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Estimated health and economic effects associated with over- and under-exposure to solar ultraviolet radiation in Australia and New Zealand using the SUNEX simulation model

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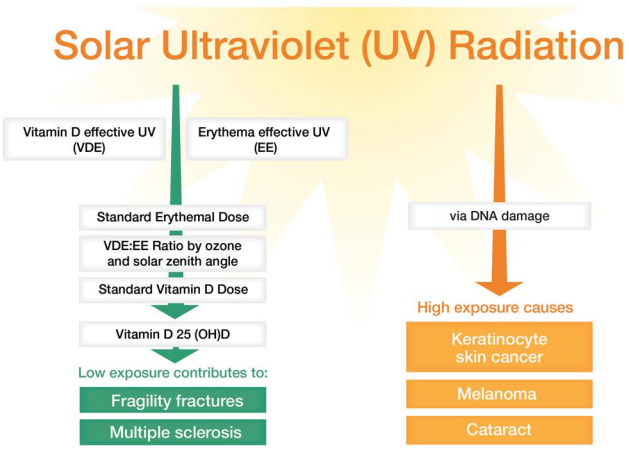
Abstract

Multiple health problems are associated with either over- or under-exposure to ultraviolet (UV) radiation. Using an agent-based microsimulation model, we examined the joint health and economic effects of conditions arising from over-exposure to sunlight (i.e., melanoma, keratinocyte skin carcinoma (KC) and cataract) and under-exposure to sunlight via vitamin D deficiency (i.e., fragility fractures and multiple sclerosis). We developed an agent-based model to estimate and compare incident cases, disease-specific deaths, healthcare costs and losses in quality-adjusted life years (QALYs) attributable to over- or under-exposure to UV radiation. Simulations were performed over a 20-year period for populations in 14 locations across Australia and New Zealand. Conditions caused by over-exposure to UV radiation were predicted to result in 6.0 and 1.2 million new cases compared with 0.12 and 0.08 million cases from under-exposure in Australia and New Zealand, respectively. However, the number of deaths due to under-exposure (Australia: 58,503; New Zealand: 20,104) were higher than those arising from over-exposure (Australia: 49,320; New Zealand: 7136), but this was dependent on the definition of vitamin D deficiency used. The expected healthcare costs from over-exposure to UV radiation were AU$12.4 billion in Australia and NZ$5.2 billion in New Zealand, three-fold higher than costs for conditions attributable to under-exposure in both countries. Despite the enormous burden of skin cancers, highlighting the importance of sun protection, avoidable deaths and healthcare costs of fragility fractures due to a lack of UV radiation requires a reduction in vitamin D deficiency in Australians and New Zealanders.

Graphical abstract



Keywords Sun exposure · Ultraviolet radiation · 25-hydroxyvitamin D · Agent-based model · Healthcare costs · Quality-adjusted life years

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1 Introduction

Ultraviolet (UV) radiation from the sun has both harms and benefits to health. Solar UV radiation is the main cause of malignant melanoma and other skin cancers, and it contributes to common eye diseases such as cataract and pterygium [1]. The key beneficial effect of UV radiation is the generation of vitamin D within the skin, which is critical for calcium metabolism and musculoskeletal health. Other benefits of vitamin D sufficiency might include protection against acute respiratory infections and autoimmune diseases [1]. Although research is still emerging, other benefits of sunlight have also been suggested, such as improving immune function and, at non-UV wavelengths, improving mood, regulating circadian rhythm, and preventing myopia [1]. Given the duality of sun exposure, when assessing the effects of interventions designed to reduce exposure to UV radiation, a balanced approach is needed to consider multiple disease outcomes and their relative health and cost impacts.

Australia and New Zealand experience high ambient UV radiation throughout most of the year and consequently have much higher incidence of malignant melanoma and other skin cancers than other countries with largely fair-skinned populations [2]. For example, the age-standardised rates of malignant melanoma are 33.5 per 100,000 in Australia and New Zealand compared with 15.3 per 100,000 in the United Kingdom, standardised to the world population [2]. Public health interventions to encourage sun protection have occurred over many decades in Australia and New Zealand, with the goal of reducing the incidence of skin cancers [3]. Ongoing primary prevention interventions for skin cancer are critical, since 26% of Australian adolescents and 17% of adults continue to get sunburnt each summer [4]. However, despite high ambient UV radiation through much of the year, around 23% of Australians and New Zealanders are reported to be vitamin D deficient (defined by the biomarker serum 25 hydroxyvitamin D (25(OH)D) < 50 nmol/L) [5, 6], and this proportion is higher in people living in the high-latitude southern regions in winter. Further, due to potential non-vitamin D benefits of exposure to solar UV radiation, vitamin D supplementation may not be the optimal solution for all people. Rather, obtaining some sunlight may be warranted.

With input from epidemiologists, environmental physicists, modellers, health economists, medical doctors and patient advocates, we designed a sun exposure simulation model (hereafter, the SUNEX model) to synthetically replicate the 25(OH)D concentrations of people living in Australia and New Zealand [7]. Here we extend the SUNEX model by adding separate disease modules to investigate downstream disease-related outcomes. Using a comprehensive microsimulation model, the purpose of this study was to estimate the disease burden and healthcare costs of five diseases attributable to over- or under-exposure to sunlight (i.e., over-exposure referring to melanoma, keratinocyte skin cancers (KCs), cataract, and under-exposure referring to fragility fractures, and multiple sclerosis). This descriptive information allows a relative comparison across the conditions and provides a benchmark for evaluating new interventions aimed at changing behaviours to promote health with greater balance of the harms and benefits of sun exposure.

