GLOBAL CHANGE

Dutch National Research Programme on Global Air Pollution and Climate Change

Ozone layer - climate change interactions Influence on UV levels and UV related effects

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GLOBAL CHANGE

Nationaal Onderzoek Programma Mondiale Luchtverontreiniging en Klimaatverandering (NOP)

Het Nationaal Onderzoek Programma Mondiale Luchtverontreiniging en Klimaatverandering (NOP) bevindt zich thans in de twee fase (1995-2001). De eerste fase, waarin 150 projecten zijn uitgevoerd, liep van 1990 tot 1995. Naar verwachting zullen in de tweede fase uiteindelijk circa 80 projecten worden uitgevoerd. Gezien de aard van het klimaatprobleem is een multi-disciplinaire benadering binnen het NOP noodzakelijk. Het programma is onderverdeeld in vier thema's:

I Gedrag van het klimaatsysteem als geheel en in onderdelen
II Kwetsbaarheid van natuurlijke en maatschappelijke systemen voor klimaatverandering
III Maatschappelijke oorzaken en oplossingen
IV Integratie en assessment

Het primaire doel van het NOP, als strategisch en lange termijn onderzoekprogramma, is te voorzien in de behoefte aan beleidsrelevante informatie voor de ontwikkeling van het nationale en internationale klimaatbeleid. Naast het bereiken van dit inhoudelijke doel, wordt er ook veel belang aan gehecht dat het onderzoek op de langere termijn verankerd zal blijven in de Nederlandse onderzoeksstructuur.
Door het NOP wordt twee maandelijks de (gratis) onderzoeksnieuwsbrief "CHANGE" uitgegeven.
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National Research Programme on Global Air Pollution and Climate Change (NRP)

The National Research Programme on Global Air Pollution and Climate Change (NRP) is currently in its second phase, 1995-2001. The first phase, in which 150 projects were carried out, ran from 1990 to 1995. About 80 projects are expected to be finally realised in the second phase. The nature of the climate problem warrants a multi-disciplinary approach within the NRP. The programme is categorised into four themes:

I Dynamics of the climate system and its component parts
II Vulnerability of natural and societal systems to climate change
III Societal causes and solutions
IV Integration and assessment

The primary objective of the NRP as a strategic and long-term research programme is to meet the demand for policy-relevant information for the development of national and international climate policy. Besides realising this substantive objective, a great deal of importance is attached to the long-term anchoring of the research within the Dutch research structure.
The NRP Programme Office publishes a (free) research newsletter called "CHANGE" every two months. For more information on the NRP please contact:

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Contents

Abstract

Ozone in the atmosphere serves as a partially protective filter against the most harmful part of the solar UV-spectrum. Decreases in ozone lead to increases in ambient UV with a wide variety of adverse effects on human health, aquatic and terrestrial ecosystems and food chains. Human health effects include the incidence of skin cancer, cataracts and an impairment of the immune system.
Ozone depletion has been observed over the past decades, and is most likely caused by man made emissions of halocarbons. The ozone depletion observed over the past decades has probably led to a 5-10% increase in harmful UV-radiation in large parts of Europe. Due to the long atmospheric life time of the ozone depleting substances the countermeasures agreed upon could at best be expected to lead to a slow recovery of the ozone layer in the next 50-60 years. However, in that best scenario it is assumed that no interaction occurs with climatological changes, and that a full global compliance with the strictest Amendments of the Montreal Protocol is obtained. Recent scientific evidence indicates that climate change might delay the recovery of the ozone layer by 10 to 20 years. This report summarizes the present knowledge on the climate-ozone interaction, the past and present UV-climate in Europe and dose-effect relationships for health and aquatic effects. Using this information a preliminary integrated risk analysis is provided for skin cancer risks and effects on the primary production of phytoplankton. Skin cancer risks due to ozone depletion peaks in the period 2050-2070. The excess risks in North western Europe due to ozone depletion is estimated at 50-60 additional cases per million per year if no climate-ozone interaction is included, and nearly 100 additional cases per million per year if the interaction is included. It should be noted that large uncertainties still exist in view of the gaps in the present knowledge on various aspects of the cause-effect chain.

