



Research paper

Solar Ultraviolet Radiation, Stratospheric Ozone Dynamics, and Photocarcinogenesis in Australia

An Updated Narrative Review of Mechanisms, Clinical Burden, Prevention, and Emerging Technologies

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ARTICLE INFO	ABSTRACT
Keywords ultraviolet radiation ozone depletion photocarcinogenesis melanoma basal cell carcinoma squamous cell carcinoma photoaging	Background: Solar ultraviolet (UVR) radiation is the prime etiological environmental agent for most UV-related cutaneous malignancies. Australia is exposed to exceptionally high ambient levels of UVR. The ongoing international control of ozone-depleting substances has started the repair of the stratospheric ozone layer but the reduction in ozone-depletion-related risk cannot offset Australia's high UV exposure. Objective: This narrative review aims to examine the interactions between stratospheric ozone dynamics, solar UVR exposure, molecular mechanisms of injury, clinical manifestations, contemporary diagnosis and treatment, and population-level prevention strategies. Methods: A narrative literature review. Publications from January 2000 to June 2025 were prioritized. Landmark publications predating 2000 were included. A search strategy included the key concepts of solar ultraviolet radiation, ultraviolet-A and ultraviolet-B, stratospheric ozone, photocarcinogenesis, melanoma, various forms of keratinocyte, and actinic keratosis. Priority was given to systematic reviews, meta-analysis, randomized trials, cohort studies, experimental studies, and reports from international and Australian health agencies. Results: UV-B radiation is associated with direct formation of DNA photolesions. UV-A is a significant contributor to oxidative stress through reactive oxygen species. Failure of DNA repair mechanisms, genomic instability, impaired immunity and mutations in TP53, BRAF, NRAS, NF1, and TERT are implicated in the development of actinic keratoses, keratinocyte carcinomas and melanoma. Chronic UV exposure produces a continuum from sunburn and photoaging to premalignant lesions and invasive malignancy. Improvements in photoprotection, dermoscopy and digital surveillance, molecular characterization, targeted therapy and immune checkpoint inhibition improve diagnosis and management. However, prevention remains at the forefront as a substantial proportion of UV-associated skin disease is preventable. Conclusion: Australia is a unique natural laboratory, where atmospheric science, UV photobiology, molecular carcinogenesis, dermatology, and public health intersect. Enhancement of the stratospheric ozone layer is an important environmental health achievement, but should not be interpreted as a reduction in the immediate need for UV protection. Population-level photoprotection, occupational interventions, early detection, risk-based surveillance, and the inclusion of digital and molecular technologies are needed to reduce the ongoing burden of UV-associated skin disease.
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1. Introduction

Solar UV radiation (UVR) is an important causative agent in the pathophysiology of skin damage, photoaging, actinic keratosis, keratinocyte

carcinomas and melanoma. Solar UV-B has been associated with direct DNA damage by damaging specific DNA bases via formation of cyclobutane dimers, while UV-A causes indirect DNA damage

through the generation of reactive oxygen species that promote oxidative stress and photoageing [2,3]. Prolonged or repeated exposure can thus lead to significant alterations that result in photocarcinogenesis.

Australia has an important research domain in terms of UV-related skin diseases, as compared to other regions of the world. Population studies have documented the high incidence of melanoma that has been documented in Australia, with cutaneous squamous cell carcinomas representing an additional significant burden [6,12]. Indeed, global estimates suggest that there is a considerable burden of cutaneous melanoma, which is likely to increase in the coming decades [13]. Thus research into the environmental and biological determinants of UV-associated skin cancer are of significant interest.

Stratospheric ozone in the atmosphere is an important determinant of sunlight exposure due to its ability to absorb UV-B wavelengths of solar radiation. Recent research has specifically noted the impact of changes in the ozone layer on exposure in Australia and the United States, through the impact of ozone-depleting substances [1]. Scientific assessment of recent ozone depletion trends has documented ongoing change in stratospheric ozone following international control measures of ozone-depleting substances [22]. Consequently, the Montreal Protocol plays a particularly critical role in controlling factors contributing to ozone depletion, while ensuring the long-term health of the stratosphere [24].

Despite improvements in the long-term outlook for the stratospheric ozone, Australia still experiences significant levels of UV exposure that impact the general public. Contemporary research has assessed recent risks and potential benefits of ultraviolet and infrared radiation in the Australian setting [2]. In addition to exposure and environmental factors, individual behaviours significantly contribute to the overall cumulative UV exposure experienced in a population. The long-term evaluation of the sunsmart program in Melbourne has indeed demonstrated changing patterns of sun protection following sun exposure in the local population throughout the decades [7]. Thus, population-based prevention remains particularly important.

At a molecular level, UVR interacts with a variety of biological agents to cause damage. UV-B exposure can lead to characteristic DNA photoproducts that can

be repaired by DNA repair enzymes, but inadequate repair can induce characteristic UV-associated mutations [14,15]. UV exposure can also induce oxidative stress and oxidatively-induced DNA lesions, which further contribute to genomic instability and photocarcinogenesis [15,20]. These biological processes provide a significant underpinning to the development of UV-associated skin malignancies.

The clinical consequences of chronic exposure to UVR are varied. Photoageing, actinic keratoses and keratinocyte carcinomas are all important contributors to the overall burden of disease. UV exposure, genetic alterations and host susceptibility play a complex role in the aetiology of both actinic keratosis and melanoma [3,6]. The high prevalence of cutaneous squamous cell carcinomas in Australia further underscores the importance of chronic UV exposure on a clinical level [6]. Evidence from Australian randomized trials has demonstrated that regular sunscreen application can provide significant protection against melanoma and squamous cell carcinomas [9,10].