2 Methods

2.1 Model overview

The SUNEX model is an agent-based microsimulation model of the relationship between exposure to UV radiation and health. The first phase of the SUNEX model has been published and represents the observed prevalence of vitamin D deficiency in the populations of Australia and New Zealand [7]. The model accounted for the range of latitudes and three climate zones: temperate in New Zealand; and arid, tropical, and temperate in Australia. The intensity of ambient UV radiation, temperature, and behaviour of residents differs substantially across locations. The model estimates the mean serum 25(OH)D concentration and the prevalence of vitamin D deficiency each month across the major cities. Large population datasets containing data on sun behaviours, socio-demographic variables, and UV radiation from ground-level measurements, ozone, and solar zenith angle were used. Full details on the development, data sources, calculations and validation of the first 'vitamin D' phase of the model is provided elsewhere [7]. The software used was *AnyLogic*™ (Version 7.3) and a read-only version is available online (https://cloud.anylogic.com/model/188db23c-3601-4116-8532-f22cf7227072). We constructed and added modules for five conditions with evidence of being causally associated with exposure to UV radiation either directly (i.e., melanoma, KC, cataracts) or indirectly via vitamin D deficiency (i.e., fragility fractures and multiple sclerosis). Over the model duration, it was possible for a person to have more than one of these conditions. Technical details of the model and its validation are provided in the Online Resource. Ethical approval for the study was received by the QIMR Berghofer Human Ethics Research Committee (P3743).

3 Model structure and features

SUNEX is an agent-based microsimulation model; the agents comprised persons and geographic locations (major cities), representing the populations of Australia and New Zealand. The 14 location agents were assigned a state or region and a continually updating standard vitamin D dose (SDD). An SDD (100 Jm^2 vitamin D weighted UV radiation) is the vitamin D equivalent of a Standard Erythemal Dose (SED: 100 Jm^2 erythemally weighted UV radiation). The relation between SDD and SED is not constant, but is a function of solar zenith angle and atmospheric ozone.

Each person in the model has attributes of age, sex, socio-demographic group, initial 25(OH)D concentration, propensity for skin to tan or burn, time spent outside, and body surface area exposed. Data values for each attribute were drawn from data distributions representing a range of values from real-world data sources. Several variables in the formulae to calculate the monthly change in serum 25(OH)D concentration and daily probability of a severe sunburn, were estimated to ensure they aligned well with broader population records of vitamin D deficiency and history of severe sunburn (Online Resource). Namely, the variables used to estimate serum 25(OH)D concentration included when people went outside, how often they were in direct sunlight, and when the saturation of 25(OH)D production occurs. For the daily probability of a severe sunburn, the formula was a function of the propensity for skin to burn and number of daily SEDs (Online Resource).

Key features of the extended SUNEX model are provided in Table 1 while full details of the model development, design, data inputs, and validation are provided in the Online Resource.

4 Model inputs and sources

Model inputs for disease-related variables and risk factors are summarised below and in Table 2 with full details provided in the Online Resource.

4.1 Incidence rates

The incidence rates for each condition were extracted from the latest national sources and, where available, by age, sex, and state or region [8–14]. A person could be diagnosed with multiple sclerosis or cataracts (in one or both eyes) once only, and 51% of people had cataract in their second eye [15]. For melanoma, KC, and fragility fractures, it was possible these could occur multiple times for a person over the model duration. Following the first event, new occurrences of melanoma and KC were based on the age- and gender-based incidence rates [8, 9, 11–14, 16], and risk ratios for subsequent fractures were based on the initial risk and fracture type [17]. Incidence rates were converted to monthly probabilities in the model.

Table 1 Extended SUNEX model design features

Feature	Details
Model type	Agent-based microsimulation model
Time step	Continuous time, run-in period 10 years, outcomes produced monthly
Model duration	20 years (tested at 10 and 30 years in sensitivity analysis)
Population	Persons 15 + year olds (aged 25 + by end of run-in period) residing in Australia and New Zealand, Age distribution represents the general populations of those countries, Population is static (closed), no new members are added with each successive year
Outcomes	New cases (person-based), disease-specific deaths, healthcare costs, quality-adjusted life years (QALYs) lost due to disease
Cost perspective	Healthcare provider and patient out-of-pocket costs
Discounting	3% costs and QALYs, incident cases and deaths were undiscounted
Costs	Australian and New Zealand dollars at 2023 prices, costs were adjusted for inflation
Base analysis	Probabilistic analysis, mean results of 30 iterations of ~ 900,000 microsimulations
Uncertainty analysis	Deterministic: one-way sensitivity analysis
Sub-group analyses	Country (Australia, New Zealand) Sex (male, female) Age groups: < 45 years, 45–64 years, 65 + years
Software	*AnyLogic*™ (Version 7.3) available to view at https://cloud.anylogic.com/model/188db23c-3601-4116-8532-f22cf7227072