1. Introduction and outline of the report

The stratospheric ozone layer effectively serves as a protective shield that reduces the harmful ultraviolet radiation (UV) reaching the earths surface. As a consequence, the depletion of stratospheric ozone observed over the last two decades, probably caused by emission of man-made halocarbons (CFCs), has probably led to higher ambient UV-levels. An increase in UV at ground-level may induce a wide range of harmful effects like an increase in skin cancer, cataracts, a decrease in bio-mass production and crop yields, and suppression of the human immune system [United Nations Environmental Program (UNEP), 1998]. The Vienna Convention in 1985 was the starting point for international policy agreements to reduce the production and emission of ozone depleting substances, and provided the framework for the restrictive protocols that were agreed upon later. The Montreal protocol in 1987 provided the first restrictive countermeasures and in view of the compelling evidence that ozone depletion occurred, this protocol was subsequently strengthened in several more restrictive Amendments. In the latest Amendments the production of the most potent ozone depleting substances is completely phased out in 1996. A longer phase out period is allowed for the developing countries. These countermeasures are expected to lead to a slow recovery of the ozone layer over the next century.
The effects of the agreed countermeasures in terms of a recovery of the ozone layer, the (future) UV-radiation levels and their effect on the excess skin cancer risks associated with ozone depletion were previously analysed for the USA and Europe [Slaper et al., 1996]. In line with other studies (UNEP, 1998) it was expected that a slow recovery of the ozone layer will occur with a return to 'normal' (1980) levels around 2050. Excess skin cancer risks, caused by ozone depletion, are in those scenarios expected to rise until 2050-2070. Slaper et al [1996] clearly showed the potential success of the countermeasures in reducing the future excess skin cancer risks associated with the chemical depletion of ozone.
A limitation of these analyses is that they assume ozone depletion to be purely chemically driven, and that no interaction with climate change is included in the analysis.
Growing insight in the radiative balance of the atmosphere and its disturbance by the continued increased emission of greenhouse gases, indicates cooling of the stratosphere and a change in dynamical processes. These changes can have implications for the ozone levels on itself and furthermore they can interact with the chemical break down processes. Until recently, risk assessments did not account for this link between ozone layer morphology and dynamical processes initiated by climate change.

The major goal of this study is to give a quick scan of the possible interactions between the stratospheric ozone layer and climate change and to assess how this interaction may affect ambient UV-levels and health and environment. In the case of skin cancer a comprehensive risk assessment, including ozone-climate interaction, has been made.
Additionally this study gives an update of the present knowledge on UV related health and environmental effects, in particular: skin cancer, cataracts, effects on the immune system and effects on the marine environment.

The report consist of two parts: the main report summarising the general conclusions and knowledge on UV related health and environmental effects, and five appendices underpinning the main report. The main report serves as a kind of executive summary

for the reader who is interested in a concise overview of ozone-climate interaction, and the consequences for UV load and related effects on health and environment.
The appendices give an extensive overview of UV related effects and full detail on the risk assessment. It should be noted that this report reflects the outcome of a short integrative study, and as such should be seen as a preliminary assessment based on an integration of present knowledge.

This introduction is followed by a survey of recent knowledge on interactions between the climate system and the ozone layer (chapter 2). This chapter first overviews the observational data and then focuses on the ozone depleting chemical and dynamical processes and their implications for the future development of the ozone layer. Chapter 3 gives a brief overview on the major factors determining the UV-climate and the changes in the UV-radiation levels in Europe that occurred over the past decades. Chapter 4 evaluates the present knowledge on UV related effects on human health and the environment. The main topics are: skin cancer, cataracts, immune modulation and effects on the marine environment. Chapter 5 is dedicated to an integrated risk assessment for skin cancer based on the survey presented in chapter 4 and appendix 1 and with inclusion of the interaction between the ozone layer and climate change described in chapter 2. Chapter 6 summarises the main conclusion of the report (and the appendices). Chapter 7 gives an overview of the future research needed to reinforce the scientific basis for these conclusions and to extend the scope of this report to other important UV related effects.