The changing landscape of modern medicine has also contributed to the increased capacity of diagnosing skin malignancies. Dermoscopy, digital imaging and structured surveillance can allow for early identification of suspicious lesions in an increased-risk population [16,27], but screening strategies must consider the cost-benefit ratios of diagnostic procedures and unnecessary biopsies and treatment [28]. Artificial intelligence and deep-learning approaches have been increasingly applied to the assessment of dermoscopic melanoma images, contributing to potential additional diagnostic technologies [17,18].

The interaction of factors surrounding atmospheric ozone and environment, individual exposure, molecular damage and the development of skin cancers is thus complex. While international agreements have improved the outlook for the stratospheric ozone layer, Australia's high rate of UV exposure means that it is still particularly vulnerable to UV-induced skin disease [1,2]. This narrative review considers the contemporary relationship between solar UV radiation, the stratospheric ozone and photocarcinogenesis in Australia, covering atmospheric, environmental, molecular, clinical and preventative aspects.

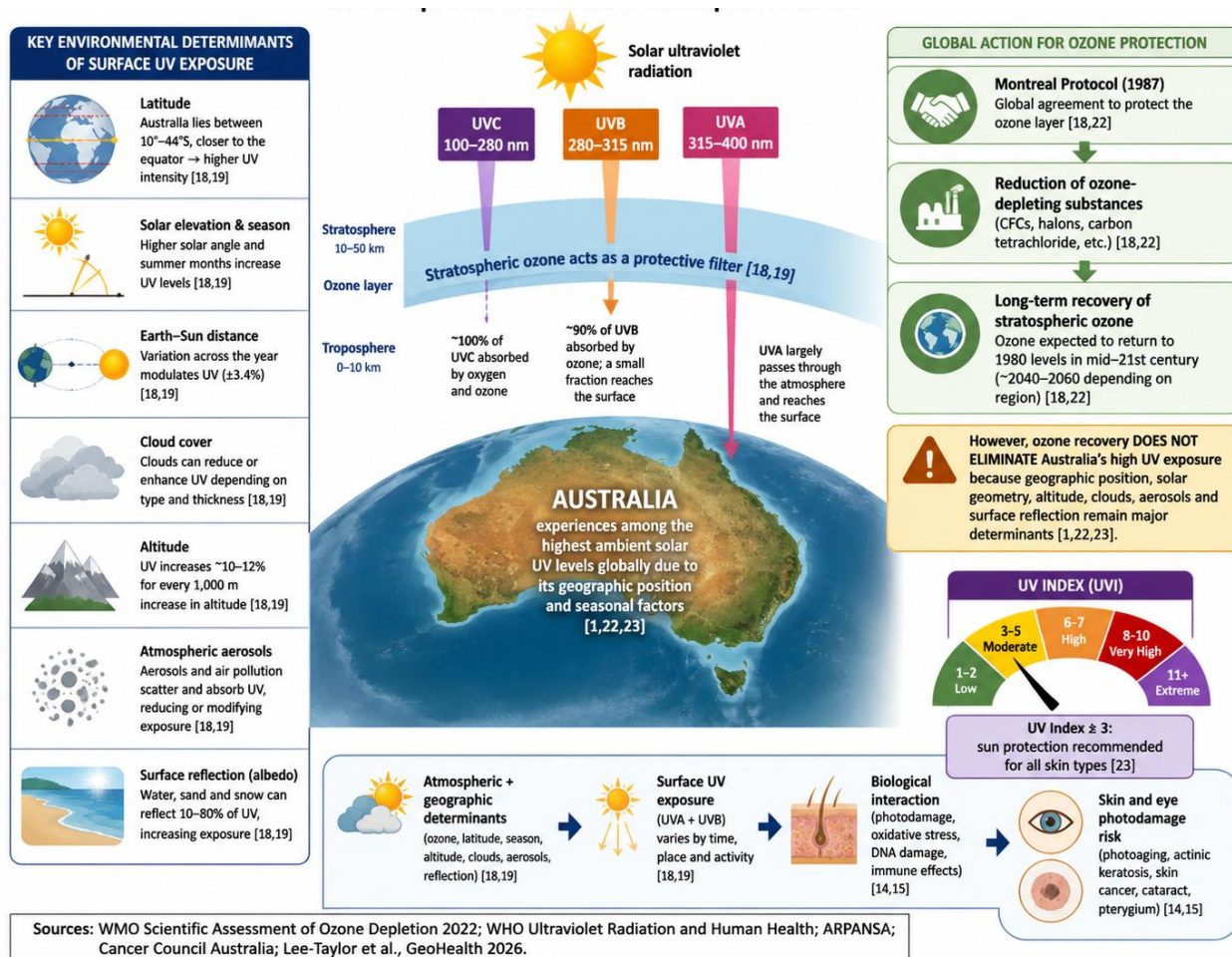


Fig. 1 Environmental determinants of solar ultraviolet radiation exposure in Australia and the protective role of stratospheric ozone

2. Methodology

2.1 Review design

This review was conducted as a structured narrative synthesis of evidence relevant to solar ultraviolet radiation (UVR), stratospheric ozone, UV-induced photocarcinogenesis, skin-cancer burden, prevention and novel diagnostics, with a specific focus on Australia. Atmospheric, environmental, health, photobiological, molecular, dermatological, epidemiological and public health domains were all interrogated in this review. The aim of this review was to provide a transparent and replicable evidence identification and synthesis strategy while acknowledging the primarily qualitative nature of the study.