Table 2 Summary of disease-related variables and sources

	Melanoma	Keratinocyte skin cancer	Cataract	Fragility fracture	Multiple sclerosis
Risk factors	Severe sunburns RR 1.3–1.6 [21]; Tanning ability RR 1.6–2.6 [21]; Past skin cancer RR 1.7–3.7 [21]; Sunscreen use RR 0.3–0.7 [18]	Sunscreen use RR 0.7 [18]	Average weekend hours outside RR 0.9 [20]; Past skin cancer RR 1.2 [22]	Vitamin D deficiency RR 1.7 (vertebrae) & 1.8 (hip) [19]	Vitamin D deficiency RR 1.5 [49]
Incidence[a]	By 5-year age group, sex and location. [QLD, Female, age 60–64: 131 per 100,000 PY] (Cancer Registry data Aust/NZ)[b]	By 5-year age group, sex and location. [QLD, Female, age 60–64: 2091 per 100,000 PY] [9]	By 10-year age group < 55, 55, 65, 75 [Female Age 65: 6038 per 100,000 persons] (MBS items)	By 5-year age groups and sex and fracture type [Female, age 60: 0.8 per 1000 PY] (AIHW 2024) [50]	By 10-year age group and sex, range [Female, age 60–69: 11 per 100,000 PY] [10]
Disease sub-categories	Single, multiple In situ, stage I, II, III, IV tumours	Single, multiple 2 +	Not applicable	Single, multiple. Type: hip, vertebrae	Mild, moderate, severe disability
Mortality	Hazard ratios by stage II (1.8) III (2.5) [51], IV (Weibull dist., mean 22 mths) [52–55]	Assumed no excess mortality	Assumed no excess mortality	Hazard ratios by ages 60/75 years, sex, fracture type [56]	Hazard ratios by mild (1.3), mod. (1.5), severe (3.6) [57, 58]
Health utility	Disutilities when diagnosed by stage in situ/I & II −0.03 [28], III −0.24, IV −0. 24 [29]	Disutilities when diagnosed by Single KC −0.01, Multiple KC −0.03 [28]	Disutilities during waiting time for surgery -0.09 [27]	Disutilities by time since fracture, changing at 2 week, 4 mth, 12 mth by fracture type, sex [30]	Health state utilities by stage of disease[d]: Mild 0.61; Moderate 0.51; Severe 0.40 [31] Relapse −0.01 [32]
Costs – Australia AU$	First year—stage in situ/I $892, II $7570, III $61,614, IV $104,483 [35] Following year—stage in situ/I/II $192, III $3436, IV $40,579 [35, 38]	First year $544 Following years $83 [35]	First year $707 Second year $463 (Supp materials)	By sex and fracture type, ± 70 years old Female, Hip < 70: $26,311 Female, Hip > 70: $43,157 [36]	Annual by severity Mild $23,900 Mod. $25,313 Severe $22,927 [34]
Costs – New Zealand NZ$	First year—stage in situ/I $1708, II $8935, III $28,673, IV $108,553 Following year—stage in situ/I/II $1000, III/IV $5739 [35, 38]	First year $1373 Following years $251 [74]	Australian costs converted to NZ$	Australian costs converted to NZ$	Australian costs converted to NZ$

ECCERT Eye Care Comparative Effectiveness Research Team, *KC* keratinocyte skin cancer, *PY* person years, *RR* relative risk

[a]Incidence is annual per 100,000 persons (melanoma, skin cancer & MS), per 100 people over 10 years (cataract) or per 1000 person-years (fragility fractures)

[b]NZ from New Zealand cancer registry[16]; QLD from Queensland Cancer Statistics On-line [13]; NSW from Cancer Institute NSW [8]; VIC from Cancer Council Victoria [59]; WA from Western Australian Cancer Registry [14]; SA from South Australian Cancer Registry [11]

[c]Fracture type is categorised into 3 groups: hip, vertebral, non-hip nonvertebral (NHNV) fractures

[d]The difference between baseline health utilities and the MS health utilities were the disutilities applied in the model

4.2 Inputs for the associations between UV radiation and condition

The SUNEX model focused solely on the *modifiable* risk factors in the pathways from UV radiation to the five conditions. This enables future analyses on the impact of any interventions that could modify risk behaviours to improve health outcomes. For example, we considered the association between sunscreen use and skin cancers, number of severe sunburns as an adult and melanoma, and vitamin D deficiency and fractures and multiple sclerosis. Each month, people could be diagnosed with any of the five conditions based on their underlying risk. The data on the relevant relative risks were obtained from published meta-analyses and other high-quality studies [18–22]. For each disease, we used a population attributable risk (PAR) equation to estimate the proportion of the condition attributable to the *modifiable* risk factors and those not attributable, based on the methods used in the Global Burden of Disease studies [23].

4.3 Mortality

In any given month, each person in the model could die of any unrelated cause, including either directly from or living with any of the five modelled diseases. We extracted mortality rates for the general population from Australian and New Zealand life tables [24]. Compared with general population mortality rates, a higher risk of death was applied for malignant melanoma, multiple sclerosis, and fragility fractures. We used specific mortality hazard ratios for disease severity for multiple sclerosis (i.e., mild, moderate, severe) and melanoma (i.e., stages II–IV) and type of fracture (i.e., hip or vertebrae). As it is rare for people among the general population to die from cataract, KC, melanoma in situ and stage I melanoma, no excess mortality was applied for people with these diseases. Competing risk of death was addressed by selecting the highest mortality hazard ratios across conditions.

4.4 Health utilities

Health utilities are similar to quality of life scores and are anchored between 0 meaning 'death' to 1 meaning 'perfect health'. These were used to weight a person's survival time and generate quality-adjusted life years (QALYs). QALYs are a widely used generic measure and are especially useful for comparing across diseases to assess the benefits of interventions that aim to maximise QALYs (i.e., improve quality of life and/or survival). Each person had a baseline health utility value according to Australian and New Zealand general population utilities by age and sex [25, 26]. From the baseline utility, a disutility was calculated and assigned when any of the five conditions occurred, by severity where relevant [27–32]. When cataracts and KCs occurred, the applied disutilities were temporary due to their rapid resolution following treatment, within the context of a long-term model. If a person had multiple co-occurring conditions, the minimum utility value was used [33]. We performed rapid literature reviews to obtain health utilities for each of the five conditions by severity, where available (Online Resource).

4.5 Healthcare costs

The study took both healthcare provider and patient cost perspectives. Healthcare providers comprised national and state governments providing services to Australians and New Zealanders. Healthcare costs for each condition included diagnosis, treatment and follow-up healthcare obtained from recent published reports [34–36]. Unit costs were specific for different severity levels for melanoma and multiple sclerosis, and for types of fragility fractures (hip and vertebrae), as reported in published costing studies [34–36]. In the absence of published cost estimates for cataracts, mean healthcare costs were generated using a decision tree analysis with diagnosis and treatment pathways (Online Resource). All model costs were inflated to 2023 Australian or New Zealand dollars using the Health Price Index and were discounted at 3%, as were QALYs, aligning with other population modelling studies [37, 38].