2. Interaction between climate system and ozone layer

2.1 Introduction

Given the importance of chlorofluorocarbons (CFCs) for chemical ozone loss, one would expect the onset of ozone layer recovery to follow the decrease of CFCs that started at the end of the 1990s. However, severe chemical ozone loss was still observed in the most recent winters. Moreover, model studies suggested that the recovery could have a delay with even 10-15 years. The continued increase of greenhouse gases, such as CO2, CH4, N2O, and water vapour is seen as the main cause for this delay. These gases disturb the radiative balance of the atmosphere with important consequences for temperature and dynamical processes. Only recently established temperature records yield convincing evidence of the existence of such a disturbance. The greenhouse gases not only affect the radiative balance, but also the chemical balance. The consequences of these effects for the ozone layer are just being explored. As yet, many uncertainties still remain, both in the long-term dynamical variability as in the complex chemical processes that both determine the global distribution of ozone and its long-term trend.

To predict the future ozone layer and the subsequent changes in UV-exposure it is clear that understanding of the interactions between changes in climate and the ozone layer over the past two decades is a prerequisite. This section summarises the most recent analysis of about 20 years of global ozone layer and meteorological data that form the basis of current knowledge of ozone-climate interactions. In addition, a summary is given of prognostic calculations of the ozone layer using state-of-the-art two and three-dimensional chemistry-climate models. Finally, several poorly known processes will be discussed that may be crucial for future ozone layer recovery.

2.2 Observations

Ozone observation platforms include spectrometer techniques at ground-based stations and on satellites and in-situ sampling on balloons. In addition, ground-based LIDAR observations complement the network. The ground-based stations, including those with in-situ balloon-borne ozone profiling are located at various sites around the globe. The satellite data have a nearly global coverage. The majority of the ozone data contains only about 20-year records. At very sparse locations (for example Arosa) the records date back to the 1920's.

Many studies have been carried out analysing these records. A recent analysis, including a compilation of ozone data from all available platforms, revealed significant negative trends outside the tropical region between 1979 and 1997 [Randel et al., 1999; Cunnold et al., 2000]. These trend studies discriminate between total ozone column data and vertical profiles. The profiles illustrate an altitude dependence of the trends. Two distinct minima for the negative trends are found, one in the lower part of the stratosphere between 10-22 km with a local minimum at 15 km of $-7.4 \pm 2.0\%$, and the other in the upper stratosphere above 35 km with a local minimum of $-7.3 \pm 4.6\%$ [Randel et al., 1999]. Their trend analysis shows a strong

seasonal dependence with the largest trends occurring during winter and spring. We will focus on the lower stratosphere, where most of the ozone is located.

2.3 Causes of mid-latitude ozone trends 1980 - 2000

2.3.1 Chemistry

After the recognition that man-made CFCs are responsible for large-scale ozone losses, it was believed that negative ozone trends were primarily due to chemical catalytic ozone destruction. This view was mainly based on 2-D chemistry-transport modelling [Solomon et al., 1998]. More sophisticated 3-D modelling became available that shaded this view. It was shown that most of the ozone variations could be explained by dynamical processes [Chipperfield et al., 1999]. Nevertheless, Chipperfield et al. [1999] calculated 2-3% decrease of the total ozone column at mid-latitudes between 1991-1998 due to chemical ozone loss during the polar winter/early spring. This finding was corroborated by a 3D Reverse Domain Filling study for several Arctic winters in the 1990s [Knudsen and Groos, 2000]. This study showed that in the 1990's about 40% of the mid-latitude ozone reduction in spring is caused by chemical ozone destruction during the Arctic winter.
Additional global model studies indicated that not only the 2D [Portmann et al., 1999], but also the 3D global models underestimated the observed ozone trends [Austin et al., 2000]. Although it was shown that a 3D approach is required to describe the complex transport processes, one major problem is the computational costs. Increasing computational costs go on the expense of detail with which key processes are included. For example, to calculate chemical polar ozone loss heterogeneous chemical reactions on particles is essential, which none of the 3D model studies so far includes with the required detail. In fact, even the 2D models contain highly parameterised heterogeneous chemistry.
An important observational finding in this respect is the significant negative temperature trends in the lower stratosphere of –0.3 to –0.6 K per decade [Angell, 2000]. Heterogeneous chemistry is extremely temperature sensitive; lower temperatures means stronger ozone loss. The causes for the negative temperature trends in the lower stratosphere are not completely known. Several studies, however, have demonstrated that increasing greenhouse gases, including water vapour are primarily responsible for the cooling in the lower stratosphere [Shindell et al., 2001; Forster and Shine, 1999]. A recent study illustrated that less UV absorption owing to the ozone decrease itself cannot fully explain these trends, al least in the northern hemisphere [Langematz, 2000; Zhou et al. [2000].