2.2 Literature search strategy

PubMed/MEDLINE, Scopus, Web of Science, Embase and Google Scholar databases were interrogated for relevant studies. The search strategy consisted of a combination of controlled vocabulary and free-text terms, with an emphasis on the key concepts of the review. The search was restricted to the period between January 2000 and June 2025, with a few key earlier studies on ozone depletion mechanisms, UVR-induced DNA damage and photocarcinogenesis added

manually if published prior to 2000. Some of the search terms and concepts included in the database searches are as follows:

("ultraviolet radiation" OR UVR OR "UV-B" OR "UV-A") AND ("ozone depletion" OR "stratospheric ozone" OR "ozone recovery") AND ("skin cancer" OR melanoma OR "cutaneous squamous cell carcinoma" OR "basal cell carcinoma" OR photocarcinogenesis) AND (Australia OR Australian)

Additional searches included combinations of terms related to DNA repair, oxidative stress, photoageing, actinic keratosis, sunscreen, sun protection, SunSmart, dermoscopy, artificial intelligence, melanoma screening, and UV exposure. Relevant reviews, as well as highly cited original studies, were hand-searches for additional publications and key older references not identified in the initial database searches.

2.3 Eligibility criteria

Eligible studies had to address at least one of the key areas related to the aims of this review, which include: (1) atmospheric ozone trends and solar ultraviolet radiation; (2) biological response to ultraviolet exposure; (3) skin cancer epidemiology and burden; (4) diagnosis, surveillance, and treatment

of skin cancer; and (5) population-level and individual skin cancer prevention. The following study designs were considered eligible for inclusion: peer-reviewed original research, systematic and narrative reviews, epidemiological, clinical and randomized control trials, major international assessments, as well as Australian and international public health reports. Additionally, key older studies published prior to 2000 were included in the review if they provided critical context or background for better understanding of the reviewed topic.

2.4 Exclusion criteria

Duplicate records, conference abstracts, letters to the editor, non-peer-reviewed articles, non-scientific web-pages, as well as studies not reporting relevant data were excluded from this review. Similarly, studies not pertinent to UVR, ozone trends, photocarcinogenesis, or skin cancer, as well as those lacking sufficient information to determine relevance to any of the key areas addressed by this review were excluded.

2.5 Study selection and evidence synthesis

The titles and abstracts of the retrieved studies were screened for relevance to the key areas addressed by this review. Following the initial screening, all relevant articles underwent a full-text review. Relevant articles were then classified according to the key areas they addressed, including: atmospheric and environmental, molecular mechanisms, epidemiology, surveillance/diagnosis/treatment, and sun protection/prevention. Following this, the evidence was synthesized thematically, using the key areas as conceptual frameworks to structure the review. Additional emphasis was placed on discussing Australian findings, if available, as well as incorporating relevant international evidence.

Due to the heterogeneity in reviewed study designs, populations, outcomes, and interventions, as well as the primarily qualitative nature of this review, the synthesis was limited to the descriptive and narrative discussion of evidence. No quantitative analyses, pooled estimates or meta-analysis of the findings of the retrieved studies were performed. Particular attention was paid to recent high-quality studies, large-scale epidemiological analyses, randomized prevention trials, systematic reviews and key international and Australian publications.

2.6 Reporting and transparency

Transparency in this review was ensured by reporting all databases interrogated, the search dates, key search terms, eligibility criteria, study selection procedures, and evidence synthesis strategy. This review was not registered as a systematic review, and no PRISMA-based quantitative study selection flow

diagram was produced, due to the primarily descriptive and qualitative nature of this study.

2.7 Ethical considerations

This review did not involve any human participants, animals, human data or tissue. Therefore, the ethical approval and informed consent from participants were not necessary.

3. Results

3.1 Overview of the Evidence

The literature synthesis highlighted associations between solar ultraviolet (UVR) radiation and molecular skin damage, cumulative effect, and the development of pre-malignant and malignant skin disease. The body of evidence included atmospheric and environmental analyses, molecular and experimental studies, epidemiology, clinical studies, prevention, and modern digital diagnostic approaches.

Evidence was grouped into five key areas: atmospheric and environmental UVR; molecular mechanisms and photocarcinogenesis; epidemiology and clinical presentation; diagnosis and modern management approaches; and prevention and emerging technologies. Particular emphasis was placed on local evidence relevant to Australia, with supplementary international research providing critical biological and clinical contextualization.

3.2 Stratospheric and Environmental Determinants of UV Exposure

The evidence highlighted the regulatory role of stratospheric ozone as a determinant of biologically effective UVR reaching the Earth's surface. While strongly protective of shorter wavelength UV-B, ozone is relatively transparent to longer wavelength UV-A radiation. Consequently, changes in stratospheric ozone profiles can lead to changes in biologically effective UV radiation.

There are multiple environmental determinants of surface UV exposure, and these interact with each other and with human behaviour to determine cumulative exposure. Latitude, solar zenith angle, season, weather, atmospheric conditions, aerosols, the Earth-Sun distance, and human behaviours are key factors. Australia is an example of a country with high population UV exposure due to its latitudinal spread and large population living in regions characterized by high solar UV exposure. Evidence suggests that the Australian population's UV exposure follows broad latitudinal and seasonal patterns. Thus, Australia's high skin cancer burden is primarily driven by these local environmental characteristics, not stratospheric ozone depletion.

The international regulation of ozone-depleting substances has impacted atmospheric ozone trends. However, recovery is a protracted process, and stratospheric ozone levels are projected to return to 1980 levels by 2040 at the earliest. Critically, recovery will take place over multiple decades, and this will have limited impact on Australia's exposure to solar UV radiation, which is inherently high due to its latitude.

The overall evidence supports the premise that stratospheric ozone is only one determinant among many, and that Australia's environmental exposure to UV radiation is largely driven by latitude and seasonality, with additional contributions from the built environment and human behaviour.