5 Validation

We took several steps to construct and validate the SUNEX model. First, conceptualising the model development and advising on data sources involved a workshop of 24 experts, consumers and stakeholders from different disciplines, held in late 2021. A pre-workshop survey was administered asking for preferences on which diseases to include in the model, and these were discussed during the workshop. Second, a senior health economist (author TC) and experienced mathematical modeller and *AnyLogic*™ trainer (author AF) reviewed the model for operational validity. This resulted in minor modifications to improve model efficiency. Third, extensive internal coherence checks of: input values; calibrations; and coding against the original sources were undertaken by three researchers (authors TE, LC and JK). We tested for extreme values and reviewed outputs. Fourth, external validation occurred by comparing the modelled findings (e.g., incident cases) to known observational data, where available.

Two key model parameters (i.e., the probability of severe sunburns and the change in 25(OH)D concentration) have not been measured reliably in published studies; therefore,

we used model calibration to estimate them. Calibration is a tool used to estimate or impute parameters in a model. For example, it is unknown exactly how long a person needs to be in the sun to cause severe sunburn but there are reports of the number of severe sunburns in our adult population. Calibration imputes the probability of severe sunburns for the model to produce the reported number of severe sunburns (i.e., adult severe sunburns from the QSkin Study) and identifies parameter values that achieve a good fit. There were eight calibrated parameters to estimate the probability of severe sunburn due to the following formula and the multiple categories of erythema burning category and 'AccFactor':

$$\text{Prob. of Severe Sunburn} = e^{-\text{ERY}_{\text{Burning Category}}/\text{Accumated SED}^{\text{AccFactor}}}$$

where 'ERY Burning category' is the number of SEDs required to enable a severe sunburn and 'AccFactor' is an exponential factor. We used the exponential factor because the accumulated SED and 'ERY Burning category' was not a linear relationship. 'ERY Burning category' and 'AccFactor' were calibrated so that the frequency of severe sunburns for each burning category matched the population. The calibration result for people who were sunburnt, and had skin that burns moderately when unprotected, was 46.2% with 1 to 5 severe sunburns that were sore for at least 2 days or resulted in skin peeling (Table C.7.4.2). The two calibrations and the limitations of interpretation are explained in the Online Resource (C.7.3–C7.4).

6 Analysis

For each of the five conditions, we modelled new cases (person-based), number of deaths, QALYs lost, and government and patient out-of-pocket healthcare costs over the next 20 years. Total counts and their percentage as a total of the five conditions were calculated. We calculated the burden of disease attributable to over- or under-exposure to UV radiation for each outcome through disease-specific PARs. The PARs, calculated within the model, represent the association between UV radiation and cataracts, fractures and multiple sclerosis. Since UV radiation is the primary cause of skin cancers, we applied a population attributable fraction reporting that UV radiation was responsible for 95% (male: 97%; female: 92%) of melanoma and 100% of KC cases [39].

The model was populated with ~ 600,000 simulated Australians and ~ 300,000 New Zealanders who were distributed proportionally to the actual population size within the 14 locations. These numbers were chosen as they comprised sufficient persons across locations and allowed analyses with reasonable computer efficiency. The cohort memberships were fixed and no new members entered the model. The model ran with all disease modules at the same time, with a run-in period of 10 years which allowed for relevant historical characteristics to develop; for example, number of severe sunburns as an adult, previous KC and fragility fractures. Outcomes were generated over 20 years in aggregate and tested over 10 and 30 years in sensitivity analyses. We also re-ran the analyses for fragility fractures with vitamin D deficiency defined as a 25(OH)D concentration of < 30 nmol/L. We entered tabulated data by age, sex or location (e.g., incidence, background mortality) as look-up tables; values were not subject to variation. Other variables such as probabilities, health utilities, and costs were assigned distributions to account for heterogeneity in the populations. We applied beta distributions to probabilities and utilities, log normal distributions to relative risk ratios, and gamma distributions to costs [40] (Online Resource). The outcomes presented are the mean counts from 30 iterations of Monte Carlo simulations involving re-sampling from the parameter probability distributions. Results are presented by each condition in aggregate for over- or under-exposure and by sex, age-group and country. Melanoma, KC and cataracts were grouped into over-exposure and fragility fractures and multiple sclerosis were grouped into under-exposure. The findings presented were extrapolated to the actual adult population sizes of Australia (20,932,520) and New Zealand (3,775,854).

7 Results

Averaged over the two countries, over-exposure to UV radiation was responsible for 95% of melanoma cases, 100% of KCs, and 1% of cataracts, whereas under-exposure via vitamin D deficiency was responsible for 11% of fragility fractures and 12% of new diagnoses of multiple sclerosis. Over the next 20 years, an estimated 12.8 million Australians and 3.3 million New Zealanders are expected to develop at least one of the five conditions. Of these, an estimated 6.0 million new cases in Australia and 1.2 million in New Zealand will be attributable to over-exposure to UV radiation, compared with 0.12 million cases in Australia and 0.09 million cases in New Zealand attributable to under-exposure to UV radiation (Table 3). The estimated number of deaths from UV radiation were higher from under-exposure (58,503 for Australia and 20,104 for New Zealand) compared with over-exposure (49,320 for Australia and 7136 for New Zealand). For government budgets, the expected healthcare cost burden from over-exposure to UV radiation will be AU$12.4 billion in Australia and NZ$5.2 billion in New Zealand, approximately three times higher than costs for under-exposure to UV radiation in both countries.

