Environmental Burden of Disease Series, No. 13

Solar Ultraviolet Radiation

Global burden of disease from solar ultraviolet radiation

Robyn Lucas
Tony McMichael
Wayne Smith
Bruce Armstrong

Editors
Annette Prüss-Üstün, Hajo Zeeb, Colin Mathers, Michael Repacholi

World Health Organization
Public Health and the Environment
Geneva 2006

WHO Library Cataloguing-in-Publication Data

Solar ultraviolet radiation : global burden of disease from solar ultraviolet radiation / Robyn Lucas ... [et al.] ; editors, Annette Prüss-Üstün ... [et al.].

(Environmental burden of disease series ; no. 13.)

1.Sunlight - adverse effects. 2.Ultraviolet rays - adverse effects. 3.Risk assessment. 4.Cost of illness. 5.Skin - radiation effects. 6.Eye - radiation effects. I.Lucas, Robyn. II.Prüss-Üstün, Annette. III.World Health Organization. IV.Series: Environmental burden of disease series ; no. 13.

ISBN 92 4 159440 3 (NLM classification: WD 605)
ISBN 978 92 4 159440 0
ISSN 1728-1652

Printed by the WHO Document Production Services, Geneva, Switzerland.

Table of Contents

List of tables

List of figures

Preface

Human exposure to solar ultraviolet radiation has important public health implications. Evidence of harm associated with overexposure to UV has been demonstrated in many studies. Skin cancer and malignant melanoma are among the most severe health effects, but a series of other health effects have been identified. The current report provides a quantification of the global disease burden associated with UV. The information presented forms a knowledge base for the prevention of adverse effects of UV exposure that is achievable with known and accessible interventions. UV prevention focuses on protecting the skin and other organs from UV radiation. On the other hand, a moderate degree of UV exposure is necessary for the production of Vitamin D which is essential for bone health. Additionally, evidence emerges that low Vitamin D levels are likely to be associated with other chronic diseases. Thus, public health policy on ultraviolet radiation needs to aim at preventing the disease burden associated both with excessive and with insufficient UV exposure.

This volume is part of a series on global estimates of disease burden caused by environmental risks, and guides for estimating the disease burden from specific risks at country or local level. This Environmental Burden of Disease (EBD) series responds to the need to quantify environmental health risks as input to rational policy making. Quantification of disease will provide information on the health gains that could be achieved by targeted action on protecting against specific environmental risks to health. An introductory volume (No. 1 of the series) provides further details on methods used for such quantification.

The methods for environmental burden of disease are part of a larger initiative - WHO has recently analysed 26 risk factors worldwide in the World Health Report (WHO, 2002). In 2006, a global estimate of the health impacts from environmental risks has shown that the 24% of global disease is due to the "modifiable" part of the environment[1].

A separate guide is being prepared to assist in the estimation of health impacts from UV radiation at country level.

[1] Preventing disease through healthy environments - towards an estimate of the global burden of disease. WHO, Geneva, 2006.

Affiliations and acknowledgements

The World Health Organization, through its INTERSUN programme, is actively engaged in protecting the public from health hazards of ultraviolet radiation. In the framework of this programme, an assessment of the global disease burden associated with solar ultraviolet radiation was performed by the National Centre for Epidemiology and Population Health (NCEPH) in Australia, implementing a contract between WHO and the New South Wales Cancer Council.

The principal authors of this report are:

- Dr. Robyn Lucas, National Centre for Epidemiology and Population Health, Canberra, Australia
- Prof. Tony McMichael, National Centre for Epidemiology and Population Health, Canberra, Australia
- Prof. Wayne Smith, Centre for Clinical Epidemiology and Biostatistics, Newcastle University, Australia.
- Prof. Bruce Armstrong, School of Public Health, The University of Sydney, Australia

The WHO and the authors wish to acknowledge the assistance of Ivan Hanigan (NCEPH) with reference retrieval and GIS mapping of population and UVR; Dr Diarmid Campbell-Lendrum (WHO) for his discussion of comparative risk assessment methodology; Dr Jenny Lucas (Bone Fellow, Auckland Hospital, New Zealand) for her help in the understanding of influences of vitamin D on the skeletal system; Dr Robin Marks for his helpful comments on disease models for skin cancers; and Dr Simon Hales for GIS expertise. Dr William B. Grant (Sunarc, USA), Reviewers at the German Bundesamt für Strahlenschutz and Professor Rona M MacKie (University of Glasgow, UK) reviewed earlier drafts of the document.

Editorial and scientific support at WHO was provided by Drs. Annette Prüss-Üstün, Hajo Zeeb, Colin Mathers and Michael Repacholi.

Abbreviations

BCC	Basal cell carcinoma
CMM	Cutaneous malignant melanoma
DALY	Disability-adjusted life year
GBD	Global burden of disease
NMSC	Non-melanoma skin cancer
PAF	Population attributable fraction
RHL	Reactivation of herpes labialis
SCC	Squamous cell carcinoma
SCCC	Squamous cell carcinomas of the cornea and the conjunctiva
UVR	Ultraviolet radiation

Summary

A burden of disease analysis was undertaken to evaluate solar ultraviolet radiation as a risk factor for human illness. The objective was to assess the contribution of solar ultraviolet radiation to human ill health in both mortality and morbidity and taking account of the future stream of disability following disease diagnosis (using the disability – adjusted life year (DALY) as a common metric).

The initial step involved an analysis of the strength of the causal relationship between UVR exposure and a number of diseases identified in the literature as probably being related. Having identified nine disease outcomes with strong evidence of a causal relationship with excessive UVR exposure, and three diseases associated with under-exposure, an estimation of the population attributable fraction for UVR exposure was made for each of these outcomes, on the basis of published epidemiological studies.

Three separate methods were used to calculate the global burden of disease due to the above-identified diseases. The global burden of disease due to melanoma was already calculated as part of WHO's global burden of disease assessment. Calculated population attributable fractions for UVR exposure were applied directly to these estimates. For other diseases for which there are good epidemiological data on incidence and mortality, population level exposure-response relationships were developed. Using country-level population-weighted average (1997-2003) annual ambient UVR, incidence and mortality rates were imputed from these exposure-response curves and the burden of disease calculated and aggregated to WHO sub-regions. For those diseases for which much weaker epidemiological data were available, exposure to UVR was approximated by latitudinal position in ten-degree bands. Incidence and mortality rates were extrapolated from the available data to regions of similar latitude and the burden of disease calculated for each WHO sub-region.

Disease duration and disability weights for various health states were derived from the literature or estimated from diseases of similar severity based on the appreciation of a working group established for this study.

Globally, excessive solar UVR exposure caused the loss of approximately 1.5 million DALYs (0.1% of the total global burden of disease) and 60 000 premature deaths in the year 2000. The greatest burden results from UVR-induced cortical cataracts, cutaneous malignant melanoma and sunburn (although the latter estimates are highly uncertain due to paucity of data). Notably, a counterfactual of zero UVR exposure would not result in a minimum disease burden, but rather a high disease burden due to diseases of vitamin D deficiency.

1. Background

1.1 Introduction

Living organisms on Earth have evolved over millions of years as the planet and its atmosphere have changed. Selection pressures related to ultraviolet radiation (UVR) have likely been instrumental in the development of different skin pigmentation in humans, as they have migrated from areas of high ambient UVR to areas of lower ambient UVR (*1*). The contrasting requirements of protection from excessive ultraviolet radiation and receiving sufficient sunlight to promote the production of vitamin D by the skin have meant that those inhabiting low latitudes, with high UVR intensity, have darker skin pigmentation for protection from the deleterious effects of UVR, while those in higher latitudes have developed fair skin to maximize vitamin D production from much lower ambient ultraviolet radiation.

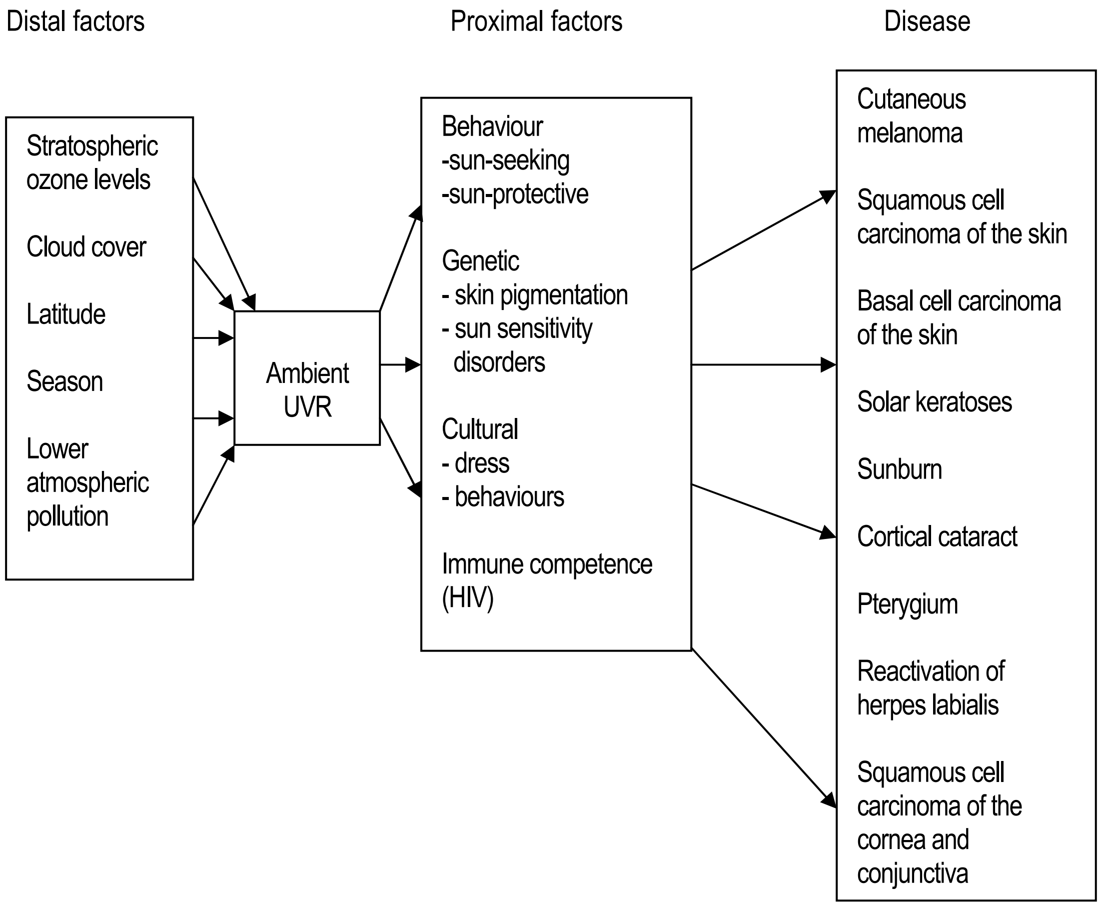
In the last few hundred years however, there has been more rapid human migration out of the areas in which we evolved, to all other parts of the world. No longer is our skin pigmentation necessarily suited to the environment in which we live. While dark-skinned populations at low latitudes have very low levels of melanoma and cancers of the skin, migration of these people to areas of high latitude has seen an increase in the incidence of rickets and osteomalacia (*2*). Fair skinned populations who have migrated to low latitudes have experienced a rapid rise in the incidence of melanoma and non-melanoma skin cancers. In addition, behavioural and cultural changes in the twentieth century have meant that many of us are now exposed to more, or less, ultraviolet radiation than ever before. Figure 1.1 presents an outline of the determinants of the health impacts of ultraviolet radiation.

Meanwhile, our industrialized society has produced chlorofluorocarbons (CFCs) that react chemically with the stratospheric ozone that has shielded Earth from most of the harmful wavelengths of ultraviolet radiation. The resulting loss of stratospheric ozone has been associated with increasing levels of some types of ultraviolet radiation reaching the Earth's surface. It is difficult to assess changes in UVR due to stratospheric ozone depletion, using ground-based measurements, due to UVR changes associated with fluctuations in cloud cover and increase in lower atmospheric pollution. However, monitoring in the Swiss Alps, where the atmosphere is relatively clear has indicated slightly increased levels of UVR in the northern hemisphere, while monitoring in Australia has demonstrated increased levels of ambient UVR in months when cloud cover has been particularly low (*3*). Increases in ambient UVR will be associated with increased adverse health effects due to excessive UVR exposure in the absence of behavioural changes and efforts at sun protection. Recent research has highlighted the beneficial effects to health of adequate UVR exposure due to UVR-induced vitamin D synthesis. The net health gain or loss from higher levels of ambient UVR will thus depend on the interaction of increased ambient UVR levels, skin pigmentation of those exposed and behavioural changes influencing personal exposure.

Ultraviolet radiation is ubiquitous. Almost everyone has some exposure to ultraviolet radiation on a daily basis. It is an exposure we cannot entirely avoid and, anyway, to strive for zero exposure would create a huge burden of skeletal disease from vitamin D deficiency. However, evaluation of the burden of disease created by excess exposure to UVR is very important since avoidance of excess exposure is a relatively simple public health message.

The purpose of this study is to evaluate the beneficial effects of adequate UVR exposure and the harmful effects of excess UVR exposure on human health, using the common metric, the DALY, to place into perspective the global burden of disease related to this ubiquitous risk factor.

Figure 1.1 Causal Web for Health Impacts due to Ultraviolet Radiation



1.2 Comparative risk assessment

Burden of disease risk factor assessment uses a comparative risk assessment framework designed to produce comparable and reliable analyses of risks to health (*4*). A detailed description of the conceptual framework and methodological issues is published elsewhere (*4*). In brief, there are four essential elements:

The burden of disease due to an observed exposure distribution in a population is compared with the burden of disease from a hypothetical, or counterfactual, exposure distribution(s).
A causal network including interactions among risk factors is developed for each disease outcome to allow making inferences about the effect of changes in combinations of risk factors.
The health loss due to a risk factor is calculated as a time-indexed stream of disease burden.
The burden of disease is calculated using a summary measure of population health, which allows the inclusion of mortality and morbidity data.

The following sections consider steps 1 and 2 in relation to UVR exposure as the risk factor.

1.3 Definition of the risk factor

Ultraviolet radiation is part of the spectrum of electromagnetic radiation emitted by the sun. It is arbitrarily divided into three bands of different wavelength although the exact wavelength at which the divisions are made differ for different disciplines (*5*). The divisions first proposed by the Second International Congress on Light in 1932 were as follows:

UVA	400-315nm
UVB	315-280nm
UVC	280-100nm

However, environmental and dermatological photobiologists commonly use slightly different divisions, more closely associated with the biological effect of the different wavelengths. That is:

UVA	400-320nm
UVB	320-290nm
UVC	290-200nm

UVC is totally absorbed by atmospheric ozone, has minimal penetration to the surface of the Earth and thus has little effect on human health. 90% or more of UVB is absorbed by atmospheric ozone (*6*), while UVA passes through the atmosphere with little change. Thus, the solar ultraviolet radiation of importance to human health consists of UVA and UVB.

While UVA penetrates the human skin more deeply than UVB, action spectra for biological responses indicate that it is radiation in the UVB range that is absorbed by DNA – subsequent damage to DNA appears to be a key factor in the initiation of the carcinogenic process in skin (*7, 8*).

The effect of solar radiation on human health depends on the amount and type of radiation impinging on the body. This in turn depends on, firstly, the concentration of atmospheric ozone that is available to absorb ultraviolet radiation, particularly UVB. Next, the amount and spectral structure of radiation reaching the body is dependent on the angle at which the sun's rays pass through the atmosphere – at low latitudes (closer to the equator) there is more intense solar UVR with a greater proportion of shorter wavelengths, related to the low angle of incidence of the incoming radiation (*9*). This strongly influences biological activity. Increasing altitude increases UVR intensity by decreasing the air mass through which solar radiation must pass. Similarly, time of day and season as well as presence of clouds, dust, haze and various organic compounds can alter the intensity of incident solar radiation. Variations in cloud cover usually reduce ground level UVR, although this effect is highly variable, depending on the characteristics of the cloud itself. Indeed, cloud cover can result in increased ground level UVR if both direct sunlight and light scattered from clouds, reach the earth's surface (*10*).

Moderating effect of behaviour

While levels of total annual ultraviolet radiation vary approximately four-fold across the globe (*11*), in any area there is likely to be at least a ten-fold difference in personal UVR exposure which is related to behavioural and cultural factors. Thus, even in areas of relatively low ambient UVR, it is possible to have high personal exposure.

Gies et al (*12*) have summarized our knowledge of variation in personal exposure to solar UVR. For most subjects, UVR exposures vary from between 5% to 15% of total ambient UVR, with the exception of outdoor workers whose exposures can reach 20-30% of ambient UVR. Groups of similar age tend to receive a similar proportion of ambient UVR in different locations, with boys consistently having higher UVR exposure than girls. However, individual exposure within population groups may vary from one tenth to ten times the mean exposure in a particular location. In some persons or sub-populations, much of the annual exposure to UVR may be concentrated in a brief annual summer holiday.

Effect modification by skin pigmentation

For studies of the effects of UVR exposure on human health there is an effect modifier that may be stronger than that found in any other exposure-disease relationship. Skin pigmentation alters the exposure-disease relationship for all UVR-induced disease where the primary exposure of interest is skin exposure. Deeply pigmented skin provides important sun protection, with quantitative estimates varying, but including a skin protection factor of 13.4 (*13*), and an MED 33-fold higher than fair skin (*14*). Intermediate skin types have intermediate values of protection.

The most common classification of skin types for UVR sensitivity is the Fitzpatrick scale (Table 1.1).

Table 1.1 Fitzpatrick skin pigmentation scale

Type	Description
I	Fair skinned Caucasians who burn very easily and never tan
II	Fair skinned Caucasians who burn easily and tan slowly and with difficulty
III	Medium skinned Caucasians who burn rarely and tan relatively easily
IV	Darker skinned Caucasians who virtually never burn and tan readily, e.g. some individuals with Mediterranean ancestry.
V	Asian or Indian skin
VI	Afro-Caribbean or Black skin

Table adapted from (*15*).

For this analysis, the global population was broken down into three broad skin pigmentation groups, as there are insufficient data to separately quantify skin types I to IV:

Lightly pigmented – this includes skin types I to IV
Intermediate pigmentation – skin type V
Deeply pigmented – skin type VI

1.4 Measurement of the risk factor

Ambient UVR may be measured in purely physical units or weighted using an erythemal response function[2] to give biologically effective UVR, expressed as joules per square metre (Jm^{-2}), minimal erythemal dose (MED), standard erythemal dose (SED) or the solar UV index (Box2.1).

Unfortunately the MED is sometimes used in populations of different skin types where it means the dose of UVR required to produce a minimal erythemal response in a particular skin type – thus the dose of UVR may not be 200 Jm^{-2}, but must be defined for the skin type(s) under study. For example, in an investigation of the photoprotection of epidermal melanin pigmentation, the ratio of the values for the MED between skin type V and skin type I and II was 2.29 (*16*). The lack of a consistent baseline for MED measurement decreases its value for interstudy comparisons.

[2] A representation of the wavelength variation in production of erythema of the skin.

The SED (standard erythemal dose) has been developed as an erythemally weighted measure of radiant exposure, equivalent to 100 Jm^{-2}. The SED is independent of skin type and a particular exposure dose in SED may cause erythema in fair skin but none in darker skin (*5*). The global solar UV index was developed as an easy-to-understand measure of biologically effective UVR to promote public awareness of the risks of UVR exposure and to promote sun protection. Weather forecasts in many countries include a forecast of the solar UV index to guide public sun exposure.

Latitude provides a rough approximation to global variation in UVR (Figure 1.2). However, because of the elliptical nature of the earth's orbit around the sun there is a 7% difference in intensity between the hemispheres for any level of latitude, with the southern hemisphere having a greater intensity (*11*). In addition, clearer skies in the southern hemisphere can increase this difference in ambient UVR to 10-15% (*12*).

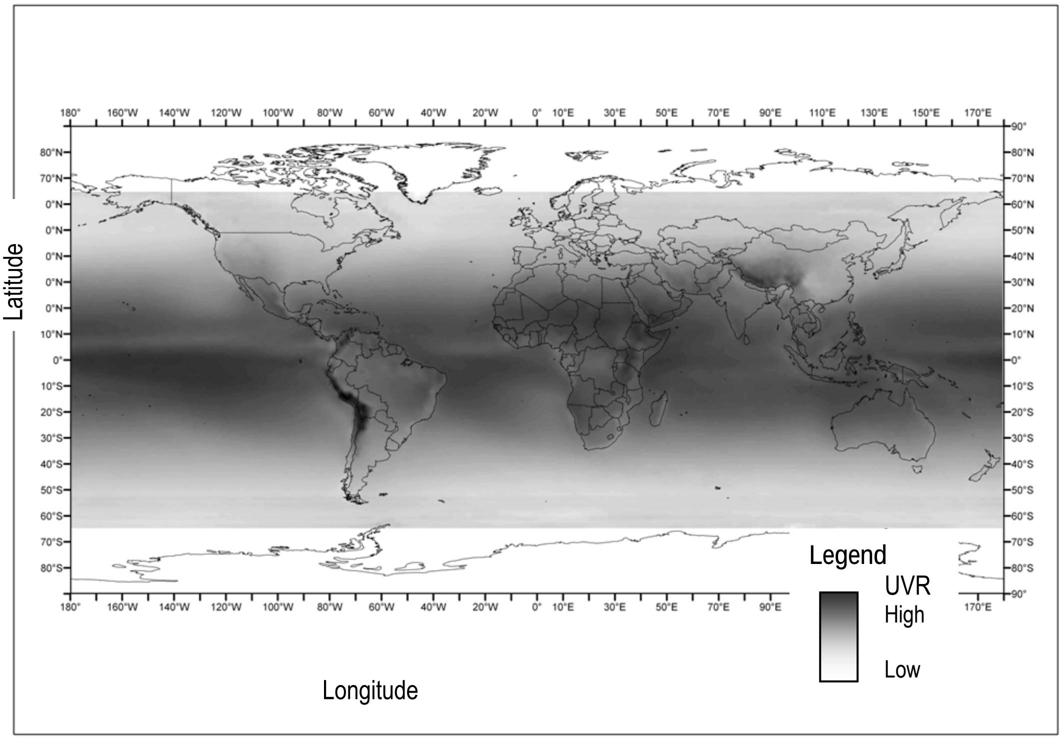
Box 2.1

MED: that dose of UVR required to produce a barely perceptible erythema in people with skin type 1 (200 Jm^{-2} of biologically effective UVR).

SED: erythemally weighted radiant UVR equivalent to 100 Jm^{-2}

Solar UV index: time weighted average effective UV irradiance in Wm^{-2} multiplied by 40 (Watts = joules/sec).

Figure 1.2 Monthly averaged annual ambient erythemally weighted UVR, 1997-2003



Ambient solar UVR is measured continuously by ground-level monitors, with publication of current values for particular locations. In addition, global ambient UVR levels, weighted to biologically effective wavelengths, calculated from satellite data are available online from 1978 to 1993 and 1996 to 2004[3].

Personal UVR exposure is usually measured in epidemiological studies by recalled exposure over a number of years. This can include a measure of the number of sunburns experienced at various times of life, hours spent outdoors during recreational activities, or occupational history. Many of the studies examining the effects of UVR exposure on the eye have quantified ocular exposure by adjusting ambient UVR (years in a location for which average ambient UVR is known) for use of a hat, sunglasses and surface albedo (*17*). However, such indices also rely on recall of the use of these sun-protective devices. Thus the estimation of the risk factor exposure level at the individual level in epidemiological studies is imprecise, given in varying "natural" units which have no fixed relationship to the physical units used to measure ambient UVR, and is particularly subject to recall inaccuracy.

We stress that even if extensive networks to precisely measure ground level UVR existed, this would not accurately represent the population distribution of individual UVR exposure. One problem is the geometrical difference between a (usually) horizontal fixed detector and the curved body surface that will produce significant deviations in exposure. These deviations have recently been quantified. But, Gies et al note that "population groups are not homogeneous as regards UVR exposure" and "Some subjects have consistently high or consistently low exposures in comparison to the mean…, from a tenth to ten times the mean" (*12*). As already noted, behavioural and cultural differences mean that for any ground level measure of UVR, there may be a hundred-fold difference in personal UVR exposure. It would be erroneous to interpret highly precise estimates of ground-level UVR as accurate estimates of personal UVR exposure. Furthermore, variations in skin pigmentation and use of sunscreen determine the exposure to biological structures in the context of variations in ambient UVR.

The estimations for this burden of disease assessment involve assuming a population-level exposure represented by annual ambient erythemally weighted UVR (calculated from satellite data) or a proxy such as latitudinal position.

1.5 Defining the counterfactual exposure

The disease burden attributable to a particular risk factor should generally be estimated as compared to an alternative exposure (or "counterfactual" exposure). This counterfactual exposure may represent the exposure resulting in a theoretical minimum disease risk, a plausible or feasible decrease in exposure and thus disease risk, or the cost-effective decrease in exposure level for decreased disease risk (*4*).

One possible choice of counterfactual exposure might be a "feasible" reduction in exposure to the risk factor. Sun avoidance and protection messages have been widespread for more than twenty years. Hill et al (*18*) described a reduction in sunburn and increased sun protective behaviours following an intensive health promotion campaign in Melbourne. Such decreases in exposure are relatively small (crude proportion of sunburnt fell from 11% to 7%, increase in hat wearing from 19% to 29% and sunscreen use from 12% to 21% over three years) but could cause a significant decrease in incidence of skin cancers and UVR-related eye diseases (*18*).

A preferable choice of counterfactual exposure for UVR might be that required to produce a theoretical minimum risk of disease. Murray et al (*4*) describe the choice of theoretical minimum exposure distributions based on categories of risk factors: physiological,

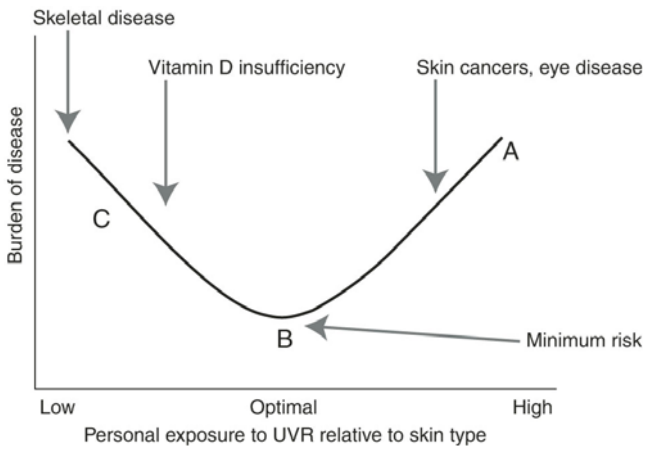
[3] http://iridl.ldeo.columbia.edu/SOURCES/.NASA/.GSFC/.TOMS/.

behavioural, environmental and socioeconomic. UVR exposure could fit into any of the first three of these categories:

Environmental toxicity for most environmental risk factors increases monotonically with increasing exposure, so that the theoretical minimum would be the lowest physically achievable level of exposure. Although solar UVR is an environmental exposure, there is clearly not a monotonic association between health risks and UVR exposure.
Physiological (e.g. vitamin D levels) and behavioural (sun exposure patterns) risk factors may demonstrate U or J shaped exposure response relationships. UVR exposure is best considered within this type of exposure-disease association.

Some UVR exposure is required for induction of synthesis of vitamin D, which is essential for musculo-skeletal health. Clearly, the minimum burden of disease for UVR exposure would thus not occur under a scenario of no UVR exposure (see Figure 2.1). Such a lack of exposure to UVR would lead to vastly increased disease load due to the increase in vitamin D deficiency. Conventionally we view this as causing only rickets, osteomalacia and osteoporosis, but recent research suggests that vitamin D may also have an extremely important role in the immune system, such that even subclinical hypovitaminosis D may have a causal role in the development of several cancers and contribute to the development of autoimmune disorders such as multiple sclerosis and type 1 diabetes (*19*). The theoretical minimum risk is therefore the turning point of the exposure-response curve. For UVR exposure this would equate to the minimum population distribution of UVR exposure that maintains vitamin D sufficiency, given the current diet. This distribution is, as yet, undefined, and varies by age, sex and skin type.

Figure 2.1 Schematic diagram of the relation between ultraviolet radiation (UVR) exposure and the burden of disease



Points A and C represent inappropriate UVR exposure. Fair-skinned populations in Australia with high outdoor UVR exposure typify point A. Point C represents people with insufficient UVR exposure, whose dietary vitamin D intake will also be important in determining their vitamin D status. Point B represents optimal UVR exposure: a person with careful titration of correct UVR dose for skin type.

Lucas, RM and Ponsonby, AL. Ultraviolet radiation and health: friend and foe. MJA 177:594-598

Holick et al (*20*) estimate that exposure of the whole body in a bathing suit to 1 (individual) MED is equivalent to ingesting 10,000 IU of vitamin D. Thus exposure of 6-10% of the body surface to 1 MED is equivalent to ingesting 600-1000 IU. The current recommended daily intake of vitamin D for children is 400 IU and for adults is 200 IU (*21, 22*), although recent research suggests that this should be increased to 600 IU (with some suggesting daily intake of up to 4000IU) in the absence of sunlight exposure. Based on these data, daily exposure of 6-10% of the body surface (one arm, one lower leg, or face and hands) to 1 MED should be sufficient to maintain vitamin D sufficiency (>50nmo/l). It should be noted however that recent research suggests that the lower level of vitamin D sufficiency should be raised to at least 80nmo/l (*23*).

Although it should be possible to calculate the mean daily UVR exposure required to maintain vitamin D sufficiency, at any location for a particular skin type using available global data on annual ambient UVR (*12*), this has yet not been done. At higher latitudes there is insufficient UVB to produce vitamin D over the winter months (*24*). Inhabitants of such areas would need to achieve higher levels of vitamin D synthesis in other seasons and rely on stored vitamin D over the winter. Even so, in the limited dose-response data available for basal cell carcinoma and melanoma (*25, 26*) this level of exposure would result in a zero incidence of cutaneous melanoma and an odds ratio of 1.0 for developing basal cell carcinoma.

A counterfactual exposure distribution of minimum UVR exposure to allow adequate synthesis of vitamin D is likely to represent a minimum risk for diseases of both over- and under-exposure, that is, there should be no need to accept an increased risk of diseases of excessive exposure, in order to achieve minimal risk of diseases of underexposure.

To summarize, for UVR exposure there are some difficulties with the comparative risk assessment methodology used in burden of disease assessment:

While there is a theoretical counterfactual exposure required to achieve a minimum disease burden (that required to maintain vitamin D levels), there is a lack of data that transfer this theoretical exposure into a measurable population exposure distribution.

The exposure distribution of populations is unclear. While data on ambient UVR are available, these do not easily translate to actual population exposure distribution. To achieve such data would require individuals of various ages and skin types to wear personal UV monitors continuously, and for a number of years, to evaluate both acute and chronic effects on health. Epidemiological studies have not been able to measure past UVR exposure with accuracy, but rather use measures such as number of sunburns or estimated hours in the sun. Further, these imprecise measures are based on recall of events usually well in the past.

2. Methods

2.1 Outcomes to be assessed

That there are effects of ultraviolet radiation on human health is clear. Absence of exposure to UVR causes a lack of vitamin D with subsequent effects on calcium and phosphorus levels and eventually rickets, osteomalacia and osteoporosis. Excess exposure to ultraviolet radiation is a relatively new problem, occasioned by less coverage by clothing, migration of pale-skinned peoples to areas of high ambient UVR and behavioural practices such as sunbathing.

There are both direct, e.g. skin cancers, and indirect effects, e.g. altering food productivity of plant and aquatic ecosystems, of ultraviolet radiation on human health. The current assessment is confined to direct effects due to human solar UVR exposure.

A systematic review of the epidemiological literature review was undertaken to ascertain a list of diseases where UVR exposure was implicated as a risk factor.

Initially a search was undertaken for major review papers in this area (*8, 27*), using search terms for the disease and "ultraviolet radiation". The Environmental Health Criteria 160 (EHC 160) document of 1994 included an extensive review of diseases possibly associated with UVR exposure so that subsequent searches were limited to references since 1994 in cases where there were a large number of "hits" for the initial search terms. A Medline search was undertaken for more recent evidence on these diseases, supplemented by searches of the bibliographies of other papers.

Following this, Medline was searched for "ultraviolet radiation" AND "health". The retrieved references were scanned for any new diseases that may have an association with ultraviolet radiation and then further more specific searches were undertaken for these diseases and UVR.

Secondly, the association between UVR and the identified disease outcomes was explored in more detail. Medline was searched using the following search terms: each disease, ultraviolet radiation and "ecologic studies" or "case-control studies" – again limited to after 1994 if the "hits" were greater than 100. Using the latter, an assessment of the current evidence for a causal relationship with ultraviolet radiation was undertaken, using Hill's criteria for causality (*28*), but particularly examining the biological plausibility of a causal relationship, the consistency of the results and the strength of the association between each disease and UVR exposure. This builds on work undertaken for EHC 160 and is described for each health state in Appendix 1.

Most information on diseases related to UVR exposure comes from white populations in developed countries, so areas such as Asia, the Middle East, Africa and South America were selectively searched to try to get as broad a global picture as possible.

Table 2.1 outlines the diseases that were considered, those that were found to have strong evidence of a causal relationship with UVR exposure and those that were subsequently included in this burden of disease analysis.

