The Prevention and Treatment of Skin Cancer

Kyra Kuriakose

INTRODUCTION

An individual's skin is the largest organ of the human body and serves as a protective barrier. It consists of three layers: the epidermis, dermis and the hypodermis. The epidermis is the most superficial and visible layer. It is made up of keratinocytes and serves as a protective barrier, preventing bacteria and germs from entering the body and bloodstream. Underneath the epidermis, lies the dermis. The dermis makes up 90% of the skin's thickness. It plays a crucial role in thermoregulation and includes other vital components such as the blood vessels, hair follicles, sweat glands, and nerve endings.[1] The hypodermis, also known as the deepest, most innermost layer, is the fatty adipose layer. This adipose tissue protects underlying muscles and bones from external injury and helps with thermoregulation. Together, the skin plays a vital role in regulating temperature, preventing dehydration, and pathogens.[2]

Protecting and preventing the skin from damage is crucial. There are three general methods for prevention known as the primary, secondary, and tertiary methods. The primary method of prevention aims to prevent disease or injury before it occurs, such as sunscreen application, wearing hats and protective clothing. Secondary prevention consists of primary prevention behaviors as well as screening and testing for pathogens. Tertiary prevention is the last form of prevention and is used typically to mitigate and manage effects of damage after it has already occurred. This can include continuous medical care and even surgical intervention.[3]

Skin cancer is the most common form of cancer worldwide, affecting over five million individuals per year in the United States alone and typically arises from damage to the epidermis and dermis secondary to harmful ultraviolet (UV) radiation.[4-5] The most common type of skin cancer is basal cell carcinoma (BCC), followed by squamous cell carcinoma (SCC) and melanoma. The practice of primary prevention is highly effective in reducing the risk of developing skin cancer, along with minimizing the treatment-related morbidity and costs.[6] In this review article, we will discuss the pathophysiology of skin cancer, preventative measures, and its impact on public health.

PRIMARY, SECONDARY, AND TERTIARY PREVENTION

Primary prevention aims to prevent disease or injury before it occurs. With respect to skin cancer, the proper use of sunscreen is a crucial component to avoid skin damage which may result in the development of skin cancer. The Sun Protection Factor (SPF) is used to categorize sunscreens, and their ability to block UVB rays, which is the predominant type of UV light responsible for skin burning. This number can tell you how much UVB light the sunscreen filters out. Sunscreen with a higher SPF provides greater sun protection. For example, SPF 15 filters only 93% of the sun's UVB rays, while SPF 30 filters out 97%.[7] There are two main types of sunscreen: mineral and chemical. Mineral sunscreen, also known as organic/physical sunscreen, is composed of minerals and protects the skin by reflecting UV light from the sun. Titanium dioxide and zinc oxide are two common active ingredients in mineral sunscreen.[8] When applied, sunscreen creates a protective film on the skin's surface, preventing harmful UV damage from penetrating the underlying dermis. Contrast this to chemical sunscreen, which is composed of chemical ingredients such as avobenzone, octinoxate and oxybenzone, is absorbed directly into the skin.[9] This allows the chemical sunscreen to absorb the UV rays, which is then converted into heat and released from the body. When comparing the two types of sunscreen, mineral sunscreens are more effective, as it starts to work at the moment of application, reflecting UV light before it is absorbed by our skin; whereas, chemical sunscreen must be fully absorbed into the skin prior to sun exposure.[9] Since it is absorbed into our skin, there is less of a thick residue, and is more resistant to water and sweat.[10] Individuals with sensitive skin may develop more irritation with the application of chemical sunscreen.

A critical component to ensure sunscreen's effectiveness is proper application. Adults require about one ounce of sunscreen to effectively cover their body. It is recommended to apply sunscreen 15 minutes prior to going outside to all exposed parts of the body. This allows chemical sunscreen to properly absorb into the skin. Other common rules of thumb include, reapplication every two hours, and immediately after swimming or sweating as the protective layer could have worn off.[11]

Even though sunscreens are deemed safe and promoted by doctors, there can be some side effects, which include the development of acne, burning, redness, and even itching following application.[12] This is more commonly observed with chemical sunscreen as particular ingredients such as benzophenone-3 can interfere with neurotransmitters, growth factors, and upset hormonal balance.[13] Another common chemical ingredient, octinoxate, is known to be an endocrine disruptor as it mimics estrogen and can disrupt thyroid function.[14] Remaining proactive as a consumer and reviewing the ingredient list in sunscreen products in order to avoid potentially toxic chemicals is recommended.

In addition to sunscreen, there are many other forms of primary photoprotection, such as the use of protective clothing (ie. hats, covered clothing, and sunglasses), avoidance of peak daylight hours (ie. 10 AM to 4 PM) and tanning beds. Protective clothing offers a physical barrier

against UV rays. Sun protective fabric such as Ultraviolet Protection Factor (UPF) clothing blocks UV radiation from reaching your skin.[15] Another method is to simply avoid the outdoors when solar radiation is the strongest typically between the hours of 10am to 4pm.[16] Many people are under the impression that tanning beds are safer than tanning in the sun. However, this is not true as tanning beds also emit harmful UV rays, which may increase an individual's risk of permanent skin damage and skin cancer.[17] Failure to practice these forms of photoprotection can lead to non-malignant consequences such as wrinkles, finelines, discoloration, skin damage or skin cancer.