Table 3 Absolute number and percentage of the total burden across all 5 diseases and UVR-attributable outcomes[a] over 20 years, in Australia and New Zealand

	Melanoma		KC		Cataract		Fractures		Multiple sclerosis		Over-exposure		Under-exposure	
Australia														
Total outcomes														
New cases (persons)	1,197,727	9%	4,833,671	38%	5,735,690	45%	1,014,199	8%	19,874	0%	11,767,088	92%	1,034,073	8%
No. deaths	51,916	8%	–	–	–	–	559,025	91%	2,115	0%	51,916	8%	561,139	92%
QALYs lost	48,079	6%	222,589	26%	369,610	43%	178,813	21%	40,233	5%	640,278	75%	219,046	25%
Govt costs (AU$B)	5.9	10%	6.8	12%	6.5	11%	35.3	61%	3.8	6%	19.1	33%	39.0	67%
OOP costs (AU$B)	0.3	1%	1.0	5%	13.5	64%	5.3	25%	1.0	5%	14.8	70%	6.3	30%
Outcomes attributable to over- or under-exposure to UV radiation														
New cases (persons)	1,137,841	19%	4,833,671	79%	57,409	1%	119,259	2%	2,250	0%	6,028,921	98%	121,508	2%
No. deaths	49,320	46%	–	–	–	–	58,275	54%	228	0%	49,320	46%	58,503	54%
QALYs lost	45,675	15%	222,589	75%	3,759	1%	19,504	7%	4,565	2%	272,023	92%	24,069	8%
Govt costs (AU$B)	5.6	33%	6.8	40%	0.1	0%	3.9	23%	0.4	3%	12.4	74%	4.3	26%
OOP costs (AU$B)	0.3	14%	1.0	47%	0.1	7%	0.6	27%	0.1	5%	1.4	67%	0.7	33%
New Zealand														
Total outcomes														
New cases (persons)	213,853	7%	995,552	31%	1,184,850	36%	853,033	26%	4,019	0%	2,394,254	74%	857,052	26%
No. deaths	7,512	3%	–	–	–	–	238,142	97%	205	0%	7512	3%	238,347	97%
QALYs lost	8505	3%	47,106	15%	77,184	25%	174,697	56%	6473	2%	132,795	42%	181,170	58%
Govt costs (NZ$B)	1.2	5%	4.0	15%	1.4	5%	19.4	72%	0.8	3%	6.7	25%	20.3	75%
OOP costs (NZ$B)	0.1	2%	0.6	9%	3.0	44%	2.9	43%	0.2	3%	3.7	54%	3.1	46%
Outcomes attributable to over- or under-exposure to UV radiation														
New cases (persons)	203,160	16%	995,552	77%	11,937	1%	82,891	6%	496	0%	1,210,649	94%	83,387	6%
No. deaths	7136	26%		–	–	–	20,079	74%	25	0%	7136	26%	20,104	74%
QALYs lost	8080	11%	47,106	66%	773	1%	14,632	20%	796	1%	55,959	78%	15,428	22%
Govt costs (NZ$B)	1.2	16%	4.0	58%	0.0	0%	1.7	24%	0.1	1%	5.2	74%	1.8	26%
OOP costs (NZ$B)	0.1	11%	0.6	59%	0.0	3%	0.3	25%	0.0	3%	0.7	72%	0.3	28%

B billion, *Govt* government, *KC* keratinocyte skin cancer, *OOP* patient out-of-pocket, *QALYs* quality-adjusted life years, *UV* ultraviolet radiation

[a]uv-attributable outcomes are the sub-set of total outcomes estimated to be caused or prevented by UV radiation alone. Percentages for individual diseases and over- and under-exposure are fractions of the total of all 5 conditions. Over-exposure outcomes are the sum of melanoma, KC and cataract. Under-exposure is for fractures and multiple sclerosis

[b]No mortality outcomes were assumed for KCs and cataracts

[c]QALYs lost—represent the subset of overall QALYs generated for the population that are reduced due to the condition compared with the general population without the disease and combine years of life lost with quality of life decrements

Driving the disease burden of UV radiation were KCs with 79% of new cases for all five conditions in Australia and 77% of cases in New Zealand (Table 3). The relative percentages of new cases were next highest for melanoma at 19% for Australia and 16% for New Zealand and were less than 6% for the remaining conditions. In Australia, the proportion of all deaths attributable to either over- or under-exposure to UV radiation was 54% for fragility fractures followed by 46% for melanoma. These values were with 74% and 26% in New Zealand (Table 3). The proportion of deaths from multiple sclerosis were 0.21% in Australia and 0.09% in New Zealand. The proportions of government healthcare costs were highest for KCs (40%), melanoma (33%) and fractures (23%) in Australia. In New Zealand, the percentage for KCs was also highest (58%), but a greater percentage of government costs were due to fractures (24%) compared with melanoma (16%). Patient out-of-pocket cost proportions were relatively high for KCs (47%) and fractures (27%) in Australia and similarly, 59% for KCs and 25% for fractures, in New Zealand. KCs also accounted for over two-thirds of the lost QALYs in both countries, out of all five diseases. Despite fractures making up 2% of all new cases, the relative cost burden was high at 23% (AU$3.9 billion in Australia) and proportionally similar for New Zealand.

For the three conditions attributable to over-exposure to UV radiation, all the outcomes were higher for men than women, by at least 30% (Table 4). However, while the absolute numbers were substantially smaller for fractures and multiple sclerosis, collectively, compared to conditions from over-exposure to UV radiation, Australian women had 60% more deaths and incurred 2.5-fold higher government costs than for men (Fig. 1) due to having both more fractures and multiple sclerosis. The age-group findings indicated that new cases of multiple sclerosis were the highest among adults < 45 years old, 1450 (0.14%) in Australia and 317 (0.17%) in New Zealand. For those aged 65 years and over, new cases were highest for KCs and fragility fractures (Table 5). Very high cases and associated spending were

Table 4 Estimated UVR-attributable outcomes by sex for five conditions over 20 years, in Australia and New Zealand