Table 2.1 Candidate, and selected, health outcomes to be assessed for the burden of disease related to ultraviolet radiation

Outcomes associated with UVR	Strong evidence of causality	Included in the Burden of Disease study
Immune effects		
Acute		
Suppression of cell-mediated immunity		
Increased susceptibility to infection		
Impairment of prophylactic immunization		
Activation of latent virus infection - herpes labialis	Activation of latent virus infection - herpes labialis	Activation of latent virus infection - herpes labialis
Chronic		
Activation of latent virus infection - papilloma virus		
Rheumatoid arthritis*		
Type 1 diabetes mellitus*		
Multiple sclerosis*		
Effects on the eyes		
Acute		
Acute photokeratitis and conjunctivitis	Acute photokeratitis and conjunctivitis	
Acute solar retinopathy	Acute solar retinopathy	
Chronic		
Climatic droplet keratopathy		
Pterygium	Pterygium	Pterygium
Pinguecula		
Squamous cell carcinoma of the cornea	Squamous cell carcinoma of the cornea	Squamous cell carcinoma of the cornea
Squamous cell carcinoma of the conjunctiva	Squamous cell carcinoma of the conjunctiva	Squamous cell carcinoma of the conjunctiva
Cataract	Cortical cataract	Cortical cataract
Ocular melanoma		
Macular degeneration		
Effects on the skin		
Acute		
Sunburn	Sunburn	Sunburn
Photodermatoses	Photodermatoses	
Chronic		
Cutaneous malignant melanoma	Cutaneous malignant melanoma	Cutaneous malignant melanoma
Cancer of the lip		
Basal cell carcinoma of the skin	Basal cell carcinoma of the skin	Basal cell carcinoma of the skin
Squamous cell carcinoma of the skin	Squamous cell carcinoma of the skin	Squamous cell carcinoma of the skin
Chronic sun damage/solar keratoses	Chronic sun damage/solar keratoses	Solar keratoses
Other direct effects		
Acute		
Medication reactions		
Chronic		
Vitamin D production* - rickets, osteomalacia, osteoporosis -tuberculosis	Vitamin D production - rickets, osteomalacia, osteoporosis	Vitamin D production - rickets, osteomalacia, osteoporosis
Non-Hodgkins lymphoma*		
Other cancers *- -Prostate -Breast -Colon		
Hypertension*		
Psychiatric disorders* -Seasonal affective disorder -Schizophrenia -General well-being		
Indirect effects		
Effect on climate, food supply, disease vectors, atmospheric chemistry		

* Possible beneficial effects of adequate UVR exposure

On further examination, although there is strong evidence of causality, the following diseases were excluded from the analysis because of lack of availability of data on incidence or prevalence:

Acute photokeratitis and photoconjunctivitis (snow blindness)
Acute solar retinopathy (eclipse blindness)

In addition, this assessment did not include disability due to the group of diseases known as the photodermatoses. These disorders are an idiosyncratic reaction to sunlight rather than diseases of excess or insufficient UVR exposure. Actinic prurigo, solar urticaria, photoallergic contact dermatitis and hydroa vacciniforme are rare disorders for which there are insufficient data for incidence or prevalence to include them in this analysis. Polymorphic light eruption is common, but data on the prevalence and clinical course are limited.

Although not included in this analysis, as evidence of causality is not yet persuasive, we believe that it is likely that other diseases may need to be considered in future analyses of burden of disease related to ultraviolet radiation. These include:

Diseases with increasing incidence where UVR exposure/vitamin D is inadequate:

Autoimmune diseases:
Multiple sclerosis
Type 1 diabetes
Rheumatoid arthritis

Cancers:
Prostate
Breast cancre
Colorectal cancer
Ovary cancer
Non-Hodgkin lymphoma

Psychiatric disorders:
Seasonal affective disorder
Mood disorders
Schizophrenia

Diseases with increasing incidence where UVR exposure is excessive

Acute macular degeneration
Posterior subcapsular cataract
Nuclear cataract
Ocular melanoma

2.2 Estimation of risk factor-disease relationships

Measurements of ambient UVR give an indication of "possible" UVR exposure of a population. However, the relationship between an outcome and the risk factor occurs at an individual level. As already indicated, understanding the population distribution of personal UVR exposure under a particular level of ambient UVR is not straightforward. In addition to difficulties in ascertaining accurate exposure data, for many diseases there is a long lag period between exposure to the risk factor and development of disease. And, for some diseases, such as cutaneous melanoma and basal cell carcinoma of the skin, it is likely that the relationship is not a simple dose-response relationship, but may involve thresholds of UVR exposure as well as critical life stages of exposure.

The epidemiological literature and international disease databases were searched to ascertain as much incidence and prevalence data as possible from diverse regions of the world, recording all data by geographical position of the study region and year of publication for studies from 1979 (when the first satellite data for UVR were available) to 2003.

Where possible, direct estimates of whole population incidence, prevalence and mortality were taken from published data (*29, 30*). Where this was not available, data from epidemiological studies on subpopulations were used. Studies were excluded where it was clear that the study population was very small or where incidence and prevalence estimates were from a non-population based sample – both situations where the sample may not be representative of the population as a whole, e.g measuring prevalence of ocular disease in an ophthalmology clinic, a clearly non-representative sample (*31*). For cataract and pterygium, preference was given to studies for which there were uniformly defined diagnostic criteria, such as the LOCS system of cataract classification. Some studies sought to prove a link to ultraviolet radiation by proving a link to another disease thought to be caused by UVR exposure, without a critical evaluation of the evidence for this second link, e.g. using the association between cataract and pinguecula to infer an association between cataract and UVR exposure (*32*). Such studies were not included in this evaluation.

In the absence of data on the population distribution of personal UVR exposure, annual ambient erythemally weighted UVR was used as the "exposure" to develop exposure-disease relationships for those diseases for which there are adequate global incidence data, i.e. the non-melanoma skin cancers. Spreadsheets were developed (Microsoft Excel) to record data on incidence, prevalence and mortality for the diseases under consideration, by sex and age group. Age group data were converted to WHO age groups[4] using DISMOD II[5]. Annual ambient erythemally weighted UVR for grids of one degree of latitude and 1.25 degrees of longitude was calculated for each year that a full year of data was available (*33*). For each study providing incidence data we therefore recorded age and sex-specific incidence (in WHO age groups) and annual ambient UVR for that study location and year (of publication).

Using these data, population-level exposure-response curves (annual ambient erythemal UVR vs. incidence rate) were constructed for each WHO age group, for lightly pigmented populations. Based on scanty literature comparing comparative disease rates by different levels of skin pigmentation (*34*), the exposure–response relationships were then adjusted for medium and deeply pigmented groups. These "dose-response" curves were then used to derive incidence rates for those areas for which no data were available.

Using ambient UVR as the exposure measure does not overcome the difficulties of not understanding the true population exposure experience (of individuals within the population). By using available data to extrapolate to data-poor regions, we are assuming that such regions have a similar pattern of personal UVR exposure, for a certain level of ambient UVR, as those regions for which there are data. Since most data come from fair-skinned populations in developed countries, such generalizations may not be warranted. Similarly, by using data accumulated over the past twenty five years (for the relation of ambient UVR to disease incidence), to provide estimates of current disease incidence, we implicitly assume that the relationship between ambient UVR and the population exposure history and distribution, has remained constant over time.

For other diseases in the assessment (sunburn, solar keratoses, reactivation of herpes labialis, pterygium and squamous cell carcinoma of the cornea and conjunctiva), for which global incidence/prevalence data are limited, "exposure" was approximated by the latitudinal

[4] WHO age groups: 0-4 years, 5-14 years, 15-29 years, 30-44 years, 45-59 years, 60-69 years, 70-79 years, 80+ years.

[5] DISMOD II is a program that estimates parameters of diseases that are unknown, by iteration, based on those data that are available (incidence, prevalence, remission rate, case fatality etc) for various age groups. It is available at http://www.who.int/evidence/bod.

position of the study, within ten-degree bands of latitude. Use of smaller units of UVR variation, while desirable, will depend on the availability of more extensive epidemiological data. While recognizing the inadequacies of latitude as a proxy for actual UVR exposure, it is used in an attempt to gain some initial understanding of the global burden of disease related to UVR exposure.

Incidence rates were recorded by age group, skin type and study location within ten-degree latitude bands. Data from northern and southern hemisphere ten-degree latitude bands were aggregated, as data were too sparse to consider these separately. (note that during summer, ambient UVR is 10-15% higher for equivalent latitudinal position (*12*) in the southern hemisphere due to elliptical orbit of the sun (and thus the sun and earth are closer during the southern summer than during the northern summer), ozone depletion and clearer skies. This difference is less marked in winter).

Available age and sex-specific incidence data were then used to extrapolate to data-poor regions within the same latitude band and to age groups for which there were no data, using Excel spreadsheets and graphs. For example, in one latitude band, data may be available for all age groups; in a second latitude band data may be available for only three age groups. Using the age group incidence pattern of the first band, missing cells were calculated in the second band. Similarly if data were available for all latitude bands in one age group, but only for three or four latitude bands for a second age group, incidence rates were calculated for missing cells using the latitudinal pattern of the first age group to extrapolate to the second age group. Using this technique it was possible to complete cells in the table, albeit with a high level of uncertainty.

In view of limited data on the population distribution of UVR exposure, we have derived ecological dose-response associations, with varying levels of precision, for the purpose of calculating disease risk in populations for which there are no available data.

2.3 Evaluation of population attributable fraction

In order to calculate the burden of disease due to a risk factor using a counterfactual risk assessment approach, we must know what proportion of each disease is attributable to the risk factor. We know that the incidence of most UVR-related diseases varies by latitude (and therefore ambient UVR), at least in white populations (although there is some evidence that this relationship is declining) (*35*). However, there are exceptions that may be explained on pigmentary characteristics of different populations (*36*). In fact, many of the countries in the areas of highest ambient UVR have deeply pigmented populations as their native inhabitants. In addition, many of these populations have adapted to the high ambient UVR with behavioural adaptations as well as pigmentary adaptations – not sunbathing, staying out of the sun in the middle of the day, covering up – and presumably as a result, have very low incidence rates of UVR-induced disease. It seems likely that the countries of highest risk of UVR-related disease are actually those with pale skinned inhabitants who have either relocated to areas of high ambient UVR or, with the advent of international travel and a degree of affluence, are able to holiday in areas of high ambient UVR.

In addition to incidence variation by latitude, we might suspect that the fraction of disease caused by UVR exposure (the population attributable fraction) may also vary by latitude e.g., risk factors for squamous cell carcinoma of the skin include UVR exposure and chronic irritation. In high ambient UVR locations, UVR may be relatively more important than chronic irritation, while the reverse may be true in situations of low UVR exposure. Again this is likely to be affected by the moderating effect of behaviour (including clothing and sunscreen usage) and skin pigmentation on actual exposure of susceptible tissues.

There is little consistency in the epidemiological literature on measures of sun exposure, making inter-study comparison difficult. Sun exposure measures vary from calculated accumulated hours of exposure over a lifetime (*37*), average annual UVB exposure (*38*), average daily global irradiance (*25*) to number of sunburns and/or number of holidays in a sunny environment. All of these are examined in the context of case-control studies with a long lag time from exposure to disease, so that accurate recall may be a problem. In addition, it seems likely that several of the UVR-related disorders have a complex relationship to UVR exposure that may not be directly 'more is worse'. Thus, both melanoma and basal cell carcinoma may be more related to the intermittency of high-dose exposure than high-dose exposure per se (*39*).

For each disease, a Microsoft Excel spreadsheet was developed to record data from case-control and ecological studies for each disease. The location of the study was recorded and latitude assigned using the Longman Atlas (*40*).

Population attributable fractions (PAFs) were calculated using the method of Bruzzi (*41*), i.e.

$$AR_C = 1 - \sum_j \frac{p_j}{\tilde{R}_j}$$

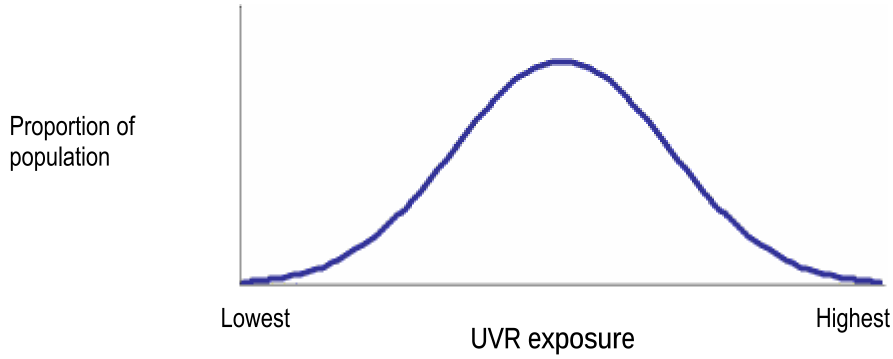
where AR_c is the attributable risk adjusted for confounding, p_j is the proportion of cases in the jth stratum of exposure, and R_j is the adjusted relative risk for the jth stratum of exposure compared to the unexposed group

Appendix 2 and Appendix 3 give details of the results of these calculations. PAF was graphed according to the latitude at which the study was undertaken and a PAF for each disease for each ten degree band of latitude was then derived from the line of best fit.

For those diseases for which there are both ecologic and case-control studies, there are very wide differences in calculated PAF. Thus for cutaneous malignant melanoma, Armstrong calculated a PAF of 0.96 for males and 0.92 for females by comparing the incidence of disease in US white populations with US black populations (*42*). The PAF calculated from case-control studies is however of the order of 0.2, with a small (non-significant) latitudinal gradient (independent of the exposure measure used in the study). In such cases, lower and upper estimates of the PAF were provided to take account of this variation.

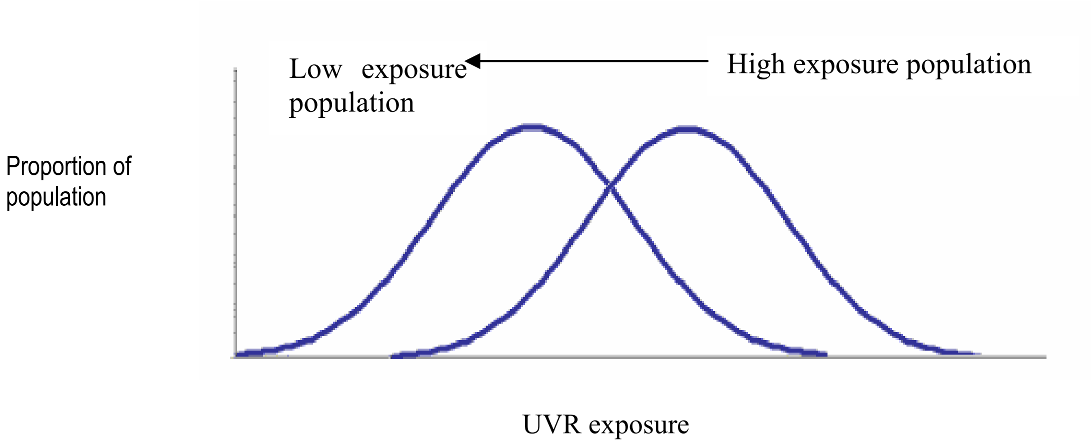
It is clear that PAFs calculated from different study types are estimating quite different parameters. The low PAFs, based on individual-level data and comparisons, are subject to substantial recall error, and this (as predominantly random misclassification of individual exposure) will generally cause an attenuation of the estimated relative risk. Further, that type of study does not compare exposed and unexposed groups (or even absolutely high and low groups) – rather, it compares individual level risks between relatively higher and lower exposure groups within a single population. For both reasons, the calculated PAF from case-controls studies does not truly capture the full attributable risk within the study population overall. Figure 2.2 represents the distribution of UVR exposure in a theoretical population. The PAF calculated from case control studies examines the risk of disease in those with highest UVR exposure, compared to those with lower UVR exposure, under this distribution of UVR exposure.

Figure 2.1 Distribution of UVR exposure in a theoretical population



On the other hand, the PAF calculated from ecologic studies compares the incidence of disease in quite different populations. It represents a distribution of exposure in one population that could be shifted to a lower level of exposure, on a population basis (see Figure 2.3).

Figure 2.2 Distribution of UVR exposure in two different (theoretical) populations



In summary, comparative risk assessment using counterfactual analysis uses the population attributable fraction (PAF), defined as "the proportional reduction in disease that would occur if exposure to the risk factor were reduced to zero" (*4*). PAF is based on relative risk, which provides an estimate of disease risk under a certain exposure distribution, compared to disease risk under a counterfactual exposure distribution – in case control studies this counterfactual is specific to the population under consideration and consists of "lesser exposure" (rather than no exposure, since in most populations everyone has some UVR exposure). In addition, "exposure" is difficult to measure with accuracy, being based on recall of events, often from many years earlier. Estimates of PAF from case control studies will thus be conservatively biased. In ecological studies, we can compare the disease incidence in populations having high ambient UVR (our current best measure of population UVR exposure) to disease incidence in populations with low exposure – either in low ambient locations (in which case the counterfactual is lower "exposure" and the calculated PAF will tend to be conservatively biased) or in deeply pigmented populations (in which case, the effective biological exposure may be very low, or zero). However even the latter may be conservatively biased, since paler populations tend to live in low sun exposure areas and more deeply pigmented populations in higher sun exposure areas.

We have presented the data using calculations of PAF from both ecologic and case control studies in an “upper estimates” and “lower estimates” form. It is likely that the true burden of disease attributable to UVR exposure lies somewhere between.

2.4 Development of disease models

Data on disease course, case fatality rates etc from varied parts of the world were recorded to enable construction of disease outcome models. (See Appendix 2 for details of the studies used for these data). Disease models were then refined in consultation with clinical experts.

Development of disease models recognizes that for every diagnosis of a disease there may be a continuing stream of disability over the remaining life course. Diagnosis may be followed by premature death after some period of morbidity, cure with no subsequent disease but initial morbidity, or initial cure, followed by relapse. Disability is calculated for each stage of the disease model.

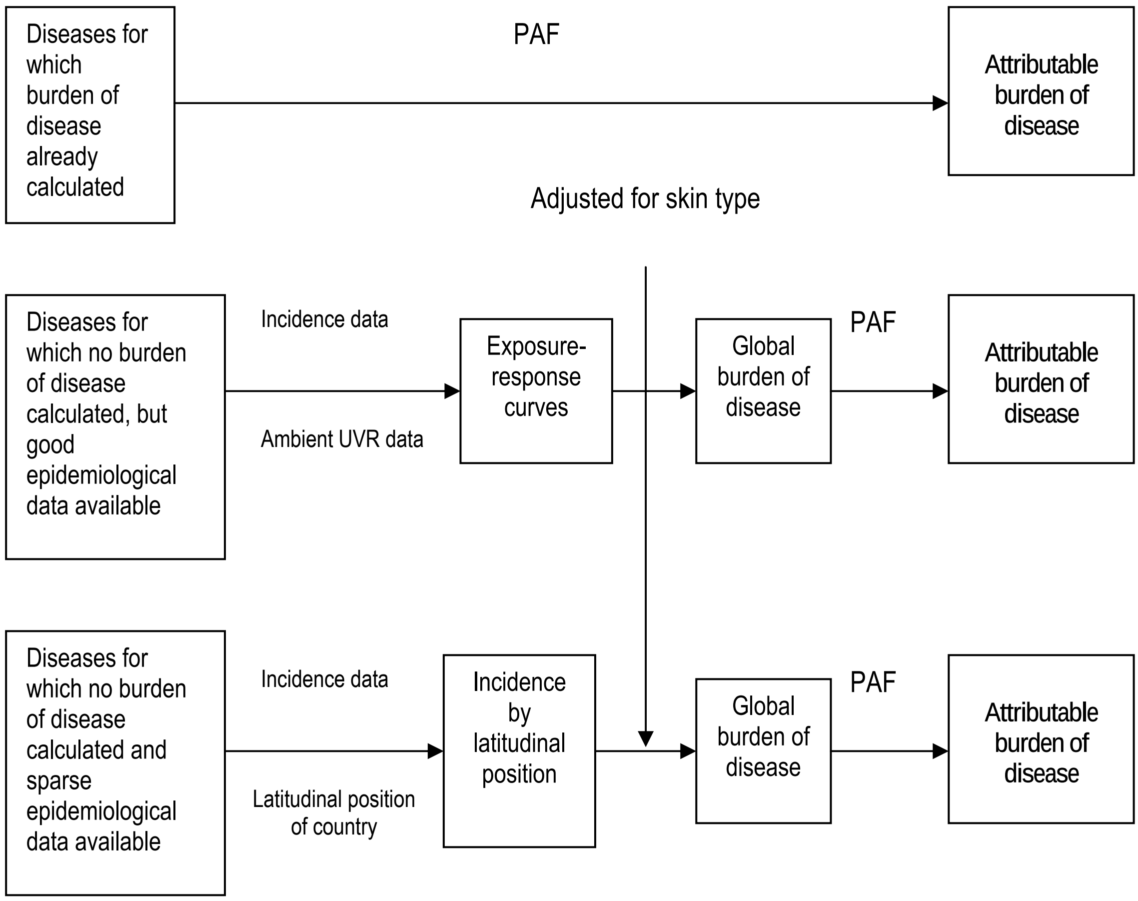
As disease outcome may vary with adequacy of available health services, separate disease models were developed for WHO ABC subregions and DE subregions (see Annex 4). The disease burden was estimated for the year 2000.

Disability weights were assigned according to the GBD 1990 study (*43*) in the first instance. Those not available from this study were taken from the Dutch study (*44*) or the Australian Burden of Disease Study (*45*). For those diseases for which no disability weight was available, we imputed a weight based on diseases or illnesses that we considered to have similar disability, as it was outside the scope of this study to carry out a thorough estimate for new disability weights.

3. Burden of Disease Assessment

The three different methodologies used to calculate the burden of disease are represented schematically in Figure 3.1.

Figure 3.1 Methods of calculating attributable burden



3.1 Diseases with pre-existing BOD analyses completed

The burden of disease from these diseases is available in the Global Burden of Disease statistics (available at www.who.int/evidence/bod). The calculated attributable fractions for UVR exposure were applied to these estimates.

3.2 Diseases where adequate epidemiological data are available

Exposure response curves were developed as outlined in Section 2.2 and disease models as outlined in Section 2.4.

Population-weighted annual averaged (1997-2003) ambient erythemally weighted UVR for each country was calculated. Using the exposure-incidence rate curves (Section 2.2), age, sex and country specific incidence rates were derived and applied to the population of each country to obtain estimates of the number of cases in each age and gender group in each country.

These case numbers were then summed to the WHO sub-region level. Incidence rate to mortality rate ratios were derived from the Australian Burden of Disease and Injury Study (*45*) and applied to the age and country-specific incidence rates to obtain mortality rates. These were applied to the country population (by age and gender group) to obtain estimates of number of deaths, which were then summed to the WHO sub-region level. Overall regional mortality rates were calculated from the total number of deaths for the region per year, divided by the total population (by age and gender).

3.3 Diseases with scanty global data

For each WHO region, countries were assigned to bands of ten degrees of latitude. For those countries that spanned several bands, a proportion of the population was assigned to each band by inspection of maps of population density (*46*). (See Appendix 4).

For each country, the population was separated into three pigment groups using available data on race and ethnicity by country (*47*). The proportions in each pigment group were assumed to hold for each age group and similar proportions were assumed to inhabit each different band of latitude for that country. (See Appendix 5).

For each latitude band, the population in each pigment group was summed to give, for each WHO sub-region, several bands of latitude, with a total population for each band, subdivided into three groups by pigmentation.

Using available data, incidence and mortality rates (or prevalence) were extrapolated to areas that were data-poor but with similar populations at similar latitudes (as outlined in Section 2.2).

Tables of disease incidence (or prevalence) and mortality for each age group, pigment group and gender, for each latitude band were constructed. See Appendix 6.
A detailed model of each disease and its sequelae was constructed, assigning disability weights and duration of disease stage, either from the literature or estimated from similar diseases or sequelae.

Using the incidence and mortality data from 3.2 and 3.3 above, the burden of disease in DALYs was calculated for each WHO region. Following this the calculated population attributable fraction was applied to the estimated disease burden to obtain upper and lower estimates of the burden of disease attributable to excess UVR exposure.

Note that in order to evaluate the burden of disease due to UVR exposure we have estimated the global incidence of diseases that are related to UVR exposure and used PAFs to estimate the proportion of that disease that is due to UVR exposure. This means that although we have defined the theoretical counterfactual exposure of least disease burden, this is not specifically used in this assessment due to the lack of global data on its distribution. Although the PAF is calculated from case-control studies, there are no data on how the exposure of the control groups compares to this theoretical counterfactual. Control groups are not unexposed, but may already represent populations that have higher exposure than the counterfactual, thus causing us to underestimate the true risk from the exposure in case groups.

4. Outcome assessment for diseases caused by excessive UVR exposure

4.1 Cutaneous malignant melanoma

Incidence

For cutaneous melanoma, global data are available on incidence and mortality. The global burden of disease estimates for the year 2000 (available at www.who.int/evidence/bod) used incidence and mortality estimates from Globocan 2000 (*29*) to calculate the burden of disease due to melanoma. The assessment of the burden of disease due to UVR from melanoma was derived in the current work by applying the calculated population attributable fraction estimates to these data.

Population attributable fraction

The fraction of disease in the population attributable to UVR exposure has been estimated at 96% in males and 92% in females in the USA, by comparison of white and black populations (*42*). Comparison of white populations in New South Wales, Australia, with ethnically similar populations in England and Wales gives a PAF of 89% (males) and 79% (females) (*42*).

Examination of ecological and individual-level studies indicates little relationship of PAF to latitude (see Appendix 3). There is also little relationship between PAFs estimated from ecologic studies and those estimated from case-control studies. As discussed in section 2.3 above, this presumably reflects both a difficulty with measuring exposure and the difficulty in finding a truly non-exposed population as the control group in epidemiological studies.

We therefore did not apply a PAF which varies with latitude, but used constant PAFs for upper and lower estimates of the burden of disease from CMM, that is caused by UVR.

Estimation of disease burden

There is generally an increase in incidence of melanoma with decreasing latitude. This has been shown within the Nordic countries, the USA and Australia. However, this relationship does not persist across non-homogeneous populations – mortality from melanoma is four to six times higher in Nordic countries than in the Mediterranean countries (*48*) and there is an opposite relationship of melanoma incidence to latitude in Italy (*36*). Since melanoma is likely to be related to intermittent high intensity sun exposure, particularly in fair-skinned individuals, those at greatest risk are likely to be fair skinned people from higher latitudes who intermittently are exposed to high intensity UVR on holidays (*49*).

Langford used multilevel modeling to examine the relationship between melanoma mortality and UVB exposure in several countries (*50*). He found that the United Kingdom, Ireland, Belgium and the Netherlands generally showed a positive relationship, whereas France showed very little relationship, Italy showed a negative relationship. Germany and Denmark, while having higher rates of melanoma mortality, did not show a positive relationship of UVB exposure with mortality.

Few studies have been done in dark-skinned populations and these have been mainly descriptive. In these populations, the incidence of melanoma is very low and the behaviour of the disease is quite different – melanoma occurs at a later age and affects the plantar and palmar surfaces of the feet and hands. This is unlikely to be due to UVR exposure (lack of exposure to this site) and may represent a baseline of incidence of cutaneous melanoma.

WHO has estimated the burden of disease for the year 2000 (*51*, *52*) from cutaneous malignant melanoma using incidence and mortality data derived from Globocan 2000 (*29*). As noted in Appendix 3, case control studies indicate that the population attributable fraction is approximately 0.2. However, it seems likely that there is a great deal of error inherent in the exposure measurement in these individual-level epidemiological studies that may systematically bias the effect estimate towards the null. Thus, upper (0.9, derived from ecological data) and lower (0.5, based on a consensus of expert opinion) estimates for population attributable fraction were applied to the WHO melanoma GBD estimates (see Appendix 3 for full explanation).

The global incidence and mortality from cutaneous malignant melanoma are summarized in Tables 4.1 and 4.2. The global burden of disease as estimated by WHO is summarized in Table 4.3. The attributable burden of disease was obtained by multiplying the PAF with the burden of disease in each age group and WHO subregion. The disease burden attributable to UVR exposure in the year 2000 is summarized in Tables 4.4 (upper estimates) and 4.5 (lower estimates).

Table 4.1 Incident cases of Malignant Melanoma 2000 by 17 WHO subregions (see Appendix 4)

MALE

AGE	RO1	RO2	RO3	RO4	RO5	RO6	RO7	RO8	RO9	RO10	RO11	RO12	RO13	RO14	RO15	RO16	RO17	Total
0-4	18	32	21	0	4	0	1	6	0	0	3	14	44	0	0	1	0	144
5-14	13	12	0	25	57	1	4	60	1	1	0	5	95	0	1	2	1	277
15-29	177	410	1 492	201	32	19	28	668	100	14	153	42	131	139	80	8	4	3 696
30-44	300	600	9 507	920	82	32	50	3 197	515	26	787	91	191	663	173	12	8	17 155
45-59	1 045	1 057	18 376	1 307	235	117	44	5 884	891	72	1 277	330	402	1 709	909	33	28	33 715
60-69	942	771	13 054	1 189	194	84	33	5 179	755	94	1 075	439	583	1 509	778	33	20	26 733
70-79	778	504	15 606	1 235	196	63	20	5 727	726	86	757	241	489	1 883	520	33	13	28 876
80+	305	222	6 609	668	165	20	6	2 811	314	16	212	82	204	1 001	146	22	7	12 812
Total	3 577	3 608	64 665	5 546	963	336	185	23 533	3 303	309	4 264	1 244	2 139	6 904	2 606	143	82	123 408

FEMALE

AGE	RO1	RO2	RO3	RO4	RO5	RO6	RO7	RO8	RO9	RO10	RO11	RO12	RO13	RO14	RO15	RO16	RO17	Total
0-4	7	1	0	6	0	0	0	7	3	0	0	0	24	0	4	1	0	55
5-14	7	2	32	23	16	2	3	12	10	1	5	0	81	21	23	4	1	245
15-29	130	218	1 149	368	54	48	42	1 282	169	31	364	75	88	278	114	10	4	4 423
30-44	210	363	5 574	1 088	136	86	73	4 096	587	28	1 267	268	121	872	424	27	13	15 233
45-59	591	597	7 693	1 343	211	72	93	6 348	805	54	1 353	493	464	1 103	675	20	33	21 950
60-69	1 024	1 198	5 202	981	185	84	43	4 452	634	71	1 311	472	442	786	425	20	8	17 337
70-79	969	1 413	4 736	878	163	52	40	5 206	694	55	1 048	399	286	839	353	6	4	17 140
80+	321	473	2 157	973	181	17	9	5 134	576	53	588	166	164	1 116	194	5	2	12 131
Total	3 258	4 266	26 542	5 660	946	362	304	26 537	3 477	294	5 937	1 873	1 671	5 016	2 214	93	66	88 514

BOTH SEXES

AGE	RO1	RO2	RO3	RO4	RO5	RO6	RO7	RO8	RO9	RO10	RO11	RO12	RO13	RO14	RO15	RO16	RO17	Total
0-4	25	34	21	6	4	1	2	13	3	0	3	14	68	0	4	2	0	199
5-14	20	14	32	48	73	3	7	72	11	2	5	5	176	21	24	6	2	521
15-29	306	628	2 641	569	86	66	70	1 950	269	45	517	117	219	418	193	17	7	8 119
30-44	510	963	15 080	2 008	218	119	122	7 293	1 102	54	2 054	359	313	1 535	597	39	22	32 387
45-59	1 636	1 654	26 069	2 650	446	189	137	12 232	1 696	125	2 630	823	867	2 812	1 584	53	62	55 665
60-69	1 966	1 969	18 256	2 170	379	168	76	9 632	1 390	165	2 386	911	1 025	2 295	1 203	53	28	44 070
70-79	1 746	1 917	20 342	2 113	358	115	59	10 932	1 420	141	1 805	640	775	2 722	874	39	17	46 017
80+	626	695	8 767	1 641	346	37	15	7946	889	70	801	248	369	2 118	340	27	10	24 943
Total	6 835	7 874	91 207	11 206	1 909	698	489	50 070	6 780	603	10 200	3 117	3 810	11 919	4 820	236	147	211 921

Table 4.2 Mortality from Malignant Melanoma 2000 (0.1% of total global mortality) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	7	12	1	3	2	0	1	1	0	0	1	18	2	0	48
5-14	4	4	1	16	3	0	1	2	3	4	0	34	0	0	74
15-29	48	185	105	84	8	24	43	121	64	39	3	87	17	27	853
30-44	88	300	745	293	13	61	79	716	222	386	8	132	102	98	3 244
45-59	327	599	1 947	704	46	55	270	1 661	477	1 093	85	384	320	378	8 344
60-69	458	575	1 715	610	46	117	215	1 660	497	1 060	177	187	351	397	8 066
70-79	573	399	2 014	590	67	149	31	2 102	464	1 007	105	268	454	283	8 508
80+	304	229	1 730	429	48	48	16	1 716	307	435	51	183	409	129	6 035
TOTAL	1 810	2 303	8 258	2 729	232	455	656	7 980	2 034	4 023	429	1 294	1 655	1 313	35 171

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	6	1	2	9	0	0	6	0	7	2	0	4	0	2	39
5-14	3	1	2	3	0	1	16	1	4	0	0	11	2	8	51
15-29	20	66	56	60	7	69	49	100	28	72	17	48	20	33	646
30-44	52	163	385	233	20	11	81	505	180	418	62	77	76	129	2 391
45-59	222	314	831	364	48	45	124	1 126	352	900	123	251	160	225	5 085
60-69	669	800	728	368	56	35	148	1 072	328	924	129	212	142	196	5 809
70-79	864	1 298	1 031	506	74	100	94	1 710	537	1 202	226	122	237	195	8 199
80+	317	469	1 405	497	58	11	36	2 598	592	976	100	69	483	158	7 770
TOTAL	2 152	3 113	4 441	2 040	263	273	555	7 112	2 027	4 495	658	794	1120	947	29 990

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	13	13	3	12	2	0	7	1	7	2	1	22	2	2	87
5-14	7	5	3	19	3	1	17	3	7	4	0	45	2	8	125
15-29	68	251	161	144	15	93	92	221	92	111	20	135	37	60	1 499
30-44	140	463	1 130	526	33	72	160	1 221	402	804	70	209	178	227	5 635
45-59	349	913	2 778	1 068	94	100	394	2 787	829	1 993	208	635	480	603	13 429
60-69	1 127	1 375	2 443	978	102	152	363	2 732	825	1 984	306	399	493	593	13 875
70-79	1 437	1 697	3 045	1 096	141	249	125	3 812	1 001	2 209	331	390	691	478	16 707
80+	621	698	3 135	926	106	59	52	4 314	899	1 411	151	252	892	287	13 805
TOTAL	3 962	5 416	12 699	4 769	495	727	1211	15 092	4 061	8 517	1 087	2 089	2 775	2 260	65 161

Table 4.3 Disease burden due to malignant melanoma in DALYs (000) by 14 WHO subregions (see Annex 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.241	0.425	0.031	0.103	0.059	0.005	0.031	0.044	0.000	0.000	0.021	0.625	0.083	0.003	1.672
5-14	0.164	0.150	0.040	0.614	0.135	0.005	0.049	0.083	0.122	0.141	0.014	1.306	0.000	0.015	2.839
15-29	1.625	6.200	3.658	2.805	0.273	0.830	1.416	4.219	2.157	1.293	0.105	2.975	0.622	0.901	29.077
30-44	2.249	7.697	19.531	7.230	0.300	1.568	1.972	18.658	5.581	9.362	0.215	3.290	2.830	2.434	82.916
45-59	5.129	9.329	32.651	11.123	0.707	0.867	4.114	27.022	7.874	17.962	1.205	6.184	5.487	5.881	135.536
60-69	4.079	5.360	16.767	5.629	0.427	1.095	2.060	16.018	4.578	10.007	1.665	1.675	3.565	3.709	76.633
70-79	2.854	1.987	10.997	3.048	0.342	0.736	0.177	11.370	2.398	5.372	0.534	1.331	2.658	1.433	45.235
80+	0.721	0.548	3.829	0.920	0.108	0.089	0.041	3.652	0.632	0.874	0.117	0.412	0.986	0.306	13.235
TOTAL	17.062	31.696	87.505	31.471	2.350	5.195	9.859	81.067	23.341	45.011	3.876	17.798	16.230	14.681	387.144