Efficacy varies with each preventative method. Sunscreen is very effective, when applied correctly. Many dermatologists recommend SPF 30 or higher, which blocks about 97% of the sun's UV rays.[18] With higher SPF products, there is marginal benefit as SPF 50 increases UV blockage by just one more percent.[19] Wearing protective clothing offers constant protection, with no need for reapplication. However, it may not be practical in settings where it is too hot. Avoiding the sun during peak hours and tanning beds provides protection from harmful UV rays. If all of these methods are practiced together, it confers the best defense against harmful UV damage.

Measures taken to prevent and control a disease are referred to as secondary prevention. In the context of skin cancer, prevention methods include chemoprevention and skin cancer screenings. Chemoprevention is the use of substances and agents to prevent skin cancer development.[20] This is usually practiced in individuals who are at a higher risk of skin cancer compared to the general population, which includes people who have a personal or family history with skin cancer, unusual and large amounts of moles, fair skin, sunburns, and those above the age of 40.[21] Screening for skin cancer predominantly takes form in visual and physical examination, oftentimes involving a dermascope to more carefully evaluate skin lesions. If a lesion is suspected to be cancer, a dermatologist will follow with a skin biopsy, which samples the abnormality to detect whether there are precancerous or cancerous cells.[22] The use of chemoprevention agents and regular skin examinations, can lead to early detection of cancer, less morbid treatments, and a greater survival rate for skin cancer.[23]

Tertiary prevention focuses on individuals who have already been affected by the disease, aiming to prevent and slow the progression of skin cancer, and prevent recurrence.[24] Common treatment modalities for skin cancer include surgery, radiotherapy, systemic therapy, or a combination of these regimens.[25] The type of surgical intervention depends on the type, size, and stage of cancer.[26] When the cancer has progressed to regional or distant metastatic disease and can no longer be cured with local therapy, systemic therapy is considered. Common cytotoxic chemotherapies include cisplatin, carboplatin, 5-fluorouracil (5-FU) and paclitaxel, which are administered typically once every few weeks intravenously.[27] Other systemic options include targeted therapy and immunotherapy.[28] Follow-up visits for patients treated for skin

cancer are typically done every three to six months to ensure there are no additional suspicious lesions and/or signs of recurrence.

The primary, secondary, and tertiary prevention methods are critical in preventing the development and progression of skin cancer (Table 1). By following these methods, individuals can significantly reduce the risk of developing skin cancer and avoid potentially significant treatment-related morbidity and mortality.

Table 1. The Prevention Methods of Skin Cancer

	Methods	Reference
Primary Prevention	Sunscreen, protective clothing, and avoidance of tanning beds	7,15–17
Secondary Prevention	Skin cancer screenings and chemoprevention	20,22
Tertiary Prevention	Regular skin exams, surgical intervention, radiotherapy, and systemic therapy	25,28

THE PATHOPHYSIOLOGY OF SKIN CANCER

Skin cancer is predominantly caused by unprotected exposure to UV light. UV light, as compared to visible light, is higher in frequency and energy on the electromagnetic (EM) spectrum. It can be subclassified into UVA, UVB, and UVC based on the wavelength.[5] The majority of skin cancers arise from UVA exposure. Its longer wavelength permits deeper penetration into the dermis, resulting in the formation of free radicals, which lead to carcinogenesis. A small minority of cancers develop as a result of UVB exposure, which impacts only the epidermis and generates pathogenic thymine dimers.[29] Thymine dimers are formed when there is an abnormal covalent bond between two adjacent thymine bases on a single strand of DNA.[30]

In addition to UV light exposure and lack of photoprotection, other factors contribute to the development of skin cancer, including an immunosuppressed state, pre-existing genetic mutations, or certain types of Fitzpatrick's skin. Fitzpatrick's skin type is a skin classification method that describes how skin tones are susceptible to sunburn, with darker skin tones being less susceptible to sunburn than lighter tones due to melanin production.[31]