	Melanoma		KC		Cataract		Fractures		Multiple sclerosis		Over exposure		Under exposure	
Australia														
Female														
New cases (persons)	465,642	17%	2,129,782	79%	25,612	1%	81,418	3%	1646	0%	2,621,036	97%	83,065	3%
No. deaths	19,666	34%	0	0%	0	0%	37,395	65%	158	0%	19,666	34%	37,553	66%
QALYs lost	19,241	16%	78,438	67%	1726	1%	14,284	12%	3244	3%	99,405	85%	17,528	15%
Govt costs (AU$B)	2.4	29%	2.6	32%	0.0	0%	2.8	34%	0.3	4%	5.0	62%	3.1	38%
OOP costs (AU$B)	0.1	11%	0.4	36%	0.1	6%	0.4	39%	0.1	7%	0.6	54%	0.5	46%
Male														
New cases (persons)	670,847	19%	2,703,889	78%	31,797	1%	37,840	1%	603	0%	3,406,532	99%	38,443	1%
No. deaths	29,623	59%	0	0%	0	0%	20,880	41%	70	0%	29,623	59%	20,950	41%
QALYs lost	26,350	15%	144,151	80%	2033	1%	5220	3%	1321	1%	172,534	96%	6541	4%
Govt costs (AU$B)	3.2	37%	4.1	48%	0.0	0%	1.1	13%	0.1	1%	7.4	86%	1.2	14%
OOP costs (AU$B)	0.2	16%	0.6	58%	0.1	7%	0.2	16%	0.0	3%	0.9	82%	0.2	18%
New Zealand														
Female														
New cases (persons)	80,034	14%	431,958	76%	5015	1%	49,374	9%	372	0%	517,007	91%	49,745	9%
No. deaths	2590	20%	0	0%	0	0%	10,577	80%	17	0%	2590	20%	10,594	80%
QALYs lost	3202	11%	15,313	51%	333	1%	10,782	36%	595	2%	18,848	62%	11,377	38%
Govt costs (NZ$B)	0.5	14%	1.5	47%	0.0	0%	1.1	36%	0.1	2%	1.9	62%	1.2	38%
OOP costs (NZ$B)	0.0	9%	0.2	48%	0.0	3%	0.2	36%	0.0	4%	0.3	60%	0.2	40%
Male														
New cases (persons)	123,053	17%	563,594	78%	6922	1%	33,518	5%	124	0%	693,569	95%	33,642	5%
No. deaths	4556	32%	0	0%	0	0%	9502	68%	8	0%	4556	32%	9509	68%
QALYs lost	4874	12%	31,793	77%	439	1%	3849	9%	202	0%	37,107	90%	4051	10%
Govt costs (NZ$B)	0.7	18%	2.5	66%	0.0	0%	0.6	15%	0.0	1%	3.2	84%	0.6	16%
OOP costs (NZ$B)	0.1	12%	0.4	68%	0.0	3%	0.1	15%	0.0	1%	0.5	83%	0.1	17%

B billion, *Govt* government, *KC* keratinocyte skin cancer, *OOP* patient out-of-pocket, *QALYs* quality-adjusted life years, *UV* ultraviolet radiation
Fractures include hip and vertebrae fractures only. Hip fractures are higher in elderly males

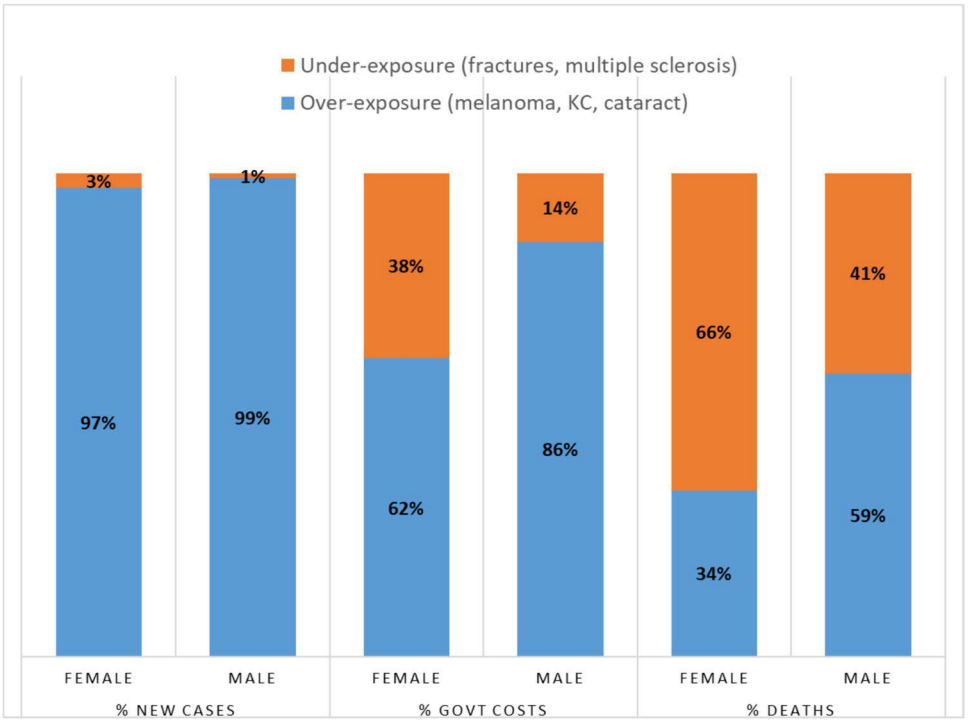

Fig. 1 Proportional outcomes attributable to over- or under-exposure to UV radiation by sex (absolute figures for these proportions are presented in Table 4), Australia

Table 5 Estimated UVR-attributable new cases and government costs by age-group over 20 years, in Australia and New Zealand