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.217	0.039	0.080	0.323	0.000	0.006	0.208	0.000	0.255	0.055	0.000	0.146	0.000	0.057	1.386
5-14	0.106	0.034	0.075	0.116	0.000	0.029	0.590	0.040	0.141	0.000	0.001	0.442	0.092	0.308	1.974
15-29	0.709	2.294	2.158	2.082	0.236	2.375	1.690	3.804	0.959	2.496	0.587	1.682	0.839	1.151	23.064
30-44	1.351	4.180	10.977	5.907	0.491	0.274	2.041	13.954	4.580	10.586	1.586	1.991	2.318	3.295	63.533
45-59	3.610	5.151	15.257	6.233	0.803	0.842	2.070	19.808	6.029	15.228	2.086	4.158	3.032	3.788	88.094
60-69	6.502	7.674	7.847	3.680	0.542	0.382	1.521	11.453	3.283	9.469	1.267	2.146	1.598	1.985	59.349
70-79	4.975	7.447	6.213	2.844	0.430	0.565	0.559	10.264	3.003	6.977	1.294	0.701	1.495	1.127	47.895
80+	0.830	1.241	3.136	1.098	0.142	0.031	0.093	5.731	1.355	2.212	0.253	0.172	1.110	0.405	17.810
TOTAL	18.301	28.061	45.742	22.285	2.644	4.505	8.772	65.052	19.606	47.024	7.075	11.438	10.484	12.117	303.104

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.458	0.464	0.111	0.426	0.059	0.011	0.239	0.044	0.255	0.055	0.021	0.771	0.083	0.060	3.058
5-14	0.270	0.184	0.115	0.730	0.135	0.034	0.639	0.123	0.263	0.141	0.015	1.748	0.092	0.323	4.812
15-29	2.333	8.495	5.815	4.887	0.509	3.205	3.106	8.023	3.116	3.789	0.693	4.657	1.460	2.052	52.141
30-44	3.600	11.877	30.508	13.137	0.791	1.842	4.013	32.612	10.161	19.948	1.801	5.280	5.148	5.729	146.449
45-59	8.739	14.480	47.908	17.357	1.509	1.710	6.184	46.830	13.902	33.190	3.291	10.342	8.519	9.669	223.630
60-69	10.581	13.034	24.614	9.310	0.968	1.477	3.580	27.471	7.861	19.476	2.932	3.821	5.163	5.694	135.982
70-79	7.830	9.434	17.210	5.892	0.772	1.301	0.736	21.633	5.401	12.350	1.828	2.032	4.153	2.560	93.130
80+	1.551	1.790	6.965	2.018	0.250	0.120	0.134	9.383	1.988	3.086	0.370	0.584	2.095	0.710	31.045
TOTAL	35.363	59.757	133.247	53.756	4.994	9.700	18.631	146.120	42.948	92.034	10.950	29.237	26.715	26.797	690.248

Table 4.4 Disease burden from malignant melanoma attributable to ultraviolet radiation DALYs (000) – upper estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.217	0.383	0.028	0.092	0.053	0.004	0.028	0.040	0.000	0.000	0.019	0.563	0.075	0.003	1.505
5-14	0.147	0.135	0.036	0.553	0.121	0.004	0.044	0.075	0.110	0.127	0.012	1.176	0.000	0.013	2.555
15-29	1.462	5.580	3.292	2.524	0.245	0.747	1.274	3.797	1.941	1.164	0.095	2.677	0.560	0.811	26.170
30-44	2.024	6.927	17.578	6.507	0.270	1.411	1.774	16.792	5.023	8.426	0.194	2.961	2.547	2.190	74.625
45-59	4.616	8.396	29.386	10.011	0.636	0.781	3.703	24.320	7.086	16.166	1.085	5.566	4.938	5.293	121.982
60-69	3.671	4.824	15.090	5.066	0.384	0.985	1.854	14.416	4.120	9.006	1.498	1.508	3.208	3.338	68.970
70-79	2.569	1.788	9.897	2.743	0.308	0.662	0.159	10.233	2.158	4.835	0.480	1.198	2.392	1.289	40.712
80+	0.649	0.493	3.446	0.828	0.097	0.080	0.037	3.287	0.569	0.786	0.106	0.371	0.887	0.275	11.912
TOTAL	15.356	28.527	78.755	28.324	2.115	4.675	8.873	72.961	21.007	40.510	3.488	16.019	14.607	13.212	348.429

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.195	0.035	0.072	0.291	0.000	0.006	0.187	0.000	0.229	0.049	0.000	0.131	0.000	0.051	1.248
5-14	0.096	0.030	0.067	0.105	0.000	0.026	0.531	0.036	0.127	0.000	0.001	0.398	0.083	0.278	1.776
15-29	0.638	2.065	1.942	1.874	0.212	2.138	1.521	3.424	0.863	2.247	0.529	1.514	0.755	1.036	20.757
30-44	1.216	3.762	9.879	5.317	0.442	0.247	1.837	12.558	4.122	9.527	1.427	1.792	2.086	2.966	57.179
45-59	3.249	4.636	13.731	5.610	0.722	0.758	1.863	17.827	5.426	13.705	1.878	3.742	2.729	3.410	79.285
60-69	5.852	6.907	7.062	3.312	0.487	0.344	1.369	10.307	2.955	8.522	1.141	1.932	1.438	1.786	53.414
70-79	4.478	6.702	5.591	2.560	0.387	0.509	0.503	9.237	2.703	6.280	1.165	0.631	1.346	1.015	43.106
80+	0.747	1.117	2.823	0.988	0.128	0.027	0.084	5.158	1.220	1.991	0.228	0.155	0.999	0.364	16.029
TOTAL	16.471	25.255	41.168	20.056	2.379	4.054	7.895	58.547	17.645	42.321	6.367	10.294	9.436	10.905	272.794

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.412	0.418	0.100	0.383	0.053	0.010	0.215	0.040	0.229	0.049	0.019	0.694	0.075	0.054	2.752
5-14	0.243	0.165	0.104	0.657	0.121	0.031	0.575	0.111	0.237	0.127	0.013	1.573	0.083	0.291	4.331
15-29	2.100	7.645	5.234	4.398	0.458	2.885	2.795	7.221	2.805	3.410	0.623	4.191	1.314	1.846	46.927
30-44	3.240	10.690	27.457	11.823	0.712	1.658	3.612	29.351	9.145	17.953	1.621	4.752	4.633	5.156	131.804
45-59	7.865	13.032	43.117	15.621	1.358	1.539	5.565	42.147	12.512	29.871	2.962	9.308	7.667	8.702	201.267
60-69	9.523	11.731	22.152	8.379	0.871	1.329	3.222	24.724	7.075	17.528	2.639	3.439	4.647	5.125	122.384
70-79	7.047	8.490	15.489	5.303	0.695	1.171	0.662	19.470	4.861	11.115	1.645	1.829	3.738	2.304	83.817
80+	1.396	1.611	6.269	1.816	0.225	0.108	0.120	8.445	1.789	2.777	0.333	0.525	1.886	0.639	27.940
TOTAL	31.826	53.782	119.922	48.381	4.495	8.730	16.768	131.508	38.653	82.831	9.855	26.313	24.043	24.117	621.223

Table 4.5 Disease burden from malignant melanoma attributable to ultraviolet radiation DALYs (000) – lower estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.120	0.213	0.016	0.051	0.030	0.002	0.016	0.022	0.000	0.000	0.010	0.313	0.042	0.002	0.836
5-14	0.082	0.075	0.020	0.307	0.067	0.002	0.025	0.042	0.061	0.070	0.007	0.653	0.000	0.007	1.419
15-29	0.812	3.100	1.829	1.402	0.136	0.415	0.708	2.110	1.078	0.646	0.053	1.487	0.311	0.450	14.539
30-44	1.125	3.848	9.766	3.615	0.150	0.784	0.986	9.329	2.790	4.681	0.108	1.645	1.415	1.217	41.458
45-59	2.565	4.664	16.326	5.562	0.353	0.434	2.057	13.511	3.937	8.981	0.603	3.092	2.743	2.940	67.768
60-69	2.039	2.680	8.383	2.815	0.213	0.547	1.030	8.009	2.289	5.003	0.832	0.838	1.782	1.855	38.317
70-79	1.427	0.993	5.499	1.524	0.171	0.368	0.088	5.685	1.199	2.686	0.267	0.666	1.329	0.716	22.618
80+	0.361	0.274	1.915	0.460	0.054	0.045	0.020	1.826	0.316	0.437	0.059	0.206	0.493	0.153	6.618
TOTAL	8.531	15.848	43.753	15.736	1.175	2.597	4.930	40.534	11.671	22.505	1.938	8.899	8.115	7.340	193.572

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.108	0.020	0.040	0.162	0.000	0.003	0.104	0.000	0.127	0.027	0.000	0.073	0.000	0.028	0.693
5-14	0.053	0.017	0.037	0.058	0.000	0.014	0.295	0.020	0.071	0.000	0.000	0.221	0.046	0.154	0.987
15-29	0.354	1.147	1.079	1.041	0.118	1.188	0.845	1.902	0.480	1.248	0.294	0.841	0.419	0.575	11.532
30-44	0.675	2.090	5.489	2.954	0.246	0.137	1.021	6.977	2.290	5.293	0.793	0.995	1.159	1.648	31.766
45-59	1.805	2.576	7.628	3.117	0.401	0.421	1.035	9.904	3.014	7.614	1.043	2.079	1.516	1.894	44.047
60-69	3.251	3.837	3.923	1.840	0.271	0.191	0.760	5.726	1.641	4.735	0.634	1.073	0.799	0.992	29.675
70-79	2.488	3.723	3.106	1.422	0.215	0.283	0.280	5.132	1.502	3.489	0.647	0.350	0.748	0.564	23.948
80+	0.415	0.621	1.568	0.549	0.071	0.015	0.046	2.866	0.678	1.106	0.126	0.086	0.555	0.202	8.905
TOTAL	9.150	14.031	22.871	11.142	1.322	2.252	4.386	32.526	9.803	23.512	3.537	5.719	5.242	6.058	151.552

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.229	0.232	0.055	0.213	0.030	0.005	0.120	0.022	0.127	0.027	0.010	0.386	0.042	0.030	1.529
5-14	0.135	0.092	0.058	0.365	0.067	0.017	0.320	0.062	0.132	0.070	0.007	0.874	0.046	0.162	2.406
15-29	1.167	4.247	2.908	2.444	0.254	1.603	1.553	4.012	1.558	1.895	0.346	2.329	0.730	1.026	26.070
30-44	1.800	5.939	15.254	6.568	0.396	0.921	2.006	16.306	5.080	9.974	0.901	2.640	2.574	2.865	73.224
45-59	4.370	7.240	23.954	8.678	0.755	0.855	3.092	23.415	6.951	16.595	1.646	5.171	4.260	4.835	111.815
60-69	5.291	6.517	12.307	4.655	0.484	0.738	1.790	13.735	3.930	9.738	1.466	1.911	2.581	2.847	67.991
70-79	3.915	4.717	8.605	2.946	0.386	0.650	0.368	10.817	2.700	6.175	0.914	1.016	2.077	1.280	46.565
80+	0.776	0.895	3.483	1.009	0.125	0.060	0.067	4.692	0.994	1.543	0.185	0.292	1.048	0.355	15.522
TOTAL	17.681	29.879	66.623	26.878	2.497	4.850	9.316	73.060	21.474	46.017	5.475	14.618	13.357	13.399	345.124

4.2 Squamous cell carcinoma

Disease incidence

We reviewed epidemiologic studies examining the incidence, and mortality of squamous cell carcinoma of the skin (SCC). While incidence varies with latitude (decreasing incidence with increasing latitude) and is increasing over time (*53*), there are great difficulties in obtaining comprehensive global data on current incidence rates.

Few cancer registries record incidence of non-melanoma skin cancers and those that do rely on notification, with or without histological proof, of the diagnosis of SCC. A number of SCC may be misclassified as solar keratoses, and many may be removed in a way that destroys tissue, making histological confirmation impossible. It is likely that there is considerable underreporting of SCC and we are reliant on those studies that have prospectively surveyed a random sample of the population with dermatological examination, and then repeated this at a later time.

The disadvantage of such studies is that unless the sample size or the incidence is great, the number of incident cases may be small, giving an unreliable estimate (*54*). In addition, most studies are carried out on predominantly white populations, so that the incidence and risk factors for SCC in black populations are even less clear.

The incidence of SCC is rising by 3-7% per year in most countries, so that deriving incidence data from studies undertaken at different times does not give comparable results that can be used as an incidence rate in 2000. To take account of this, incidence data from epidemiological studies were recorded by age group, study year and study location. All age group data were converted to the standard age groups used in burden of disease analysis, using DISMOD II. Latitude and longitude coordinates for each study location were assigned according to the Longman Atlas (*40*). Annual erythemally weighted UVR data were derived from monthly estimates for the year of the study. Thus for each study location age-specific incidence and annual ambient UVR data were available. These data formed the basis of “dose-response” plots for each gender within each age group. Subsequent incidence rate data were derived from the averaged annual ambient UVR (1997-2003) for each country, weighted by population distribution, and applied to the population estimates (by age and gender) for 2000 (*46*).

Incidence rates for those of intermediate and deeply pigmented skins were calculated by applying a multiplier to the rates for lightly-pigmented populations, based on studies that compared rates in different groups (*34, 55*), i.e. 0.1 for intermediate pigmentation, 0.018 for deeply pigmented populations. These rates were then generalized to populations with no data, on the basis of annual ambient UVR levels and skin pigmentation distribution. Note that Hoy (*34*) found a gender difference in the comparison of incidence rates in Hispanic and non-Hispanic whites, i.e. for age standardized incidence rates, Hispanic males had one-tenth the incidence rate for non-Hispanic males, whereas for females the incidence rate in Hispanic women was 0.4 times that of non-Hispanic women. In this study non-Hispanic women had very low rates of SCC compared to those in white populations in other epidemiological studies and this may have a behavioural explanation peculiar to this population. For this reason, the comparative rate for males was used to adjust the incidence rate for lightly pigmented populations to an incidence rate for populations of intermediate pigmentation for both genders.

In deeply pigmented populations, SCC seems to arise in areas of chronic inflammation and scarring, e.g. sites of tropical ulcers. While this has been interpreted as possibly due to the effects of UVR exposure on the depigmented scar tissue (*56*), it also may be unrelated to UVR exposure as many SCC occur on non-sun-exposed sites (*13*). There does appear to be a latitudinal gradient in the incidence of SCC in deeply pigmented persons (*57*) and SCC, while uncommon, is more common than BCC.

Population attributable fraction

The population attributable fraction was estimated from case-control studies using the methods described in section 2.3 (see Appendix 3). PAF was graphed by latitude. While the trendline is suggestive of a latitudinal gradient in PAF, this is not significant ($p = 0.55$). The PAF applied to the burden of disease estimates was constant across all latitudes.

The mean PAF from case-controls studies was 0.35, intercept (extrapolated) is 0.5 and there is no significant latitudinal gradient. As case-control studies tend to give low PAF because of difficulties in measuring exposure and in defining a non-exposed population we assumed a lower estimate of PAF of 0.5 and an upper estimate of 0.7 in lightly pigmented groups, based on the extensive epidemiological experience of members of this working group. We could find no studies examining the PAF in intermediate and deeply pigmented populations, however it is likely that UVR is considerably less important in the causation of SCC in these populations. Based on limited epidemiological data (see Appendix 3), we have assigned a PAF for intermediate pigmented populations that is one-fifth that of white populations, and for deeply pigmented populations, a PAF one-fifth of that of the intermediate populations.

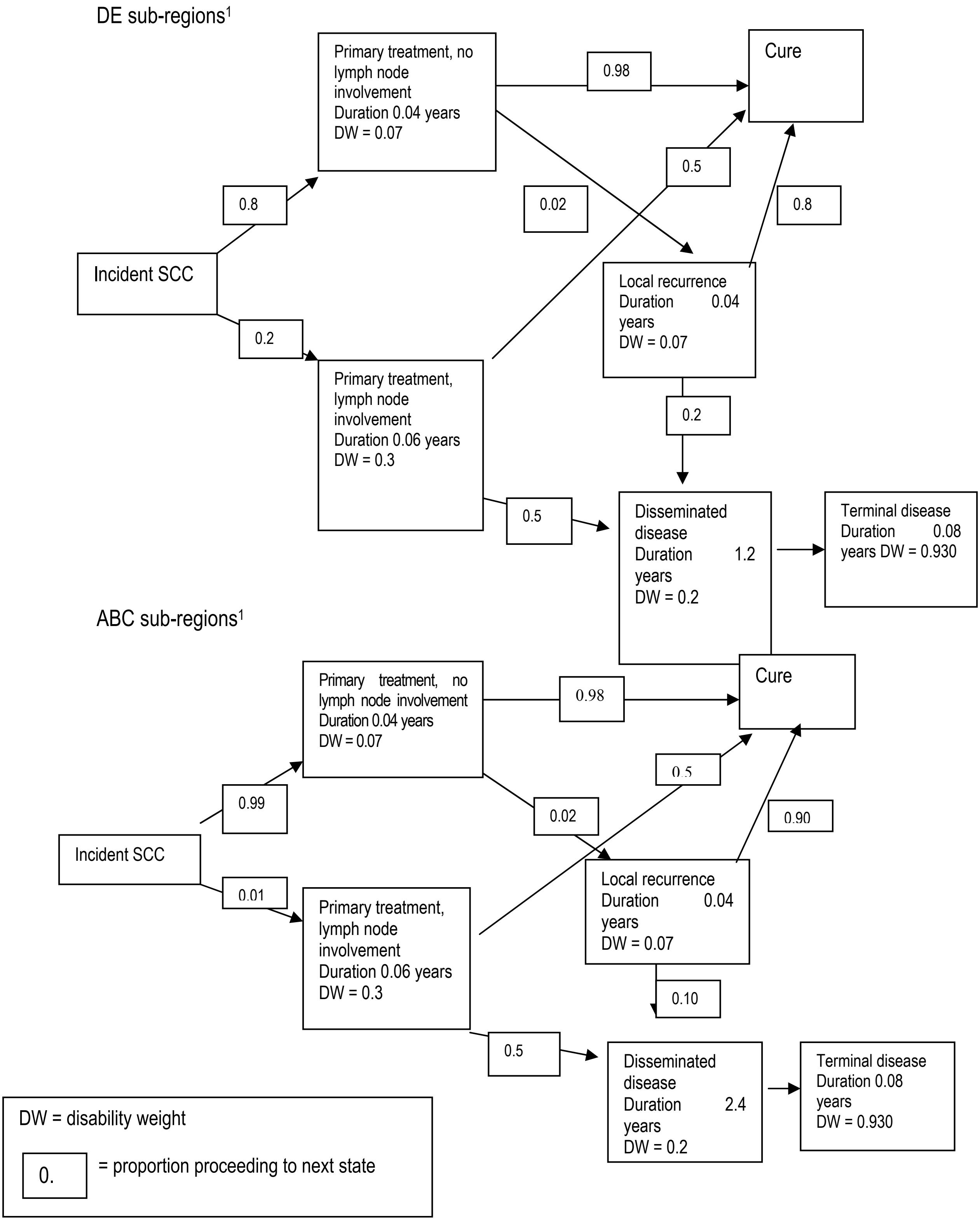
Disease model

Mortality rates were estimated by investigating the relationship between incidence and mortality rates in the Australian setting, for non-melanoma skin cancer (NMSC) (*45*). Weinstock notes that SCC is twelve times more likely to lead to death than BCC (*55*). Using these proportions, the mortality rate for NMSC was split into a rate for SCC and a rate for BCC. This incidence/mortality rate ratio was then applied to the incidence rate estimates for different age groups to define the mortality rate (see Appendix 3). Black populations, even in developed countries have much higher mortality rates from SCC – the disease presents later and tends to be more aggressive. In the series examined by Mora, there was an overall death rate of 18.4% (*58*). Marks (*59*) cites a case fatality rate in lightly pigmented populations, of 7/1000. The mortality to incidence rate ratio in black populations was assumed to be ten times that in white populations, with population groups with intermediate pigmentation having rate ratios between lightly and deeply pigmented populations (i.e. five times that of lightly pigmented populations). Few data are available for mortality rates in DE countries. While mortality rates are likely to be higher in DE countries than in ABC countries, no further adjustments were made to the mortality rates.

Figure 4.1 outlines the flow chart of the disease course for SCC. A, B, C and D,E countries were analyzed separately to take account of differences in stage of presentation and subsequent disease course due to variation in access to health care.

Incidence and mortality for SCC are summarized in Table 4.6 and Table 4.7 respectively. The burden of disease due to SCC in the year 2000 is summarized in Table 4.8 and the upper and lower estimates of disease burden due to SCC are summarized in Tables 4.9 and 4.10.

Figure 4.1 Disease model for SCC



[1]NB: See Annex 4 for definition of sub-regions

Table 4.6 Incident cases of SCC
by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	5	7	46	78	7	73	51	44	47	29	15	55	21	315	793
15-29	16	24	166	349	29	274	179	163	176	91	79	228	102	1 224	3 099
30-44	485	766	3 757	12 172	1 212	7 227	5 830	2 617	2 585	945	3 484	7 337	1 901	26 281	76 599
45-59	1981	3 092	30 641	57 450	5 050	33 637	21 715	27 052	16 095	10 461	14 507	34 823	20 924	164 562	441 990
60-69	2 129	3 038	37 760	63 063	5 706	33 642	23 436	46 550	23 613	17 888	16 721	39 824	32 224	201 972	547 567
70-79	1 829	2 420	56 028	64 320	5 221	32 754	19 116	66 691	25 335	19 611	15 034	35 805	41 085	197548	582 798
80+	291	314	28 590	13 716	844	6 632	2 991	35 846	7 236	7 016	2 387	6 460	17 931	46 679	176 932
TOTAL	6 737	9 661	156 987	211 147	18 069	114 239	73 318	178 963	75 087	56 041	52 228	124 532	114 188	638 580	1 829 777

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	1	2	13	19	2	19	13	14	15	10	4	13	6	83	213
15-29	12	18	121	257	21	196	125	117	134	67	57	156	74	868	2 225
30-44	363	569	5 742	10 165	749	5 646	3 985	4 484	4 010	1 938	2 386	5 639	2 967	35 668	84 312
45-59	1 280	1 992	15 023	36 138	3 410	15 127	14 417	12 000	8 648	4 842	9 472	19 461	9 923	76 573	228 306
60-69	1092	1 648	15 856	31 695	2 866	13 481	11 507	18 663	11 677	8 741	8 569	18 059	13 034	76 837	233 724
70-79	790	1 203	26 444	29 656	2 150	11 912	7 721	34 405	14 877	15 644	6 384	13 982	19 566	84 703	269 438
80+	414	707	37 264	22 427	1 466	7 080	3 830	42 057	9 483	12 487	4 017	8 200	23 684	61 925	235 042
TOTAL	3 953	6 140	100 464	130 357	10 663	53 461	41 597	111 739	48 844	43 730	30 890	65 511	69 254	336 657	1 053 260

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	6	8	60	97	8	92	64	58	62	39	19	68	27	398	1 006
15-29	28	42	287	606	49	470	304	280	310	158	136	384	176	2 092	5 324
30-44	848	1 335	9 499	22 337	1 961	12 873	9 815	7 102	6 595	2 883	5 870	12 976	4 869	61 948	160 911
45-59	3 261	5 085	45 663	93 588	8 460	48 763	36 133	39 052	24 743	15 303	23 979	54 284	30 847	241 135	670 296
60-69	3 221	4 686	53 616	94 758	8 572	47 123	34 943	65 212	35 290	26 629	25 291	57 883	45 259	278 809	781 291
70-79	2 619	3 623	82 472	93 975	7 371	44 666	26 837	101 096	40 212	35 255	21 419	49 787	60 651	282 251	852 235
80+	706	1 021	65 854	36 143	2 310	13 713	6 820	77 903	16 719	19 503	6 404	14 660	41 614	108 604	411 974
TOTAL	10 690	15 800	257 452	341 504	28 732	167 700	114 915	290 702	123 931	99 771	83 118	190 043	183 442	975 237	2 883 037

Table 4.7 Deaths from SCC
by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30-44	1	1	1	4	1	1	2	1	1	0	3	7	0	7	29
45-59	23	25	49	128	20	50	60	39	23	15	85	246	30	279	1 072
60-69	42	44	101	233	38	83	106	112	57	43	166	474	78	572	2 149
70-79	41	43	160	272	41	91	104	167	65	47	174	491	106	599	2 402
80+	27	24	384	250	29	82	80	438	88	85	114	390	219	637	2 846
TOTAL	133	136	696	886	128	307	353	757	233	191	543	1 608	434	2 094	8 498

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
45-59	12	13	19	63	10	17	29	13	10	5	44	107	11	106	459
60-69	15	16	30	83	13	24	36	32	21	15	61	153	22	161	684
70-79	20	21	92	139	19	38	47	109	46	49	81	218	62	314	1 254
80+	27	32	342	279	33	60	64	351	81	104	128	338	198	603	2 639
TOTAL	74	83	483	565	76	139	176	505	157	173	313	815	293	1 184	5 036

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30-44	1	1	1	4	1	1	2	1	1	0	3	7	0	7	29
45-59	35	38	67	191	30	67	89	52	33	20	129	353	41	385	1 531
60-69	57	60	132	316	51	106	142	144	78	58	227	627	101	733	2 833
70-79	61	64	253	410	60	129	152	275	110	97	255	709	168	913	3 656
80+	54	56	726	529	62	142	144	789	169	189	242	727	417	1 240	5 485
TOTAL	208	219	1179	1450	204	446	529	1262	390	364	856	2423	727	3 278	13 534

Table 4.8 Disease burden due to SCC in DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.002	0.000	0.002	0.008
15-29	0.001	0.001	0.001	0.002	0.001	0.001	0.007	0.001	0.001	0.000	0.000	0.009	0.001	0.006	0.032
30-44	0.038	0.052	0.040	0.158	0.062	0.073	0.272	0.026	0.026	0.009	0.087	0.454	0.019	0.298	1.616
45-59	0.520	0.610	1.101	2.778	0.574	1.147	1.994	0.884	0.530	0.345	1.722	6.085	0.686	6.293	25.269
60-69	0.654	0.713	1.580	3.520	0.733	1.307	2.348	1.774	0.897	0.686	2.374	8.008	1.230	8.863	34.687
70-79	0.447	0.482	1.733	2.805	0.574	0.999	1.678	1.852	0.725	0.543	1.680	5.852	1.178	6.507	27.057
80+	0.150	0.136	2.056	1.327	0.177	0.445	0.523	2.326	0.468	0.453	0.600	2.247	1.174	3.569	15.651
TOTAL	1.810	1.993	6.511	10.590	2.122	3.973	6.825	6.863	2.647	2.038	6.465	22.656	4.287	25.538	104.320

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002
15-29	0.000	0.001	0.001	0.001	0.001	0.001	0.005	0.001	0.001	0.000	0.000	0.006	0.000	0.004	0.022
30-44	0.014	0.022	0.030	0.053	0.028	0.029	0.151	0.023	0.021	0.010	0.012	0.214	0.015	0.184	0.806
45-59	0.290	0.344	0.462	1.493	0.342	0.433	1.141	0.335	0.248	0.136	0.944	2.933	0.278	2.583	11.965
60-69	0.277	0.314	0.546	1.442	0.314	0.430	0.987	0.585	0.381	0.275	0.975	3.029	0.410	2.863	12.829
70-79	0.240	0.272	1.091	1.612	0.278	0.465	0.797	1.303	0.558	0.600	0.895	2.831	0.746	3.738	15.427
80+	0.178	0.215	2.040	1.689	0.245	0.375	0.523	2.089	0.491	0.627	0.766	2.286	1.201	3.796	16.521
TOTAL	0.999	1.168	4.169	6.290	1.209	1.734	3.604	4.337	1.700	1.649	3.593	11.300	2.651	13.170	57.573

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.003	0.000	0.002	0.010
15-29	0.001	0.002	0.001	0.003	0.002	0.002	0.012	0.001	0.002	0.001	0.001	0.015	0.001	0.011	0.054
30-44	0.052	0.073	0.070	0.211	0.090	0.103	0.423	0.049	0.047	0.019	0.100	0.667	0.035	0.483	2.422
45-59	0.810	0.954	1.563	4.272	0.916	1.580	3.135	1.219	0.779	0.481	2.667	9.018	0.964	8.876	37.234
60-69	0.931	1.027	2.125	4.962	1.048	1.738	3.335	2.359	1.279	0.962	3.350	11.037	1.639	11.727	47.517
70-79	0.687	0.754	2.824	4.417	0.852	1.464	2.475	3.156	1.283	1.143	2.575	8.683	1.924	10.246	42.484
80+	0.328	0.351	4.096	3.016	0.422	0.820	1.046	4.414	0.959	1.081	1.366	4.534	2.375	7.364	32.172
TOTAL	2.808	3.161	10.680	16.881	3.331	5.707	10.429	11.199	4.348	3.687	10.058	33.956	6.938	38.709	161.892

Table 4.9 Disease burden from SCC attributable to ultraviolet radiation DALYs (000) – upper estimates (by 14 WHO subregions, see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.004
15-29	0.000	0.000	0.001	0.001	0.000	0.001	0.004	0.001	0.001	0.000	0.000	0.001	0.000	0.004	0.015
30-44	0.003	0.017	0.027	0.099	0.029	0.051	0.156	0.018	0.018	0.007	0.023	0.066	0.013	0.201	0.730
45-59	0.045	0.196	0.755	1.738	0.264	0.798	1.145	0.618	0.371	0.241	0.456	0.890	0.479	4.251	12.249
60-69	0.057	0.229	1.083	2.202	0.337	0.910	1.348	1.241	0.628	0.480	0.628	1.172	0.859	5.988	17.162
70-79	0.039	0.155	1.189	1.755	0.264	0.696	0.964	1.296	0.507	0.380	0.445	0.856	0.823	4.396	13.764
80+	0.013	0.044	1.410	0.830	0.081	0.310	0.300	1.627	0.327	0.317	0.159	0.329	0.821	2.411	8.978
TOTAL	0.158	0.639	4.465	6.625	0.975	2.766	3.918	4.800	1.852	1.427	1.711	3.315	2.996	17.254	52.902

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
15-29	0.000	0.000	0.000	0.001	0.000	0.001	0.003	0.000	0.000	0.000	0.000	0.001	0.000	0.003	0.011
30-44	0.001	0.007	0.020	0.033	0.013	0.020	0.088	0.016	0.015	0.007	0.003	0.031	0.011	0.124	0.390
45-59	0.025	0.116	0.317	0.936	0.158	0.302	0.665	0.235	0.174	0.095	0.255	0.431	0.195	1.735	5.637
60-69	0.024	0.106	0.374	0.903	0.145	0.300	0.575	0.409	0.267	0.193	0.263	0.445	0.286	1.923	6.214
70-79	0.021	0.092	0.748	1.010	0.128	0.324	0.464	0.912	0.391	0.420	0.241	0.416	0.522	2.511	8.199
80+	0.015	0.073	1.400	1.059	0.113	0.262	0.305	1.461	0.343	0.439	0.207	0.336	0.839	2.549	9.400
TOTAL	0.087	0.395	2.860	3.941	0.558	1.209	2.100	3.033	1.190	1.154	0.970	1.659	1.853	8.845	29.853

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.004
15-29	0.000	0.001	0.001	0.002	0.001	0.002	0.007	0.001	0.001	0.001	0.000	0.002	0.001	0.007	0.026
30-44	0.004	0.024	0.048	0.132	0.042	0.072	0.244	0.035	0.033	0.014	0.026	0.098	0.024	0.325	1.120
45-59	0.070	0.312	1.072	2.674	0.422	1.100	1.810	0.853	0.545	0.337	0.711	1.321	0.674	5.987	17.886
60-69	0.081	0.335	1.457	3.105	0.482	1.210	1.923	1.650	0.895	0.673	0.891	1.616	1.146	7.911	23.377
70-79	0.060	0.246	1.937	2.764	0.392	1.020	1.428	2.207	0.898	0.800	0.686	1.272	1.345	6.907	21.963
80+	0.029	0.116	2.810	1.888	0.195	0.571	0.605	3.087	0.671	0.757	0.365	0.664	1.660	4.960	18.379
TOTAL	0.244	1.034	7.325	10.566	1.533	3.975	6.018	7.833	3.042	2.581	2.680	4.974	4.849	26.099	82.754

Table 4.10 Disease burden from SCC attributable to ultraviolet radiation DALYs (000) – lower estimates (by 14 WHO subregions, see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.003
15-29	0.000	0.000	0.000	0.001	0.000	0.001	0.003	0.000	0.000	0.000	0.000	0.001	0.000	0.003	0.011
30-44	0.002	0.012	0.020	0.071	0.020	0.037	0.112	0.013	0.013	0.005	0.017	0.047	0.010	0.144	0.521
45-59	0.032	0.139	0.540	1.241	0.188	0.570	0.818	0.442	0.265	0.172	0.326	0.636	0.342	3.037	8.748
60-69	0.040	0.163	0.774	1.573	0.241	0.650	0.963	0.886	0.448	0.343	0.449	0.837	0.614	4.277	12.258
70-79	0.027	0.110	0.849	1.253	0.189	0.497	0.688	0.925	0.362	0.272	0.318	0.612	0.588	3.140	9.830
80+	0.009	0.031	1.007	0.593	0.058	0.221	0.214	1.162	0.234	0.227	0.113	0.235	0.586	1.722	6.413
TOTAL	0.111	0.455	3.189	4.732	0.697	1.976	2.799	3.429	1.323	1.019	1.222	2.368	2.140	12.324	37.784

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
15-29	0.000	0.000	0.000	0.001	0.000	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.002	0.008
30-44	0.001	0.005	0.015	0.024	0.009	0.015	0.063	0.012	0.011	0.005	0.002	0.022	0.008	0.088	0.279
45-59	0.018	0.083	0.226	0.668	0.113	0.216	0.475	0.168	0.124	0.068	0.182	0.308	0.139	1.239	4.026
60-69	0.017	0.076	0.267	0.645	0.104	0.214	0.411	0.292	0.191	0.138	0.188	0.318	0.205	1.374	4.438
70-79	0.015	0.066	0.535	0.721	0.092	0.232	0.331	0.651	0.279	0.300	0.172	0.297	0.373	1.793	5.856
80+	0.011	0.052	1.000	0.756	0.081	0.187	0.218	1.043	0.245	0.314	0.148	0.240	0.599	1.821	6.714
TOTAL	0.061	0.281	2.043	2.815	0.398	0.863	1.500	2.167	0.850	0.825	0.693	1.185	1.323	6.318	21.322

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.004
15-29	0.000	0.000	0.001	0.001	0.001	0.001	0.005	0.001	0.001	0.000	0.000	0.002	0.000	0.005	0.018
30-44	0.003	0.017	0.034	0.094	0.030	0.051	0.174	0.025	0.023	0.010	0.019	0.070	0.017	0.232	0.800
45-59	0.050	0.222	0.766	1.910	0.301	0.786	1.293	0.609	0.389	0.240	0.508	0.943	0.481	4.276	12.774
60-69	0.057	0.238	1.041	2.218	0.344	0.864	1.374	1.179	0.639	0.481	0.637	1.155	0.818	5.651	16.696
70-79	0.042	0.175	1.384	1.975	0.280	0.728	1.020	1.577	0.641	0.572	0.490	0.908	0.961	4.934	15.687
80+	0.020	0.083	2.007	1.349	0.139	0.408	0.432	2.205	0.479	0.540	0.261	0.475	1.186	3.543	13.127
TOTAL	0.172	0.737	5.232	7.547	1.095	2.839	4.298	5.595	2.173	1.844	1.914	3.553	3.464	18.642	59.106

4.3 Basal cell carcinoma

Disease incidence

Basal cell carcinomas (BCCs) are the most frequent cancers in a number of countries (*53*). While mortality from these cancers is low, there may be substantial morbidity from disfigurement (they are most often on the skin of the head and neck) and because of their high prevalence they represent a considerable medical expense. Many countries do not record incidence of BCC or only as a part of "non-melanoma skin cancer" (NMSC). Unfortunately, this category, as well as including SCC, can include Kaposi's sarcoma, histiocytoma of the skin and other skin tumours (*55*). This means that even those cancer registries that do record 'non-melanoma skin cancer' cannot be used as a source of incidence/prevalence/mortality data for BCC.