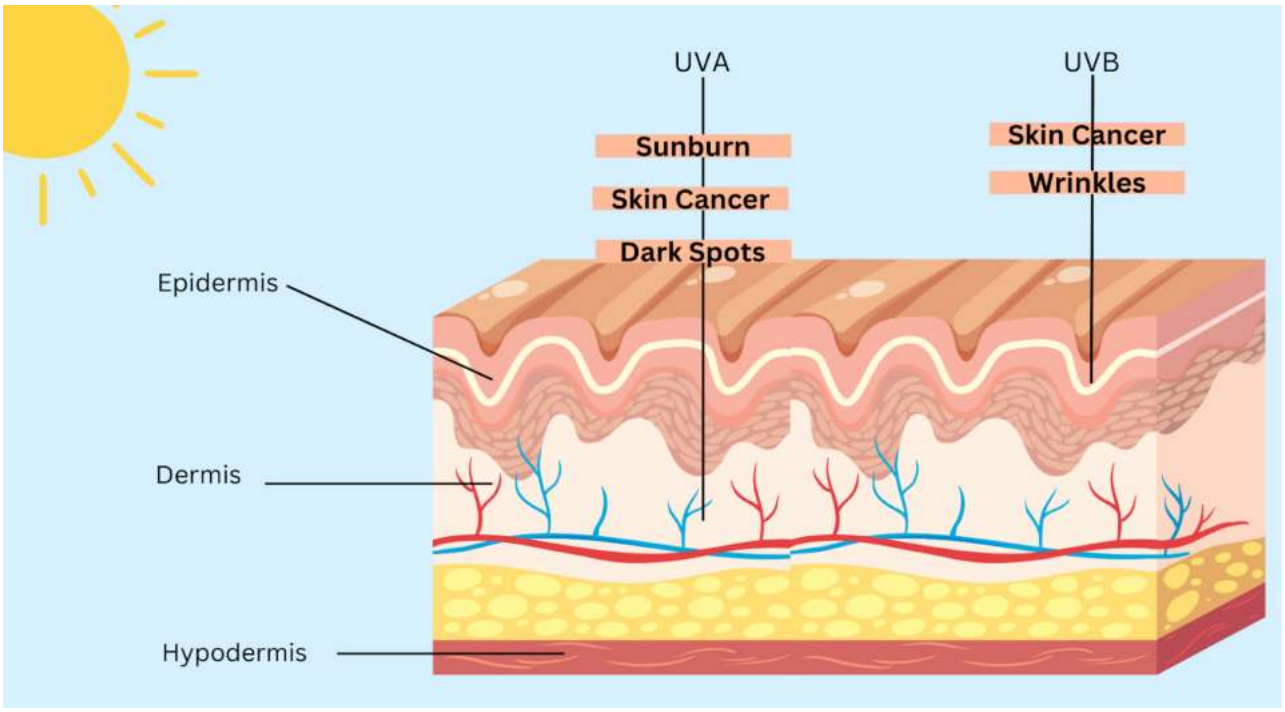

Figure 1. Skin layers affected by UV rays; UVA with a wavelength of 315-400 nm penetrates the dermis of the skin. UVB penetrates the epidermis with a wavelength of 280-315 nm.

Table 2. Properties of UV Rays [16]

Types of UV rays	Wavelength	Energy	Ability to penetrate in the skin
UVA	315-400 nm	Lowest	Deep penetration of the dermis
UVB	280-315 nm	Greater than UVA, less than UVC	Reaches the basal layer of the epidermis
UVC	100-280 nm	Highest	Little to no penetration

NON-CANCEROUS CONSEQUENCES OF SKIN DAMAGE

Outside of skin cancer, there are additional benign consequences of UV exposure which can lead to premature aging such as wrinkles, melasma, sun spots, an uneven skin tone, and telangiectasias (Figure 1). Signs of photoaging usually first appear in the teens to early 20's, which can be delayed with the practice of primary prevention.[32] In addition to the natural aging process, sun damage to the skin is a major cause of wrinkles, which is the result of free radical

injury to elastin fibers in the skin.[33] Elastin fibers allow the skin to stretch and contract, while also maintaining its structure.[34] Melasma occurs in the skin when UV rays stimulate the production of melanocytes, which are the cells responsible for pigment production (melanin).[35] Sun spots are also a visual outcome of high melanin production.[36] In addition to sun damage, there are other causes of melasma such as genetic and hormonal changes (ie. pregnancy), whereas sun spots are solely due to sun damage. On examination, sunspots are better demarcated and circular as compared to melasma, which often presents as gray brown patches and seen only on the face.[37] The variable production of melanin in the skin further contributes to an individual's uneven skin tone. Another consequence of photoaging are telangiectasias, also known as spider veins, which are dilated blood vessels within the dermis. This is the result of UV rays damaging and thinning the blood vessel walls, making them visible to the human eye.[38] Photoaging can be prevented and delayed by practicing photoprotection through primary prevention.

There are various treatment options to address photoaging. Laser therapy, also known as photorejuvenation, is one of the most common treatments, and improves skin color, texture and tone, while reducing wrinkles and fine lines. This is achieved by stimulating the growth of collagen, elastin, and melanin using the laser.[39] The laser beam penetrates deep into the skin and targets certain tissues to provoke the body's natural wound healing process and production of essential proteins such as collagen which tightens and firms the skin. Furthermore, the production of elastin fibers allows the skin to stretch while the production of melanin can lead to a more even skin tone. Additional treatment options include the use of topical creams, such as retinoid, chemical peels, and the application of antioxidants. Botulinum toxin (botox), is commonly used to reduce and prevent the development of fine wrinkles; however, is not as effective in treating static and deep wrinkles caused by photoaging.[40]

‘

Figure 2. Clinical signs of photoaging [41–46]

SKIN CANCER

Skin cancer is one of the most common types of cancer, affecting every one in five Americans. It results from the uncontrolled and abnormal proliferation of skin cells with unrepaired DNA mutations.[41] Skin cancer can be categorized as non-melanomatous and melanoma. The most common types of skin cancer are both non-melanomatous and include basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).[42] Figure 2 indicates the skin layers that get affected due to cancerous growth.