3.3 Molecular Mechanisms of Photocarcinogenesis

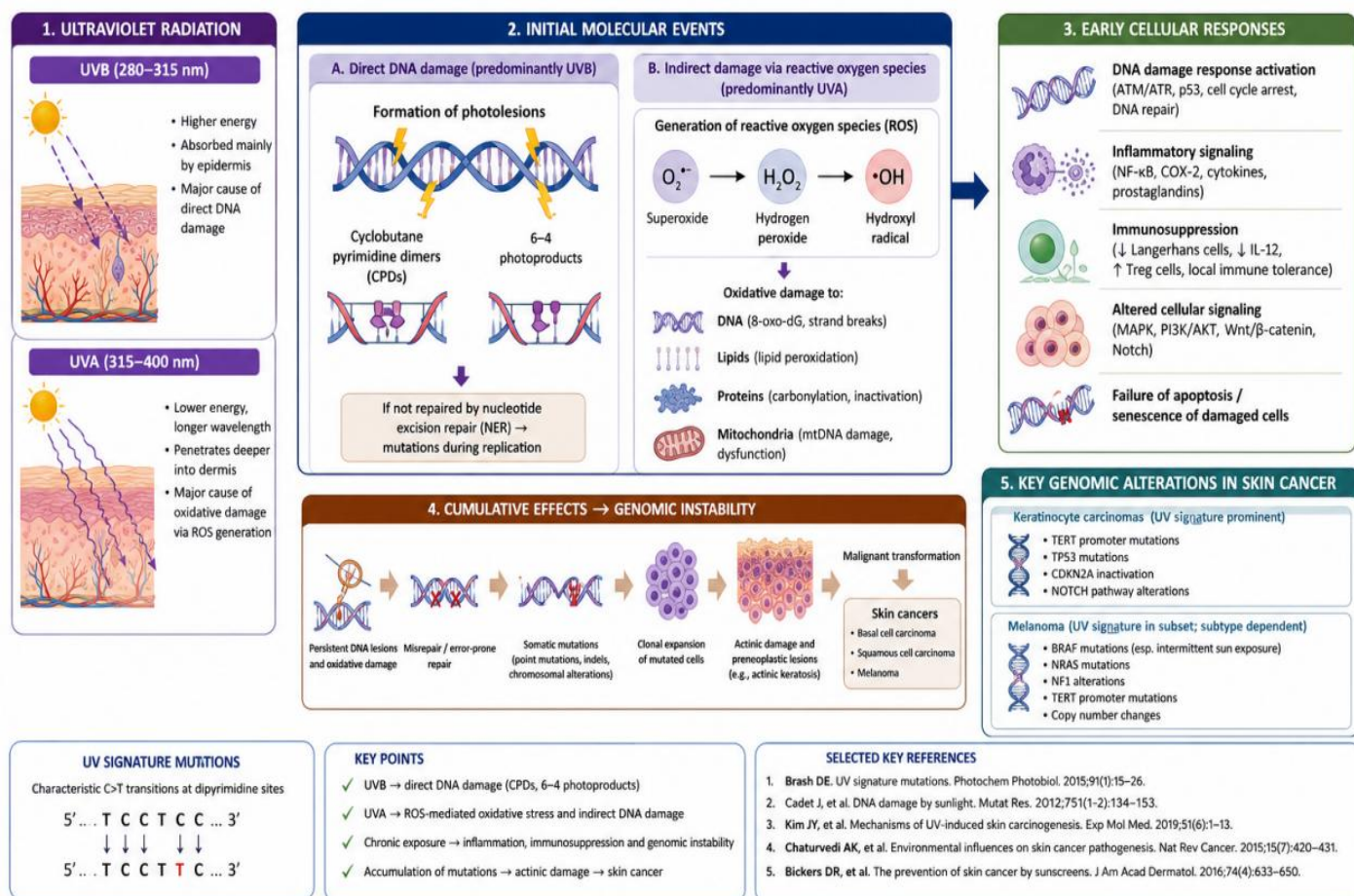
The literature synthesis revealed that photocarcinogenesis is a multi-step process, which is initiated by DNA damage and oxidative stress, leading to molecular and cellular dysfunction and neoplastic transformation. UV-B radiation induces direct DNA damage while UV-A produces indirect DNA damage via photosensitized oxidation processes. Both forms of DNA damage play a role in driving photocarcinogenesis and photo-ageing.

The response to DNA damage determines the outcome. Cells unable to repair UV-induced DNA damage can undergo apoptosis or, when the repair response is defective, proceed to malignant transformation. Defective nucleotide excision repair is implicated in the pathogenesis of melanoma. Other molecular changes that contribute to melanoma initiation and progression include defects in DNA repair mechanisms and telomerase activation.

UV-induced immunomodulation is another contributor to photocarcinogenesis. Persistent pro-inflammatory responses to DNA damage and UV-induced immunosuppression may drive malignant transformation. UV exposure has also been implicated in melanoma progression through its impact on the tumour microenvironment, promotion of neo-angiogenesis, and modulation of the extracellular matrix.

The accumulation of mutations and oncogenic changes results in transformation and tumorigenesis. Overall, the evidence indicates that melanoma is a multi-factorial disease driven by a combination of UV-induced molecular changes, defective DNA repair mechanisms, and immunological changes.

UV radiation induces direct DNA damage and oxidative stress leading to genomic instability, altered cellular signaling, immune modulation and malignant transformation



Abbreviations: CPDs, cyclobutane pyrimidine dimers; ROS, reactive oxygen species; NER, nucleotide excision repair; ATM, ataxia telangiectasia mutated; ATR, ATM and Rad3-related; NF-κB, nuclear factor kappa B; MAPK, mitogen-activated protein kinase; TERT, telomerase reverse transcriptase.

Fig. 2 Molecular mechanisms of UV-induced skin injury and photocarcinogenesis

3.4 Clinical and Epidemiological Disease Burden

The clinical manifestations of chronic UV exposure range from cosmetic photo-ageing to UV-induced keratoses and skin cancers. The body of evidence demonstrated that the Australian population bears a significant burden of UV-related skin cancers, with high incidence of both melanoma and keratinocyte carcinomas. The latter is an important contributor to overall morbidity due to its substantial clinical impact.