Many BCC are dealt with by a primary care physician and no histological confirmation of the diagnosis may be requested, or the method of removal may result in a specimen that is unsuitable for histological examination. Incidence must often be investigated by epidemiological studies of populations over several years. BCC and SCC are commonly multiple – studies may count number of people with lesions, or number of lesions, so care must be taken when using these data.

NMSC is uncommon in Asians, blacks and Hispanics. Unlike SCC, it appears that BCC in black patients is related to UVR exposure and is clinically and histologically similar to BCC in white patients (*60*). However, while the ratio of BCC to SCC in white populations appears to lie between 4:1 (higher latitudes) and 2.5:1(lower latitudes), SCC is more common than BCC in deeply pigmented populations.

Incidence of BCC was recorded as for SCC. Population level dose response curves were plotted and age-specific incidence derived from these as already outlined for SCC. Much of the epidemiological data on BCC comes from Australia, which has extremely high rates of incident BCC. Thus, efforts were made to also find non-Australian studies to contribute to the incidence rate data.

Basal cell carcinoma is uncommon in people of intermediate pigment and rare in those who are deeply pigmented. Data are scarce, so the data for the lightly pigmented were adjusted with multipliers across all latitudes and age groups as follows: intermediate skin pigmentation – female - 0.21, male - 0.14 (*34*); deeply pigmented – 0.002 (*61, 62*).

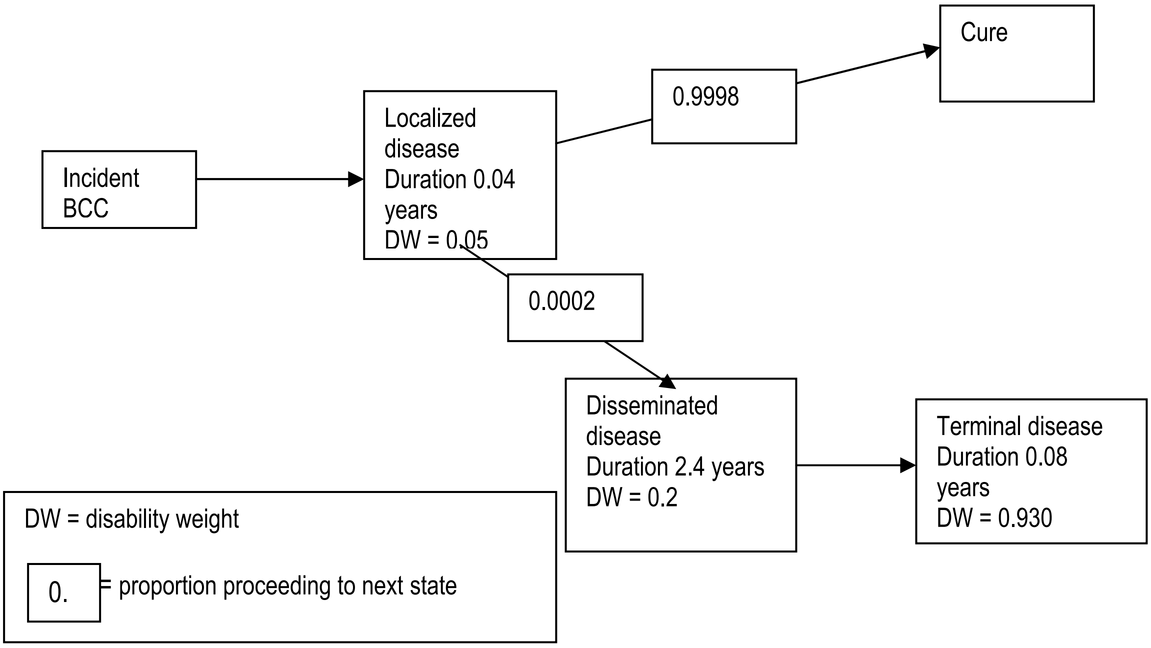
Population attributable fraction

Case-control studies were examined to calculate PAF. Similarly to melanoma, there is little latitudinal gradient of PAF ($p = 0.32$) and the calculated PAF seems quite low (intercept = 0.33). If one applies a similar analysis of PAF based on the difference in incidence in Caucasian and African Americans that Armstrong has done for melanoma (*42*), the PAF would similarly be of the order of 0.9 to 1.00, (see Appendix 3). Basal cell carcinoma, like melanoma, may have a complicated dose-response relationship, which is difficult to examine with case-control studies. A lower estimate of 0.50 and an upper estimate of 0.9 were applied to the calculated burden of disease estimates, (see Appendix 3).

Disease characteristics

Metastasis and mortality due to BCC are very rare. Case fatality rates vary from <1 in 4000 (< 0.025%) (*63*) to 0.05% (1 in 2000) (*64*). Information on mortality rates is scarce, with most references quoting rates for non-melanoma skin cancer, with no distinction between SCC, BCC and other types of skin cancer. Mortality rates were calculated as for SCC, by using a ratio in relation to incidence. The results of this method were compatible with the few published mortality rates for BCC (*55, 65*). Figure 4.2 summarizes the flow diagram for the disease course for BCC.

Figure 4.2 Disease model for BCC – all regions



Many of those with non-melanoma skin cancer have multiple lesions, particularly at lower latitudes (*66*). Most studies to date have recorded the incidence rate as number of persons with incident disease (and this is used in this assessment). However, this clearly does not truly capture the burden of disease due to non-melanoma skin cancers. A person having multiple BCC removed has a higher burden of disease than a person having one BCC removed – but how much higher? Presumably removal of ten BCC does not attract ten times the disability of having one removed. The epidemiological data are too sparse to include multiple lesions in the current assessment, but future disease models should attempt to include multiple lesions in the analysis. Tables 4.11 and 4.12 summarize the incidence and mortality for BCC; Table 4.13 summarizes the burden of disease due to BCC; Tables 4.14 and 4.15 summarize the burden of disease from BCC that is attributable to UVR exposure in the year 2000 (upper and lower estimates).

Table 4.11 Incident cases of BCC by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	1	2	12	34	4	27	31	8	13	4	9	32	6	86	270
5-14	15	19	184	437	47	371	303	143	187	87	116	407	82	1 347	3 744
15-29	536	737	7 658	19 910	1 918	14 380	10 585	6 684	8 048	3 450	5 844	17 110	4 647	59 103	160 611
30-44	3 474	5 179	32 573	171 459	30 156	92 300	113 117	26 257	22 218	11 158	73 678	134 157	16 338	237 911	969 975
45-59	4 408	6 752	95 771	244 201	33 593	135 982	109 865	95 175	51 293	40 052	89 573	189 944	65 003	520 668	1 682 280
60-69	2 744	3 659	135 758	146 494	11 290	80 687	52 059	194 807	87 079	83 691	41 519	122 279	119 901	682 871	1 764 837
70-79	1 952	2 125	147 879	116 638	8 271	61 366	33 407	199 778	69 107	65 052	29 389	85 091	111 101	493 261	1 424 417
80+	658	600	51 973	49 890	5 848	19 529	13 615	57 557	12 517	10 517	14 216	31 354	31 279	92 499	392 053
TOTAL	13 789	19 072	471 807	749 063	91 128	404 644	332 982	580 409	250 462	214 012	254 344	580 374	348 357	2 087 745	6 398 187

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	5	5	56	111	13	89	79	58	63	40	37	137	25	367	1 084
15-29	292	328	1 824	9 552	1 630	5 141	5 859	1 690	2 189	936	4 442	9 684	1 062	15 069	59 697
30-44	4 157	4 663	34 848	169 306	30 186	63 342	91 958	29 642	24 641	13 758	86 356	156 331	17 397	246 483	973 067
45-59	3 691	4 383	70 526	163 317	22 131	59 447	72 775	73 481	40 864	36 432	72 390	155 993	46 792	347 473	1 169 694
60-69	2 136	2 404	52 561	91 690	11 253	34 914	36 489	81 165	42 115	46 862	40 915	94 066	44 017	242 024	822 610
70-79	1 067	1 115	52 911	52 449	5 091	19 020	15 330	87 303	33 799	46 477	18 378	45 078	39 490	160 913	578 420
80+	553	679	83 878	39 112	2 656	11 741	7 118	105 700	21 570	33 928	9 675	25 983	53 680	133 678	529 950
TOTAL	11 900	13 575	296 604	525 538	72 959	193 694	229 606	379 037	165 242	178 434	232 193	487 272	202 463	1 146 007	4 134 524

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	1	2	12	34	4	27	31	8	13	4	9	32	6	86	270
5-14	20	24	240	547	60	460	383	202	250	127	153	544	107	1 713	4 829
15-29	828	1 064	9 481	29 463	3 548	19 522	16 444	8 373	10 237	4 386	10 286	26 794	5 709	74 173	220 308
30-44	7 631	9 842	67 421	340 765	60 342	155 642	205 074	55 899	46 860	24 916	160 034	290 488	33 735	484 394	1 943 042
45-59	8 099	11 135	166 296	407 518	55 724	195 429	182 639	168 656	92 157	76 484	161963	345 937	111 795	868 141	2 851 974
60-69	4 879	6 063	188 320	238 184	22 543	115 601	88 548	275 971	129 194	130 553	82 434	216 345	163 918	924 895	2 587 447
70-79	3 019	3 239	200 790	169 087	13 362	80 386	48 737	287 081	102 906	111 529	47 767	130 169	150 591	654 173	2 002 837
80+	1 211	1 279	135 851	89 002	8 504	31 270	20 733	163 257	34 087	44 445	23 891	57 337	84 959	226 178	922 004
TOTAL	25 689	32 648	768 410	1 274 600	164 087	598 337	562 589	959 447	415 704	392 445	486 537	1 067 646	550 820	3 233 752	10 532 711

Table 4.12 Deaths from BCC in 2000
by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30-44	0	1	3	17	3	9	11	3	2	1	7	13	2	24	97
45-59	1	1	14	36	5	20	16	14	8	6	13	28	10	77	249
60-69	1	1	36	39	3	22	14	52	23	22	11	33	32	182	471
70-79	1	1	87	69	5	36	20	118	41	38	17	50	66	291	841
80+	1	1	68	65	8	25	18	75	16	14	19	41	41	121	511
TOTAL	4	5	209	226	24	113	79	262	90	82	68	165	150	695	2 170

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30-44	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
45-59	1	1	14	32	4	11	14	14	8	7	14	30	9	67	226
60-69	0	0	10	17	2	7	7	15	8	9	8	18	8	46	157
70-79	0	0	18	18	2	7	5	30	13	16	6	16	14	56	203
80+	1	1	77	36	2	11	7	98	20	31	9	24	50	123	489
TOTAL	2	2	120	103	11	36	33	158	50	63	37	88	81	293	1 076

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30-44	0	1	3	17	3	9	11	3	2	1	7	13	2	24	97
45-59	1	2	28	68	9	32	30	28	15	13	27	58	19	144	475
60-69	1	1	46	57	5	28	21	67	32	31	19	51	40	228	628
70-79	2	2	106	87	7	43	25	148	54	55	24	66	79	347	1044
80+	1	1	145	101	10	36	24	173	37	45	27	65	90	244	1001
TOTAL	6	7	328	330	34	148	112	419	140	145	105	253	230	988	3245

Table 4.13 Disease burden due to BCC in DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
5-14	0.000	0.000	0.000	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.003	0.008
15-29	0.001	0.002	0.016	0.042	0.004	0.030	0.022	0.014	0.017	0.007	0.012	0.036	0.010	0.124	0.338
30-44	0.016	0.023	0.147	0.777	0.137	0.418	0.513	0.119	0.100	0.050	0.334	0.608	0.074	1.079	4.393
45-59	0.022	0.034	0.477	1.217	0.167	0.680	0.549	0.472	0.256	0.200	0.446	0.946	0.322	2.600	8.388
60-69	0.016	0.021	0.781	0.845	0.065	0.464	0.300	1.120	0.500	0.485	0.240	0.705	0.689	3.932	10.164
70-79	0.015	0.016	1.097	0.872	0.062	0.459	0.251	1.487	0.520	0.495	0.221	0.639	0.832	3.705	10.671
80+	0.006	0.005	0.446	0.433	0.051	0.169	0.120	0.488	0.106	0.089	0.125	0.276	0.267	0.825	3.406
TOTAL	0.075	0.101	2.964	4.186	0.486	2.222	1.756	3.700	1.500	1.327	1.379	3.211	2.193	12.268	37.369

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.002
15-29	0.001	0.001	0.004	0.020	0.003	0.011	0.012	0.004	0.005	0.002	0.009	0.020	0.002	0.032	0.126
30-44	0.009	0.010	0.073	0.357	0.064	0.133	0.194	0.062	0.054	0.029	0.182	0.329	0.037	0.519	2.051
45-59	0.022	0.027	0.429	0.994	0.135	0.363	0.444	0.445	0.246	0.222	0.440	0.948	0.283	2.121	7.119
60-69	0.011	0.012	0.263	0.460	0.056	0.175	0.183	0.406	0.218	0.236	0.206	0.472	0.220	1.213	4.132
70-79	0.006	0.006	0.303	0.303	0.029	0.110	0.089	0.500	0.209	0.269	0.107	0.261	0.227	0.930	3.351
80+	0.004	0.005	0.595	0.286	0.020	0.086	0.054	0.743	0.156	0.241	0.072	0.195	0.383	0.993	3.833
TOTAL	0.053	0.061	1.667	2.420	0.307	0.879	0.976	2.160	0.888	1.000	1.017	2.227	1.152	5.808	20.614

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
5-14	0.000	0.000	0.001	0.001	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.001	0.000	0.004	0.010
15-29	0.002	0.002	0.020	0.062	0.007	0.041	0.035	0.018	0.022	0.009	0.022	0.056	0.012	0.156	0.464
30-44	0.025	0.033	0.220	1.133	0.200	0.551	0.706	0.181	0.154	0.079	0.516	0.937	0.111	1.598	6.445
45-59	0.044	0.060	0.905	2.211	0.302	1.043	0.992	0.917	0.503	0.422	0.886	1.894	0.604	4.721	15.506
60-69	0.027	0.033	1.044	1.305	0.122	0.640	0.484	1.526	0.719	0.721	0.446	1.178	0.909	5.144	14.296
70-79	0.021	0.022	1.400	1.175	0.091	0.570	0.340	1.987	0.729	0.764	0.328	0.900	1.059	4.635	14.022
80+	0.010	0.010	1.041	0.718	0.071	0.255	0.174	1.231	0.262	0.331	0.198	0.471	0.650	1.818	7.239
TOTAL	0.128	0.162	4.631	6.607	0.794	3.100	2.732	5.860	2.389	2.326	2.396	5.438	3.345	18.076	57.983

Table 4.14 Disease burden from BCC attributable to ultraviolet radiation DALYs (000) – upper estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
5-14	0.000	0.000	0.000	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.003	0.007
15-29	0.001	0.001	0.015	0.038	0.004	0.027	0.020	0.013	0.015	0.007	0.011	0.032	0.009	0.112	0.304
30-44	0.014	0.021	0.132	0.699	0.123	0.376	0.461	0.107	0.090	0.045	0.300	0.547	0.066	0.971	3.954
45-59	0.020	0.030	0.429	1.095	0.151	0.612	0.494	0.425	0.231	0.180	0.401	0.852	0.289	2.340	7.549
60-69	0.014	0.019	0.703	0.760	0.059	0.418	0.270	1.008	0.450	0.436	0.216	0.635	0.620	3.539	9.147
70-79	0.013	0.014	0.987	0.785	0.056	0.413	0.226	1.339	0.468	0.445	0.199	0.575	0.749	3.335	9.604
80+	0.005	0.005	0.401	0.389	0.046	0.152	0.108	0.439	0.095	0.080	0.113	0.249	0.240	0.743	3.065
TOTAL	0.068	0.091	2.667	3.768	0.438	1.999	1.580	3.330	1.350	1.194	1.241	2.890	1.974	11.041	33.632

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.002
15-29	0.001	0.001	0.003	0.018	0.003	0.010	0.011	0.003	0.004	0.002	0.008	0.018	0.002	0.029	0.113
30-44	0.008	0.009	0.066	0.321	0.057	0.120	0.174	0.056	0.048	0.026	0.164	0.296	0.033	0.467	1.846
45-59	0.020	0.024	0.386	0.895	0.121	0.326	0.399	0.400	0.222	0.200	0.396	0.853	0.254	1.909	6.407
60-69	0.010	0.011	0.237	0.414	0.051	0.158	0.165	0.366	0.196	0.212	0.185	0.425	0.198	1.091	3.719
70-79	0.006	0.006	0.273	0.273	0.027	0.099	0.080	0.450	0.188	0.242	0.096	0.235	0.204	0.837	3.016
80+	0.004	0.005	0.536	0.257	0.018	0.077	0.048	0.668	0.140	0.217	0.065	0.176	0.345	0.893	3.450
TOTAL	0.048	0.055	1.500	2.178	0.277	0.791	0.878	1.944	0.799	0.900	0.915	2.004	1.037	5.227	18.553

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
5-14	0.000	0.000	0.000	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.003	0.009
15-29	0.002	0.002	0.018	0.056	0.007	0.037	0.031	0.016	0.019	0.008	0.019	0.051	0.011	0.141	0.417
30-44	0.022	0.030	0.198	1.020	0.180	0.496	0.636	0.163	0.139	0.071	0.464	0.843	0.099	1.438	5.800
45-59	0.040	0.054	0.815	1.990	0.272	0.939	0.893	0.825	0.452	0.380	0.798	1.705	0.544	4.249	13.956
60-69	0.024	0.030	0.939	1.175	0.109	0.576	0.435	1.374	0.647	0.649	0.401	1.060	0.818	4.630	12.866
70-79	0.019	0.020	1.260	1.058	0.082	0.513	0.306	1.788	0.657	0.687	0.295	0.810	0.953	4.171	12.620
80+	0.009	0.009	0.937	0.647	0.064	0.229	0.156	1.107	0.236	0.297	0.178	0.424	0.585	1.636	6.515
TOTAL	0.115	0.146	4.168	5.946	0.714	2.790	2.458	5.274	2.150	2.094	2.156	4.894	3.011	16.268	52.184

Table 4.15 Disease burden from BCC attributable to ultraviolet radiation DALYs (000) – lower estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.004
15-29	0.001	0.001	0.008	0.021	0.002	0.015	0.011	0.007	0.008	0.004	0.006	0.018	0.005	0.062	0.169
30-44	0.008	0.012	0.073	0.388	0.068	0.209	0.256	0.059	0.050	0.025	0.167	0.304	0.037	0.539	2.197
45-59	0.011	0.017	0.238	0.609	0.084	0.340	0.274	0.236	0.128	0.100	0.223	0.473	0.161	1.300	4.194
60-69	0.008	0.011	0.390	0.422	0.033	0.232	0.150	0.560	0.250	0.242	0.120	0.353	0.344	1.966	5.082
70-79	0.007	0.008	0.548	0.436	0.031	0.230	0.125	0.744	0.260	0.247	0.111	0.319	0.416	1.853	5.336
80+	0.003	0.003	0.223	0.216	0.026	0.084	0.060	0.244	0.053	0.045	0.063	0.138	0.134	0.413	1.703
TOTAL	0.038	0.051	1.482	2.093	0.243	1.111	0.878	1.850	0.750	0.663	0.690	1.605	1.097	6.134	18.685

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
15-29	0.000	0.000	0.002	0.010	0.002	0.005	0.006	0.002	0.002	0.001	0.005	0.010	0.001	0.016	0.063
30-44	0.004	0.005	0.037	0.178	0.032	0.067	0.097	0.031	0.027	0.014	0.091	0.165	0.018	0.260	1.026
45-59	0.011	0.013	0.214	0.497	0.067	0.181	0.222	0.222	0.123	0.111	0.220	0.474	0.141	1.060	3.559
60-69	0.005	0.006	0.132	0.230	0.028	0.088	0.092	0.203	0.109	0.118	0.103	0.236	0.110	0.606	2.066
70-79	0.003	0.003	0.151	0.151	0.015	0.055	0.045	0.250	0.105	0.135	0.053	0.131	0.114	0.465	1.675
80+	0.002	0.003	0.298	0.143	0.010	0.043	0.027	0.371	0.078	0.121	0.036	0.098	0.192	0.496	1.917
TOTAL	0.026	0.030	0.834	1.210	0.154	0.439	0.488	1.080	0.444	0.500	0.508	1.113	0.576	2.904	10.307

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.002	0.005
15-29	0.001	0.001	0.010	0.031	0.004	0.021	0.017	0.009	0.011	0.005	0.011	0.028	0.006	0.078	0.232
30-44	0.012	0.017	0.110	0.567	0.100	0.276	0.353	0.091	0.077	0.040	0.258	0.468	0.055	0.799	3.222
45-59	0.022	0.030	0.453	1.106	0.151	0.521	0.496	0.458	0.251	0.211	0.443	0.947	0.302	2.360	7.753
60-69	0.013	0.017	0.522	0.653	0.061	0.320	0.242	0.763	0.359	0.360	0.223	0.589	0.454	2.572	7.148
70-79	0.010	0.011	0.700	0.588	0.046	0.285	0.170	0.994	0.365	0.382	0.164	0.450	0.530	2.317	7.011
80+	0.005	0.005	0.521	0.359	0.035	0.127	0.087	0.615	0.131	0.165	0.099	0.236	0.325	0.909	3.620
TOTAL	0.064	0.081	2.315	3.303	0.397	1.550	1.366	2.930	1.194	1.163	1.198	2.719	1.673	9.038	28.991

4.4 Chronic sun damage/solar keratoses

Disease incidence

Although we may not like the appearance of our ageing skin, there is no disability in health terms from the wrinkling, actinic lentigines and actinic (solar) keratoses that constitute photoageing. There is however, a disability related to removal of solar keratoses and there is a recognized progression of solar keratoses (SK) to SCC. It appears that SK, dysplasia, SCC-in-situ and invasive SCC are a continuum and it may be difficult to delineate these clinically. Current treatment options include local destruction with cryotherapy, curettage, electrodessication, or topical application of aminolevulinic acid and light.

It is clear that not only is there a latitudinal gradient in the prevalence of persons with solar keratoses, but at lower latitudes, it is more likely that there will be multiple solar keratoses. It is important in evaluating studies to be clear whether they are measuring prevalent lesions, or ‘persons with lesions’ as some people have a large number of lesions. In the Nambour study (*67*) 10% of the population had more than one lesion, while in South Wales there was a median of 2 solar keratoses in those aged over 60 years (*54*). In the later part of the Nambour study (*68*), 18% of the study population had 11 or more solar keratoses.

A few studies have examined the prevalence of solar keratoses and using these data we have extrapolated to achieve a theoretical distribution of prevalence of solar keratoses by latitude and age (*54, 68-72*). From this the incidence rates for removal of SK and for malignant transformation were estimated.

Population attributable fraction

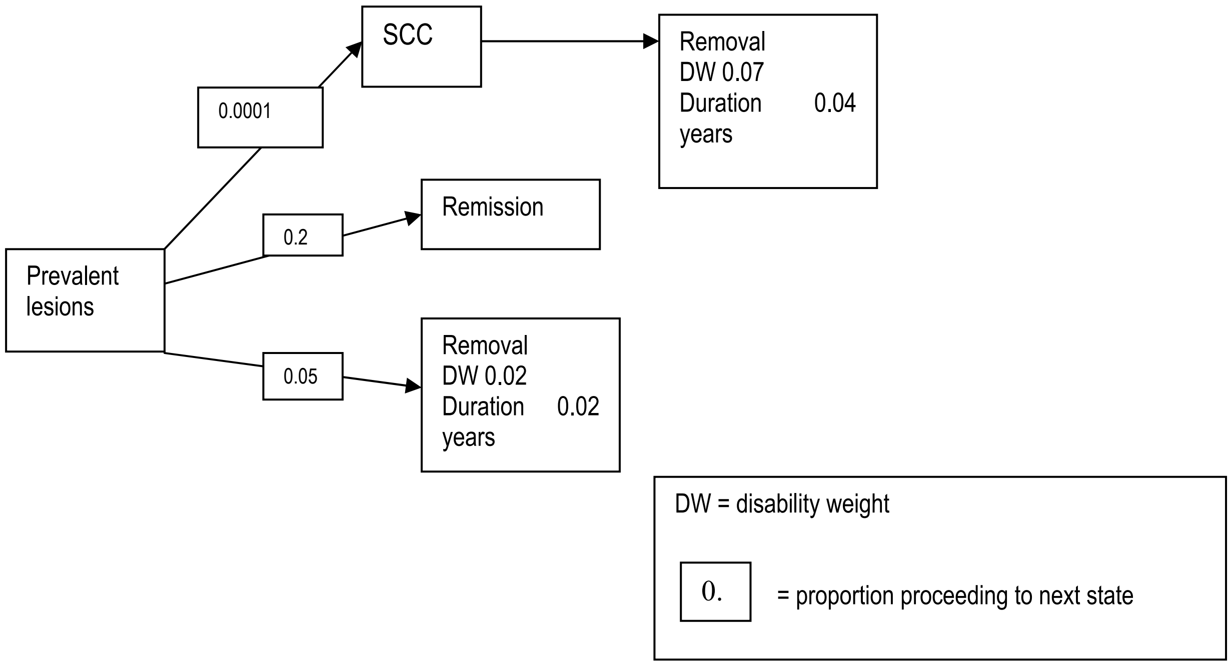
Chronic sun damage to the skin, or photoageing includes those sun-induced changes to the skin that, combined with the changes of intrinsic or chronologic ageing, represent the characteristic signs of ageing skin. Many of the changes in the skin that are evident with ageing are photo-induced (*73*).

Only solar keratoses are assessed in this report and they are considered to be entirely related to UVR exposure. (See appendix 3)

Disease model

From the epidemiological data we have assumed a removal rate of 5% (of those solar keratoses that do not remit) in developed countries, a zero removal rate in under-developed countries, a remission rate of 20% per year, (*54, 74*) and a progression to SCC of 0.01% per year (*75*). Figure 4.3 presents the disease model for solar keratoses.

Figure 4.3 Disease model for solar keratoses



Tables 4.16 to 4.17 summarize the prevalence and burden of disease due to solar keratoses (as part of the photoageing process).

Table 4.16 Prevalent persons with solar keratoses by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	1 270	27 580	358 289	767 805	43 427	554 168	289 306	308 131	336 321	85 589	50 008	7 935	316 817	3 446 324	6 592 970
30-44	6 586	186 617	5 872 608	5 734 145	239 382	4 013 297	1 802 422	6 995 676	4 170 761	2 813 945	390 819	52 517	3 713 439	38 410 568	74 402 782
45-59	5 503	174 078	8 754 162	5 909 085	203 461	4 095 124	1 609 478	10 554 675	4 912 268	3 981 146	311 019	41 899	7 920 583	46 772 556	95 245 037
60-69	2 625	77 791	5 634 194	3 214 432	104 333	2 191 993	836 400	10 548 280	4 246 878	4 113 056	162 098	24 186	5 921 548	27 340 613	64 418 427
70-79	1 303	31 779	4 457 224	1 875 245	55 224	1 212 758	371 928	8 264 776	2 561 876	2 830 309	86 443	11 466	3 838 172	14 031 807	39 630 310
80+	307	5 950	2 029 818	577 161	17 049	326 917	88 401	3 278 006	612 261	684 429	26 926	3 134	1 409 415	3 187 199	12 246 973
TOTAL	17 594	503 794	27 106 294	18 077 874	662 876	12 394 257	4 997 935	39 949 545	16 840 365	14 508 475	1 027 313	141 137	23 119 975	133 189 067	292 536 501

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30-44	3 172	102 062	2 849 348	3 103 000	118 051	2 063 058	919 582	2 743 052	1 821 289	1 090 194	187 503	27 182	2 043 947	20 476 801	3 7548 242
45-59	5 917	188 813	8 969 150	6 339 515	214 578	3 637 145	1 703 897	10 688 037	5 063 708	4 565 229	325 348	44 340	7 973 923	43 680 059	9 3399 659
60-69	2 893	85 008	4 219 774	3 126 162	108 236	1 649 817	735 003	7 053 434	3 060 191	3 240 080	174 741	24 527	4 672 050	20 054 940	4 8206 856
70-79	1 513	46 070	4 541 544	2 202 398	60 398	1 085 944	371 117	7 730 689	2 571 785	3 159 231	100 128	12 096	4 282 375	14 187 061	4 0352 349
80+	429	14 753	3 379 996	878 219	21 604	335 179	99 124	5 085 134	929 380	1 333 264	39 627	3 278	2 603 518	5 235 202	19 958 702
TOTAL	13 924	436 707	23 959 813	15 649 289	522 866	8 771 143	3 828 723	33 300 347	13 446 352	13 388 000	827 347	111 423	21 575 814	103 634 063	239 465 811

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	1 270	27 580	358 289	767 805	43 427	554 168	289 306	308 131	336 321	85 589	50 008	7 935	316 817	3 446 324	6 592 970
30-44	9 758	288 679	8 721 956	8 837 146	357 433	6 076 356	2 722 004	9 738 729	5 992 050	3 904 140	578 321	79 699	5 757 386	58 887 369	111 951 026
45-59	11 420	362 891	17 723 312	12 248 600	418 039	7 732 268	3 313 375	21 242 712	9 975 976	8 546 375	636 367	86 239	15 894 506	90 452 615	188 644 695
60-69	5 518	162 799	9 853 968	6 340 594	212 569	3 841 809	1 571 402	17 601 714	7 307 069	7 353 137	336 840	48 713	10 593 598	47 395 553	112 625 284
70-79	2 816	77 849	8 998 768	4 077 643	115 622	2 298 702	743 046	15 995 466	5 133 660	5 989 540	186 571	23 562	8 120 547	28 218 869	79 982 661
80+	737	20 703	5 409 814	1 455 375	38 653	662 097	187 525	8 363 140	1 541 641	2 017 694	66 553	6 412	4 012 933	8 422 400	32 205 677
TOTAL	31 518	940 501	51 066 107	33 727 164	1 185 742	21 165 400	8 826 658	73 249 892	30 286 717	27 896 475	1854 660	252 561	44 695 788	236 823 130	532 002 313

Table 4.17 Burden of disease due to solar keratoses (=attributable BOD) DALYs (000) by 14 WHO subregions (see Appendix 4

(note that there is no mortality due to solar keratoses and the disease burden is fully attributable to UVR exposure)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.004	0.012	0.000	0.009	0.000	0.002	0.003	0.000	0.001	0.000	0.005	0.055	0.091
30-44	0.000	0.000	0.065	0.093	0.000	0.065	0.001	0.044	0.033	0.023	0.006	0.000	0.056	0.603	0.989
45-59	0.000	0.000	0.131	0.096	0.000	0.067	0.000	0.142	0.074	0.058	0.005	0.000	0.125	0.758	1.456
60-69	0.000	0.000	0.101	0.052	0.000	0.036	0.000	0.165	0.069	0.065	0.003	0.000	0.096	0.450	1.037
70-79	0.000	0.000	0.080	0.031	0.000	0.020	0.000	0.167	0.060	0.061	0.001	0.000	0.065	0.238	0.723
80+	0.000	0.000	0.047	0.009	0.000	0.005	0.000	0.102	0.030	0.025	0.000	0.000	0.026	0.060	0.304
TOTAL	0.000	0.000	0.429	0.294	0.000	0.201	0.001	0.622	0.268	0.232	0.017	0.000	0.374	2.163	4.601

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
30-44	0.000	0.000	0.036	0.050	0.000	0.034	0.000	0.020	0.017	0.009	0.003	0.000	0.032	0.325	0.526
45-59	0.000	0.000	0.113	0.103	0.000	0.059	0.000	0.095	0.050	0.047	0.005	0.000	0.123	0.694	1.289
60-69	0.000	0.000	0.091	0.051	0.000	0.027	0.000	0.146	0.065	0.062	0.003	0.000	0.079	0.338	0.862
70-79	0.000	0.000	0.071	0.036	0.000	0.018	0.000	0.116	0.045	0.051	0.002	0.000	0.070	0.233	0.642
80+	0.000	0.000	0.060	0.014	0.000	0.005	0.000	0.109	0.032	0.037	0.001	0.000	0.044	0.090	0.392
TOTAL	0.000	0.000	0.369	0.254	0.000	0.143	0.001	0.487	0.209	0.206	0.013	0.000	0.347	1.681	3.711

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.004	0.012	0.000	0.009	0.000	0.002	0.003	0.000	0.001	0.000	0.005	0.055	0.091
30-44	0.000	0.000	0.100	0.143	0.000	0.099	0.001	0.064	0.049	0.032	0.009	0.000	0.088	0.928	1.513
45-59	0.000	0.000	0.244	0.199	0.000	0.126	0.001	0.237	0.124	0.104	0.010	0.000	0.248	1.453	2.746
60-69	0.000	0.000	0.192	0.103	0.000	0.062	0.000	0.311	0.133	0.127	0.005	0.000	0.175	0.788	1.896
70-79	0.000	0.000	0.151	0.066	0.000	0.037	0.000	0.283	0.105	0.112	0.003	0.000	0.135	0.471	1.363
80+	0.000	0.000	0.107	0.024	0.000	0.011	0.000	0.211	0.062	0.062	0.001	0.000	0.070	0.150	0.698
TOTAL	0.000	0.000	0.798	0.548	0.000	0.344	0.002	1.108	0.477	0.438	0.030	0.000	0.721	3.844	8.311

4.5 Sunburn

Disease incidence

There is a paucity of data on the incidence of sunburn globally. Many studies report incidence over one or two weekends in the summer, (*76-78*) or hospital experience of sunburn (*79*) without relating this to a population incidence.