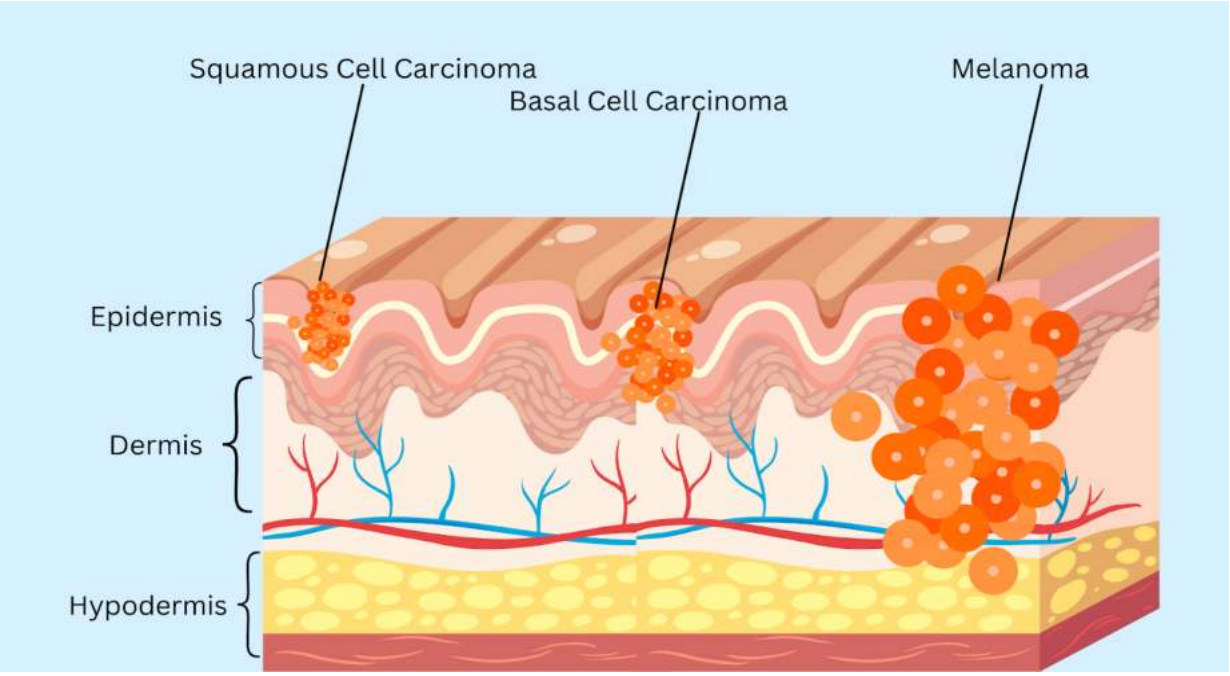

Figure 3. Affected skin layers in three different types of skin cancer [41,42]

Basal cell carcinoma is the most common type of skin cancer and is a result of the abnormal proliferation of basal cells within the epidermis. Basal cells serve as a regenerative layer which create new skin cells and push older cells toward the skin surface to eventually, slough off.[43] BCC most commonly occurs on sun-exposed areas such as the face, ears, neck, scalp, shoulders and back, and is commonly described as a pearly bump in the shades of white, pink, red, and brown (Figure 2).[42] It rarely metastasizes and confers in an excellent prognosis if diagnosed and treated early.[31]

Squamous cell carcinoma is another non-melanomatous type of skin cancer and originates from squamous cells, also within the epidermal layer of the skin. Similar to BCC, SCC also develops in sun-exposed areas, and can appear as a nodule on the skin, rough scaly patches, or open sores (Figure 2). However, unlike BCC, SCC tends to be more aggressive and prone to regional

and distant metastasis.[44] It is also more likely to be associated with perineural invasion (PNI) which may compromise neurologic function. Typically, SCC requires aggressive multimodality treatment if diagnosed at a later stage and has higher rates of morbidity and mortality, when compared to BCC.

Melanoma develops from melanocytes which are also present in the epidermis and are responsible for pigment production.[42] Individuals can distinguish moles from melanoma through a visual exam by looking for the “ABCDEs” of melanoma. The “ABCDEs” include lesion asymmetry, irregular border, variation in color, a diameter greater than six millimeters, and abnormal change of the lesion over time (Figure 2).[45] It is the most aggressive form of skin cancer, as it is a type of neuroendocrine cancer, and proliferates quickly, resulting in the highest incidence of skin cancer-related deaths.[39]

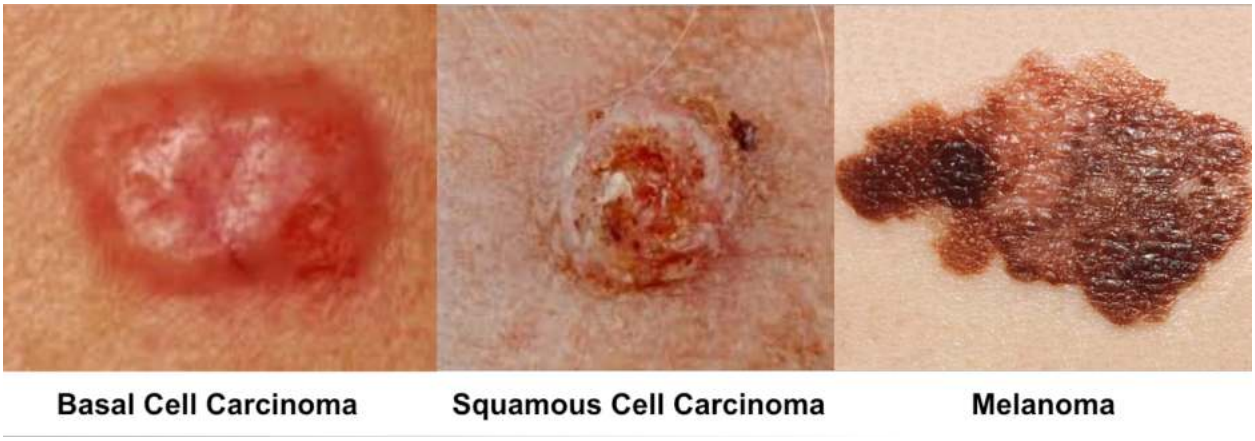

Figure 4. The appearance of cutaneous cancers [44,47,48]

GENETIC SYNDROMES

When mutated, specific genes in the body pose a threat of developing skin cancer.
Gorlin syndrome, also known as basal cell nevus syndrome, impacts an estimated one in 31,000 people and can affect multiple body systems, including the skin, eyes, reproductive system, hormone glands, and bones. This syndrome is caused by a mutation in the *PTCH1* gene, resulting in an increased risk of developing cancer. Individuals with Gorlin syndrome are at the greatest risk of developing BCC and are predisposed to develop benign tumors in the jaw, heart, and ovaries.[46]