Although overall melanoma incidence is of major public health significance, the burden varies greatly between different population groups across Australia. It varies according to age, sex, population background, cumulative UV exposure, preventative health behaviours, and access to clinical assessment and treatment. Similar patterns are evident for keratinocyte carcinomas, although to a lesser extent. The evidence highlights the association between population-level UV exposure and melanoma incidence. However, it also demonstrates that the interaction between environmental exposure, individual susceptibility, and healthcare-related factors is complex.

3.5 Evidence for Photoprotection and Prevention

The prevention literature demonstrates that the mitigation of UV exposure decreases the incidence of skin cancers and their precursors. Evidence from cohort studies highlights the protective effect of regular sunscreen application. In particular, long-term sunscreen use was associated with a reduced incidence of melanoma. Consistent results were reported for UV-induced keratoses, with prolonged sunscreen application associated with reduced incidence of cutaneous squamous cell carcinomas.

The evidence indicates that sunscreen is an important element of a broader photoprotection strategy, which also includes seeking shade, wearing protective clothing, and using UV-protective sunglasses when outdoors. It also highlights the importance of sun-protective health behaviours, particularly for populations at higher risk of UV damage. At the population level, the Australian sun protection campaigns have been associated with increased sun protection adherence across the population over time.

3.6 Contemporary Diagnostic Approaches

The diagnostic approaches to UV-related skin cancers have evolved considerably over the past decade. They now include a range of conventional and innovative methods, including dermoscopy, total/full-body photography, sequential imaging, histopathological assessment, and selected molecular tests. Dermoscopy is an essential element of diagnostic

evaluation, as it allows for the visualization of features not available to the naked eye. It enables the assessment of subsurface structures and can help guide the management of suspicious lesions. For patients at higher risk of developing melanoma, sequential digital monitoring is an important tool that allows for the objective measurement of changes over time.

At the same time, the evidence highlights the need for careful clinical judgment to avoid overtreatment. Increased surveillance can lead to the identification of lesions that would have otherwise remained undetected but may turn out to be benign. Therefore, a balanced approach is required, with regular surveillance and timely interventions for suspicious lesions that warrant further assessment. The definitive role of histopathological examination in the diagnostic algorithm is still undisputed, and a biopsy should always be considered in suspicious cases. For confirmed malignancies, pathology results, stage, anatomical location, and selected molecular tests inform further management.

3.7 Artificial Intelligence and Digital Technologies

The literature synthesis identified a growing body of evidence on the use of artificial intelligence (AI), machine learning, deep learning, digital dermoscopy, and teledermatology in the management of patients with UV-related skin cancers. AI systems have been developed for a range of applications, from assisting with the diagnosis of melanoma to providing triage support for patients presenting with suspicious lesions. The evidence suggests that these approaches have the potential to increase access to care, particularly in rural and remote areas where specialist care is limited. However, the reliability and applicability of these approaches remain controversial. Particular concerns include the validity of the training sets used to develop AI systems, the ability to generalize across different populations and skin types, and the accuracy of diagnosis under varying clinical settings. Therefore, the overall evidence indicates that AI systems are valuable tools that can complement conventional diagnostic approaches but are unlikely to replace them in the foreseeable future.

3.8 Integrated Commentary

The evidence identified a range of mechanisms linking environmental exposure to the development of skin cancer. Specifically, DNA photodamage and oxidative stress initiated by UV radiation, lead to molecular, cellular, and tissue-level changes that contribute to neoplastic transformation. These changes can also manifest as photo-ageing. UV radiation exposure can also trigger persistent pro-inflammatory responses that contribute to photocarcinogenesis.

A range of interventions can be implemented at various stages to reduce individual and population health risk. Ozone layer protection plays an essential role in reducing overall population exposure to UV radiation, but other measures are also necessary. Public health campaigns can increase overall awareness and modify population behaviours, while

individual measures such as sun avoidance and photoprotection can reduce personal exposure. Surveillance and early diagnosis are also important, as they allow for timely interventions to reduce the malignant potential of suspicious lesions. Treatment follows as the final step in managing diagnosed malignancies.