Characteristically, sunburn is uncommon in the very young, although if it does occur, it may be severe and even life threatening (*80*). The incidence rises through childhood and reaches a peak in adolescence and early adulthood (*81*). Studies vary as to relative incidence by sex (*78, 82*).

Many of the studies examining incidence of sunburn come from Australia and New Zealand and are confined to narrow age groups of later childhood and adolescence. Recent studies report that the incidence of sunburn, particularly amongst the young, continues to be very high. In the United States, 72% of youths 11-18 years reported at least one summer sunburn, and 12% reported at least 5 sunburns (*83*). In the United Kingdom, 48% of parents stated that their child had had at least one sunburn in the previous year (*84*). Even in Sweden, a high latitude country, 55% of respondents reported sunburn in the previous year (*85*). Diffey suggests that sunscreen may often be applied incorrectly, resulting in high doses of UVR exposure as people erroneously assume their skin is protected; doses of UVA may be particularly high if narrow-spectrum sunscreen is used (*86*).

We have used the age distribution outlined by Boldeman et al (*85*) for the Swedish population aged 13-50 years and incidence studies from other parts of the world, to derive a theoretical distribution of sunburn incidence by age and latitude (see Appendix 6).

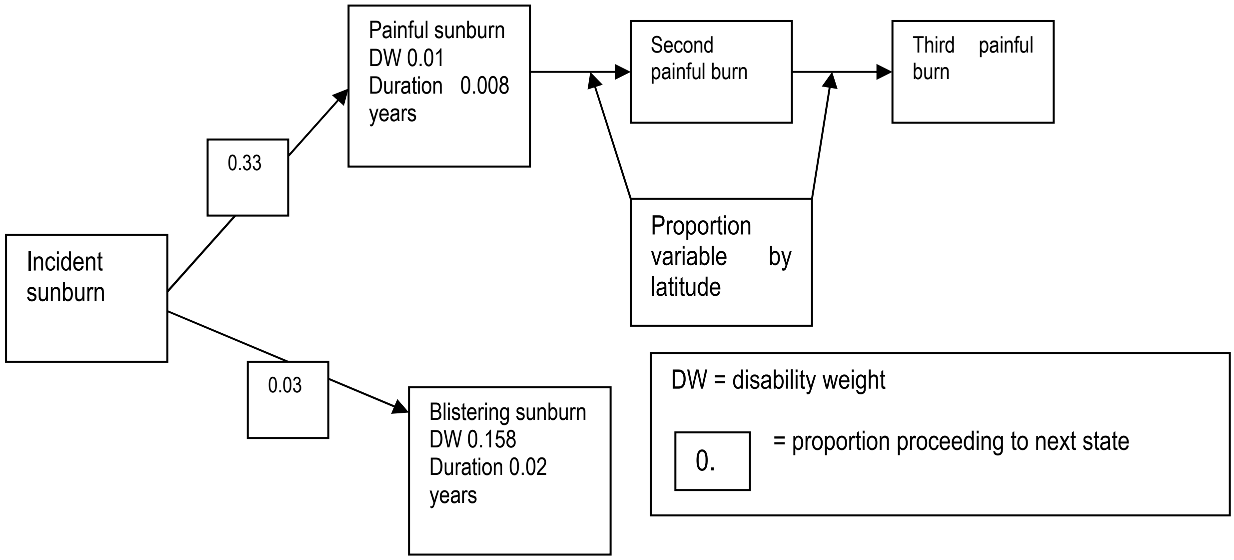
Population attributable fraction

Sunburn is considered totally attributable to UVR exposure, i.e. PAF = 100%

Disease model

Approximately 33% of all recorded sunburns are painful sunburns (*87-89*). Approximately 3% of all burns are severe, blistering burns (*87, 88*). The incidence of a second and third severe burn seems to vary with latitude, from 57% of those with painful sunburn having a second burn and 32% of these having a third burn at the lowest latitudes, to 15% and 8% respectively at higher latitudes. Figure 4.4 shows the disease model used for sunburn.

Figure 4.4 Disease model for sunburn



Sunburn per se is not considered to cause a disability, but there is a disability related to severe and blistering sunburns.

Almost all the available data on sunburn involves white populations. However, Hall et al (*90*) note that 6% of African Americans reported being extremely sensitive to the sun and had suffered severe sunburning, while 9% reported mild burns. This is in contrast to overall rates of any sunburn of 84% for lightly pigmented populations. There is no published detail regarding the depth of pigmentation in those who have suffered severe sunburn, but on the basis of these data (84% lightly pigmented report sunburn, compared to 9% deeply pigmented), and assuming it is applicable to deeply pigmented persons, we have applied a multiplier to the distribution of sunburn incidence in fair-skinned populations of 0.1 for those with deep pigment (9% is approximately 0.1*84%) and 0.5 for those of intermediate pigment (halfway between deeply pigmented and lightly pigmented persons) to obtain an incidence distribution in these populations. We have then applied the same breakdown of painful sunburn and blistering sunburn to this incidence distribution, with duration and disability weights as for lightly pigmented populations.

Tables 4.18 and 4.19 summarize the incidence and burden of disease due to sunburn, but it should be noted that these estimates are highly uncertain due to the paucity of good epidemiological data.

Table 4.18 Incident cases of sunburn 2000
by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	854 925	802 746	1 579 535	3 436 242	584 572	1 987 848	3 194 318	1 471 602	1 489 794	735 602	1 851 959	7 919 779	809 178	11 439 715	38 157 815
5-14	3 857 723	3 663 400	10 680 544	19 173 192	2 796 064	12 184 612	15 178 505	11 801 964	10 172 833	7 929 205	9 649 675	44 391 359	4 759 849	74 534 048	230 772 973
15-29	4 169 002	3 651 086	16 800 360	26 230 559	3 240 908	15 719 390	16 892 545	23 906 063	17 668 507	16 065 886	13 956 763	56 725 595	10 056 333	112 428 380	337 511 377
30-44	1 815 561	1 565 226	14 712 885	14 193 593	1 446 684	7 416 760	8 084 110	21 165 584	10 495 391	11 775 258	7 672 841	29 946 165	7 205 341	79 486 508	216 981 907
45-59	753 059	649 617	9290 128	6 769 027	658 861	3 198 697	3 371 934	14 354 750	5 694 382	7 253 988	3 393 441	14 116 708	6 271 210	40 025 310	115 801 112
60-69	69 921	56 107	930 421	644 250	65 242	295 882	298 011	1 963 380	692 758	1 011 341	341 885	1 373 359	796 020	4 016 660	12 555 237
70-79	16 013	11 997	335 190	172 823	16 203	76 463	66 189	646 089	187 562	252 935	81 170	320 034	242 822	962 247	3 387 737
80+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	11 536 203	10 400 179	54 329 062	70 619 686	8 808 534	40 879 652	47 085 612	75 309 432	46 401 228	45 024 215	36 947 735	154 792 997	30 140 753	322 892 868	955 168 156

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	837 728	791 810	1 504 717	3 305 412	562 587	1 903 656	3 052 637	1 392 341	1 432 383	702 512	1 783 665	7 461 028	766 854	10 356 001	35 853 331
5-14	3 793 035	3 651 991	10 192 122	18 509 522	2 705 370	11 665 983	14 558 734	11 182 676	9 767 696	7 614 522	9 334 635	41 544 773	4 526 363	67 561 348	216 608 770
15-29	4 112 907	3 658 879	16 224 249	26 012 735	3 206 347	15 080 051	15 856 575	22 769 368	16 990 212	15 736 970	13 619 714	52 396 696	9 639 269	105 658 235	320 962 207
30-44	1 831 465	1 573 480	14 460 326	14 707 862	1 511 273	6 727 285	7 543 093	20 667 118	10 427 808	12 028 628	7 741 538	27 703 180	7 099 048	75 611 970	209 634 074
45-59	785 228	695 295	9 507 641	7 255 204	693 119	2 817 028	3 351 875	14 453 014	5 908 228	8 326 781	3 606 462	13 490 429	6 313 312	37 665 127	114 868 743
60-69	80 451	67 908	1 027 960	747 381	71 017	292 143	316 736	2 174 969	816 304	1 460 494	389 672	1 436 944	862 444	3 949 701	13 694 124
70-79	19 674	16 504	439 463	226 816	19 155	79 926	76 018	919 439	275 033	548 698	98 022	359 979	321 760	1 155 523	4 556 010
80+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	11 460 487	10 455 867	53 356 477	70 764 931	8 768 869	38 566 071	44 755 667	73 558 925	45 617 664	46 418 605	36 573 709	144 393 028	29 529 049	301 957 904	916 177 253

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	1 692 653	1 594 555	3 084 252	6 741 654	1 147 160	3 891 504	6 246 955	2 863 942	2 922 177	1 438 114	3 635 625	15 380 807	1 576 031	21 795 716	74 011 145
5-14	7 650 758	7 315 391	20 872 666	37 682 714	5 501 434	23 850 595	29 737 238	22 984 640	19 940 529	15 543 727	18 984 310	85 936 131	9 286 212	142 095 396	447 381 741
15-29	8 281 908	7 309 964	33 024 608	52 243 293	6 447 254	30 799 441	32 749 120	46 675 432	34 658 720	31 802 856	27 576 478	109 122 291	19 695 601	218 086 615	658 473 581
30-44	3 647 025	3 138 706	29 173 211	28 901 455	2 957 957	14 144 044	15 627 203	41 832 703	20 923 199	23 803 886	15 414 379	57 649 345	14 304 389	155 098 478	426 615 980
45-59	1 688 658	1 344 912	18 797 769	14 024 231	1 351 980	6 015 725	6 723 808	28 807 764	11 602 610	15 580 769	6 999 903	27 607 137	12 584 522	77 690 437	230 820 225
60-69	150 371	124 015	1 958 381	1 391 631	136 259	588 025	614 747	4 138 349	1 509 062	2 471 835	731 557	2 810 303	1 658 465	7 966 360	26 249 360
70-79	35 687	28 501	774 653	399 638	35 358	156 389	142 207	1 565 528	462 596	801 633	179 192	680 013	564 582	2 117 769	7 943 746
80+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	23 147 061	20 856 045	107 685 540	141 384 617	17 577 402	79 445 723	91 841 278	148 868 358	92 018 892	91 442 819	73 521 444	299 186 026	59 669 803	624 850 772	1 871 495 780

Table 4.19 Burden of disease due to sunburn (attributable BOD) DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.145	0.136	0.268	0.584	0.099	0.338	0.543	0.250	0.253	0.125	0.315	1.345	0.137	1.943	6.481
5-14	0.655	0.612	1.761	3.237	0.467	2.138	2.627	1.797	1.622	1.170	1.611	7.467	0.835	12.941	38.940
15-29	0.733	0.671	2.594	4.562	0.583	2.520	2.794	3.581	2.689	2.335	2.428	9.859	1.580	18.118	55.049
30-44	0.302	0.265	2.253	2.290	0.240	1.154	1.273	3.239	1.597	1.821	1.220	4.807	1.119	12.332	33.914
45-59	0.088	0.076	1.059	0.781	0.077	0.363	0.384	1.677	0.654	0.867	0.390	1.630	0.711	4.536	13.294
60-69	0.010	0.008	0.135	0.093	0.009	0.043	0.043	0.284	0.100	0.146	0.049	0.199	0.115	0.581	1.816
70-79	0.002	0.002	0.048	0.025	0.002	0.011	0.010	0.093	0.027	0.037	0.012	0.046	0.035	0.139	0.490
80+	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
TOTAL	1.936	1.770	8.120	11.573	1.478	6.566	7.674	10.922	6.943	6.500	6.024	25.354	4.533	50.591	149.984

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.142	0.134	0.256	0.561	0.096	0.323	0.519	0.236	0.243	0.119	0.303	1.267	0.130	1.759	6.090
5-14	0.643	0.610	1.681	3.125	0.451	2.047	2.519	1.703	1.558	1.124	1.558	6.988	0.794	11.728	36.530
15-29	0.725	0.672	2.505	4.524	0.577	2.417	2.624	3.412	2.586	2.286	2.369	9.106	1.515	17.032	52.350
30-44	0.305	0.266	2.215	2.374	0.251	1.045	1.189	3.162	1.587	1.860	1.231	4.446	1.103	11.734	32.767
45-59	0.092	0.081	1.084	0.837	0.081	0.319	0.383	1.687	0.679	0.995	0.414	1.558	0.716	4.269	13.196
60-69	0.012	0.010	0.149	0.108	0.010	0.042	0.046	0.315	0.118	0.211	0.056	0.208	0.125	0.571	1.981
70-79	0.003	0.002	0.064	0.033	0.003	0.012	0.011	0.133	0.040	0.079	0.014	0.052	0.047	0.167	0.659
80+	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
TOTAL	1.922	1.777	7.953	11.563	1.470	6.205	7.290	10.649	6.811	6.675	5.945	23.625	4.429	47.260	143.573

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.288	0.271	0.524	1.145	0.195	0.661	1.061	0.486	0.000	0.244	0.618	2.612	0.268	3.702	12.571
5-14	1.298	1.223	3.442	6.363	0.918	4.184	5.146	3.501	0.000	2.293	3.169	14.456	1.629	24.669	75.471
15-29	1.458	1.343	5.100	9.086	1.160	4.937	5.418	6.993	0.000	4.621	4.797	18.965	3.095	35.150	107.399
30-44	0.606	0.531	4.468	4.664	0.491	2.199	2.462	6.401	0.017	3.681	2.451	9.253	2.222	24.066	66.681
45-59	0.180	0.157	2.144	1.619	0.159	0.683	0.767	3.364	0.050	1.862	0.803	3.188	1.426	8.805	26.490
60-69	0.022	0.018	0.283	0.201	0.020	0.085	0.089	0.599	0.065	0.358	0.106	0.407	0.240	1.152	3.797
70-79	0.005	0.004	0.112	0.058	0.005	0.023	0.021	0.226	0.045	0.116	0.026	0.098	0.082	0.306	1.149
80+	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.032	0.000	0.000	0.000	0.000	0.000	0.000
TOTAL	3.857	3.547	16.073	23.136	2.948	12.771	14.964	21.571	13.754	13.176	11.969	48.979	8.962	97.851	293.557

4.6 Cortical cataract

Disease incidence

Early studies on cataract used a number of different definitions to define presence of cataract, making comparison of cataract rates in different locations very difficult. However, in later studies there is consistency in the definition of the various types of cataracts, which has led to reliable estimates from a number of parts of the world as to percentage of all cataracts that are cortical cataract, and cataract incidence, prevalence and progression.

While there does seem to be a latitudinal gradient in the proportion of all cataracts that are cortical, with higher proportions of cortical cataract at lower latitudes (*91-95*) the prevalence of cataract does not vary with latitude and, if there is any latitudinal variation, prevalence of cortical cataract increases with increasing latitude.

Population attributable fraction

Population attributable fractions were calculated from case-control studies for cortical cataract, and graphed against latitude (see cortical cataract workbook, Appendix 3). There was a non-significant latitudinal gradient ($p = 0.62$) with an intercept of 0.26, mean = 0.19. A PAF for UVR exposure causing cortical cataract of 0.2 was used in this assessment. This may be low due to recall inaccuracy as already noted, but reflects the efforts made in some cataract studies to accurately quantify the ocular UVR dose.

Disease model

Cataract per se attracts no disability weight – the disability results from loss of vision, from cataract surgery and from the increased mortality associated with visual impairment.

Few studies that have measured cortical cataract have also measured visual loss in those with cortical cataract. It does however, appear likely that cortical cataract is less likely to be associated with visual impairment than other forms of cataract, particularly mixed and nuclear cataract (*91, 96*). In addition, cortical cataract has a weaker relationship with mortality than other forms of cataract and is less likely to result in cataract surgery (*97, 98*).

The Barbados Eye Study (*91*) looking at visual impairment of greater than 20/40 due to cataract, found a prevalence of cortical cataract of 20.4%, over all age groups. In the Tibet Eye Study, also looking at visual impairment of greater than 20/40, a much higher proportion of cataracts were cortical, with little variation in different age groups – around 60% (*92*). In the POLA study, the proportion of those with cortical cataract who were visually impaired due to cataracts was 13-17% with little variation due to age (*94*).

For the purposes of this burden of disease study, the proportion of all cataracts causing visual loss that is due to cortical cataract is taken as 30% (average of above is 31%, range 13% to 60%). Cortical cataracts are likely to cause mild rather than moderate or severe visual loss and thus contribute less to the global burden of disease, based on disease severity, than other forms of cataract. However, mild visual loss is likely to be more prevalent than moderate or severe visual loss, and despite its lower severity, may thus contribute strongly to the total burden of disease due to cataract. We have therefore assumed that 25% of the total burden of disease due to cataract calculated by WHO for 2000 (*99*) is due to cortical cataract. The calculated PAF was applied to the resultant estimated burden of disease due to cortical cataract. Clearly this is only a rough approximation, and further work is needed in this area.

Table 4.20 summarizes the incidence of cataract globally; Table 4.21 summarizes the burden of disease due to all cataracts; Tables 4.22 and 4.23 summarize the burden of disease due to cortical cataract and the burden of disease due to cortical cataract that is attributable to UVR exposure.

Table 4.20 Incident cataracts 2000 (from GBD 2000, (99)) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	902	717	0	158	298	160	62	0	1	0	17	17	0	0	2 331
5-14	3 974	5 274	0	753	906	1 791	1 575	0	47	0	94	475	0	14	14 903
15-29	21 352	30 176	3	4 688	2 229	7 329	8 457	33	410	177	1,071	22 195	3	5 491	103 614
30-44	73 079	92 430	462	18 733	4 052	10 392	12 172	938	1 646	1 669	57 321	154 654	62	50 475	478 086
45-59	102 486	141 795	2 736	48 828	6 549	15 262	18 109	3 731	5 572	6 080	223 906	346 629	490	168 751	1 090 924
60-69	55 616	93 519	4 913	43 829	6 400	14 614	13 911	5 424	8 887	16 407	185 984	264 242	573	209 016	923 334
70-79	47 984	57 781	4 208	37 788	6 897	14 232	9 753	3 832	9 522	15 390	107 600	185 475	509	142 700	643 672
80+	21 988	17 566	3 418	20 343	3 444	7 594	4 395	1 797	4 200	5 121	39 458	76 967	266	39 472	246 029
TOTAL	327 380	439 260	15 740	175 120	30 776	71 375	68 433	15 755	30 285	44 844	615 450	1 050 653	1 904	615 918	3 502 893

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	277	139	0	7	202	350	835	5	0	0	6	8	0	0	1 830
5-14	1 416	1 132	0	40	690	2 709	2 616	26	0	2	59	74	1	13	8 777
15-29	25 441	19 238	21	709	2 122	9 350	8 407	199	8	19	1 255	24 748	9	1 121	92 648
30-44	83 281	115 153	875	8 251	5 922	8 370	14 266	2 131	424	1 036	51 378	202 143	80	34 837	528 147
45-59	112 447	210 370	3 878	67 924	9 574	18 677	21 597	4 709	7 095	5 682	261 318	472 273	534	196 400	1 392 478
60-69	90 460	149 902	5 309	73 539	7 979	19 833	16 225	6 027	13 086	13 001	279 070	356 219	707	240 608	1 271 965
70-79	74 803	96 158	5 792	61 497	11 055	19 894	12 725	5 378	15 879	26 587	167 921	272 985	743	183 990	955 407
80+	36 753	35 973	6 682	36 956	7 901	12 332	6 616	4 064	10 462	18 531	71 926	130 312	541	77 268	456 317
TOTAL	424 878	628 064	22 558	248 923	45 448	91 514	83 288	22 538	46 954	64 858	832 932	1 458 762	2 616	734 237	4 707 569

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	1 179	856	0	165	501	510	897	5	1	0	23	25	0	0	4 161
5-14	5 390	6 406	0	793	1 597	4 500	4 191	26	47	2	154	550	1	27	23 681
15-29	46 793	49 415	25	5 397	4 351	16 678	16 864	232	418	196	2 326	46 943	12	6 612	196 262
30-44	156 360	207 583	1 337	26 984	9 975	18 763	26 438	3 069	2 070	2 705	108 699	356 797	142	85 312	1 006 233
45-59	214 933	352 165	6 614	116 752	16 123	33 939	39 706	8 440	12 667	11 762	485 223	818 902	1 024	365 151	2 483 401
60-69	146 076	243 421	10 222	117 368	14 380	34 447	30 135	11 451	21 973	29 408	465 054	620 461	1 281	449 623	2 195 300
70-79	122 787	153 939	10 000	99 285	17 952	34 126	22 479	9 210	25 401	41 977	275 521	458 459	1 253	326 691	1 599 079
80+	58 741	53 539	10 099	57 299	11 346	19 926	11 011	5 860	14 662	23 652	111 384	207 279	807	116 739	702 346
TOTAL	752 258	1 067 324	38 297	424 042	76 223	162 889	151 721	38 293	77 239	109 702	1 448 383	2 509 415	4 520	1 350 155	8 210 462

Table 4.21 Burden of disease from cataract DALYs (000) (from GBD 2000, (99)) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	1.258	1.258
30-44	168.658	112.775	2.842	75.309	5.711	48.034	82.343	3.560	3.306	7.452	85.861	120.228	2.196	124.524	842.798
45-59	286.867	221.564	9.752	66.463	24.036	46.037	210.445	2.879	12.239	30.499	154.742	855.753	4.701	292.412	2 218.390
60-69	113.922	144.264	5.568	20.655	25.209	14.339	104.655	1.221	14.700	63.526	82.781	535.272	2.042	248.419	1 376.572
70-79	38.442	54.777	2.744	7.596	12.887	4.750	32.659	0.557	8.297	26.501	32.777	168.754	0.902	80.953	472.596
80+	5.457	7.881	0.596	1.259	2.129	0.602	4.666	0.123	1.288	2.683	5.322	27.020	0.163	10.209	69.398
TOTAL	613.345	541.261	21.502	171.282	69.972	113.762	434.768	8.341	39.830	130.662	361.483	1707.026	10.004	757.776	4 981.014

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
30-44	110.430	143.874	1.844	33.892	3.426	51.339	74.738	4.052	5.793	7.144	86.569	370.889	2.671	119.752	1 016.412
45-59	254.008	228.844	10.883	97.833	20.148	33.712	208.835	3.860	22.412	34.199	169.271	941.937	4.849	332.262	2 363.055
60-69	143.472	122.754	5.944	40.193	25.829	9.478	111.749	2.319	19.767	60.794	96.201	481.880	2.222	299.408	1 422.008
70-79	59.004	63.938	3.459	16.749	17.443	3.152	48.003	1.559	10.693	39.577	39.023	242.261	1.068	131.804	677.733
80+	10.034	13.673	1.040	3.074	3.735	0.452	7.364	0.565	2.050	6.607	7.149	44.090	0.361	24.382	124.578
TOTAL	576.948	573.083	23.169	191.741	70.580	98.133	450.690	12.356	60.715	148.321	398.213	2081.056	11.172	907.609	5 603.786

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	1.258	1.258
30-44	279.088	256.649	4.685	109.201	9.137	99.372	157.081	7.612	9.099	14.596	172.430	491.116	4.868	244.276	1 859.211
45-59	540.875	450.408	20.635	164.296	44.184	79.749	419.280	6.739	34.652	64.698	324.012	1 797.690	9.550	624.674	4 581.445
60-69	257.393	267.018	11.512	60.848	51.037	23.817	216.404	3.540	34.467	124.320	178.983	1 017.152	4.263	547.828	2 798.580
70-79	97.445	118.716	6.203	24.344	30.330	7.903	80.662	2.117	18.990	66.079	71.800	411.014	1.970	212.757	1 150.329
80+	15.491	21.554	1.636	4.333	5.864	1.055	12.031	0.689	3.337	9.290	12.471	71.110	0.525	34.592	193.976
TOTAL	1 190.292	1 114.344	44.671	363.022	140.552	211.895	885.458	20.697	100.545	278.983	759.696	3 788.082	21.176	1 665.385	10 584.799

Table 4.22 Burden of disease due to cortical cataract DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.315	0.315
30-44	42.164	28.194	0.710	18.827	1.428	12.008	20.586	0.890	0.827	1.863	21.465	30.057	0.549	31.131	210.700
45-59	71.717	55.391	2.438	16.616	6.009	11.509	52.611	0.720	3.060	7.625	38.685	213.938	1.175	73.103	554.598
60-69	28.480	36.066	1.392	5.164	6.302	3.585	26.164	0.305	3.675	15.882	20.695	133.818	0.510	62.105	344.143
70-79	9.610	13.694	0.686	1.899	3.222	1.188	8.165	0.139	2.074	6.625	8.194	42.188	0.226	20.238	118.149
80+	1.364	1.970	0.149	0.315	0.532	0.151	1.167	0.031	0.322	0.671	1.330	6.755	0.041	2.552	17.350
TOTAL	153.336	135.315	5.375	42.820	17.493	28.441	108.692	2.085	9.957	32.666	90.371	426.757	2.501	189.444	1245.253

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
30-44	27.608	35.969	0.461	8.473	0.856	12.835	18.685	1.013	1.448	1.786	21.642	92.722	0.668	29.938	254.103
45-59	63.502	57.211	2.721	24.458	5.037	8.428	52.209	0.965	5.603	8.550	42.318	235.484	1.212	83.066	590.764
60-69	35.868	30.688	1.486	10.048	6.457	2.369	27.937	0.580	4.942	15.198	24.050	120.470	0.555	74.852	355.502
70-79	14.751	15.985	0.865	4.187	4.361	0.788	12.001	0.390	2.673	9.894	9.756	60.565	0.267	32.951	169.433
80+	2.508	3.418	0.260	0.769	0.934	0.113	1.841	0.141	0.512	1.652	1.787	11.023	0.090	6.096	31.144
TOTAL	144.237	143.271	5.792	47.935	17.645	24.533	112.672	3.089	15.179	37.080	99.553	520.264	2.793	226.902	1 400.946

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.315	0.315
30-44	69.772	64.162	1.171	27.300	2.284	24.843	39.270	1.903	2.275	3.649	43.108	122.779	1.217	61.069	464.803
45-59	135.219	112.602	5.159	41.074	11.046	19.937	104.820	1.685	8.663	16.175	81.003	449.423	2.388	156.169	1 145.361
60-69	64.348	66.754	2.878	15.212	12.759	5.954	54.101	0.885	8.617	31.080	44.746	254.288	1.066	136.957	699.645
70-79	24.361	29.679	1.551	6.086	7.582	1.976	20.165	0.529	4.748	16.520	17.950	102.754	0.493	53.189	287.582
80+	3.873	5.389	0.409	1.083	1.466	0.264	3.008	0.172	0.834	2.322	3.118	17.778	0.131	8.648	48.494
TOTAL	297.573	278.586	11.168	90.756	35.138	52.974	221.364	5.174	25.136	69.746	189.924	947.021	5.294	416.346	2 646.200

Table 4.23 Disease burden from cataract attributable to UVR DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.063	0.063
30-44	8.433	5.639	0.142	3.765	0.286	2.402	4.117	0.178	0.165	0.373	4.293	6.011	0.110	6.226	42.140
45-59	14.343	11.078	0.488	3.323	1.202	2.302	10.522	0.144	0.612	1.525	7.737	42.788	0.235	14.621	110.920
60-69	5.696	7.213	0.278	1.033	1.260	0.717	5.233	0.061	0.735	3.176	4.139	26.764	0.102	12.421	68.829
70-79	1.922	2.739	0.137	0.380	0.644	0.238	1.633	0.028	0.415	1.325	1.639	8.438	0.045	4.048	23.630
80+	0.273	0.394	0.030	0.063	0.106	0.030	0.233	0.006	0.064	0.134	0.266	1.351	0.008	0.510	3.470
TOTAL	30.667	27.063	1.075	8.564	3.499	5.688	21.738	0.417	1.991	6.533	18.074	85.351	0.500	37.889	249.053

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
30-44	5.522	7.194	0.092	1.695	0.171	2.567	3.737	0.203	0.290	0.357	4.328	18.544	0.134	5.988	50.821
45-59	12.700	11.442	0.544	4.892	1.007	1.686	10.442	0.193	1.121	1.710	8.464	47.097	0.242	16.613	118.153
60-69	7.174	6.138	0.297	2.010	1.291	0.474	5.587	0.116	0.988	3.040	4.810	24.094	0.111	14.970	71.100
70-79	2.950	3.197	0.173	0.837	0.872	0.158	2.400	0.078	0.535	1.979	1.951	12.113	0.053	6.590	33.887
80+	0.502	0.684	0.052	0.154	0.187	0.023	0.368	0.028	0.102	0.330	0.357	2.205	0.018	1.219	6.229
TOTAL	28.847	28.654	1.158	9.587	3.529	4.907	22.534	0.618	3.036	7.416	19.911	104.053	0.559	45.380	280.189

TOTAL

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.063	0.063
30-44	13.954	12.832	0.234	5.460	0.457	4.969	7.854	0.381	0.455	0.730	8.622	24.556	0.243	12.214	92.961
45-59	27.044	22.520	1.032	8.215	2.209	3.987	20.964	0.337	1.733	3.235	16.201	89.885	0.478	31.234	229.072
60-69	12.870	13.351	0.576	3.042	2.552	1.191	10.820	0.177	1.723	6.216	8.949	50.858	0.213	27.391	139.929
70-79	4.872	5.936	0.310	1.217	1.516	0.395	4.033	0.106	0.950	3.304	3.590	20.551	0.099	10.638	57.516
80+	0.775	1.078	0.082	0.217	0.293	0.053	0.602	0.034	0.167	0.464	0.624	3.556	0.026	1.730	9.699
TOTAL	59.515	55.717	2.234	18.151	7.028	10.595	44.273	1.035	5.027	13.949	37.985	189.404	1.059	83.269	529.242

4.7 Pterygium

Disease incidence

There are moderately good descriptive data on incidence and prevalence of pterygium worldwide (*100, 101*). However, there is a large discrepancy in the prevalence of pterygium within a small area, depending on whether one looks at urban or rural populations. Thus, in the Melbourne Visual Impairment project (*102*) the prevalence of pterygium in males, 80-89 years who lived in an urban area was 1.79%, while in those in a rural area it was 31.3%.

Despite Cameron's work on the distribution of pterygium worldwide, initial inspection of prevalence rates by latitude shows a wide range of rates at similar latitudes, with no clear latitudinal gradient and no clear racial differences. However, closer review of the prevalence rates reveals that some of the rates are for total population prevalence, while some are prevalence rates only in older age groups. For example, Wong et al (*103*) cite a prevalence of 6.9% in the Chinese population of Singapore aged 40 or older, Panchapakesan et al (*104*) a rate of 7.3% in the Blue Mountains, NSW population over the age of 49 years and Taylor et al (*105*) a rate of 44% in Aborigines over the age of 30 years in Northwestern Australia.

In order to develop a global distribution of prevalence for pterygium, prevalence rates using only parts of the population were adjusted to the total population using the World Standard Population (*106*) to derive the approximate age-standardised summary prevalence. Prevalence data from within each latitude band were then averaged to provide the representative age-standardised prevalence for each latitude band. Using this as a summary prevalence for the latitude band, and the age and sex distribution outlined in the literature (*102-104, 107*), a theoretical distribution of global pterygium prevalence was developed by back-calculating from the summary prevalence to give age and sex-specific prevalence data for each latitude band.

Population attributable fraction

Case-control studies were examined to calculate the population attributable fraction due to UVR exposure. Unfortunately, a number of these studies failed to measure confounding factors, particularly exposure to particulate matter. Also, Threlfall et al (*108*) showed that there is a difference in the PAF if different methods of sun exposure are used. There is little latitudinal gradient in the PAF for pterygium ($p = 0.35$) with an intercept of 0.33 and mean of 0.42 in studies using averaged annular ocular dose. Using daily ocular dose as the exposure measure (*108*), the PAF is 0.74. These two PAFs were used as the upper (0.74) and lower (0.42) estimates of PAF and were applied to the calculated disease burden due to pterygium. (See Appendix 3)

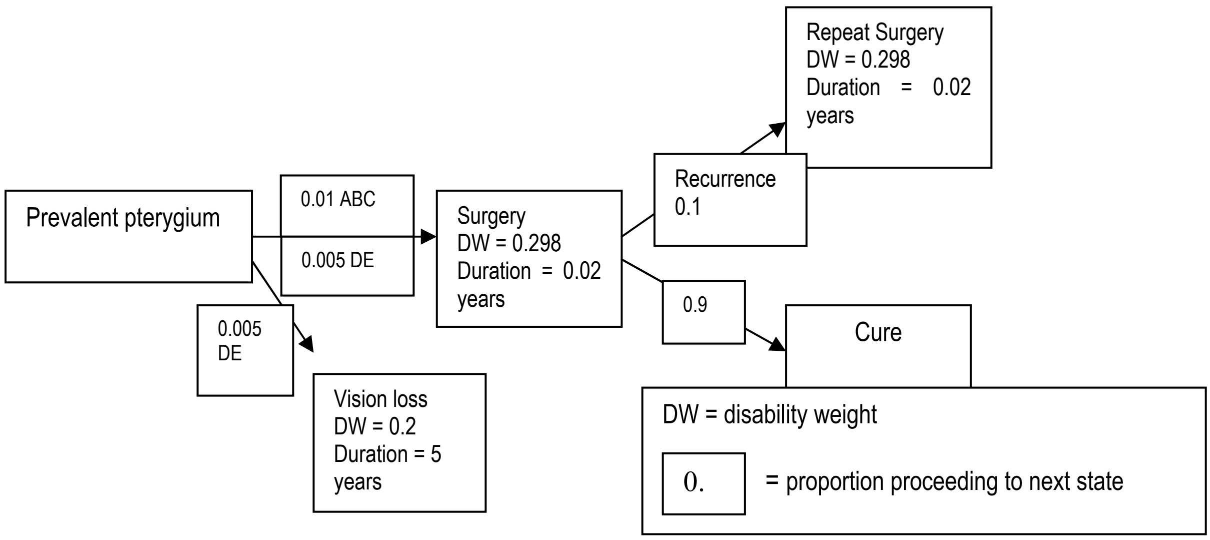
Disease model

Pterygium per se attracts no disability weight, as there is usually no associated vision loss. Only a small proportion of all pterygia are operated on in developed countries and this is likely to be less in under-developed countries. However, the incidence of operations for pterygia may have less to do with the prevalence of pterygia than with the level of ophthalmological service to the area. For example, Wlodarczyk et al have examined the cost of pterygia in Australia (*109*). The lowest rate of pterygium removal is in the Northern Territory and the highest in Queensland – yet these states have similar latitude. This could be explained if the two states had a greatly different age structure (since prevalence of pterygium increases with age) or some other risk factor for pterygium. A more likely explanation is that the Northern Territory has lower access to specialist ophthalmological services.