	Melanoma		KC		Cataract		Fractures		Multiple sclerosis		Over exposure		Under exposure	
Australia														
New cases (persons)														
< 45 years	220,626	21%	801,176	44%	2320	0%	1827	0%	1450	0%	1,024,122	100%	3277	0%
45–64 years	516,571	19%	2,126,263	44%	22,675	1%	29,236	1%	636	0%	2,665,510	99%	29,871	1%
65 + years	399,291	16%	1,906,232	44%	32,413	1%	88,196	4%	164	0%	2,337,936	96%	88,360	4%
Govt costs (AU$B)														
< 45 years	0.97	50%	0.67	25%	0.00	0%	0.03	1%	0.28	13%	1.64	84%	0.31	16%
45–64 years	2.36	37%	3.03	32%	0.03	0%	0.77	11%	0.12	2%	5.42	86%	0.89	14%
65 + years	2.22	26%	3.07	27%	0.04	0%	3.11	27%	0.02	0%	5.33	63%	3.13	37%
New Zealand														
New cases (persons)														
< 45 years	36,198	20%	143,181	44%	390	0%	4847	3%	317	0%	179,769	97%	5164	3%
45–64 years	89,385	16%	420,544	43%	4375	1%	27,947	5%	137	0%	514,304	95%	28,084	5%
65 + years	77,505	14%	431,826	43%	7171	1%	50,097	8%	42	0%	516,502	91%	50,139	9%
Govt costs (NZ$B)														
< 45 years	0.18	30%	0.31	34%	0.00	0%	0.04	5%	0.07	10%	0.50	83%	0.10	17%
45–64 years	0.48	19%	1.64	39%	0.01	0%	0.41	14%	0.03	1%	2.13	83%	0.44	17%
65 + years	0.49	13%	2.07	35%	0.01	0%	1.25	25%	0.01	0%	2.57	67%	1.26	33%

B billion, *Govt* government, *KC* keratinocyte skin cancer, *OOP* patient out-of-pocket, *QALYs* quality-adjusted life years, *UV* ultraviolet radiation
Age group includes the age a person is at the start of the model. Therefore, a larger proportion of those aged 65 + will die in the 20 year duration

predicted for KCs across all age-groups. For all age-groups, when compared with the proportions of new cases, government costs were disproportionally higher for melanoma and fractures compared with KCs. In people aged 45–64 years in both countries, government costs were fivefold higher for conditions related to over-exposure than for those related to

under-exposure to UV radiation. In those aged ≥ 65 years this reduced to less than twofold higher due to the higher incidence of fracture in older persons (Table 5).

Sensitivity analyses showed proportionally fewer or greater outcomes over 10 years and 30 years, respectively (data not shown). When a more conservative definition of vitamin D deficiency was used for calculating fragility fractures, from 25(OH)D concentration of 50 nmol/L to 30 nmol/L, the findings showed new cases of hip and vertebral fractures reduced by one half, deaths by one third and the other outcomes by one half in Australia (Table 6). Corresponding outcomes for New Zealand showed more pronounced reductions across outcomes than for Australia.

8 Discussion

The burden of disease in Australia and New Zealand due to too much and too little sun exposure is expected to be substantial over the next 20 years. Very high proportions of older adults are predicted to be diagnosed with either (or several) of these five conditions. The sheer volume of new cases of KC in both males and females of middle- and older ages will drive this UV radiation burden, far exceeding the new cases for the other diseases attributable to under-exposure to UV radiation, while multiple sclerosis affects relatively few people. Total healthcare costs will be very high for KCs and fragility fractures in both nations. Despite only being a small proportion of all conditions, UV-attributable fragility fractures will exert a relatively high mortality burden, with women more affected than men, and high costs due to the high costs associated with hospitalisation.

Several studies have used simulation models to assess the costs and outcomes for the individual conditions in this study [10, 35, 41, 42]. These include population models for disease burden and for health economic applications to assess the cost-effectiveness of interventions. However, none of the previous studies have combined multiple diseases in the same model or considered both the harms and benefits of sun exposure in their populations. Our findings suggest this might be particularly important when dealing with female mortality, since insufficient sun exposure that

Table 6 Estimated UVR-attributable fractures by definition of vitamin D deficiency over 20 years, in Australia

	50 nmol/L			30 nmol/L		
	Total fractures	Hip	Vertebral	Total fractures	Hip	Vertebral
Australia						
Female						
New cases (persons)	81,418	57,721	23,698	37,685	26,872	10,813
No. deaths	37,395	30,117	7,278	17,325	14,010	3,315
QALYs lost	14,284	10,047	4,237	6,734	4,774	1,960
Govt costs (AU$B)	2.80	2.55	0.26	1.31	1.20	0.12
OOP costs (AU$B)	0.42	0.38	0.04	0.20	0.18	0.02
Male						
New cases (persons)	37,840	28,281	9,559	17,404	13,038	4,366
No. deaths	20,880	16,954	3,926	9,612	7,826	1,786
QALYs lost	5,220	4,554	666	2,566	2,228	339
Govt costs (AU$B)	1.10	1.03	0.08	0.51	0.47	0.03
OOP costs (AU$B)	0.17	0.15	0.01	0.08	0.07	0.01
New Zealand						
Female						
New cases (persons)	49,374	12,777	36,597	18,977	4,549	14,428
No. deaths	10,577	4,311	6,266	2,509	1,050	1,459
QALYs lost	10,782	2,211	8,572	2,599	536	2,063
Govt costs (NZ$B)	1.13	0.59	0.53	0.27	0.15	0.12
OOP costs (NZ$B)	0.17	0.09	0.08	0.04	0.02	0.02
Male						
New cases (persons)	33,518	6,877	26,641	7,334	1,497	5,837
No. deaths	9,502	3,066	6,436	2,106	690	1,416
QALYs lost	3,849	1,284	2,565	857	280	577
Govt costs (NZ$B)	0.57	0.27	0.31	0.13	0.06	0.07
OOP costs (NZ$B)	0.09	0.04	0.05	0.02	0.01	0.01

exacerbates fragility fractures has a higher risk of death than melanoma for females.