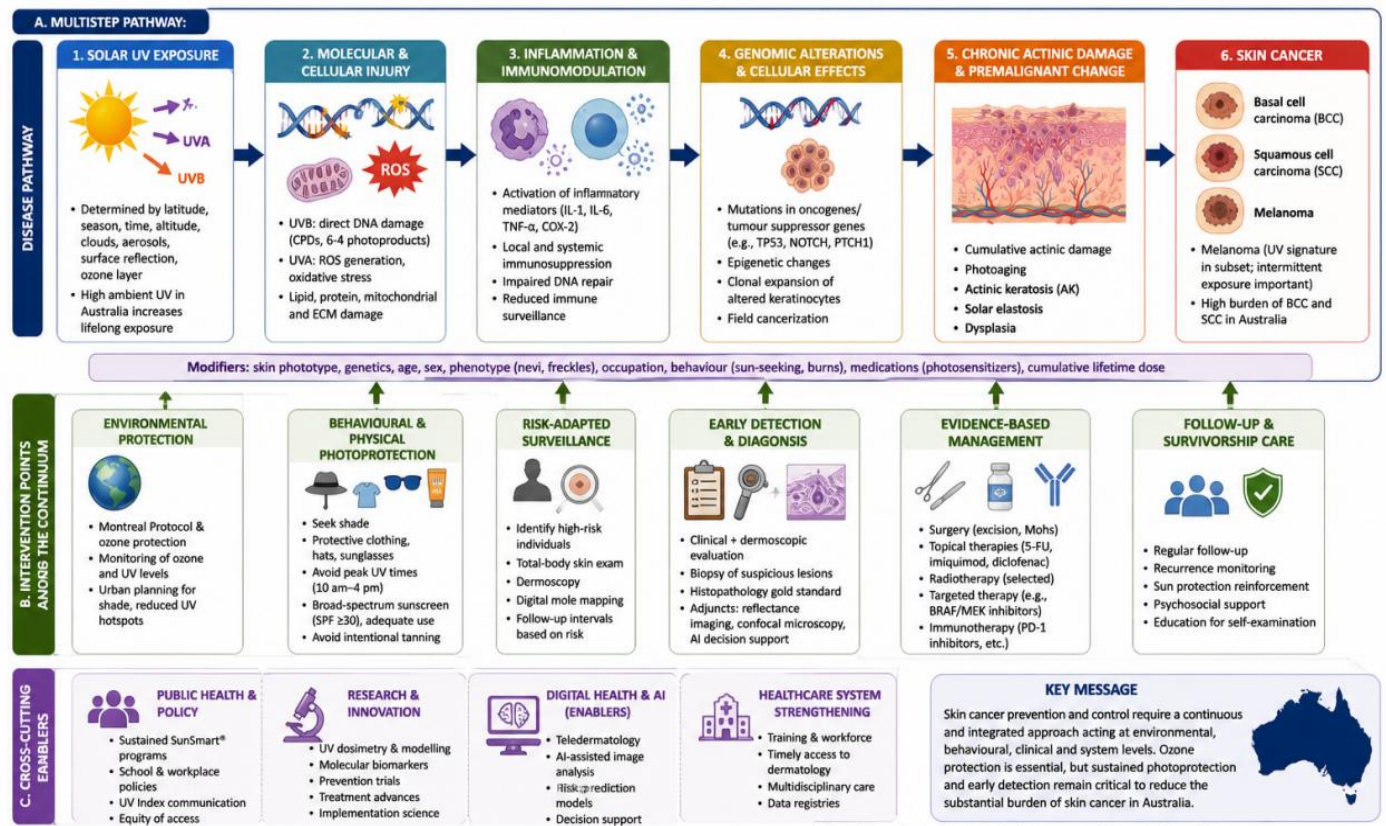


Fig. 3 Integrated pathway from solar UV exposure to skin cancer: prevention, surveillance and management at multiple levels

An integrated approach is the most effective way to reduce the health impact of UV exposure. The evidence shows that multiple factors contribute to the high incidence of UV-related skin cancers in Australia. The unique combination of Australia's geography and climate plays a significant role, but social, cultural, and behavioural factors also contribute to the rising incidence of skin cancers. These factors need to be addressed using a combination of individual behaviour change, public health approaches, and improved clinical management.

4. Discussion

The present narrative review highlights that the etiology of UV-related skin disease in Australia is multifactorial. Notwithstanding the contributions of UV exposure, geographical, climatic, historical, host-and behavioral factors, the capacity of UV to inflict persistent cellular and genomic damage plays a critical role. Recent empirical findings suggest that high levels of UV exposure in Australia are partially explained by historical depletion of stratospheric

ozone but that population-weighted UV exposure reflects a combination of latitude, solar geometry, climatic conditions, behavior, and other factors, of which ozone depletion is only one contributor [1,2]. This is an important consideration given that the projected recovery of the ozone layer will not negate the need for photoprotection.

4.1 Ozone Recovery Is Not Protective of UV Exposure

An important consideration emerging from the present analysis is the need to differentiate between ozone recovery and the reduction of ground-level UV exposure. While the Montreal protocol has had a significant impact in reducing atmospheric ozone-depleting substances and is projected to contribute to stratospheric ozone recovery, this process will be gradual [22]. With Australia's geographic location, solar UV radiation levels are projected to remain high despite ozone-layer recovery [22]. Hence, while improvements in the stratospheric ozone layer should

be regarded as an important environmental health gain, it is unlikely to offset the need for individual- and population-level UV protection.

Emerging modeling studies provide further insight into this issue by highlighting that differences in biologically effective UV radiation between Australia and the United States relate to latitude, variations in stratospheric ozone, and Earth-sun geometry, but that the historical contribution of ozone-depleting substances only explains a component of these differences [1]. This suggests that an environmental health model needs to account for a range of factors including solar geometry, seasonal variations in UV exposure, cloud cover, aerosols, behavior, and host responses in order to understand variations in ground-level UV exposure. Hence, while active measures to reduce atmospheric ozone-depleting substances should be maintained, they are unlikely to negate the need for national sun-protection policies.

4.2 UVR-Induced Photocarcinogenesis Is a Multistep Biological Process

A key finding of the present review is the need to consider a multistep biological model of photocarcinogenesis. Both UV-B and UV-A appear to play a role in driving UV-related carcinogenesis through distinct but overlapping mechanisms [14,15]. In particular, UV-B induces direct DNA damage whereas UV-A causes oxidative DNA damage and plays a role in driving inflammation and immunomodulation. These effects may interact with individual factors such as impaired DNA repair capacity, genetic predisposition, and defects in cellular signaling cascades and contribute to neoplastic transformation. These processes are relevant to skin cancer etiology in Australia given the cumulative nature of DNA damage and the potential for chronic inflammation and immunomodulation to drive malignant transformation [14]. UV-induced mutational signatures provide further evidence of a causal relationship between UV exposure and carcinogenesis [14,15].

It is noteworthy that defective apoptosis and impaired cell-cycle control following UV exposure can also contribute to photocarcinogenesis [15]. This observation is directly relevant to Australia given the high rates of skin cancer and the potential for these processes to drive tumorigenesis. Similar mechanisms appear to operate in both keratinocyte and melanoma carcinogenesis, albeit with some differences between these tumor types. Thus, in melanoma, there is growing recognition of the complexity of the molecular pathology of melanoma whereas keratinocyte carcinogenesis appears to be driven by a combination of UV-induced alterations in tumor suppressor genes and oncogenic pathways [12,14].