We have assumed a 1% surgical removal rate for ABC regions (see disease model, Figure 4.5), based on published rates of surgery (*100, 104, 109*). Pterygium surgery is performed in developing countries, probably less for cosmetic reasons and more to avoid loss of vision. In

Nigeria, Ashaye cites pterygium surgery as making up 20% of all ocular surgery (*110*). We have therefore assigned a removal rate of 0.5% of all pterygia, for DE countries (less commonly performed than in ABC countries). However, it is likely that there is a higher prevalence of visual loss due to pterygium in these countries, so that the remaining 0.5% (who are not operated on compared to ABC countries) have a disability related to visual loss.

Figure 4.5 Disease model for pterygium



The results of the burden of disease assessment are presented in Tables 4.24 – 4.26.

Table 4.24 Prevalence (persons) of pterygium 2000 by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	166 775	277 920	0	88 990	37 287	7 778	21 707	0	0	0	338 938	72 154	4048	141 723	1 157 320
30-44	1 046 540	1 206 552	1 262 990	1 884 396	285 661	677 931	1 198 860	1 117 598	673 790	402 307	1 546 098	5 328 353	593 128	7 407 246	24 631 450
45-59	2 557 073	2 851 386	3 613 688	4 992 224	753 454	1 714 730	2 706 458	2 958 852	1 432 635	924 702	4 001 299	14 300 823	2 505 757	19 003 819	64 316 900
60-69	1 266 727	1 322 600	1 651 047	2 337 530	400 988	758 656	1 125 710	1 969 401	819 261	701 121	2 146 159	6 968 459	1 423 699	8 763 120	31 654 478
70-79	698 769	726 873	1 742 730	1 609 457	244 151	505 625	698 007	1 934 711	634 107	537 795	1 236 981	4 236 987	1 287 415	5 953 637	22 047 245
80+	146 670	143 065	664 329	444 966	63 866	116 148	158 637	573 809	119 248	84 945	277 535	975 147	408 847	1 168 147	5 345 359
TOTAL	5 882 553	6 528 396	8 934 784	11 357 564	1 785 407	3 780 870	5 909 378	8 554 371	3 679 041	2 650 870	9 547 009	31 881 922	6 222 894	42 437 691	149 152 750

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30-44	534 960	606 786	620 838	979 132	149 631	302 862	559 867	547 290	335 248	205 658	780 817	2 463 047	292 325	3 539 688	11 918 149
45-59	1 368 422	1 520 004	1 898 051	2 690 857	400 315	737 092	1 369 153	1521 881	749 516	537 433	2 128 309	6 873 442	1 303 406	9 249 303	32 347 184
60-69	727 564	772 807	914 133	1 343 395	219 829	368 128	600 659	1103 006	474 894	499 946	1 221 654	3 647 272	770 385	4 383 827	17 047 499
70-79	430 750	471 567	1 145 070	1 036 393	144 598	263 593	400 221	1382 035	454 192	574 416	744 232	2 372 159	851 953	3 624 001	13 895 180
80+	99 679	116 878	648 823	345 616	43 710	66 253	89 280	625 170	115 772	149 481	196 539	603 814	418 396	1 087 915	4 607 326
TOTAL	3 161 375	3 488 042	5 226 915	6 395 393	958 084	1 737 928	3 019 180	5 179 382	2 129 621	1 966 935	5 071 551	15 959 735	3 636 465	21 884 733	79 815 339

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15-29	166 775	277 920	0	88 990	37 287	7 778	21 707	0	0	0	338 938	72 154	4 048	141 723	1 157 320
30-44	1 581 500	1 813 338	1 883 828	2 863 528	435 292	980 794	1 758 727	1 664 888	1 009 038	607 964	2 326 915	7 791 400	885 453	10 946 933	36 549 598
45-59	3 925 495	4 371 390	5 511 739	7 683 081	1 153 770	2 451 822	4 075 611	4 480 733	2 182 150	1 462 136	6 129 607	21 174 265	3 809 163	28 253 122	96 664 084
60-69	1 994 291	2 095 407	2 565 180	3 680 925	620 817	1 126 785	1 726 369	3 072 408	1 294 156	1 201 066	3 367 813	10 615 731	2 194 083	13 146 946	48 701 977
70-79	1 129 519	1 198 441	2 887 800	2 645 851	388 749	769 218	1 098 228	3 316 745	1 088 298	1 112 211	1 981 213	6 609 146	2 139 369	9 577 637	35 942 425
80+	246 349	259 943	1 313 152	790 582	107 576	182 401	247 916	1 198 979	235 020	234 427	474 074	1 578 962	827 243	2 256 061	9 952 685
TOTAL	9 043 929	10 016 438	14 161 699	17 752 957	2 743 491	5 518 798	8 928 558	13 733 752	5 808 662	4 617 805	14 618 560	47 841 657	9 859 359	64 322 423	228 968 088

Table 4.25 Burden of disease from pterygium DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.081	0.135	0.000	0.004	0.018	0.000	0.011	0.000	0.000	0.000	0.014	0.035	0.000	0.006	0.304
30-44	0.520	0.595	0.053	0.079	0.142	0.028	0.605	0.047	0.028	0.017	0.065	2.691	0.025	0.310	5.204
45-59	1.270	1.407	0.151	0.209	0.375	0.072	1.367	0.124	0.060	0.039	0.167	7.222	0.105	0.794	13.359
60-69	0.629	0.652	0.069	0.098	0.199	0.032	0.568	0.082	0.034	0.029	0.090	3.519	0.059	0.366	6.427
70-79	0.347	0.358	0.073	0.067	0.121	0.021	0.352	0.081	0.026	0.022	0.052	2.140	0.054	0.249	3.964
80+	0.073	0.070	0.028	0.019	0.032	0.005	0.080	0.024	0.005	0.004	0.012	0.492	0.017	0.049	0.909
TOTAL	2.919	3.218	0.373	0.475	0.887	0.158	2.983	0.357	0.154	0.111	0.399	16.099	0.260	1.773	30.167

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
30-44	0.268	0.300	0.040	0.045	0.074	0.013	0.293	0.027	0.019	0.009	0.033	1.253	0.022	0.238	2.635
45-59	0.684	0.752	0.127	0.126	0.199	0.031	0.715	0.078	0.043	0.022	0.089	3.493	0.102	0.617	7.078
60-69	0.363	0.382	0.060	0.063	0.109	0.015	0.313	0.056	0.026	0.021	0.051	1.852	0.061	0.289	3.662
70-79	0.215	0.233	0.077	0.051	0.072	0.011	0.209	0.070	0.024	0.024	0.031	1.206	0.067	0.244	2.535
80+	0.050	0.058	0.044	0.017	0.022	0.003	0.047	0.032	0.006	0.006	0.008	0.307	0.033	0.073	0.706
TOTAL	1.580	1.725	0.348	0.302	0.476	0.073	1.578	0.263	0.118	0.082	0.212	8.111	0.286	1.461	16.615

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.081	0.135	0.000	0.004	0.018	0.000	0.011	0.000	0.000	0.000	0.014	0.035	0.000	0.006	0.304
30-44	0.788	0.895	0.093	0.124	0.216	0.041	0.899	0.074	0.047	0.025	0.097	3.944	0.047	0.548	7.839
45-59	1.953	2.159	0.278	0.334	0.574	0.102	2.082	0.202	0.103	0.061	0.256	10.715	0.207	1.411	20.437
60-69	0.992	1.034	0.129	0.161	0.309	0.047	0.881	0.138	0.060	0.050	0.141	5.371	0.120	0.655	10.088
70-79	0.563	0.592	0.149	0.118	0.193	0.032	0.562	0.151	0.051	0.046	0.083	3.346	0.121	0.493	6.499
80+	0.123	0.128	0.072	0.036	0.053	0.008	0.127	0.056	0.011	0.010	0.020	0.800	0.050	0.122	1.615
TOTAL	4.499	4.943	0.721	0.776	1.364	0.231	4.562	0.620	0.272	0.193	0.611	24.210	0.546	3.235	46.783

Table 4.26 Disease burden from pterygium attributable to UVR DALYs (000) – upper estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.060	0.100	0.000	0.003	0.013	0.000	0.008	0.000	0.000	0.000	0.010	0.026	0.000	0.004	0.225
30-44	0.385	0.440	0.039	0.058	0.105	0.021	0.448	0.035	0.021	0.012	0.048	1.991	0.018	0.229	3.851
45-59	0.939	1.041	0.112	0.154	0.277	0.053	1.011	0.091	0.044	0.029	0.124	5.344	0.077	0.588	9.886
60-69	0.465	0.483	0.051	0.072	0.148	0.023	0.420	0.061	0.025	0.022	0.066	2.604	0.044	0.271	4.756
70-79	0.257	0.265	0.054	0.050	0.090	0.016	0.261	0.060	0.020	0.017	0.038	1.583	0.040	0.184	2.934
80+	0.054	0.052	0.021	0.014	0.023	0.004	0.059	0.018	0.004	0.003	0.009	0.364	0.013	0.036	0.673
TOTAL	2.160	2.382	0.276	0.351	0.657	0.117	2.208	0.265	0.114	0.082	0.295	11.913	0.192	1.312	22.325

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
30-44	0.198	0.222	0.030	0.034	0.055	0.009	0.217	0.020	0.014	0.006	0.024	0.927	0.017	0.176	1.950
45-59	0.506	0.556	0.094	0.093	0.147	0.023	0.529	0.058	0.032	0.017	0.066	2.585	0.075	0.457	5.238
60-69	0.269	0.283	0.045	0.047	0.081	0.011	0.232	0.041	0.019	0.015	0.038	1.370	0.045	0.214	2.710
70-79	0.159	0.173	0.057	0.037	0.053	0.008	0.155	0.052	0.018	0.018	0.023	0.892	0.050	0.181	1.876
80+	0.037	0.043	0.032	0.013	0.016	0.002	0.035	0.023	0.005	0.005	0.006	0.227	0.025	0.054	0.522
TOTAL	1.169	1.276	0.257	0.223	0.353	0.054	1.168	0.194	0.088	0.061	0.157	6.002	0.211	1.081	12.296

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.060	0.100	0.000	0.003	0.013	0.000	0.008	0.000	0.000	0.000	0.010	0.026	0.000	0.004	0.225
30-44	0.583	0.663	0.069	0.092	0.160	0.030	0.665	0.055	0.035	0.019	0.072	2.919	0.035	0.405	5.801
45-59	1.445	1.598	0.206	0.247	0.424	0.076	1.541	0.149	0.076	0.045	0.190	7.929	0.153	1.044	15.124
60-69	0.734	0.765	0.096	0.119	0.229	0.035	0.652	0.102	0.045	0.037	0.104	3.974	0.089	0.485	7.465
70-79	0.416	0.438	0.111	0.087	0.143	0.024	0.416	0.112	0.038	0.034	0.061	2.476	0.090	0.365	4.810
80+	0.091	0.095	0.053	0.026	0.040	0.006	0.094	0.041	0.008	0.007	0.015	0.592	0.037	0.090	1.195
TOTAL	3.329	3.658	0.534	0.575	1.009	0.171	3.376	0.459	0.201	0.143	0.452	17.916	0.404	2.394	34.621

Table 4.27 Disease burden from pterygium attributable to UVR DALYs (000) – lower estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.034	0.057	0.000	0.002	0.008	0.000	0.004	0.000	0.000	0.000	0.006	0.015	0.000	0.002	0.128
30-44	0.218	0.250	0.022	0.033	0.060	0.012	0.254	0.020	0.012	0.007	0.027	1.130	0.010	0.130	2.186
45-59	0.533	0.591	0.063	0.088	0.157	0.030	0.574	0.052	0.025	0.016	0.070	3.033	0.044	0.334	5.611
60-69	0.264	0.274	0.029	0.041	0.084	0.013	0.239	0.035	0.014	0.012	0.038	1.478	0.025	0.154	2.699
70-79	0.146	0.151	0.031	0.028	0.051	0.009	0.148	0.034	0.011	0.009	0.022	0.899	0.023	0.104	1.665
80+	0.031	0.030	0.012	0.008	0.013	0.002	0.034	0.010	0.002	0.001	0.005	0.207	0.007	0.021	0.382
TOTAL	1.226	1.352	0.157	0.199	0.373	0.066	1.253	0.150	0.065	0.047	0.168	6.762	0.109	0.745	12.670

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
30-44	0.112	0.126	0.017	0.019	0.031	0.005	0.123	0.011	0.008	0.004	0.014	0.526	0.009	0.100	1.107
45-59	0.287	0.316	0.053	0.053	0.084	0.013	0.301	0.033	0.018	0.009	0.037	1.467	0.043	0.259	2.973
60-69	0.153	0.160	0.025	0.026	0.046	0.006	0.132	0.023	0.011	0.009	0.021	0.778	0.025	0.121	1.538
70-79	0.091	0.098	0.032	0.021	0.030	0.005	0.088	0.029	0.010	0.010	0.013	0.507	0.028	0.102	1.065
80+	0.021	0.024	0.018	0.007	0.009	0.001	0.020	0.013	0.003	0.003	0.003	0.129	0.014	0.031	0.296
TOTAL	0.664	0.724	0.146	0.127	0.200	0.031	0.663	0.110	0.050	0.035	0.089	3.407	0.120	0.614	6.979

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
15-29	0.034	0.057	0.000	0.002	0.008	0.000	0.004	0.000	0.000	0.000	0.006	0.015	0.000	0.002	0.128
30-44	0.331	0.376	0.039	0.052	0.091	0.017	0.378	0.031	0.020	0.011	0.041	1.656	0.020	0.230	3.292
45-59	0.820	0.907	0.117	0.140	0.241	0.043	0.874	0.085	0.043	0.026	0.108	4.500	0.087	0.593	8.584
60-69	0.417	0.434	0.054	0.068	0.130	0.020	0.370	0.058	0.025	0.021	0.059	2.256	0.050	0.275	4.237
70-79	0.236	0.248	0.063	0.050	0.081	0.014	0.236	0.063	0.021	0.020	0.035	1.405	0.051	0.207	2.730
80+	0.052	0.054	0.030	0.015	0.022	0.003	0.053	0.023	0.005	0.004	0.008	0.336	0.021	0.051	0.678
TOTAL	1.890	2.076	0.303	0.326	0.573	0.097	1.916	0.260	0.114	0.081	0.257	10.168	0.229	1.359	19.650

4.8 Carcinoma of the cornea and conjunctiva

Disease incidence

Age-standardized incidence rates for eye cancers are available for a number of countries (*30*). In addition, the proportion of eye cancers that are histologically proven SCCC is given. Using this information it is possible to obtain approximate age-standardized incidence rates for SCCC globally. Using the literature to establish an age breakdown of the disease (*111, 112*), and using the Segi World Standard Population (*106*), age-specific incidence rates were back calculated (using an Excel spreadsheet and repeated iterations of possible values, to achieve age-specific incidence rates that were compatible with both the final age-standardized rate and the population distribution of the disease in that region).

It is clear that this is predominantly a rare disease of the elderly, except in sub-Saharan Africa, where the mean age at presentation is 35 years (compared to 60.4 years in Mexico City) (*112, 113*). For this reason, the same male to female ratios and age distribution of disease were applied to all regions, except AFR E for which a younger age distribution was applied.

Population attributable fraction

Squamous cell carcinomas of the cornea and conjunctiva (SCCC) are rare tumours, particularly in white populations. There appears to be a continuum from simple dysplasia to carcinoma in situ to invasive squamous cell carcinoma involving the conjunctiva as well as the cornea (*114*).

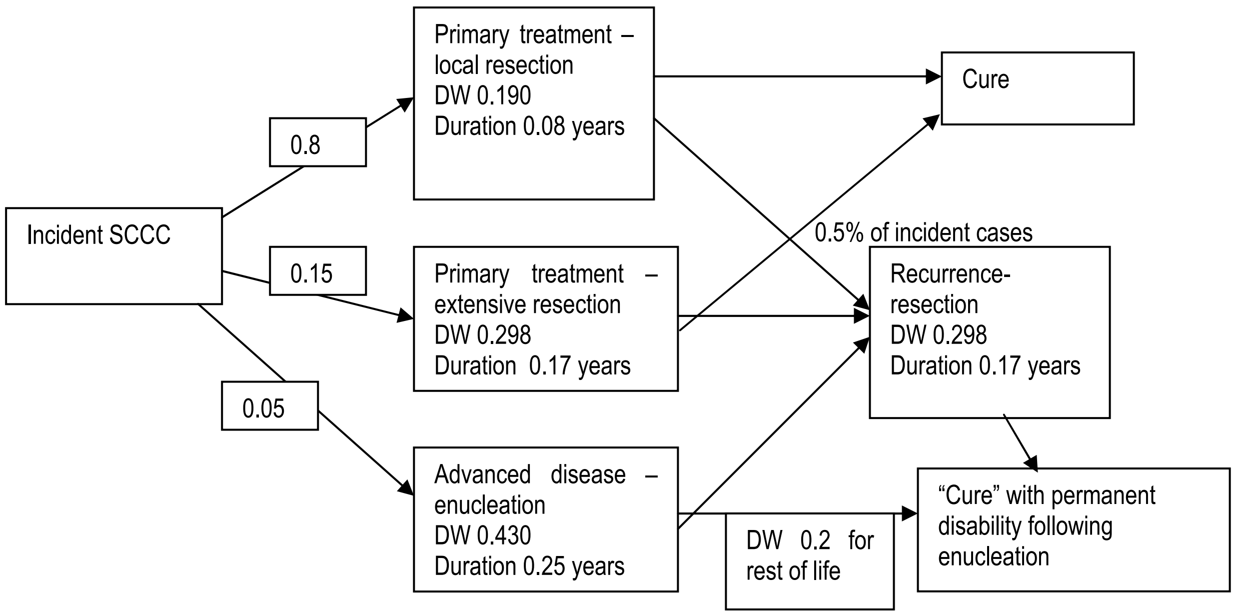
The incidence of this tumour has greatly increased in recent years associated with HIV infection. The proportion of SCCC that is attributable to AIDS (PAF for AIDS for SCCC) has been calculated to be 0.66 (*112*). Sun (*115*) found links between SCCC and ultraviolet radiation exposure of a similar magnitude to SCC of the eyelid. The PAF calculated from the single relevant study by Lee et al (using as a UV exposure measure cumulative exposure at ≤ 30° latitude for ≥ 50 years), was 0.62, based on an odds ratio of 3.9 (1.0-14.8) (*114*). We have used the same PAF as for SCC in lightly pigmented populations (lower estimate 0.5, upper estimate 0.7), and applied this to all pigment groups. This assumes that the protective effect of pigmentation present for SCC of the skin is not present when considering disease of the cornea and conjunctiva.

Disease model

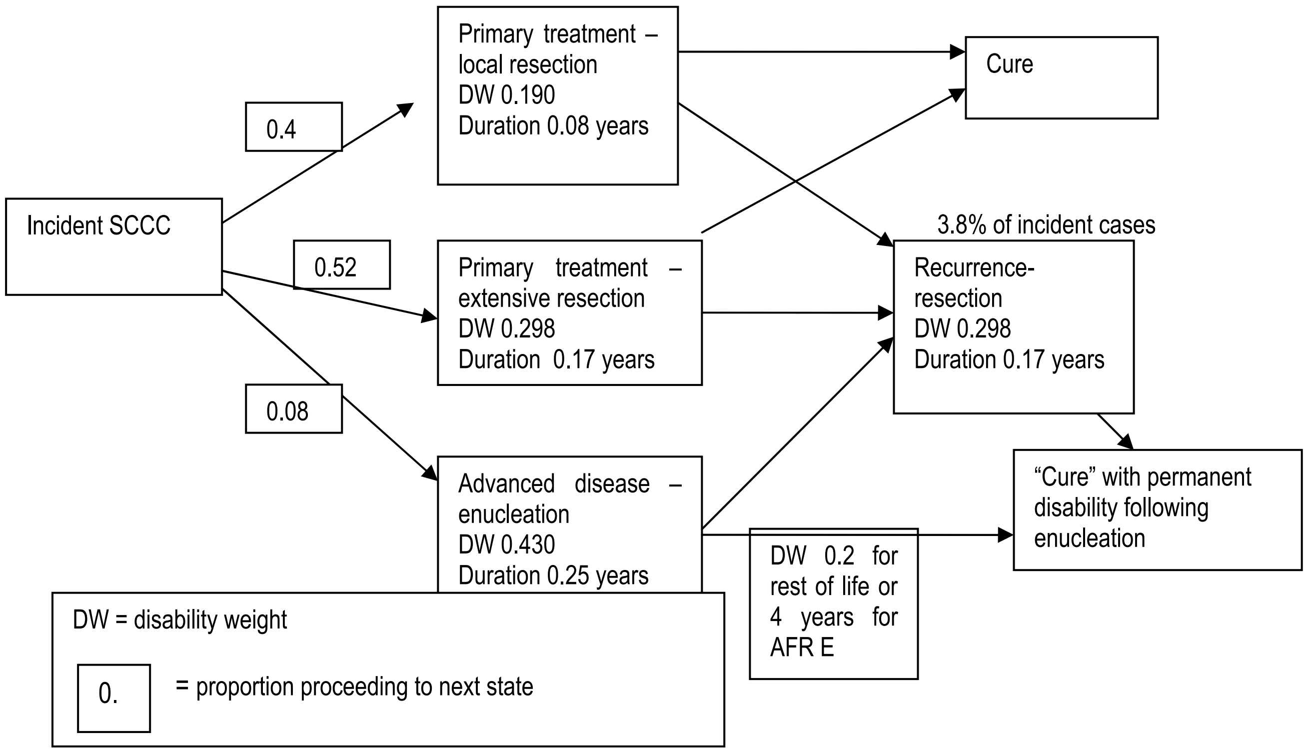
There appears to be no mortality associated with SCCC itself. Treatment is by local resection for localized disease; more extensive resection or enucleation is performed for more extensive disease.

The flow chart of the disease history is outlined in Figure 4.6.

Figure 4.6 Disease model for SCCC - ABC regions



Disease model of SCCC for DE regions



The results of the burden of disease assessment for SCCC for the year 2000 are presented in Tables 4.28 to 4.31.

Table 4.28 Incident cases of SCCC (2000)
by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	2	341	0	4	1	0	1	0	0	0	3	6	0	3	361
15-29	10	1 209	6	35	7	9	18	4	4	1	29	92	5	72	1 501
30-44	46	976	30	106	17	24	51	22	15	8	100	281	20	276	1 972
45-59	60	325	69	153	24	40	71	47	25	14	132	412	65	502	1 939
60-69	30	65	41	73	12	19	34	44	20	14	65	210	43	268	938
70-79	16	17	38	48	7	12	18	38	13	10	39	110	33	169	568
80+	5	5	21	17	2	4	5	21	4	3	11	34	14	43	189
TOTAL	170	2 937	206	436	70	107	197	176	81	50	378	1 144	181	1 332	7 465

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	2	282	0	2	1	0	1	0	0	0	3	5	0	2	298
15-29	10	555	4	27	6	6	10	3	3	1	24	51	3	52	755
30-44	25	498	21	78	14	16	30	15	10	6	90	132	15	202	1 152
45-59	48	219	54	124	19	25	56	35	19	12	118	273	49	364	1 415
60-69	23	56	39	65	10	16	29	42	19	18	63	154	42	226	802
70-79	14	15	43	48	7	11	18	47	16	18	41	93	40	166	577
80+	4	5	34	20	3	3	5	38	7	11	14	29	24	62	259
TOTAL	126	1 630	196	363	58	77	148	179	74	65	353	738	174	1 075	5 256

BOTHSEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	3	623	0	6	2	0	2	0	0	0	6	11	0	4	657
15-29	20	1764	10	62	12	15	27	7	8	2	54	143	9	125	2 258
30-44	71	1473	51	184	31	40	80	37	25	14	190	414	36	478	3 124
45-59	108	543	123	277	43	65	127	82	44	26	249	685	114	866	3 352
60-69	53	121	80	137	22	34	63	87	39	32	128	364	85	493	1 738
70-79	31	32	82	95	14	23	36	85	29	28	80	203	74	334	1 146
80+	9	10	55	37	5	7	10	58	11	14	25	63	38	106	448
TOTAL	297	4 567	402	799	129	184	345	355	155	115	731	1 883	355	2 407	12 724

Table 4.29 Burden of disease from SCCC DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0
5-14	0.001	0.035	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.001	0.003	0.000	0.001	0.044
15-29	0.005	0.123	0.002	0.010	0.003	0.003	0.009	0.001	0.001	0.000	0.009	0.044	0.002	0.022	0.234
30-44	0.020	0.099	0.008	0.028	0.007	0.006	0.022	0.006	0.004	0.002	0.027	0.121	0.005	0.074	0.429
45-59	0.021	0.033	0.015	0.033	0.008	0.009	0.025	0.010	0.005	0.003	0.029	0.143	0.014	0.109	0.457
60-69	0.008	0.007	0.007	0.012	0.003	0.003	0.009	0.007	0.003	0.002	0.010	0.054	0.007	0.043	0.175
70-79	0.003	0.002	0.004	0.005	0.001	0.001	0.003	0.004	0.001	0.001	0.004	0.020	0.004	0.019	0.072
80+	0.001	0.001	0.002	0.001	0.000	0.000	0.001	0.002	0.000	0.000	0.001	0.004	0.001	0.003	0.017
TOTAL	0.058	0.299	0.037	0.092	0.024	0.022	0.068	0.030	0.016	0.009	0.081	0.390	0.033	0.270	1.428

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0
5-14	0.001	0.029	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.003	0.000	0.001	0.036
15-29	0.005	0.056	0.001	0.008	0.003	0.002	0.005	0.001	0.001	0.000	0.007	0.025	0.001	0.016	0.131
30-44	0.011	0.051	0.006	0.021	0.006	0.004	0.013	0.004	0.003	0.002	0.025	0.058	0.004	0.055	0.263
45-59	0.018	0.022	0.012	0.028	0.007	0.006	0.021	0.008	0.004	0.003	0.027	0.100	0.011	0.084	0.351
60-69	0.007	0.006	0.007	0.011	0.003	0.003	0.008	0.008	0.003	0.003	0.011	0.044	0.007	0.040	0.161
70-79	0.003	0.002	0.006	0.006	0.001	0.001	0.004	0.006	0.002	0.002	0.005	0.019	0.005	0.021	0.083
80+	0.001	0.001	0.003	0.002	0.000	0.000	0.001	0.003	0.001	0.001	0.001	0.004	0.002	0.005	0.025
TOTAL	0.044	0.166	0.035	0.078	0.021	0.016	0.051	0.029	0.014	0.011	0.078	0.253	0.031	0.222	1.049

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0
5-14	0.002	0.063	0.000	0.002	0.001	0.000	0.001	0.000	0.000	0.000	0.002	0.005	0.000	0.001	0.077
15-29	0.010	0.180	0.003	0.019	0.006	0.004	0.013	0.002	0.002	0.001	0.016	0.069	0.003	0.038	0.366
30-44	0.031	0.150	0.014	0.050	0.013	0.011	0.035	0.010	0.007	0.004	0.051	0.179	0.010	0.129	0.694
45-59	0.039	0.055	0.027	0.062	0.015	0.014	0.045	0.018	0.010	0.006	0.056	0.244	0.025	0.192	0.808
60-69	0.014	0.012	0.014	0.023	0.006	0.006	0.017	0.015	0.007	0.005	0.022	0.099	0.014	0.083	0.337
70-79	0.006	0.003	0.010	0.012	0.003	0.003	0.007	0.010	0.003	0.003	0.010	0.039	0.009	0.040	0.158
80+	0.001	0.001	0.004	0.003	0.001	0.001	0.001	0.005	0.001	0.001	0.002	0.008	0.003	0.008	0.04
TOTAL	0.103	0.465	0.072	0.169	0.045	0.039	0.119	0.060	0.030	0.020	0.158	0.643	0.064	0.492	2.478

Table 4.30 Disease burden from SCCC attributable to UVR DALYs (000) – upper estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.001	0.025	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.001	0.002	0.000	0.001	0.031
15-29	0.004	0.086	0.001	0.007	0.002	0.002	0.006	0.001	0.001	0.000	0.006	0.031	0.001	0.015	0.164
30-44	0.014	0.069	0.006	0.020	0.005	0.004	0.015	0.004	0.003	0.001	0.019	0.085	0.004	0.052	0.300
45-59	0.015	0.023	0.011	0.023	0.006	0.006	0.018	0.007	0.004	0.002	0.020	0.100	0.010	0.076	0.320
60-69	0.006	0.005	0.005	0.008	0.002	0.002	0.006	0.005	0.002	0.001	0.007	0.038	0.005	0.030	0.123
70-79	0.002	0.001	0.003	0.004	0.001	0.001	0.002	0.003	0.001	0.001	0.003	0.014	0.003	0.013	0.050
80+	0.001	0.001	0.001	0.001	0.000	0.000	0.001	0.001	0.000	0.000	0.001	0.003	0.001	0.002	0.012
TOTAL	0.041	0.209	0.026	0.064	0.017	0.015	0.048	0.021	0.011	0.006	0.057	0.273	0.023	0.189	1.000

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.001	0.020	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.002	0.000	0.001	0.025
15-29	0.004	0.039	0.001	0.006	0.002	0.001	0.004	0.001	0.001	0.000	0.005	0.018	0.001	0.011	0.092
30-44	0.008	0.036	0.004	0.015	0.004	0.003	0.009	0.003	0.002	0.001	0.018	0.041	0.003	0.039	0.184
45-59	0.013	0.015	0.008	0.020	0.005	0.004	0.015	0.006	0.003	0.002	0.019	0.070	0.008	0.059	0.246
60-69	0.005	0.004	0.005	0.008	0.002	0.002	0.006	0.006	0.002	0.002	0.008	0.031	0.005	0.028	0.113
70-79	0.002	0.001	0.004	0.004	0.001	0.001	0.003	0.004	0.001	0.001	0.004	0.013	0.004	0.015	0.058
80+	0.001	0.001	0.002	0.001	0.000	0.000	0.001	0.002	0.001	0.001	0.001	0.003	0.001	0.004	0.018
TOTAL	0.031	0.116	0.025	0.055	0.015	0.011	0.036	0.020	0.010	0.008	0.055	0.177	0.022	0.155	0.735

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.001	0.045	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.001	0.004	0.000	0.001	0.056
15-29	0.007	0.125	0.002	0.013	0.004	0.004	0.010	0.001	0.001	0.000	0.011	0.048	0.002	0.027	0.256
30-44	0.022	0.105	0.010	0.034	0.009	0.007	0.025	0.007	0.005	0.003	0.036	0.125	0.006	0.090	0.484
45-59	0.027	0.039	0.019	0.043	0.011	0.011	0.032	0.013	0.006	0.004	0.039	0.170	0.018	0.135	0.566
60-69	0.011	0.009	0.010	0.016	0.004	0.004	0.012	0.011	0.004	0.004	0.015	0.069	0.010	0.058	0.235
70-79	0.004	0.003	0.007	0.008	0.001	0.001	0.005	0.007	0.002	0.002	0.006	0.027	0.006	0.028	0.109
80+	0.001	0.001	0.004	0.002	0.000	0.000	0.001	0.004	0.001	0.001	0.001	0.006	0.002	0.006	0.029
TOTAL	0.071	0.326	0.050	0.119	0.032	0.027	0.083	0.041	0.021	0.014	0.111	0.450	0.045	0.344	1.736

Table 4.31 Disease burden from SCCC attributable to UVR DALYs (000) – lower estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.001	0.018	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.001	0.002	0.000	0.001	0.022
15-29	0.003	0.062	0.001	0.005	0.002	0.002	0.005	0.001	0.001	0.000	0.005	0.022	0.001	0.011	0.117
30-44	0.010	0.050	0.004	0.014	0.004	0.003	0.011	0.003	0.002	0.001	0.014	0.061	0.003	0.037	0.215
45-59	0.011	0.017	0.008	0.017	0.004	0.005	0.013	0.005	0.003	0.002	0.015	0.072	0.007	0.055	0.229
60-69	0.004	0.004	0.004	0.006	0.002	0.002	0.005	0.004	0.002	0.001	0.005	0.027	0.004	0.022	0.088
70-79	0.002	0.001	0.002	0.003	0.001	0.001	0.002	0.002	0.001	0.001	0.002	0.010	0.002	0.010	0.036
80+	0.001	0.001	0.001	0.001	0.000	0.000	0.001	0.001	0.000	0.000	0.001	0.002	0.001	0.002	0.009
TOTAL	0.029	0.150	0.019	0.046	0.012	0.011	0.034	0.015	0.008	0.005	0.041	0.195	0.017	0.135	0.716

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.001	0.015	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.002	0.000	0.001	0.018
15-29	0.003	0.028	0.001	0.004	0.002	0.001	0.003	0.001	0.001	0.000	0.004	0.013	0.001	0.008	0.066
30-44	0.006	0.026	0.003	0.011	0.003	0.002	0.007	0.002	0.002	0.001	0.013	0.029	0.002	0.028	0.132
45-59	0.009	0.011	0.006	0.014	0.004	0.003	0.011	0.004	0.002	0.002	0.014	0.050	0.006	0.042	0.176
60-69	0.004	0.003	0.004	0.006	0.002	0.002	0.004	0.004	0.002	0.002	0.006	0.022	0.004	0.020	0.081
70-79	0.002	0.001	0.003	0.003	0.001	0.001	0.002	0.003	0.001	0.001	0.003	0.010	0.003	0.011	0.042
80+	0.001	0.001	0.002	0.001	0.000	0.000	0.001	0.002	0.001	0.001	0.001	0.002	0.001	0.003	0.013
TOTAL	0.022	0.083	0.018	0.039	0.011	0.008	0.026	0.015	0.007	0.006	0.039	0.127	0.016	0.111	0.528

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.001	0.032	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.001	0.003	0.000	0.001	0.040
15-29	0.005	0.090	0.002	0.009	0.003	0.003	0.007	0.001	0.001	0.000	0.008	0.035	0.002	0.019	0.183
30-44	0.016	0.075	0.007	0.025	0.007	0.005	0.018	0.005	0.004	0.002	0.026	0.090	0.005	0.065	0.346
45-59	0.020	0.028	0.014	0.031	0.008	0.008	0.023	0.009	0.005	0.003	0.028	0.122	0.013	0.097	0.404
60-69	0.008	0.007	0.007	0.012	0.003	0.003	0.009	0.008	0.003	0.003	0.011	0.049	0.007	0.042	0.168
70-79	0.003	0.002	0.005	0.006	0.001	0.001	0.004	0.005	0.002	0.002	0.005	0.020	0.005	0.020	0.078
80+	0.001	0.001	0.003	0.002	0.000	0.000	0.001	0.003	0.001	0.001	0.001	0.004	0.002	0.004	0.021
TOTAL	0.051	0.233	0.036	0.085	0.023	0.019	0.060	0.030	0.015	0.010	0.080	0.322	0.032	0.246	1.244

4.9 Reactivation of herpes labialis

Disease incidence

In developing a plausible global distribution of history of recurrent herpes, it is clear that there are racial differences as well as age differences. Some studies are not population-based and different studies use different definitions of "a history of recurrent herpes", making comparison difficult.