Xeroderma pigmentosum (XP), is an autosomal recessive inherited disorder with pathogenic variants in various genes found to be associated with XP (*XPA*, *XPB*/*ERCC3*, *XPC*, *XPD*/*ERCC2*, *XPE*/*DDB2*, *XPF*/*ERCC4*, *XPG*/*ERCC5)*.[46] It is an extremely rare condition, impacting about one in a million patients within the United States and Europe. Like Gorin syndrome, XP can also affect many body systems, including the skin, eyes, and nervous system. These patients are extremely sensitive to UV rays, and a common manifestation of this disease is the development of skin cancer (BCC, SCC or melanoma) at a young age. Other signs and symptoms of XP include vision loss, blindness, loss of hearing, and loss of reflexes. Unfortunately, the lifespan of patients with XP is typically shortened due to developing skin cancer at the young age.[49]

There have been specific point mutations detected that increase an individual's risk of cutaneous melanoma. The most well-described mutation is in the *CDKN2A* gene, which is responsible for the production of a critical tumor suppressor protein that is important in the regulation of the cell cycle. Impacted individuals are at a 30%-70% lifetime risk of developing melanoma and at a heightened risk of pancreatic cancer. If a germline mutation is detected, patients require routine skin surveillance and need to be diligent in practicing photoprevention.[50]

TREATMENTS FOR SKIN CANCER

In situ lesions or early-stage skin cancer typically warrant treatment as there are a multitude of minimally invasive local therapies that offer excellent disease control. Rarely, is observation an option unless the culprit lesion is extremely small, located in consequential areas in which treatment may be morbid, or the patient has comorbidities limiting treatment options such as surgical candidacy.

Topical chemotherapy is an anti-cancer treatment, often used in the treatment of precancerous lesions and BCC and SCC. It is referred to as a localized treatment, as the cream cannot penetrate deep into the skin. The three most common topical treatments include 5-fluorouracil (5FU), imiquimod, and tirbanibulin.[51] 5FU works by blocking the cells ability to replicate, promoting apoptosis during the cell cycle.[52] Imiquimod is a cream that is an immune system modifier, increasing the immune system's activity, to attack cancer cells.[53] Tirbanibulin is another chemotherapy ointment which inhibits tubulin polymerization and Src kinase signaling.[54] Physicians often prescribe topical chemo treatments for *in situ* or early-stage disease.[55]

Cryotherapy, also known as CryoSurgery is another common treatment used for *in situ* lesions or early-stage skin cancer. Cryotherapy uses many different types of cryogens which include liquid nitrogen (most common), carbon snow, and dimethyl ether and propane (DMEP).[56] Cryogens are substances that when cooled, cause tissue death, and are delivered through the

use of a cryospray applicator. Tissue death results in the lesion crusting over and falling off. Cryotherapy is a great treatment option that results in minimal toxicity and excellent local control with cure rates of 98.6% at 30 years.[57]

Surgical resection is another common local therapy for skin cancer. The type of surgery depends on the size, type, area, and stage of the cancerous tissue and can range from Mohs Surgery and wide local excision, among others.[26] Mohs Surgery is a unique surgical technique in which the surgeon removes one layer of skin at a time, and examines each layer with a microscope for cancer cells. If there are still more cancer cells, the surgeon will go back and remove more layers until the affected area is cancer free. This process takes more time than other surgeries; however, is a very precise and advanced treatment.[26] Wide local excision (WLE) is a surgical procedure in which a scalpel is used to cut out a tumor or abnormal tissue, and a predetermined margin of healthy skin along with it. If a large portion of skin is removed, a skin graft may be required to fill the defect and repair the area. WLE is typically recommended to treat patients with melanoma, as well as BCC and SCC.[58]

Radiation therapy is an alternative treatment for skin cancer for those who have large tumors and may not be surgical candidates. Radiotherapy works by using high energy x-rays to kill cancer cells. External beam radiation therapy (EBRT) and brachytherapy are the two main types of radiotherapy.[59] EBRT uses a linear accelerator (LINAC) to direct high energy radiation very focally to the tumor. Brachytherapy, a form of internal radiation therapy, delivers radiation directly into the tumor either through the permanent implantation of seeds or via catheters. It is used to treat smaller and more superficial tumors in the head, neck, breast, and cervix. With respect to skin cancers, radiation can be delivered in the definitive or adjuvant setting. In the adjuvant setting, this is usually employed for large tumors who have undergone surgical resection and have high risk features on pathology such as positive perineural invasion, positive lymphovascular invasion, positive lymph nodes or margins that place the patient at a higher risk for disease recurrence.

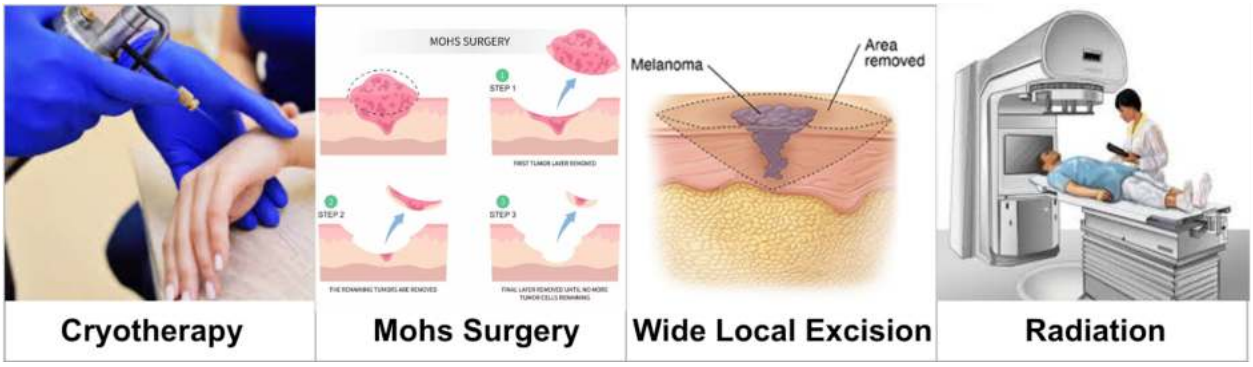

Figure 3. Treatment options for in-situ and early-stage skin cancer [60–63]