Overall, these findings highlight that UV exposure needs to be considered a carcinogen that interacts with a range of biological processes.

These molecular pathological considerations have important implications for the differing roles of UV exposure in the etiology of keratinocyte and melanoma carcinogenesis. The former is strongly related to cumulative exposure whereas the latter appears to reflect a complex interaction between intermittent exposure, host factors, and nevus biology [8,12]. Hence, in both cases, there is a need to consider the cumulative burden of UV exposure. As such, public health and clinical interventions should focus on decreasing overall UV exposure as well as implementing targeted measures to reduce the risk of neoplastic transformation in populations and patients at risk.

4.3 Australia's Skin Cancer Burden Reflects Long-Term Exposure

An important consideration in the context of skin cancer prevention and control in Australia is the long latency period between UV exposure and the development of clinically apparent malignancy. This is reflected in the high incidence of skin cancer across the country despite recent public health initiatives aimed at improving sun-protection behaviors. Indeed, the projected recovery of the ozone layer is unlikely to offset the long-term environmental health impacts of high solar UV exposure. This consideration is relevant to both melanoma and keratinocyte carcinogenesis [8]. At the same time, it is evident that sun-protection behaviors adopted in recent years will have long-term benefits for reducing the overall disease burden.

It should also be acknowledged that the burden of disease reflects a range of factors including host-, behavior-, and environment-related factors. Thus, age, sex, skin type, occupation, and recreational exposure, as well as genetic and immunological factors, contribute to interindividual variation in UV exposure and skin cancer risk. There is growing recognition of the impact of individual variability on clinical presentation and outcomes [6,13]. At the same time, the high incidence rates in Australia highlight the importance of other factors, including high ambient UV levels, which contribute to the overall disease burden [4].

4.4 Prevention Is the Most Important Modifiable Component

A key message of the present review is the central role of primary prevention in reducing the overall disease burden in Australia. Unlike many other environmental and behavioral carcinogens, UV exposure is both strongly modifiable at the individual and population levels. There is a substantial evidence

base, including several randomized controlled trials and population cohort studies conducted in Australia, that supports the role of regular sunscreen application in reducing the risk of skin cancer [9,10]. The long-term follow-up of the Nambour Skin Cancer Prevention Trial provides particularly compelling evidence of the role of regular sunscreen use in reducing the risk of cutaneous squamous cell carcinoma (SCC) and melanoma [9,10]. It should be noted that the melanoma risk reduction observed in this trial primarily related to invasive tumors.

The role of sunscreens in skin cancer prevention should be interpreted within the context of a broader public health strategy that emphasizes sun-protective measures, minimizes UV exposure, and reduces the likelihood of skin damage [5]. Within this paradigm, regular sunscreen application is an important adjunct to other measures, including seeking shade, wearing protective clothing, and using UV-protective eyewear. These individual-level measures should be complemented by population-level initiatives that promote such behaviors, including public health campaigns, workplace initiatives, and the creation of shade in public places. This approach is particularly important in Australia given the high ambient UV levels throughout much of the country and most of the year. Thus, while the projected recovery of the stratospheric ozone layer will reduce UV exposure, it will likely remain relatively high for many decades [1,22].

An important public health initiative in Australia that has contributed to improvements in sun-protection behaviors is the SunSmart program. This campaign has been associated with a stepwise change in public attitudes and sun-protective behaviors [7]. Similar approaches can be applied at the population and individual levels in order to reduce the overall UV exposure and skin cancer risk. More specifically, public health campaigns that provide continuous education and reminders about the importance of sun protection can influence individual behavior [2]. This approach can be applied in a wide range of settings, including the workplace, schools, and the built environment, to reduce UV exposure [23]. By reducing the overall UV exposure and implementing targeted skin cancer screening and surveillance initiatives, it will be possible to reduce the overall disease burden.

4.5 Early Detection and Risk-Adapted Surveillance Are Increasingly Important

The importance of early diagnosis and timely treatment of skin cancer has been increasingly recognized in recent years, particularly with regard to melanoma. These considerations apply to keratinocyte carcinogenesis as well, with several treatment modalities being available for early SCC [8].

Within this context, dermoscopy and other diagnostic adjuncts play an important role in enabling clinicians to differentiate between benign and malignant skin conditions [16]. Total-body photography and sequential digital dermoscopic surveillance can also be particularly useful in patients with multiple melanomas or at high risk of developing skin cancer [27]. However, it is important to emphasize that early diagnosis and treatment of skin cancer should be considered within the context of an individual's overall risk of developing skin cancer. A population-wide approach to skin cancer screening is unlikely to be clinically or cost-effective given the relatively low likelihood that an individual presenting for such a screen will have skin cancer [16,27].

Risk-stratified surveillance and management is likely to be the most clinically useful approach to the early diagnosis of skin cancer. This paradigm emphasizes the importance of assessing an individual's risk of developing skin cancer, with particular attention paid to cumulative UV exposure, history of melanoma or keratinocyte carcinoma, level of nevi, family history, and other risk factors [16,27]. Within this framework, high-risk patients can be offered more intensive surveillance and early treatment while the majority of the population can be encouraged to adopt sun-protective measures and participate in skin cancer screening programs [16,27].