In white populations there appears to be a weak latitudinal gradient, with lower prevalence in Swedish populations (*116*) than in southern Wisconsin (*117*) or Germany (*118*) as well as a peak of prevalence (history of recurrence in the last two years) in late adolescence and early adulthood. 52% of those with a positive history of recurrent herpes had disease onset prior to 10 years of age (*117*). In a study examining prevalence of a history of reactivation of herpes labialis (RHL) in Asian dental outpatients there was a higher incidence in Chiang Mai (latitude 18^{o} 48′ N) than in Kuala Lumpur (latitude 3^{o} 08′ N) by a factor of three. However, the number of affected individuals was too small to draw any conclusions about incidence or latitudinal gradients (*119*).

The few studies done in African, Asian and South American populations indicate that there is a lower prevalence of RHL in Asian populations, but that African populations have similar rates to European populations. Thus, the distribution of RHL is taken to be the same in lightly pigmented populations as for deeply pigmented populations but with a multiplier of 0.4 times the prevalence for Asian populations. The method used to calculate the global incidence is outlined in Appendix 6.

Population attributable fraction

There are few quantitative data either on the prevalence of recurrent herpes labialis or the factors that precipitate lesions. We do know that 80-90% of the adult population has antibodies to herpes simplex virus type 1, the causative organism for herpes labialis (*120*). Of these, around one third suffer from recurrent disease. Recurrences are precipitated by emotional stress, illness, sunlight, trauma and a variety of other anecdotal factors. Analysis of data from Young et al gives several different odds ratios for a relationship with UVR exposure, depending on the exposure measure used (*117*). (See Appendix 3). However, this is a cross-sectional study and recalled exposure may be inaccurate, with resultant underestimation of the odds ratios and thus the PAF. A PAF of 0.25 is used as the lower estimate and 0.5 as the upper estimate of the population attributable fraction.

Disease model

Recurrence rates of lesions were averaged from a number of studies (*116, 117, 121-123*). In the model used, 48.6% of people with a history of recurrent herpes labialis had one recurrence per year, 35.1% have two recurrences per year, and 16% have four or more recurrences per year. The duration of an episode was 0.014 years, disability weight 0.005. The results of the burden of disease assessment are outlined in Tables 4.32 to 4.35.

Table 4.32 Incident herpes labialis 2000
by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	7 512 354	9 621 294	2 842 909	5 448 982	969 018	3 224 926	4 303 089	2 581 515	2 344 701	1 646 880	25 93 751	10 177 772	1 239 659	19 419 936	73 926 787
15-29	15 328 480	19 376 664	8 011 907	15 046 699	2 287 586	7 772 992	9 178 835	9 129 483	7 166 187	5 650 674	78 29 730	26 255 789	4 764 667	55 129 528	192 929 221
30-44	8 129 705	10 167 267	10 678 287	10 947 228	1 286 996	5 330 339	5 957 231	12 987 218	6 612 431	7 032 971	54 67 105	18 540 622	5 080 145	56 077 651	164 295 196
45-59	3 929 823	4 673 399	8 151 937	6 043 202	657 290	2 719 617	2 905 648	10 872 786	4 365 555	5 339 151	26 94 888	10 210 786	5 217 266	33 379 625	101 160 973
60-69	1 357 976	1 517 789	2 841 169	2 089 461	239 633	902 255	938 737	4 902 177	1 800 396	2 336 636	9 92 214	3 629 725	2 368 126	12 030 873	37 947 166
70-79	509 385	574 746	1 902 027	1 009 155	100 806	433 807	375 997	2 971 305	894 071	1 065 668	3 95 649	1 525 311	1 345 214	5 368 114	18 471 254
80+	103 004	111 411	659 151	251 366	25 380	88 952	75 710	851 486	159 745	169 765	89 869	321 825	380 455	936 236	4 224 356
TOTAL	36 870 727	46 042 572	35 087 386	40 836 093	5 566 707	20 472 887	23 735 248	44 295 970	23 343 086	23 241 744	20 063 205	70 661 830	20 395 532	182 341 964	592 954 951

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	7 446 089	9 580 522	2 712 846	5 260 542	939 156	3 087 818	4 144 070	2446 053	2252 273	1 581 506	2 509 106	9 524 210	1 178 649	17 609 063	70 271 903
15-29	15 360 398	19 369 863	7 734 762	14 915 705	2 270 323	7 454 797	8 706 145	8700 403	6891 743	5 533 818	7 641 505	24 245 483	4 566 550	51 826 057	185 217 553
30-44	8 335 458	10 227 711	10 495 667	11 337 671	1 357 443	4 819 259	5625 509	12687 394	6571 515	7 184 281	5 517 043	17 145 839	5 006 412	53 316 734	159 627 936
45-59	4 208 233	4 977 081	8 346 126	6 475 304	708 590	2 383 663	2 938392	10953 563	4525 010	6 128 424	2 863 995	9 760 765	5 251 690	31 389 323	100 910 158
60-69	1 559 473	1 780 333	3 143 354	2 423 329	265 752	888 793	10 05 920	5445 277	2111 932	3 367 170	1 131 093	3 798 508	2 565 177	11 815 329	41 301 441
70-79	628 469	749 644	2 494 766	1 324 374	120 200	453 108	4 30 336	4225 344	1299 265	2 300 590	478 305	1 712 560	1 781 970	6 432 059	24 430 991
80+	143 448	184 035	1 294 359	409 067	35 342	102 019	87 626	1889 286	324 171	626 188	129 302	404 997	780 410	1 734 515	8 144 765
TOTAL	37 681 569	46 869 188	36 221 880	42 145 993	5 696 807	19 189 458	22 937 997	46347 321	23975 909	26 721 976	20 270 350	66 592 363	21 130 859	174 123 079	589 904 749

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5-14	14 958 443	19 201 816	5 555 755	10 709 524	1 908 174	6 312 744	8 447 159	5 027 567	4 596 974	3 228 386	5 102 857	19 701 982	2 418 308	37 028 999	144 198 689
15-29	30 688 878	38 746 527	15 746 669	29 962 404	4 557 909	15 227 789	17 884 981	17 829 886	14 057 930	11 184 492	15 471 235	50 501 273	9 331 217	106 955 586	378 146 775
30-44	16 465 163	20 394 978	21 173 954	22 284 899	2 644 439	10 149 597	11 582 740	25 674 612	13 183 946	14 217 251	10 984 148	35 686 460	10 086 558	109 394 385	323 923 130
45-59	8 138 056	9 650 480	16 498 062	12 518 506	1 365 879	5 103 280	5 844 040	21 826 350	8 890 565	11 467 575	5 558 883	19 971 551	10 468 956	64 768 948	202 071 131
60-69	2 917 450	3 298 122	5 984 523	4 512 790	505 385	1 791 048	1 944 657	10 347 453	3 912 328	5 703 805	2 123 307	7 428 233	4 933 303	23 846 202	79 248 606
70-79	1 137 854	1 324 390	4 396 792	2 333 529	221 006	886 915	806 333	7 196 650	2 193 336	3 366 257	873 954	3 237 871	3 127 184	11 800 173	42 902 244
80+	246 452	295 446	1 953 510	660 433	60 722	190 971	163 335	2 740 772	483 916	795 953	219 170	726 822	1 160 865	2 670 751	12 369 119
TOTAL	74 552 296	92 911 760	71 309 266	82 982 086	11 263 514	39 662 345	46 673 245	90 643 290	47 318 994	49 963 720	40 333 555	137 254 193	41 526 390	356 465 044	1 182 859 698

Table 4.33 Burden of disease from RHL DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.873	1.118	0.330	0.633	0.113	0.375	0.500	0.300	0.272	0.191	0.301	1.182	0.144	2.256	8.587
15-29	1.780	2.251	0.931	1.748	0.266	0.903	1.066	1.060	0.832	0.656	0.909	3.050	0.553	6.403	22.409
30-44	0.944	1.181	1.240	1.272	0.149	0.619	0.692	1.508	0.768	0.817	0.635	2.154	0.590	6.513	19.083
45-59	0.456	0.543	0.947	0.702	0.076	0.316	0.337	1.263	0.507	0.620	0.313	1.186	0.606	3.877	11.750
60-69	0.158	0.176	0.330	0.243	0.028	0.105	0.109	0.569	0.209	0.271	0.115	0.422	0.275	1.397	4.408
70-79	0.059	0.067	0.221	0.117	0.012	0.050	0.044	0.345	0.104	0.124	0.046	0.177	0.156	0.624	2.145
80+	0.012	0.013	0.077	0.029	0.003	0.010	0.009	0.099	0.019	0.020	0.010	0.037	0.044	0.109	0.491
TOTAL	4.283	5.348	4.075	4.743	0.647	2.378	2.757	5.145	2.711	2.700	2.330	8.207	2.369	21.179	68.872

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.855	1.100	0.311	0.604	0.108	0.355	0.476	0.281	0.259	0.182	0.288	1.093	0.135	2.022	8.068
15-29	1.763	2.224	0.888	1.712	0.261	0.856	1.000	0.999	0.791	0.635	0.877	2.784	0.524	5.950	21.264
30-44	0.957	1.174	1.205	1.302	0.156	0.553	0.646	1.457	0.754	0.825	0.633	1.968	0.575	6.121	18.327
45-59	0.483	0.571	0.958	0.743	0.081	0.274	0.337	1.258	0.520	0.704	0.329	1.121	0.603	3.604	11.585
60-69	0.179	0.204	0.361	0.278	0.031	0.102	0.115	0.625	0.242	0.387	0.130	0.436	0.295	1.356	4.742
70-79	0.072	0.086	0.286	0.152	0.014	0.052	0.049	0.485	0.149	0.264	0.055	0.197	0.205	0.738	2.805
80+	0.016	0.021	0.149	0.047	0.004	0.012	0.010	0.217	0.037	0.072	0.015	0.046	0.090	0.199	0.935
TOTAL	4.326	5.381	4.159	4.839	0.654	2.203	2.633	5.321	2.753	3.068	2.327	7.645	2.426	19.991	67.726

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	1.727	2.217	0.642	1.237	0.220	0.729	0.976	0.581	0.531	0.373	0.589	2.276	0.279	4.277	16.654
15-29	3.544	4.474	1.819	3.460	0.526	1.759	2.066	2.059	1.624	1.292	1.787	5.833	1.078	12.353	43.673
30-44	1.901	2.355	2.445	2.573	0.305	1.172	1.338	2.965	1.523	1.642	1.268	4.122	1.165	12.635	37.410
45-59	0.940	1.114	1.905	1.445	0.158	0.590	0.675	2.520	1.027	1.324	0.642	2.307	1.209	7.481	23.335
60-69	0.337	0.381	0.691	0.521	0.058	0.207	0.225	1.195	0.452	0.658	0.245	0.858	0.570	2.754	9.149
70-79	0.131	0.153	0.507	0.269	0.026	0.102	0.093	0.830	0.253	0.388	0.101	0.374	0.361	1.362	4.950
80+	0.028	0.034	0.225	0.076	0.007	0.022	0.019	0.316	0.056	0.092	0.025	0.084	0.134	0.308	1.426
TOTAL	8.609	10.729	8.234	9.582	1.301	4.581	5.390	10.466	5.464	5.767	4.658	15.853	4.795	41.170	136.598

Table 4.34 Disease burden from RHL attributable to UVR DALYs (000) – upper estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.436	0.559	0.165	0.316	0.056	0.187	0.250	0.150	0.136	0.096	0.151	0.591	0.072	1.128	4.293
15-29	0.890	1.125	0.465	0.874	0.133	0.451	0.533	0.530	0.416	0.328	0.455	1.525	0.277	3.202	11.204
30-44	0.472	0.590	0.620	0.636	0.075	0.310	0.346	0.754	0.384	0.408	0.318	1.077	0.295	3.257	9.542
45-59	0.228	0.271	0.473	0.351	0.038	0.158	0.169	0.631	0.254	0.310	0.157	0.593	0.303	1.939	5.875
60-69	0.079	0.088	0.165	0.121	0.014	0.052	0.055	0.285	0.105	0.136	0.058	0.211	0.138	0.699	2.204
70-79	0.030	0.033	0.110	0.059	0.006	0.025	0.022	0.173	0.052	0.062	0.023	0.089	0.078	0.312	1.073
80+	0.006	0.006	0.038	0.015	0.001	0.005	0.004	0.049	0.009	0.010	0.005	0.019	0.022	0.054	0.245
TOTAL	2.141	2.674	2.038	2.372	0.323	1.189	1.378	2.573	1.356	1.350	1.165	4.104	1.184	10.590	34.436

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.427	0.550	0.156	0.302	0.054	0.177	0.238	0.140	0.129	0.091	0.144	0.547	0.068	1.011	4.034
15-29	0.882	1.112	0.444	0.856	0.130	0.428	0.500	0.499	0.396	0.318	0.439	1.392	0.262	2.975	10.632
30-44	0.478	0.587	0.602	0.651	0.078	0.277	0.323	0.728	0.377	0.412	0.317	0.984	0.287	3.061	9.163
45-59	0.242	0.286	0.479	0.372	0.041	0.137	0.169	0.629	0.260	0.352	0.164	0.560	0.301	1.802	5.793
60-69	0.090	0.102	0.180	0.139	0.015	0.051	0.058	0.313	0.121	0.193	0.065	0.218	0.147	0.678	2.371
70-79	0.036	0.043	0.143	0.076	0.007	0.026	0.025	0.243	0.075	0.132	0.027	0.098	0.102	0.369	1.402
80+	0.008	0.011	0.074	0.023	0.002	0.006	0.005	0.108	0.019	0.036	0.007	0.023	0.045	0.100	0.468
TOTAL	2.163	2.690	2.079	2.419	0.327	1.102	1.317	2.661	1.376	1.534	1.164	3.823	1.213	9.995	33.863

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.864	1.109	0.321	0.618	0.110	0.365	0.488	0.290	0.265	0.186	0.295	1.138	0.140	2.139	8.327
15-29	1.772	2.237	0.909	1.730	0.263	0.879	1.033	1.030	0.812	0.646	0.893	2.917	0.539	6.177	21.837
30-44	0.951	1.178	1.223	1.287	0.153	0.586	0.669	1.483	0.761	0.821	0.634	2.061	0.582	6.317	18.705
45-59	0.470	0.557	0.953	0.723	0.079	0.295	0.337	1.260	0.513	0.662	0.321	1.153	0.604	3.740	11.668
60-69	0.168	0.190	0.345	0.260	0.029	0.103	0.112	0.597	0.226	0.329	0.123	0.429	0.285	1.377	4.575
70-79	0.066	0.076	0.254	0.135	0.013	0.051	0.047	0.415	0.127	0.194	0.050	0.187	0.180	0.681	2.475
80+	0.014	0.017	0.113	0.038	0.004	0.011	0.009	0.158	0.028	0.046	0.013	0.042	0.067	0.154	0.713
TOTAL	4.304	5.364	4.117	4.791	0.650	2.291	2.695	5.233	2.732	2.884	2.329	7.926	2.397	20.585	68.299

Table 4.35 Disease burden from RHL attributable to UVR DALYs (000) – lower estimates by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.218	0.279	0.083	0.158	0.028	0.094	0.125	0.075	0.068	0.048	0.075	0.296	0.036	0.564	2.147
15-29	0.445	0.563	0.233	0.437	0.066	0.226	0.267	0.265	0.208	0.164	0.227	0.762	0.138	1.601	5.602
30-44	0.236	0.295	0.310	0.318	0.037	0.155	0.173	0.377	0.192	0.204	0.159	0.538	0.148	1.628	4.771
45-59	0.114	0.136	0.237	0.175	0.019	0.079	0.084	0.316	0.127	0.155	0.078	0.296	0.151	0.969	2.937
60-69	0.039	0.044	0.083	0.061	0.007	0.026	0.027	0.142	0.052	0.068	0.029	0.105	0.069	0.349	1.102
70-79	0.015	0.017	0.055	0.029	0.003	0.013	0.011	0.086	0.026	0.031	0.011	0.044	0.039	0.156	0.536
80+	0.003	0.003	0.019	0.007	0.001	0.003	0.002	0.025	0.005	0.005	0.003	0.009	0.011	0.027	0.123
TOTAL	1.071	1.337	1.019	1.186	0.162	0.594	0.689	1.286	0.678	0.675	0.583	2.052	0.592	5.295	17.218

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.214	0.275	0.078	0.151	0.027	0.089	0.119	0.070	0.065	0.045	0.072	0.273	0.034	0.505	2.017
15-29	0.441	0.556	0.222	0.428	0.065	0.214	0.250	0.250	0.198	0.159	0.219	0.696	0.131	1.488	5.316
30-44	0.239	0.294	0.301	0.325	0.039	0.138	0.161	0.364	0.189	0.206	0.158	0.492	0.144	1.530	4.582
45-59	0.121	0.143	0.240	0.186	0.020	0.068	0.084	0.314	0.130	0.176	0.082	0.280	0.151	0.901	2.896
60-69	0.045	0.051	0.090	0.070	0.008	0.026	0.029	0.156	0.061	0.097	0.032	0.109	0.074	0.339	1.185
70-79	0.018	0.022	0.072	0.038	0.003	0.013	0.012	0.121	0.037	0.066	0.014	0.049	0.051	0.185	0.701
80+	0.004	0.005	0.037	0.012	0.001	0.003	0.003	0.054	0.009	0.018	0.004	0.012	0.022	0.050	0.234
TOTAL	1.082	1.345	1.040	1.210	0.164	0.551	0.658	1.330	0.688	0.767	0.582	1.911	0.606	4.998	16.931

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
5-14	0.432	0.554	0.160	0.309	0.055	0.182	0.244	0.145	0.133	0.093	0.147	0.569	0.070	1.069	4.164
15-29	0.886	1.119	0.455	0.865	0.132	0.440	0.516	0.515	0.406	0.323	0.447	1.458	0.269	3.088	10.918
30-44	0.475	0.589	0.611	0.643	0.076	0.293	0.334	0.741	0.381	0.410	0.317	1.030	0.291	3.159	9.352
45-59	0.235	0.279	0.476	0.361	0.039	0.147	0.169	0.630	0.257	0.331	0.160	0.577	0.302	1.870	5.834
60-69	0.084	0.095	0.173	0.130	0.015	0.052	0.056	0.299	0.113	0.164	0.061	0.214	0.142	0.688	2.287
70-79	0.033	0.038	0.127	0.067	0.006	0.026	0.023	0.208	0.063	0.097	0.025	0.093	0.090	0.340	1.238
80+	0.007	0.009	0.056	0.019	0.002	0.006	0.005	0.079	0.014	0.023	0.006	0.021	0.033	0.077	0.356
TOTAL	2.152	2.682	2.059	2.395	0.325	1.145	1.348	2.617	1.366	1.442	1.164	3.963	1.199	10.292	34.150

5. Potential disease burden caused by complete removal of UVR exposure

The previous chapter described the burden of disease due to excessive UVR exposure. That disease burden may be completely avoidable if personal UVR exposure was reduced to levels appropriate to an individual's skin type, given the local ambient UVR. This appropriate level is not "no UVR exposure", but the minimum exposure required to maintain vitamin D adequacy. This chapter presents an estimate of the potential burden of disease that would be incurred if, globally, there was zero UVR exposure (taking account only of these diseases that have strong, proven causal association with low UVR exposure). Notably if the association between a number of other diseases thought to possibly associated with low UVR exposure, eg cancers of the breast, colon and prostate, is proven, this potential burden of disease will be much greater.

The beneficial effect of UVR in preventing rickets in young children and osteomalacia in adults has been documented since the early 19th century (*21*). More recently the importance of UVR in maintaining vitamin D levels to prevent osteoporosis in older adults has been noted (*124*).

Vitamin D levels can also be maintained by supplementation of food. However, it is estimated that approximately 80-100 % of vitamin D is derived from the action of sunlight on the skin (*125*).

In order to evaluate the beneficial effects of UVR in preventing rickets, osteomalacia and osteoporosis, we assume a baseline exposure of no UVR exposure and examine the associated amount of disease that would occur in this situation – this is the amount of disease avoided by having adequate exposure to UVR. Jabonski and Chaplin (*1*) have defined three bands of ambient UVR which correspond to areas in which there is sufficient UVR to produce vitamin D throughout the year (latitude 30^{o}N to 30^{o}S), sufficient to produce vitamin D in some seasons only (30^o to 50^o) and insufficient to produce adequate vitamin D from UVR alone at any time of the year (50^o to 70^o).

It is likely that there is an inverse relationship between these zones and the amount of dietary intake of vitamin D. For example, in the zone where there is insufficient sunlight year round to produce sufficient vitamin D, it is likely that people who inhabit this zone have adapted to the lack of sunlight-derived vitamin D by increasing dietary vitamin D sources – fish, cod liver oil. This provides a way of separating out the contribution of diet and sunlight to the maintenance of vitamin D levels in different regions. In confirmation of this, in an examination of vitamin D intake and serum levels in Arab, Danish and ethnic Danish Moslems in Denmark, Glerup et al found that Arab women had low dietary vitamin D intake (1.04ug/day), while Danish women ingested 7.49ug/day (unveiled) and 13.53 ug/day (veiled) (*125*).

Using Jabonski and Chaplin's zones, studies were sought in which individuals had 'no' sunlight exposure – veiled women, institutionalized individuals, children who, for cultural reasons are kept wrapped up. By looking at the incidence of rickets, osteomalacia and osteoporosis in these populations, it should be possible to estimate the burden of disease avoided by sunlight exposure.

Vitamin D deficiency itself does not attract a disability weight. Thus only preventive effects on frank rickets, osteomalacia and osteoporosis have been considered in this analysis.

Clearly, this is only the tip of the iceberg of even the bone-related disorders related to vitamin D deficiency. It takes no account of minor derangements in structure and consequently of function that are sub-clinical – knock knees or bowed knees, with subsequent loss of function, possible decreased participation in physical activities and possible osteoarthritis at a later age. There is no account taken of the difficulty and morbidity associated with childbirth when pelvic malformation is the consequence of unrecognized rickets.

In addition, researchers are beginning to suspect that vitamin D has far more wide-ranging effects on the immune system (various malignancies and auto-immune disorders may be increased with vitamin D deficiency), the cardiovascular system, the muscle part of the musculoskeletal system and psychiatric disorders. Shaw et al (*2*) outline effects of maternal vitamin D deficiency on the developing fetal brain, congenital cataracts, postnatal head and linear growth.

Vitamin D status is assessed by measuring blood levels of 25-hydroxy vitamin D (25(OH)D). Unfortunately, there is little standardization in methods for measuring 25(OH)D with different methods giving vastly different results (*24*). Similarly, quoted reference ranges vary greatly. The "normal" range depends on the dietary and sun exposure habits of the reference group and may have little relationship to clinical disease. Lips has proposed stages of vitamin D deficiency based on adverse health outcomes (*24*), which are presented in Table 5.1.

Table 5.1 Proposal for staging of vitamin D deficiency[1]

Severity of deficiency	25(OH) D [nmol/l]	25(OH)D [ng/ml]	Bone histology
Mild	25-50	10-20	Normal or high turnover
Moderate	12.5-25	5-10	High turnover
Severe	<12.5	<5	Incipient or overt osteomalacia

[1] Serum levels of vitamin D are measured as 25 hydroxy vitamin D, 25(OH) D
Source: Lips et al, 2001(*24*)

We have used a serum level of 10nmol/l as the level likely to be associated with frank disease, or a clinical diagnosis of rickets or osteomalacia. Studies from Africa indicate that rickets is still a not uncommon disease with a high case fatality rate (31%) and high morbidity (*126*). It is associated with increased risk of pneumonia and congestive cardiac failure, in addition to the skeletal effects.

Case fatality due to vitamin D deficiency of 30% in DE regions and 5% in ABC regions has been assumed. Duration of rickets is taken as one year in children 0-4 years, with onset of disease at 12 months of age.

Twenty per cent of veiled ethnic Danish Moslems had serum 25(OH) D levels of less than 10nmol/l, a level at which one could expect signs of osteomalacia, bone pain, muscle weakness etc (*125*). Thus in the highest latitude band, where dietary substitutes have been found to compensate for lack of UV induced vitamin D, we have taken a figure of 20% of the population as suffering from rickets, osteomalacia or osteoporosis under a scenario of no UV exposure. Gloth et al, looking at vitamin D deficiency in the elderly found that 48% of a sunlight deprived group in Baltimore (latitude 39^{o} N) had 25(OH) D levels less than 25nmol/l (*127*). There was an equal male to female ratio and no racial differences in the levels of 25(OH) D. Indeed, recent research indicates that skin colour does not affect the amount of vitamin D that can be generated; it just takes longer sun exposure to generate a certain level of circulating vitamin D (six times as long for deeply pigmented skin, compared to lightly pigmented skin) (*19*). In Lebanon (latitude 34^{o}), 61.8% of veiled women had 25(OH) D levels less than 5ng/ml (12.5nmol/l) (*128*). Using these data, 61.8% of people in the 30-50 degree band would be expected to have clinically low vitamin D levels. The prevalence of vitamin D deficiency from the Baltimore study was not used in these calculations as USA is one of only a few countries that have vitamin D supplementation of foods. The figure of 48% is thus likely to underestimate the prevalence of vitamin D deficiency in populations at a similar latitude who do not have dietary supplementation with vitamin D.

On the basis of data presented in Jablonski and Chaplin (*1*), it is likely that the entire population of the central zone of adequate UV year round (30°N to 30°S) has developed few dietary substitutes for sunlight-induced production of vitamin D. However, more coastal populations may have higher dietary intake of vitamin D and thus be less affected by low levels of UVR (*129*). Thus, the incidence of vitamin D deficiency diseases is estimated at 85% for populations in this band under a scenario of no UV exposure.

Using these figures as the incidence of severe vitamin D deficiency, and applying a disability weight of 0.3 for rickets in the 0-4 age group, 0.2 in the 5-59 age group for adolescent rickets and then osteomalacia, and 0.1 in the older age groups for the effects of osteoporosis (see Appendix 3), the beneficial effects of UVB exposure were calculated.

The effect of dietary supplementation can be seen by examining the rates of disease avoided in AMR A (where there is dietary supplementation of vitamin D) with other regions of similar latitude and population. We have applied incidence rates for vitamin D deficiency to AMR A of 20%, assuming that dietary intake is similar to that of high latitude countries. Note that Gloth's results from Baltimore are consistent with this figure – 48% had vitamin D levels less than 25nmol/l, but a much smaller fraction would have had levels <10nmol/l (the definition of vitamin D deficiency used here). Incident cases of vitamin D deficiency and the burden of disease avoided by having adequate UVR exposure are presented in Table 5.2 and 5.3.

Table 5.2 Incident cases of vitamin D deficiency 2000 under a scenario of zero UVR exposure by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	20 298 939	24 355 501	2 211 114	18 759 318	4 063 195	6 797 361	18 677 283	4 890 825	5 061 358	2 140 675	12 300 533	59 645 237	2 564 009	45 662 839	227 428 185
5-14	32 802 301	39 515 271	4 754 818	37 008 446	7 448 261	14 131 633	31 509 011	10 752 113	10 567 325	5 593 303	24 592 452	116 355 865	5 194 311	100 226 537	440 451 647
15-29	33 409 842	39 294 480	6 589 386	49 957 726	8 759 572	16 854 779	33 476 980	18 635 462	15 619 181	9 042 631	36 400 222	147 802 974	9 886 841	138 894 466	564 624 540
30-44	18 861 972	21 860 239	7 675 552	36 154 552	5 241 108	11 074 940	21 884 763	21 360 177	12 107 818	8 615 505	27 053 236	105 487 336	9 638 511	129 254 113	436 269 820
45-59	9 768 725	10 867 422	5 866 056	20 472 819	2 888 841	5 988 034	11 169 981	17 257 800	7 656 788	6 329 230	14 585 374	60 595 161	10 088 979	77 897 175	261 432 384
60-69	3 512 523	3 702 027	2 236 435	7 316 618	1 095 917	2 028 389	3 761 986	8 867 525	3 580 226	3 211 614	5 639 821	22 608 065	4 873 112	29 895 708	102 329 966
70-79	1 557 871	1 634 161	1 610 215	3 869 245	544 230	1 025 188	1 690 424	5 916 592	1 917 520	1 638 138	2 674 354	10 549 902	2 975 110	14 267 110	51 870 060
80+	356 899	352 892	696 710	1 176 359	153 470	264 249	434 138	2 099 665	421 469	343 241	660 199	2 681 658	1 063 402	3 155 097	13 859 449
Total	120 569 072	141 581 992	31 640 286	174 715 082	30 194 594	58 164 573	122 604 566	89 780 159	56 931 684	36 914 336	123 906 191	525 726 198	46 284 275	539 253 044	2 098 266 052

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	1 9958 983	24 015 716	2 106 033	18 034 772	3 910 836	6 511 682	17 885 065	4 626 648	4 865 738	2 043 794	11 846 561	56 191 876	2 429 672	41 567 402	215 994 777
5-14	3 2468 873	39 351 661	4 537 357	35 710 671	7 210 320	13 532 897	30 265 194	10 189 719	10 151 433	5 370 572	23 790 738	108 894 954	4 938 055	91 307 572	417 720 015
15-29	3 3390 309	39 288 722	6 362 945	49 600 733	8 674 715	16 144 827	31 481 583	17 784 196	15 019 121	8 842 589	35 529 989	136 514 368	9 476 104	130 982 674	539 092 875
30-44	1 9292549	21 997 941	7 544 505	37 584 209	5 495 634	9 740 163	20 429 403	20 901 324	12 043 855	8 805 864	27 310 942	97 581 124	9 503 143	123 614 040	421 844 695
45-59	10 426 378	11 583 563	6 004 607	21 934 227	3 073 490	5 002 687	11 082 439	17 464 041	7 914 042	7 254 731	15 508 706	57 912 826	10 150 278	73 975 134	259 287 149
60-69	4 037 673	4 354 247	2 471 282	8 426 092	1 202 495	1 961 256	4 002 276	9 932 110	4 166 523	4 567 847	6 423 707	23 630 340	5 275 000	29 807 534	110 258 380
70-79	1 921 344	2 132 941	2 109 575	4 986 076	644 836	1 066 358	1 938 966	8 428 964	2 733 931	3 449 787	3 222 200	11 818 414	3 934 606	17 350 697	65 738 697
80+	490 299	589 187	1 364 304	1 847 301	213 308	303 779	488 611	4 628 243	825 380	1 209 793	944 602	3 365 342	2 176 841	5 891 422	24 338 411
Total	121 986 407	143 313 979	32 500 607	178 124 081	30 425 634	54 263 649	117 573 537	93 955 246	57 720 022	41 544 978	124 577 444	495 909 244	47 883 698	514 496 474	2 054 274 999

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	40 257 922	48 371 217	4 317 147	36 794 089	7 974 031	13 309 043	36 562 348	9 517 473	9 927 095	4 184 468	24 147 093	115 837 113	4 993 680	87 230 240	443 422 962
5-14	65 271 174	78 866 932	9 292 175	72 719 116	14 658 581	27 664 531	61 774 205	20 941 832	20 718 758	10 963 875	48 383 190	225 250 819	10 132 365	191 534 109	858 171 662
15-29	66 800 151	78 583 202	12 952 331	99 558 459	17 434 287	32 999 606	64 958 563	36 419 658	30 638 301	17 885 221	71 930 210	284 317 342	19 362 945	269 877 140	1 103 717 416
30-44	38 154 521	43 858 180	15 220 056	73 738 761	10 736 742	20 815 103	42 314 166	42 261 501	24 151 672	17 421 369	54 364 178	203 068 460	19 141 654	252 868 153	858 114 515
45-59	20 195 102	22 450 985	11 870 663	42 407 046	5 962 332	10 990 720	22 252 420	34 721 841	15 570 830	13 583 961	30 094 079	118 507 988	20 239 257	151 872 308	520 719 533
60-69	7 550 195	8 056 274	4 707 717	15 742 710	2 298 412	3 989 645	7 764 262	18 799 635	7 746 749	7 779 461	12 063 528	46 238 405	10 148 112	59 703 242	212 588 346
70-79	3 479 215	3 767 102	3 719 790	8 855 322	1 189 067	2 091 546	3 629 390	14 345 557	4 651 451	5 087 925	5 896 555	22 368 317	6 909 716	31 617 806	117 608 757
80+	847 198	942 079	2 061 014	3 023 660	366 778	568 029	922 749	6 727 908	1 246 849	1 553 034	1 604 802	6 046 999	3 240 243	9 046 519	38 197 860
Total	242 555 479	284 895 971	64 140 893	352 839 163	60 620 229	112 428 222	240 178 103	183 735 404	114 651 706	78 459 314	248 483 635	1 021 635 442	94 167 974	1 053 749 518	4 152 541 051

Table 5.3 Potential disease burden due to complete removal of UVR exposure, DALYs (000) by 14 WHO subregions (see Appendix 4)

MALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	185 718	222 974	3 652	30 984	37 162	11 227	170 691	8 078	8 360	3 536	20 316	545 056	4 235	75 419	1 327 408
5-14	29 829	355 090	472	3 673	6 603	1 403	28 126	1 067	1 049	555	2 441	99 659	516	9 948	220 931
15-29	3 316	3 900	654	4 958	869	1 673	3 323	1 850	1 550	898	3 613	14 670	981	13 786	56 041
30-44	1 872	2 170	762	3 588	520	1 099	2 172	2 120	1 202	855	2 685	10 470	957	12 829	43 301
45-59	970	1 079	582	2 032	287	594	1 109	1 713	760	628	1 448	6 014	1 001	7 732	25 948
60-69	174	184	111	363	54	101	187	440	178	159	280	1 122	242	1 484	5 078
70-79	1 538	1 606	224	542	538	144	1 674	826	270	233	377	10 339	418	2 007	20 736
80+	207	205	69	117	87	26	249	206	41	34	66	1 529	105	320	3 262
TOTAL	223 626	267 706	6 526	46 259	46 122	16 267	207 530	16 299	13 410	6 897	31 226	688 860	8 453	123 524	1 702 706

FEMALE

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	183 958	221 487	3 502	29 216	36 033	10 224	164 662	7 336	7 652	3 282	19 798	517 299	3 825	65 900	1 274 174
5-14	29 743	35 661	450	2 451	6 433	453	27 202	460	371	327	2 500	94 083	183	3 909	204 226
15-29	3 314	3 900	632	3 353	861	533	3 125	776	558	546	3 734	13 550	340	5 329	40 550
30-44	1 915	2 183	749	2 523	545	319	2 028	928	453	556	2 870	9 685	352	4 710	29 816
45-59	1 035	1 150	596	1 439	305	164	1 100	780	311	455	1 630	5 748	360	2 749	17 821
60-69	200	216	123	270	60	32	199	218	81	145	338	1 173	91	549	3 694
70-79	2 182	2 406	322	680	733	130	2 212	1 057	343	472	510	13 306	477	2 135	26 965
80+	320	382	141	162	135	22	320	350	62	104	104	2 163	155	444	4 865
TOTAL	222 667	267 385	6 515	40 096	45 105	11 878	200 847	11 904	9 831	5 887	31 484	657 007	5 783	85 724	1 602 111

BOTH SEXES

AGE	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B	TOTAL
0-4	369 677	444 461	7 154	60 200	73 194	21 451	335 354	15 414	16 011	6 818	40 115	1 062 355	8 060	141 319	2 601 581
5-14	59 572	71 250	922	6 125	13 036	1 855	55 327	1 528	1 420	882	4 941	193 743	699	13 856	425 157
15-29	6 630	7 800	1 286	8 312	1 730	2 206	6 447	2 626	2 108	1 444	7 347	28 220	1 321	19 115	96 591
30-44	3 787	4 353	1 511	6 112	1 066	1 418	4 200	3 048	1 654	1 411	5 555	20 155	1 308	17 539	73 117
45-59	2 004	2 228	1 178	3 471	592	759	2 209	2 492	1 071	1 083	3 077	11 762	1 361	10 480	43 769
60-69	375	400	234	633	114	133	385	658	259	304	617	2 295	333	2 033	8 772
70-79	3 720	4 012	546	1 222	1 271	274	3 886	1 883	613	704	887	23 645	895	4 142	47 701
80+	527	587	210	279	223	48	569	556	104	137	171	3 692	260	764	8 127
TOTAL	446 293	535 091	13 040	86 354	91 227	28 144	408 377	28 204	23 240	12 784	62 711	1 345 867	14 236	209 248	3 304 816

6. Sources of error or uncertainty

There are three major sources of uncertainty in the estimates:

1. Lack of data on a global basis for incidence and mortality estimates, disease course and disability weights.
2. Modification of the exposure-response curves due to sun-seeking behaviour or cultural influences on clothing. The “dose-response relationships” derived for non-melanoma skin cancers are averaged over regions with similar ambient UVR – despite possibly wide-ranging differences in actual exposure due to behavioural or cultural influences. Thus, the estimates are likely to be too low for sun-loving populations in Australia, and too high for culturally sun-avoidant populations in the Middle East and Asia. More accurate country-level data is required to improve these uncertainties.
3. Crudeness of the adjustment for skin pigmentation. Only rough estimates assigning populations to three levels of skin pigmentation were possible in this analysis. A single study from Tasmania has examined the distribution of skin pigmentation using spectrophotometric readings (*130*). In order to accurately adjust for skin pigmentation both the population distribution and the effect on the incidence of disease needs to be known in more detail.