Systemic therapy is often used in the treatment of patients with advanced skin cancer. In patients with locally advanced tumors that present with nodal metastasis or high risk features that would make surgical margin clearance challenging, radiographic or clinical perineural invasion, etc., oftentimes, definitive radiotherapy in combination with chemotherapy is recommended. The most common chemotherapy regimens given concurrently with radiation include cisplatin and carboplatin. Over the past several decades, immunotherapy and targeted therapies for patients with specific genetic alterations (ex. sonic hedgehog inhibitors in patients with a *PTCH1* or *SMO* gene mutation) have gained traction in the treatment landscape of skin cancers.[64] Again, these types of systemic therapy are often recommended in patients with locally advanced disease. Outside of the definitive setting, systemic therapy may be combined with radiotherapy as adjuvant treatment after the patient undergoes surgery and has high risk features for recurrence for pathology. In the metastatic setting, systemic therapy is often used as well.

PUBLIC HEALTH LENS

About 8.9 billion dollars is the annual cost in the United States to treat all types of skin cancer. Simply following primary and secondary prevention methods to prevent the development of skin cancer resulting in early detection can save lives and healthcare-related costs. Sunburns can easily be prevented by following primary and secondary methods (ie. applying sunscreen), yet yield a total estimated cost of $11.2 million dollars from emergency room (ER) visits alone. The use of tanning beds is a known risk factor for the development of skin cancer, and is unfortunately still commonly used by an estimated 7.8 million adults. Consequently, the use of tanning beds has been calculated to result in 61,000 cases of melanoma and over 6,000 melanoma-related deaths. By omission of tanning bed use, $342 million dollars could be saved.[65]

Skin cancer is the most common type of cancer in the United States with over five million cases each year, but it is also the most preventable. Skin Cancer Awareness Month (every May) is celebrated to educate the public on ways to prevent cancer and the consequences of skin cancer.[66] There are also many programs such as SPOT Skin Cancer™, launched by the American Academy of Dermatology (AAD), which raise awareness of prevention methods, how to spot the cancer early, and save lives, with the end goal of having a world where skin cancer doesn’t exist.[67]

CONCLUSION

With over five million cases every year, skin cancer is the most commonly diagnosed cancer in the United States, impacting one in five Americans. Simple and economical primary prevention

methods such as the application and use of sunscreen, and protective clothing can be extremely effective in reducing the incidence of skin cancer. If diagnosed with skin cancer, there are multiple treatment options including topical chemotherapy, cryotherapy, surgery, and radiotherapy. Although often effective in addressing an individual's disease, these treatments are not entirely benign, and can significantly impact mental and physical health as well as result in financial toxicity. This includes a public health cost of $8.9 billion dollars that is spent annually on skin cancer in the United States and highlights the importance of widespread patient education regarding the affordable and simple prevention methods that can reduce skin cancer incidence, treatment-related consequences, and financial implications to the patient and public health system.

WORKS CITED

1. Keep Your Skin Healthy. NIH News in Health. Accessed July 8, 2024. https://newsinhealth.nih.gov/2015/11/keep-your-skin-healthy
2. Skin: Layers, Structure and Function. Cleveland Clinic. Accessed July 8, 2024. https://my.clevelandclinic.org/health/body/10978-skin
3. Primary, Secondary & Tertiary Prevention | Definition & Examples. study.com. Accessed July 8, 2024. https://study.com/learn/lesson/primary-secondary-tertiary-prevention-levels.html
4. Basal & Squamous Cell Skin Cancer Statistics. Accessed July 8, 2024. https://www.cancer.org/cancer/types/basal-and-squamous-cell-skin-cancer/about/key-statistics.html
5. Gruber P, Zito PM. Skin Cancer. In: *StatPearls*. StatPearls Publishing; 2024. Accessed July 8, 2024. http://www.ncbi.nlm.nih.gov/books/NBK441949/
6. A review of skin cancer primary prevention activities in primary care settings - June 2024, Volume 34, Issue 2 | PHRP. https://www.phrp.com.au/. doi:10.17061/phrp34012401
7. How to decode sunscreen labels. Accessed July 17, 2024. https://www.aad.org/public/everyday-care/sun-protection/shade-clothing-sunscreen/understand-sunscreen-labels
8. Chemical vs. Mineral Sunscreen: What's the Difference? EverydayHealth.com. July 3, 2024. Accessed July 19, 2024. https://www.everydayhealth.com/skin-beauty/chemical-vs-mineral-sunscreen-whats-difference/
9. Mineral vs. Chemical Sunscreen: Which Is Better? Cleveland Clinic. Accessed July 17, 2024. https://health.clevelandclinic.org/mineral-vs-chemical-sunscreen
10. Mineral vs. Chemical Sunscreen: Which Is Better for My Skin? GoodRx. Accessed July 19, 2024. https://www.goodrx.com/health-topic/dermatology/mineral-vs-chemical-sunscreen
11. How to apply sunscreen. Accessed July 17, 2024. https://www.aad.org/public/everyday-care/sun-protection/shade-clothing-sunscreen/how-to-apply-sunscreen
12. Sunscreen Agent (Topical Application Route) Side Effects - Mayo Clinic. Accessed July 17, 2024. https://www.mayoclinic.org/drugs-supplements/sunscreen-agent-topical-application-route/side-effects/drg-20070255?p=1