Sun exposure behaviours throughout a person's lifespan have a considerable influence on the risk of disease, but can be modified to optimise health. With ageing populations, substantial progress on prevention is needed to curb the rise in avoidable disease [3, 43]. For skin cancer, studies have consistently shown that investment in sun protection initiatives produces a high return on investment [43]. Our analyses isolate the subset of disease burden related to over-exposure to UV radiation that could be reduced through beneficial sun behaviour changes. Typically, the types of prevention for disease control include primary, secondary, and tertiary strategies. An additional approach is primordial prevention, which focuses on structural changes to avoid the need for individual behaviour change. Examples for skin cancer prevention include shade creation in public spaces, compulsory protective clothing for outdoor workers, compulsory clothing protection by school and sports uniforms.

The economic attention on harmful risk factors for disease is growing. The Organisation for Economic Cooperation and Development now reports on risk factors in its publication on global health indicators [44]. The Australian Government also produces disease expenditure attributable to key risk factors [45] and reported that potentially avoidable risk factors were worth AU$24 billion in healthcare spending in 2018–19. Sun exposure was estimated to account for $1.24 billion using the attributable fraction approach and was the leading risk factor for cancer-related health expenditure [45]. Low bone mineral density was also a major factor costing $1.15 billion for falls-related expenditure [45]. Reducing harmful behavioural risk factors is likely to yield high health and economic gains with widespread benefits beyond a single disease, and these gains are potentially higher than for secondary prevention services [38].

For several decades, the Australian and New Zealand public health community have promoted sun safety to address the high burden of skin cancer in their populations [3]. Our recent research involving citizens' juries, conducted in Brisbane (latitude 27.5° S) and Adelaide (latitude 34.9° S) obtained the perspectives of general citizens, who were informed about the pros and cons of sun exposure, and how messaging around improving the balance could be received [46]. The jury members' recommended that skin cancer should be central to health promotion messages, yet there was scope for more nuanced advice tailored to a person's skin phenotype [46]. A revised Position Statement for managing the risks and benefits of sun exposure does this by allocating citizens into high-, medium- and low-risk of skin cancer based on skin pigment and other risk factors [47]. The Statement provides guidance on recommendations for time in sun according to location and month of the year [7, 47]. The impact of adhering to the Position Statement recommendations for maintaining vitamin D is yet to be examined at a population level, and further work could quantify the extent of health and economic improvements from the outcomes predicted here, reflecting the status quo. For people concerned about vitamin D deficiency, supplementation is a relatively easy, safe and effective option.

8.1 Strengths and limitations

A number of assumptions and uncertainties need to be considered when interpreting the results of the SUNEX model. Firstly, the definition of vitamin D deficiency we used is not universally accepted. The data showing associations with fractures at a concentration < 50 nmol/L were based on studies that used a range of imprecise assays, but they were mostly the older immunoassays that tended to read lower. Therefore, there is a disconnect in the type of assay used in the studies that assessed the association between 25(OH)D concentration and fracture, and the assay used to determine the prevalence of vitamin D deficiency in the community. It is also plausible that the risk of falls and fractures increase only when 25(OH)D drops below 30 nmol/L [48]. By using a cut-off of 50 nmol/L we may have over-estimated the percentage of fragility fractures and multiple sclerosis attributable to under-exposure to UV radiation. Our sensitivity analysis, where we redefined vitamin D deficiency as < 30 nmol/L, indicates substantially lower numbers of fragility fractures and associated costs. There are also uncertainties associated with estimates of association between exposure to UV radiation and melanoma/KC/cataract. Association does not establish causation, so while 25(OH)D levels may be lower in fracture populations, there is currently little trial evidence that intervening to increase these levels reduced fracture risk. Other sources of imprecision relate to excluding fractures at sites other than hip or vertebrae that may also be related to vitamin D deficiency, and excluding deaths from KC and cataracts, both of which would underestimate the burden.

While combining multiple diseases into simulation models is novel, it is also complex and has likely introduced uncertainty into the model processes in unknown ways. As such, our findings should be interpreted with caution. Several simplifying assumptions about model structure and inputs were necessary as we focused on modifiable risk factors. Ethnicity was not explicitly assigned to persons in the SUNEX model and the population studies have low numbers of deeply pigmented people. Ethnicity is an important indicator of skin colour, and vitamin D deficiency is higher in persons with more deeply pigmented skin; however it is not a perfect surrogate and is not asked in population surveys (country

of birth is the closest question). The model involved a closed cohort and therefore cannot be interpreted as the expected outcomes for the whole population in a snapshot of time but rather is a cohort of the population observed for 20 years. However, this is appropriate when persons age, and it was a sufficient duration for indicating disease outcomes. The SUNEX model uniquely captures outcomes from sun exposure as a single risk factor, and considers a wider scope of consequences of UV-related disease beyond skin cancer. We transparently documented the processes, inputs, and model structure and sought clinical, epidemiological, and scientific expertise to build and implement the model. We used the best-available data inputs and these may be updated as new evidence arises.

9 Conclusion

Current projections over the next 20 years suggests both over- and under-exposure to UV radiation will exert a sizable disease and cost burden in Australia and New Zealand. Over-exposure to sunlight, and more specifically the development of new KCs, is predominantly driving new cases, healthcare costs and lost QALYs. However, there is a relatively high mortality and cost burden, particularly in women, for fragility fractures from vitamin D deficiency. Balancing sun exposure by understanding and acting on new tailored advice at a population level has the potential to optimise health and save increasingly scarce healthcare resources. The role of vitamin D supplementation remains a valid solution for reducing community-level vitamin D deficiency.

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Data availability Due to confidentiality agreements, supporting individual data for our modelling study is not readily available. Data from published sources are publicly available through academic sources or through request to the authors. The numerical model simulations upon which this study is based are too large to archive or to transfer. Instead, we provide all the information needed to replicate the simulations in the supplementary materials.

Declarations

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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