To account for the effect of uncertainty or the use of aggregate information despite variation between individuals and populations, results have been expressed in terms of lower and upper estimates. This is, however, only an approximate estimate of the uncertainty, and more accurate estimates would require that additional evidence becomes available.

7. Conclusion

The full results of the burden of disease assessment are presented in Appendix 7 (including results with and without sunburn and RHL, for which the estimates are highly uncertain). Table 7.1 presents a summary of these results.

Table 7.1 Burden of disease due to excessive UVR exposure, DALYs (000) and deaths

Disease	DALYs (000) Upper estimate	DALYs (000) Lower estimate	Deaths Upper estimate	Deaths Lower estimate
CMM	621.2	345.1	58 645	32 581
SCC of skin	82.7	59.1	9 474	6 767
BCC of skin	52.1	29.0	2 921	1 623
Solar keratoses	8.3	8.3	0	0
Sunburn	293.6	293.6	0	0
Cortical cataract	529.2	529.2	0	0
Pterygium	34.6	19.7	0	0
SCCC	1.7	1.2	0	0
RHL	68.3	34.1	0	0
Total	1691.9	1319.4	71 039	40 970
Total (excluding sunburn and RHL)	1330.1	991.7	71 039	40 970

CMM: Cutaneous malignant melanoma; SCC: Squamous cell carcinoma; BCC: Basal cell carcinoma; SCCC: Squamous cell carcinomas of the cornea and conjunctiva; RHL: Reactivation of herpes labialis

Thus approximately 1.5 million DALYs and 60 000[6] lives were lost in 2000 due to excessive UVR exposure. While the loss of these 1.5 million DALYs could have been avoided through appropriate UVR exposure (minimum required to maintain vitamin D adequacy), under a scenario of zero UVR exposure 3 304 million DALYs would have been lost due to vitamin D deficiency diseases – rickets, osteomalacia and osteoporosis.

In this first assessment of the burden of disease resulting from excess exposure to ultraviolet radiation it has become clear that more research is needed in this area. Throughout the study, approximations have had to be made to fill knowledge gaps, not just from the developing parts of the globe. This study has highlighted gaps in our knowledge and areas in which further research is needed.

A detailed analysis of a large number of epidemiological studies has been undertaken to arrive at the estimates of burden of disease. The results indicate a relatively modest burden of disease from ultraviolet radiation, but highlight the important benefits from having adequate UVR to maintain vitamin D levels. It should however be noted that only selected disease outcomes have been included here, due to limited evidence or lack of globally available data. It may be that with additional evidence the estimations can become more comprehensive and the true burden will be much higher. Also indirect effects, which could not be included in this analysis, may have wide-ranging consequences on health.

All of the diseases caused by excessive ultraviolet radiation occur in adulthood and old age. They are a result of prolonged and excessive exposure to UVR or the result of a long latent period between exposure and disease. The calculation of the global burden of disease in

[6] The mid-point between the lower and upper estimate was 56 000 deaths, but the authors believe that the upper estimate was closer to reality, and therefore rounded up towards the upper estimate

DALYs favours diseases that affect the young, particularly causing mortality in the young (since this contributes the most years of life lost). In addition, several of the diseases related to UVR are of short duration or attract a low disability weight, despite being of very high prevalence.

Of note in the results is the relatively high (but most uncertain) burden of disease associated with reactivation of herpes labialis and sunburn – two highly prevalent, but relatively minor diseases. Cortical cataract is a significant cause of suffering through loss of vision.

Advocating a position of no UVR exposure is clearly not recommended, given the beneficial effect of UVR. In addition, it is important to moderate the extent of UVR-avoidance depending on the population. It would be deleterious to health to promote high degrees of sun avoidance in populations already at risk of vitamin D deficiency disorders – the deeply pigmented or otherwise sun protected populations.

8. Future directions

At the recent ICNIRP/WHO meeting in Munich (October 2005), which considered the risks and benefits of UVR exposure, the overwhelming consensus was that further research was required in many areas. To improve the precision of these burden of disease estimates and to develop more precise assessment of uncertainty using a comparative risk assessment framework we require information on the following:

What is the counterfactual distribution of minimum disease burden?

If the minimum disease burden occurs at the level of UVR exposure where vitamin D sufficiency is maintained but diseases of over-exposure do not occur, then that level of UVR exposure must be defined. In order for this to occur, further research is needed to clarify what is meant by "vitamin D sufficiency". While musculoskeletal health appears to be preserved at vitamin D levels greater than 50nmol/L, secretion of parathyroid hormone is suppressed and bone density maintained at vitamin D levels of at least 75-80nmol/L, leading to a recommendation of a lower limit of normal of 80nmol/L (*23*). However, it is not yet clear whether this level is sufficient to provide protection from autoimmune diseases or implicated cancers. Further research will be required to establish vitamin D insufficiency as a risk factor for these diseases and then to establish the level of vitamin D considered "sufficient". Similarly there should be clarification of whether there are critical ages where sufficiency is important (*131*).

Once a level of sufficiency is determined, research is then required to better understand the amount and wavelength of UVR to achieve and maintain that level. Based on current research findings, this will vary by:

- Age (*21*)
- Skin type (*132*)
- Location (*21*)
- Typical dietary intake of vitamin D

With these data, a counterfactual exposure distribution could be defined which would be one of theoretical minimum risk, providing a feasible, plausible and almost certainly cost-effective minimum risk.

What is the actual exposure distribution of the populations under consideration?

Better data are required to allow assessment of the actual exposure distribution of populations, taking into account ambient UVR, sun-seeking or avoiding behaviour, clothing habits, and use of sun protective devices (sunscreen, sunglasses, hats etc). Again, this would need to be determined in relation to age, sex and skin type. This measurement would ideally be in physical units, e.g. SED, rather than natural units, e.g. sunburns.

Diseases under consideration

This report outlines nine diseases for which there is sufficient evidence of an association with excessive UVR exposure and three diseases for which there is sufficient evidence of an association with inadequate UVR exposure.

Further data are now required to clarify the relationship between excessive UVR exposure and acute macular degeneration, nuclear and posterior subcapsular cataract and ocular melanoma. Similarly we require more evidence about the apparently complex association between UVR exposure and melanoma onset and progression (whereby excessive UVR exposure is associated with increased risk of developing melanoma, but decreased risk of progression (*133*)).

There are a large number of diseases possibly associated with insufficient UVR exposure – cancers of the colon, breast, prostate, ovary and others; autoimmune diseases such as multiple sclerosis, type 1 diabetes and rheumatoid arthritis; cardiovascular diseases such as hypertension, acute stroke and coronary artery disease; endocrine disorders such as type 2 diabetes; psychiatric disorders and disorders of mood; lymphomas including both Hodgkin and non-Hodgkin lymphoma.

Much more research will be required to elucidate the role of UVR exposure in the onset and progression of these disorders and to control for confounding from, for example, a lowered risk from being outdoors for other reasons, such as exercise. Further work is also required on the effect of solar UVR on vaccine efficacy and risk of infectious diseases.

Not only do we need to establish whether there is indeed a causal association between UVR exposure and these illnesses, but dose-response relationships should be clarified – such relationships will be complicated by the need to include time-varying exposure and perhaps critical periods of exposure.

In summary, to complete a more rigorous assessment using the comparative quantification of health risks (CQHR) framework we require attention to the following features of that methodology (*4*):

1. The burden of disease due to the observed exposure distribution in a population is compared with the burden from a hypothetical distribution, rather than a single reference level, such as non-exposed.

We have little information on either the hypothetical or the observed exposure distribution; what information we do have on the latter typically comes from fair skinned populations living in developed countries. These data may not be generalisable to the global community.

2. Multiple stages in the causal network of interactions among risk factors and disease outcome are considered, including the joint effects of changes in multiple risk factors.

Our understanding of the causal network of interactions both among risk factors and disease outcome are rudimentary. To a certain extent using the PAF derived from multiple regression analysis with adjustment for other factors allows consideration of the pure effect of this exposure. But more work is required for diseases such as cancers, autoimmune diseases and even for example the role of physical activity over the lifetime and bone density in investigating the effect of vitamin D on bone health.

3. The health loss due to a risk factor is calculated as a time-indexed stream of disease burden due to a time-indexed "stream" of exposure.

More sophisticated disease models and the interaction of disease diagnosis with exposure patterns (eg lower sun exposure following a diagnosis of skin cancer), will be required to better describe the time-indexed stream of disease burden.

Murray et al (*4*) describe using a structural model to calculate the burden of disease due to a risk factor. To examine the health effects of UVR exposure, such a model should include changing stratospheric (increasing ground level UVR) and tropospheric (decreasing ground level UVR) ozone levels, human skin pigmentation, diet, levels of physical activity, quality of health care and sun exposure behaviour. The lack of adequate data on the global distribution of the several of these parameters suggests that further research is required before such models can be of value. Modeling time-varying exposure for the diseases of UVR over-exposure may be challenging for diseases such as BCC or melanoma where high intermittent sun exposure in early life confers increased risk which may not decline over time, but accumulated exposure may be partially protective.

There is a growing body of work seeking to understand the differential effects of UVA versus UVB exposure on human health. Since it is ambient UVB that varies most with ozone depletion and with low zenith angle, and UVB is important to the induction of vitamin D synthesis, separating the health effects of different wavelengths will be crucial to predictive models.

This first global burden of disease assessment of the risks of UVR exposure has highlighted the gaps in our knowledge of the effects of this ubiquitous exposure. A great deal of further research is required across several fields to improve the precision of the estimates and to broaden the scope of the assessment.

References

1. **Jablonski, N.G. & Chaplin, G.** The evolution of human skin coloration. *Journal of Human Evolution. 39* (1): 57-106 (2000).
2. **Shaw, N.J. & Pal, B.R.** Vitamin D deficiency in UK Asian families: activating a new concern. *Archives of Disease in Childhood. 86* (3): 147-149 (2002).
3. **Diffey, B.L.** Stratospheric ozone depletion and the risk of non-melanoma skin cancer in a British population. *Physics in Medicine and Biology. 37* (12): 2267-2279 (1992).
4. **Murray, C.J. et al.** Comparative quantification of health risks conceptual framework and methodological issues. *Popul Health Metr. 1* (1): 1 (2003).
5. **Diffey, B.L.** Sources and measurement of ultraviolet radiation. *Methods. 28* (1): 4-13 (2002).
6. **Roy, C.R. et al.** The measurement of solar ultraviolet radiation. *Mutation Research. 422* (1): 7-14 (1998).
7. **Horneck, G.** Quantification of the biological effectiveness of environmental UV radiation. *Journal of Photochemistry and Photobiology B: Biology. 31* (1995): 43-49 (1995).
8. **WHO.** Environmental Health Criteria 160 - Ultraviolet radiation, World Health Organization, 1994.
9. **Sayre, R. et al.** Vitamin D vs Erythema: effects of solar angle and artificial sources. In: *Biologic Effects of Light 1998, Basel, Switzerland, 1998.*
10. **Madronich, S. et al.** Changes in biologically active ultraviolet radiation reaching the Earth's surface. *Journal of Photochemistry and Photobiology. B, Biology. 46* (1-3): 5-19 (1998).
11. **Roy, C.R. et al.** The solar UV radiation environment: measurement techniques and results. *Journal of Photochemistry and Photobiology B: Biology. 31*: 21-27 (1995).
12. **Gies, P. et al.** Trends in Ultraviolet Radiation. *Trends in Sun Protection Seminar - Anti Cancer Council of Victoria* (1999).
13. **Halder, R.M. & Bridgeman-Shah, S.** Skin cancer in African Americans. *Cancer. 75* (2 Suppl): 667-673 (1995).
14. **Clydesdale, G.J. et al.** Ultraviolet light induced injury: immunological and inflammatory effects. *Immunology and Cell Biology. 79* (6): 547-568. (2001).
15. **MacKie, R.M.** Effects of Ultraviolet Radiation on Human Health. *Radiation Protection Dosimetry. 91* (1-3): 15-18 (2000).
16. **Kollias, N. et al.** Erythema and melanogenesis action spectra in heavily pigmented individuals as compared to fair-skinned Caucasians. *Photodermatology, Photoimmunology and Photomedicine. 12* (5): 183-188 (1996).
17. **McCarty, C.A. et al.** The epidemiology of cataract in Australia. *American Journal of Ophthalmology. 128* (4): 446-465 (1999).
18. **Hill, D. et al.** Changes in sun-related attitudes and behaviours, and reduced sunburn prevalence in a population at high risk of melanoma. *European Journal of Cancer Prevention. 2* (6): 447-456 (1993).
19. **Vieth, R.** Vitamin D nutrition and its potential health benefits for bone, cancer and other conditions. *Journal of Environmental and Nutritional Medicine. 11* (4): 275-291 (2001).
20. **Holick, M.F.** Sunlight "D"ilemma: risk of skin cancer or bone disease and muscle weakness. *Lancet. 357* (9249): 4-6 (2001).
21. **Holick, M.F.** McCollum Award Lecture, 1994: vitamin D--new horizons for the 21st century. *American Journal of Clinical Nutrition. 60* (4): 619-630 (1994).
22. **Nozza, J.M. & Rodda, C.P.** Vitamin D deficiency in mothers of infants with rickets. *Medical Journal of Australia. 175* (5): 253-255 (2001).
23. **Hollis, B.W.** Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. *Journal of Nutrition. 135* (2): 317-322 (2005).
24. **Lips, P.** Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocrine Reviews. 22* (4): 477-501 (2001).
25. **Kricker, A. et al.** A dose-response curve for sun exposure and basal cell carcinoma. *International Journal of Cancer. 60* (4): 482-488 (1995).
26. **Henriksen, T. et al.** Ultraviolet-radiation and skin cancer. Effect of an ozone layer depletion. *Photochemistry and Photobiology. 51* (5): 579-582 (1990).
27. **Armstrong, B.K.** Stratospheric ozone and health. *International Journal of Epidemiology. 23* (5): 873-885. (1994).
28. **Hill, A.B.** The Environment and Disease: Association or Causation? *Proceedings of the Royal Society of Medicine. 58*: 295-300 (1965).

29. **Ferlay, J. et al.** GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0 ed, IARC CancerBase No. 5. Lyon, IARCPress, 2001.
30. **Parkin, D.M. et al.** Cancer Incidence in Five Continents. Lyon, IARC Scientific Publications No. 143, 1997.
31. **Chumbley, L.C.** Impressions of eye diseases among Rhodesian Blacks in Mashonaland. *S Afr Med J. 52* (8): 316-318. (1977).
32. **Lim, R. et al.** Cataract associations with pinguecula and pterygium: the Blue Mountains Eye Study. *American Journal of Ophthalmology. 126* (5): 717-719 (1998).
33. TOMS erythemal UV irradiance datasets, IRI/LDEO Climate Data Library, 2004.
34. **Hoy, W.E.** Nonmelanoma skin carcinoma in Albuquerque, New Mexico: experience of a major health care provider. *Cancer. 77* (12): 2489-2495. (1996).
35. **Woodhead, A.D. et al.** Environmental factors in nonmelanoma and melanoma skin cancer. *Journal of Epidemiology. 9* (6 Suppl): S102-114 (1999).
36. **Cristofolini, M. et al.** Risk factors for cutaneous malignant melanoma in a northern Italian population. *International Journal of Cancer. 39* (2): 150-154 (1987).
37. **Rosso, S. et al.** The multicentre south European study 'Helios'. II: Different sun exposure patterns in the aetiology of basal cell and squamous cell carcinomas of the skin. *British Journal of Cancer. 73* (11): 1447-1454. (1996).
38. **Vitasa, B.C. et al.** Association of nonmelanoma skin cancer and actinic keratosis with cumulative solar ultraviolet exposure in Maryland watermen. *Cancer. 65* (12): 2811-2817. (1990).
39. **Armstrong, B.K. & Kricker, A.** The epidemiology of UV induced skin cancer. *Journal of Photochemistry and Photobiology. B, Biology. 63* (1-3): 8-18 (2001).
40. **Ralph, B. & Stacey, M.** *Longman Atlas*. Melbourne, Addison-Wesley Longman Australia Pty Limited, 1999.
41. **Bruzzi, P. et al.** Estimating the population attributable risk for multiple risk factors using case-control data. *American Journal of Epidemiology. 122* (5): 904-914 (1985).
42. **Armstrong, B.K. & Kricker, A.** How much melanoma is caused by sun exposure? *Melanoma Research. 3* (6): 395-401 (1993).
43. **Murray, C. & Lopez, A.** The Global Burden of Disease. *Global Burden of Disease and Injury Series* (1996).
44. **Stouthard, M. et al.** *Disability Weights for Diseases in The Netherlands*, Department of Public Health, Erasmus University, Rotterdam, the Netherlands, 1997.
45. **Mathers, C. et al.** The burden of disease and injury in Australia. Canberra, Australian Institute of Health and Welfare, 1999, pp. 245.
46. **United Nations.** World Population Prospects: the 2000 Revision, United Nations Population Division Department of Economic and Social Affairs, 2001.
47. **Rosati, G.** The prevalence of multiple sclerosis in the world: an update. *Neurological sciences 22* (2): 117-139. (2001).
48. **Osterlind, A.** Epidemiology of malignant melanoma in Europe. *Acta Oncologica. 31* (8): 903-908 (1992).
49. **Osterlind, A. et al.** The Danish case-control study of cutaneous malignant melanoma. II. Importance of UV-light exposure. *International Journal of Cancer. 42* (3): 319-324 (1988).
50. **Langford, I.H. et al.** Multi-level modelling of geographically aggregated health data: a case study on malignant melanoma mortality and UV exposure in the European Community. *Statistics in Medicine. 17* (1): 41-57 (1998).
51. **Shibuya, K. et al.** Global and regional estimates of cancer mortality and incidence by site: II. Results for the global burden of disease 2000. *BMC Cancer. 2* (1): 37 (2002).
52. **Mathers, C.D. et al.** Global and regional estimates of cancer mortality and incidence by site: I. Application of regional cancer survival model to estimate cancer mortality distribution by site. *BMC Cancer. 2* (1): 36 (2002).
53. **Stern, R.S.** The mysteries of geographic variability in nonmelanoma skin cancer incidence. *Archives of Dermatology. 135* (7): 843-844 (1999).
54. **Harvey, I. et al.** Non-melanoma skin cancer and solar keratoses. I. Methods and descriptive results of the South Wales Skin Cancer Study. *British Journal of Cancer. 74* (8): 1302-1307. (1996).
55. **Weinstock, M.A. et al.** Nonmelanoma skin cancer mortality. A population-based study. *Archives of Dermatology. 127* (8): 1194-1197 (1991).
56. **Foster, H.M. & Webb, S.J.** Skin cancer in the North Solomons. *Australian and New Zealand Journal of Surgery. 58* (5): 397-401 (1988).
57. **Schottenfeld, D. & Fraumeni, J.F., Jr.** Cancer Epidemiology and Prevention, 2nd ed, Oxford University Press, Inc, 1996.

58. **Mora, R.G. & Perniciaro, C.** Cancer of the skin in blacks. I. A review of 163 black patients with cutaneous squamous cell carcinoma. *Journal of the American Academy of Dermatology. 5* (5): 535-543 (1981).
59. **Marks, R.** Squamous cell carcinoma. *Lancet. 347* (9003): 735-738 (1996).
60. **Matsuoka, L.Y. et al.** Basal cell carcinoma in black patients. *Journal of the American Academy of Dermatology. 4* (6): 670-672 (1981).
61. **Altman, A. et al.** Basal cell epithelioma in black patients. *Journal of the American Academy of Dermatology. 17* (5 Pt 1): 741-745 (1987).
62. **Halder, R.M. & Bang, K.M.** Skin cancer in blacks in the United States. *Dermatologic Clinics. 6* (3): 397-405 (1988).
63. **Preston, D.S. & Stern, R.S.** Nonmelanoma cancers of the skin. *New England Journal of Medicine. 327* (23): 1649-1662. (1992).
64. **Weinstock, M.A.** Death from skin cancer among the elderly: epidemiological patterns. *Archives of Dermatology. 133* (10): 1207-1209. (1997).
65. **Hannuksela-Svahn, A. et al.** Basal cell skin carcinoma and other nonmelanoma skin cancers in Finland from 1956 through 1995. *Archives of Dermatology. 135* (7): 781-786 (1999).
66. **Raasch, B.A. & Buettner, P.G.** Multiple nonmelanoma skin cancer in an exposed Australian population. *International Journal of Dermatology. 41* (10): 652-658 (2002).
67. **Green, A. et al.** Skin cancer in a Queensland population. *Journal of the American Academy of Dermatology. 19* (6): 1045-1052. (1988).
68. **Frost, C.A. et al.** The prevalence and determinants of solar keratoses at a subtropical latitude (Queensland, Australia). *British Journal of Dermatology. 139* (6): 1033-1039 (1998).
69. **Massa, A. et al.** [Prevalence of cutaneous lesions in Freixo de Espada a Cinta]. *Acta Medica Portuguesa. 13* (5-6): 247-254. (2000).
70. **Araki, K. et al.** Incidence of skin cancers and precancerous lesions in Japanese--risk factors and prevention. *Journal of Epidemiology. 9* (6 Suppl): S14-21 (1999).
71. **Suzuki, T. et al.** Incidence of actinic keratosis of Japanese in Kasai City, Hyogo. *Journal of Dermatological Science. 16* (1): 74-78. (1997).
72. **Naruse, K. et al.** Prevalence of actinic keratosis in Japan. *Journal of Dermatological Science. 15* (3): 183-187. (1997).
73. **Griffiths, C.E.** Dowling Oration delivered at the Royal College of Physicians, London, Friday 5 June 1998. Retinoids: renaissance and reformation. *Clinical and Experimental Dermatology. 24* (4): 329-335 (1999).
74. **Thompson, S.C. et al.** Reduction of solar keratoses by regular sunscreen use. *New England Journal of Medicine. 329* (16): 1147-1151. (1993).
75. **Marks, R. et al.** Malignant transformation of solar keratoses to squamous cell carcinoma. *Lancet. 1* (8589): 795-797. (1988).
76. **McGee, R. et al.** A community survey of sun exposure, sunburn and sun protection. *New Zealand Medical Journal. 108* (1013): 508-510 (1995).
77. **McGee, R. et al.** Sunburn and sun protection among young children. *Journal of Paediatrics and Child Health. 33* (3): 234-237 (1997).
78. **Richards, R. et al.** Sunburn and sun protection among New Zealand adolescents over a summer weekend. *Australian and New Zealand Journal of Public Health. 25* (4): 352-354 (2001).
79. **MacGregor, D.M. & White, M.I.** Sunburn in children -- the Aberdeen experience. *Clinical and Experimental Dermatology. 26* (2): 137-140 (2001).
80. **Cronin, K.J. et al.** A 1-year prospective study of burns in an Irish paediatric burns unit. *Burns. 22* (3): 221-224 (1996).
81. **Schofield, P.E. et al.** Trends in sun protection behaviour among Australian young adults. *Australian and New Zealand Journal of Public Health. 25* (1): 62-65 (2001).
82. **Piccolo-Lobo, M.S. et al.** Sun tanning-related burns--a 3-year experience. *Burns. 18* (2): 103-106 (1992).
83. **Davis, K.J. et al.** Summer sunburn and sun exposure among US youths ages 11 to 18: national prevalence and associated factors. *Pediatrics. 110* (1 Pt 1): 27-35 (2002).
84. **Bourke, J.F. & Graham-Brown, R.A.** Protection of children against sunburn: a survey of parental practice in Leicester. *British Journal of Dermatology. 133* (2): 264-266 (1995).
85. **Boldeman, C. et al.** Tanning habits and sunburn in a Swedish population age 13-50 years. *European Journal of Cancer. 37* (18): 2441-2448 (2001).
86. **Diffey, B.L.** Sunscreens, suntans and skin cancer. People do not apply enough sunscreen for protection. *BMJ. 313* (7062): 942. (1996).

87. **Reynolds, K.D. et al.** Predictors of sun exposure in adolescents in a southeastern U.S. population. *Journal of Adolescent Health. 19* (6): 409-415 (1996).
88. **Morris, J. et al.** Sun protection behaviours and the predictors of sunburn in young children. *Journal of Paediatrics and Child Health. 34* (6): 557-562 (1998).
89. **Hall, H.I. et al.** Factors associated with sunburn in white children aged 6 months to 11 years. *American Journal of Preventive Medicine. 20* (1): 9-14 (2001).
90. **Hall, H.I. & Rogers, J.D.** Sun protection behaviors among African Americans. *Ethnicity and Disease. 9* (1): 126-131 (1999).
91. **Leske, M.C. et al.** Prevalence of lens opacities in the Barbados Eye Study. *Archives of Ophthalmology. 115* (1): 105-111. (1997).
92. **Hu, T.S. et al.** Age-related cataract in the Tibet Eye Study. *Archives of Ophthalmology. 107* (5): 666-669 (1989).
93. **West, S.K. et al.** Sunlight exposure and risk of lens opacities in a population-based study: the Salisbury Eye Evaluation project. *JAMA. 280* (8): 714-718 (1998).
94. **Delcourt, C. et al.** Light exposure and the risk of cortical, nuclear, and posterior subcapsular cataracts: the Pathologies Oculaires Liees a l'Age (POLA) study. *Archives of Ophthalmology. 118* (3): 385-392 (2000).
95. **Congdon, N. et al.** Prevalence of the different types of age-related cataract in an African population. *Investigative Ophthalmology and Visual Science. 42* (11): 2478-2482 (2001).
96. **Klein, B.E. et al.** Incidence of age-related cataract: the Beaver Dam Eye Study. *Archives of Ophthalmology. 116* (2): 219-225 (1998).
97. **Klein, B.E. et al.** Incident cataract surgery: the Beaver Dam eye study. *Ophthalmology. 104* (4): 573-580 (1997).
98. **Wang, J.J. et al.** Visual impairment, age-related cataract, and mortality. *Archives of Ophthalmology. 119* (8): 1186-1190. (2001).
99. **WHO.** World Health Report 2001, World Health Organization, 2001.
100. **Hirst, L.W.** Distribution, Risk Factors, and Epidemiology of Pterygium. In: Taylor, H., ed. *Pterygium*, Kugler Publications, The Hague, The Netherlands, 2000, pp. 15-27.
101. **Cameron, M.** *Pterygium Throughout the World*. Illinois, Thomas, 1965.
102. **McCarty, C.A. et al.** Epidemiology of pterygium in Victoria, Australia. *British Journal of Ophthalmology. 84* (3): 289-292 (2000).
103. **Wong, T.Y. et al.** The prevalence and risk factors for pterygium in an adult Chinese population in Singapore: the Tanjong Pagar survey. *American Journal of Ophthalmology. 131* (2): 176-183 (2001).
104. **Panchapakesan, J. et al.** Prevalence of pterygium and pinguecula: the Blue Mountains Eye Study. *Australian and New Zealand Journal of Ophthalmology. 26 Suppl 1*: S2-5 (1998).
105. **Taylor, H.R.** The prevalence of corneal disease and cataracts in Australian aborigines in Northwestern Australia. *Australian Journal of Ophthalmology. 8* (4): 289-301 (1980).
106. **Ahmad, O. et al.** Age Standardization of Rates: A New WHO Standard, World Health Organization.
107. **Rasanayagam, R.T.** The incidence and racial distribution of pterygium in West Malaysia. *Transactions of the Ophthalmological Society of New Zealand. 25*: 56-59 (1973).
108. **Threlfall, T.J. & English, D.R.** Sun exposure and pterygium of the eye: a dose-response curve. *American Journal of Ophthalmology. 128* (3): 280-287 (1999).
109. **Wlodarczyk, J. et al.** Pterygium in Australia: a cost of illness study. *Clinical and Experimental Ophthalmology. 29* (6): 370-375 (2001).
110. **Ashaye, A.O.** Pterygium in Ibadan. *West African Journal of Medicine. 10* (3-4): 232-243 (1991).
111. **Malik, M.O. & El Sheikh, E.H.** Tumors of the eye and adnexa in the Sudan. *Cancer. 44* (1): 293-303. (1979).
112. **Waddell, K.M. et al.** Carcinoma of the conjunctiva and HIV infection in Uganda and Malawi. *British Journal of Ophthalmology. 80* (6): 503-508. (1996).
113. **Cervantes, G. et al.** Squamous cell carcinoma of the conjunctiva: clinicopathological features in 287 cases. *Canadian Journal of Ophthalmology. 37* (1): 14-19; discussion 19-20. (2002).
114. **Lee, G.A. et al.** Risk factors in the development of ocular surface epithelial dysplasia. *Ophthalmology. 101* (2): 360-364 (1994).
115. **Sun, E.C. et al.** Epidemiology of squamous cell conjunctival cancer. *Cancer Epidemiology, Biomarkers and Prevention. 6* (2): 73-77 (1997).
116. **Axell, T. & Liedholm, R.** Occurrence of recurrent herpes labialis in an adult Swedish population. *Acta Odontologica Scandinavica. 48* (2): 119-123 (1990).
117. **Young, T.B. et al.** Cross-sectional study of recurrent herpes labialis. Prevalence and risk factors. *American Journal of Epidemiology. 127* (3): 612-625 (1988).

118. **Reichart, P.A.** Oral mucosal lesions in a representative cross-sectional study of aging Germans. *Community Dentistry and Oral Epidemiology. 28* (5): 390-398 (2000).
119. **Axell, T. et al.** Prevalence of oral soft tissue lesions in out-patients at two Malaysian and Thai dental schools. *Community Dentistry and Oral Epidemiology. 18* (2): 95-99 (1990).
120. **Barkvoll, P. & Attramadal, A.** Recurrent herpes labialis in a military brass band. *Scandinavian Journal of Dental Research. 95* (3): 256-258 (1987).
121. **Young, S.K. et al.** A clinical study for the control of facial mucocutaneous herpes virus infections. I. Characterization of natural history in a professional school population. *Oral Surgery, Oral Medicine, Oral Pathology. 41* (4): 498-507 (1976).
122. **Embil, J.A. et al.** Prevalence of recurrent herpes labialis and aphthous ulcers among young adults on six continents. *Canadian Medical Association Journal. 113* (7): 627-630 (1975).
123. **Gibson, J.J. et al.** A cross-sectional study of herpes simplex virus types 1 and 2 in college students: occurrence and determinants of infection. *Journal of Infectious Diseases. 162* (2): 306-312 (1990).
124. **Rosen, H.** 1,25(OH)2 vitamin D for osteoporosis. *Annals of Internal Medicine. 114* (6): 519-520 (1991).
125. **Glerup, H. et al.** Commonly recommended daily intake of vitamin D is not sufficient if sunlight exposure is limited. *Journal of Internal Medicine. 247* (2): 260-268. (2000).
126. **Lulseged, S.** Severe rickets in a children's hospital in Addis Ababa. *Ethiopian Medical Journal. 28* (4): 175-181. (1990).
127. **Gloth, F.M., 3rd et al.** Vitamin D deficiency in homebound elderly persons. *JAMA. 274* (21): 1683-1686. (1995).
128. **Gannage-Yared, M.H. et al.** Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. *Journal of Bone and Mineral Research. 15* (9): 1856-1862 (2000).
129. **Ekanem, E.E. et al.** Nutritional rickets in Calabar, Nigeria. *Annals of Tropical Paediatrics. 15* (4): 303-306. (1995).
130. **Dwyer, T. et al.** The use of spectrophotometry to estimate melanin density in Caucasians. *Cancer Epidemiology, Biomarkers and Prevention. 7* (3): 203-206 (1998).
131. **van der Mei, I.A. et al.** Past exposure to sun, skin phenotype, and risk of multiple sclerosis: case-control study. *BMJ. 327* (7410): 316 (2003).
132. **Clemens, T.L. et al.** Increased skin pigment reduces the capacity of skin to synthesise vitamin D3. *Lancet. 1* (8263): 74-76 (1982).
133. **Berwick, M. et al.** Sun exposure and mortality from melanoma. *Journal of the National Cancer Institute. 97* (3): 195-199 (2005).