13. Maliyil BT, Koshy RR, Madhavan AT, Korrapati NH. Trust your sunscreen with caution: A literature review on the side effects of sunscreen. *Cosmoderma*. 2023;3. doi:10.25259/CSDM_52_2023
14. Octinoxate. Safe Cosmetics. Accessed July 17, 2024. https://www.safecosmetics.org/chemicals/octinoxate/
15. Sun Protective Clothing. The Skin Cancer Foundation. Accessed July 19, 2024. https://www.skincancer.org/skin-cancer-prevention/sun-protection/sun-protective-clothing/
16. US EPA O. Ultraviolet (UV) Radiation and Sun Exposure. November 26, 2018. Accessed July 17, 2024. https://www.epa.gov/radtown/ultraviolet-uv-radiation-and-sun-exposure
17. Tanning. The Skin Cancer Foundation. Accessed July 17, 2024. https://www.skincancer.org/risk-factors/tanning/
18. Sunscreen FAQs. Accessed July 17, 2024. https://www.aad.org/media/stats-sunscreen
19. Foundation SC. Ask the Expert: Does a High SPF Protect My Skin Better? The Skin Cancer Foundation. May 1, 2023. Accessed July 19, 2024. https://www.skincancer.org/blog/ask-the-expert-does-a-high-spf-protect-my-skin-better/
20. Tsao AS, Kim ES, Hong WK. Chemoprevention of Cancer. *Chemoprevention Cancer*. 2004;54(3).
21. Dermatology P. How Often Should You Get a Skin Cancer Screening? Prizant Dermatology. September 10, 2021. Accessed July 25, 2024. https://prizantderm.com/how-often-should-you-get-a-skin-cancer-screening/
22. DermNet® - Principles of dermatological practice. Examination of the skin. DermNet®. March 3, 2024. Accessed July 25, 2024. https://dermnetnz.org/cme/principles/examination-of-the-skin
23. Cutaneous squamous cell carcinoma: Primary and secondary prevention - UpToDate. Accessed July 25, 2024. https://www.uptodate.com/contents/cutaneous-squamous-cell-carcinoma-primary-and-secondary-prevention
24. Tertiary Prevention | HealthLink BC. Accessed July 25, 2024. https://www.healthlinkbc.ca/tertiary-prevention
25. 1 in 5 people get skin cancer. Cleveland Clinic. Accessed July 25, 2024. https://my.clevelandclinic.org/health/diseases/15818-skin-cancer
26. Surgery for Skin Cancer. June 12, 2024. Accessed July 25, 2024. https://www.hopkinsmedicine.org/health/conditions-and-diseases/surgery-for-skin-cancer
27. Basal & Squamous Cell Skin Cancer Chemo | Non-melanoma Chemo. Accessed July 25, 2024. https://www.cancer.org/cancer/types/basal-and-squamous-cell-skin-cancer/treating/systemic-chemotherapy.html
28. Aboul-Fettouh N, Morse D, Patel J, Migden MR. Immunotherapy and Systemic Treatment of Cutaneous Squamous Cell Carcinoma. *Dermatol Pract Concept*. 2021;11(Suppl 2):e2021169S. doi:10.5826/dpc.11S2a169S
29. Sander M, Sander M, Burbidge T, Beecker J. The efficacy and safety of sunscreen use for the prevention of skin cancer. *CMAJ Can Med Assoc J*. 2020;192(50):E1802-E1808. doi:10.1503/cmaj.201085
30. Thymine Dimer - an overview | ScienceDirect Topics. Accessed July 26, 2024. https://www.sciencedirect.com/topics/chemistry/thymine-dimer
31. Gruber P, Zito PM. Skin Cancer. In: *StatPearls*. StatPearls Publishing; 2024. Accessed July 8, 2024. http://www.ncbi.nlm.nih.gov/books/NBK441949/
32. Sun-damaged Skin: Photoaging, Signs, Causes & Treatment. Cleveland Clinic. Accessed July 26, 2024. https://my.clevelandclinic.org/health/diseases/5240-sun-damage-protecting-yourself
33. Services D of H& H. Wrinkles. Accessed August 1, 2024. http://www.betterhealth.vic.gov.au/health/conditionsandtreatments/wrinkles
34. What Is Elastin? The Beauty Benefits of. Accessed August 1, 2024. https://www.venustreatments.com/en-gl/blog/what-is-elastin-the-beauty-benefits-of-elastic-fibers/
35. Melasma: Treatment, Causes & Prevention. Cleveland Clinic. Accessed August 1, 2024.