Several emerging technologies can contribute to this individualized approach to skin cancer surveillance. Thus, dermoscopy has been shown to be an important diagnostic adjunct in both research and clinical settings [16]. Reflectance confocal microscopy and other similar non-invasive imaging approaches can be particularly useful in selected clinical scenarios, for example, when the clinical diagnosis is uncertain [28]. It should be emphasized, however, that histopathological examination of suspect skin lesions remains central to the diagnosis of skin cancer. It is likely that the future management of patients with melanoma will increasingly focus on the integration of clinical, dermoscopic, and pathological data rather than rely on any one of these approaches.

4.6 Artificial Intelligence Offers Opportunity but Needs Clinical Validation

Artificial intelligence (AI) is set to play an important role in a number of fields, including dermatology. There is a growing evidence base, including several recent systematic reviews, that highlights the potential of AI systems to contribute to the diagnosis of melanoma [17,18]. Of particular note, several studies have reported that AI-assisted diagnosis can perform similarly to human experts in diagnostic melanoma challenges [17,18]. Nevertheless, it is important to emphasize that the diagnostic accuracy

of AI systems needs to be validated against standard-of-care approaches in clinical practice.

At present, there are significant limitations in the clinical application of AI in dermatology. Thus, diagnostic performance is often determined using test sets that include only a limited range of images, and external validation is frequently lacking [17]. Furthermore, diagnostic accuracy tends to decrease with more complex cases, including those involving patients with different skin tones [17]. The ability of an AI system to perform accurately and reliably across a range of conditions and populations needs to be demonstrated prospectively. Finally, evidence suggests that the most clinically useful applications of AI in dermatology are likely to be found in collaboration with human experts rather than as standalone diagnostic tools [17,18].

Dermatology in Australia is uniquely positioned to benefit from innovations in digital health. Thus, the introduction of teledermatology and AI-assisted diagnostic tools can improve access to care for patients, particularly those in rural and remote areas [2]. Nevertheless, it is critical to ensure that these innovations are implemented with appropriate clinical governance and that they complement rather than replace standard-of-care approaches. Thus, teledermatology, when supported by clinicians, can be a useful tool in the initial assessment of patients with suspected melanoma or other skin cancers.

4.7 Implications for Australian Public Health and Clinical Practice

The present findings have important implications for public health and clinical practice in Australia. First, it is evident that multiple levels of intervention will be necessary in order to reduce the overall disease burden. At the environmental level, adherence to the Montreal protocol and investment in continued monitoring of the ozone layer and UV exposure are critical [22,24]. At the population level, public health initiatives, including the SunSmart program, need to be maintained and expanded, particularly in relation to occupational UV exposure [7,23]. At the individual level, a comprehensive approach to sun protection is critical in reducing the overall UV exposure.

At the clinical level, it is increasingly evident that surveillance and early diagnosis are core components of skin cancer management, particularly for patients at high UV exposure risk. Thus, there is a need for clinicians to adopt a risk-adapted approach to skin cancer surveillance, which also has implications for resource allocation. Within this framework, dermoscopy and other emerging diagnostic technologies appear to have an important role to play in both research and clinical practice. For patients with advanced malignant melanoma, there has been considerable progress in molecular characterization

and treatment, with targeted and immunotherapeutic agents providing durable treatment responses in many cases [12].

Finally, it is important to emphasize the need for a dynamic and integrated skin cancer control program that spans environmental, public health, and clinical domains. Thus, the findings of the present review highlight the need for a continuous focus on primary prevention, early diagnosis, and treatment of skin cancer in Australia. At the same time, improvements in molecular characterization of melanoma and new treatment modalities will ensure that optimal care is available for patients with advanced disease.

4.8 Strengths and Limitations of the Present Review

The present review includes a broad range of literature, including publications on atmospheric sciences, UV photobiology, molecular pathology, epidemiology, clinical dermatology, and digital health. This is an important strength, given the multifactorial etiology of skin cancer and the fact that the burden in Australia is related to both environmental and host factors. Nevertheless, there are several limitations that should be acknowledged. First, the present review is a narrative review rather than a systematic review with a meta-analysis. Second, the body of evidence on which the present review is based is heterogeneous in terms of study design, populations studied, and outcomes. Third, much of the evidence on AI relates to its diagnostic performance in test sets of images, which may not be generalizable to clinical practice [17,18]. Fourth, the estimates of UV exposure and its impact are based on modeling and make assumptions about exposure. Finally, much of the evidence comes from populations with largely Caucasian skin types, and the applicability to other populations should be carefully considered.

5. Future Research Priorities

Future research should focus on understanding the complex interplay between environmental UV exposure, individual risk factors, and disease outcomes. Thus, there is a need for population cohort studies, including those conducted in Australia, that prospectively examine the relationship between lifetime exposure and multiple risk factors, including individual UV exposure, skin type, behavior, and molecular pathology. This will enable the development of individual risk profiles and more accurate prediction of an individual's likelihood of developing skin cancer. Such studies could utilize novel approaches to estimating individual UV exposure, including wearable devices, and be combined with clinical outcome data.

There is also a need to examine the impact of individual- and population-level interventions on UV exposure. Thus, future studies should assess the impact of occupational, school-based, and other sun-protection initiatives, as well as the role of digital technologies in encouraging such measures [2,23]. In the clinical setting, there is a need for prospective validation of emerging technologies, including AI-assisted diagnosis, in multiple populations and a range of clinical settings before they can be recommended for routine use [17,18]. Finally, future research should explore how best to integrate the wide range of available data, including clinical, molecular pathological, and digital health information, into individualized skin cancer surveillance and management approaches.

6. Overall Interpretation

The present review has provided a comprehensive overview of the key aspects of UV-related disease in Australia. These include the fact that high ambient UV exposure levels are related to both geographic and host factors, the complexity of UV-induced skin cancer etiology, and the range of interventions that can be used to reduce individual UV exposure and disease risk. Thus, it is evident that a multifactorial approach, which spans the environmental, public health, and clinical domains, will be critical to reducing the skin cancer disease burden in the long term.

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