https://my.clevelandclinic.org/health/diseases/21454-melasma
36. Do your age spots bother you?-Age spots (liver spots) - Symptoms & causes. Mayo Clinic. Accessed August 1, 2024. https://www.mayoclinic.org/diseases-conditions/age-spots/symptoms-causes/syc-20355859
37. Green DM. What is the Difference Between Melasma and Sun Spots? Dr. Michele Green M.D. October 6, 2023. Accessed August 2, 2024. https://www.michelegreenmd.com/what-is-the-difference-between-melasma-and-sun-spots
38. MD DLT. Broken Veins from the Sun. News-Medical. August 22, 2017. Accessed August 1, 2024. https://www.news-medical.net/health/Broken-Veins-from-the-Sun.aspx
39. Torgerson DC. Collagen & How Do Lasers Stimulate Collagen Production. Toronto Facial Plastic Surgery and Laser Centre | Dr. Torgerson. August 18, 2016. Accessed August 8, 2024. https://drtorgerson.com/what-is-collagen-and-how-do-lasers-stimulate-collagen-production-on-the-face/
40. Is Botox a fix for facial wrinkles? Mayo Clinic Health System. Accessed August 9, 2024. https://www.mayoclinichealthsystem.org/hometown-health/speaking-of-health/is-botox-the-fix-for-all-facial-wrinkles
41. Skin cancer. Accessed August 1, 2024. https://www.aad.org/media/stats-skin-cancer
42. Skin Cancer Information. The Skin Cancer Foundation. Accessed August 1, 2024. https://www.skincancer.org/skin-cancer-information/
43. Basal cell carcinoma-Basal cell carcinoma - Symptoms & causes. Mayo Clinic. Accessed August 1, 2024. https://www.mayoclinic.org/diseases-conditions/basal-cell-carcinoma/symptoms-causes/syc-20354187
44. Squamous cell carcinoma of the skin - Symptoms and causes. Mayo Clinic. Accessed August 1, 2024. https://www.mayoclinic.org/diseases-conditions/squamous-cell-carcinoma/symptoms-causes/syc-20352480
45. What to look for: ABCDEs of melanoma. Accessed August 2, 2024. https://www.aad.org/public/diseases/skin-cancer/find/at-risk/abcdes
46. Genetics of Skin Cancer (PDQ®) - NCI. July 29, 2009. Accessed August 9, 2024. https://www.cancer.gov/types/skin/hp/skin-genetics-pdq
47. Basal Cell Carcinoma Southaven, MS. Dermatology Clinic of North Mississippi. Accessed September 14, 2024. https://www.dcnms.com/basal-cell-carcinoma-southaven-ms/
48. Melanoma - Symptoms and causes. Mayo Clinic. Accessed September 14, 2024. https://www.mayoclinic.org/diseases-conditions/melanoma/symptoms-causes/syc-20374884
49. Xeroderma Pigmentosum (XP): Symptoms, Causes & Treatment. Cleveland Clinic. Accessed August 9, 2024. https://my.clevelandclinic.org/health/diseases/24088-xeroderma-pigmentosum-xp
50. Pauley K, Khan A, Kohlmann W, Jeter J. Considerations for Germline Testing in Melanoma: Updates in Behavioral Change and Pancreatic Surveillance for Carriers of CDKN2A Pathogenic Variants. *Front Oncol*. 2022;12. doi:10.3389/fonc.2022.837057
51. Chemotherapy Cream: Types, Uses, Effectiveness, and Side Effects. Healthline. December 8, 2023. Accessed August 31, 2024. https://www.healthline.com/health/cancer/what-to-know-about-chemotherapy-cream-for-skin-cancer
52. Fluorouracil (5-FU): What to Expect, Side Effects, and More. Accessed August 31, 2024. https://www.breastcancer.org/drugs/fluorouracil
53. Imiquimod Topical: MedlinePlus Drug Information. Accessed August 31, 2024. https://medlineplus.gov/druginfo/meds/a698010.html
54. Tirbanibulin Topical: MedlinePlus Drug Information. Accessed August 31, 2024. https://medlineplus.gov/druginfo/meds/a621013.html
55. Chemotherapy cream: What to know. June 30, 2021. Accessed August 31, 2024.

https://www.medicalnewstoday.com/articles/chemotherapy-cream
56. Cryotherapy: Uses, Cautions, and Aftercare — DermNet. DermNet®. October 26, 2023. Accessed September 2, 2024. https://dermnetnz.org/topics/cryotherapy
57. Kuflik EG. Cryosurgery for skin cancer: 30-year experience and cure rates. *Dermatol Surg Off Publ Am Soc Dermatol Surg Al*. 2004;30(2 Pt 2):297-300. doi:10.1111/j.1524-4725.2004.30090.x
58. Wide Local Excision for Melanoma. Melanoma Research Alliance. Accessed August 31, 2024. https://www.curemelanoma.org/patient-eng/melanoma-treatment/surgery/wide-local-excision/
59. Radiotherapy for skin cancer. Accessed August 31, 2024. https://www.cancerresearchuk.org/about-cancer/skin-cancer/treatment/radiotherapy/radiotherapy-skin-cancer
60. External Beam Radiation Therapy for Cancer - NCI. May 1, 2018. Accessed September 14, 2024. https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy/external-beam
61. How Mohs Surgery Works · Conway Medical Center. Accessed September 14, 2024. https://www.conwaymedicalcenter.com/news/topic/how-mohs-surgery-works/
62. Melanoma Removal Surgery | Saint Luke's Health System. Accessed September 14, 2024. https://www.saintlukeskc.org/health-library/melanoma-removal-surgery
63. Cryotherapy Clinic Treatment - Dorset, Bournemouth, Christchurch. Accessed September 14, 2024. https://www.southfaceskin.com/medical-dermatology/cryotherapy/
64. Efficacy and safety of sonic hedgehog pathway inhibitors in cancer - PMC. Accessed September 2, 2024. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6434684/
65. CDC. Health and Economic Benefits of Skin Cancer Interventions. National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP). July 17, 2024. Accessed September 2, 2024. https://www.cdc.gov/nccdphp/priorities/skin-cancer.html
66. Skin Cancer Awareness Month. The Skin Cancer Foundation. Accessed September 5, 2024. https://www.skincancer.org/get-involved/skin-cancer-awareness-month/
67. SPOT Skin Cancer™ seeks a world without skin cancer. Accessed September 5, 2024. https://www.aad.org/public/public-health/skin-cancer-awareness