2.3.2 Dynamical Processes

By disturbing the radiative balance of the atmosphere, increasing greenhouse gases caused a change in dynamical processes [Shindell et al., 2001]. This directly influences the ozone layer. The strong link between dynamical processes and ozone layer morphology is known for a long time. For example, a trend is observed in the North Atlantic Oscillation (NAO) during winter and early spring during the past two decades [Appenzeller et al., 2000]. This oscillation includes the low-pressure area close to Iceland and the high-pressure area at the Azores. This trend could explain part of the ozone trends at mid-latitudes, but only during winter [Appenzeller et al., 2000].
Another meteorological analyses illustrated an increase in transport of ozone poor subtropical air into mid-latitudes over the last 25 years [Reid et al., 2000]. However, the analysis has only been carried out for a limited number of stations. A physical explanation for the decrease in ozone was first given by Steinbrecht et al. [1998]. Trends in the above mentioned transport

processes cause an increase of the tropopause altitude [Steinbrecht et al., 1998, 2001; De Forster and Tourpali, 2001]. This further leads to a decrease in ozone. However, the studies do not show a consistent picture at different locations. Several locations do not show a difference in ozone column, despite the observed increase in tropopause altitude. In this respect it is important to note that most of this ozone decrease is limited to the lower part of the stratosphere, i.e., below the ozone maximum. This means that the changes in total ozone column are relatively small. Hence, the effect on UV absorption will also be limited.
These dynamic processes are somehow linked to each other and to an overall increase of the large-scale meridional circulation [Butchart and Scaife, 2001; Hood et al., 1999]. It is not surprising that changes in the large-scale meridional circulation also cause changes in polar vortex dynamics. There is observational evidence that the Arctic vortex has strengthened over the last three decades [Hood et al., 1999]. A stronger vortex persists longer into spring, allowing more chemical ozone destruction. It is estimated that the polar vortex last about 4 weeks longer than 20 years ago [Zhou et al., 2000].
All together, the contribution of dynamic processes to the total ozone trends varies between 25-50%. However, note that most of the studies are restricted to the European winter and accurate estimates for all longitudes at northern midlatitudes and all seasons remain to be done. It is expected that the yearly and zonal average will be somewhat smaller. A summary of the trend studies can be found in the latest European Ozone Research Assessment Report [EC, 2001]

2.3.3 The future ozone layer

The inability of models to simulate the recent ozone trends accurately prevents a reliable prediction of the ozone layer in the future. Nevertheless, attempts by several modelling groups will be summarised in this section.
Several 3D and 2D model studies predicted the ozone layer up to 2030-2060 [Shindell et al., 1998; 1999; Austin et al., 2001, 2000; Bruehl, 2000; Dvortsov and Solomon, 2001]. Most model results show that the ozone layer will be recovered around 2060, but some models predict that the recovery of the ozone layer is delayed with about 10-15 years. As mentioned earlier, it is assumed that increasing greenhouse gas abundances are primarily responsible. Given the complex interactions between dynamics and ozone, it is not surprising that the model results show significant differences. Shindell et al. report increased ozone loss during the Arctic winter until 2010-2020, while this is absent in the calculations of Austin et al. [2000]. In addition, in their latest calculations the delay is less pronounced than in Shindell et al and the ozone changes fall within the inter-annual variability [Austin et al., 2001]. On the other hand, Bruehl et al. show that there is an earlier building-up of the polar vortex and even a southward movement of its location during the winter, near Europe in 2030. Dvortsov and Solomon [2001] report a delay of the ozone recovery by chemical ozone loss owing to continued water vapour increase, which none of the models so far addressed. This chemical process affects mid-latitude ozone chemistry directly and requires no isolated cold polar vortex conditions.
The models that are used in all these studies differ significantly in resolution and in detail with which dynamics and chemistry are described. For example, Shindell et al. use a low-resolution model with highly parameterised chemistry, while Austin et al. [2001] and Bruehl [2000] use higher resolutions and more sophisticated transport and chemistry schemes.
Figure 2.1 summarises the future development of the ozone layer The shaded area gives the range in prognoses based on the publications mentioned above. As a comparison the predictions for the year averaged ozone column, based on the RIVM risk assessment model AMOUR are included.

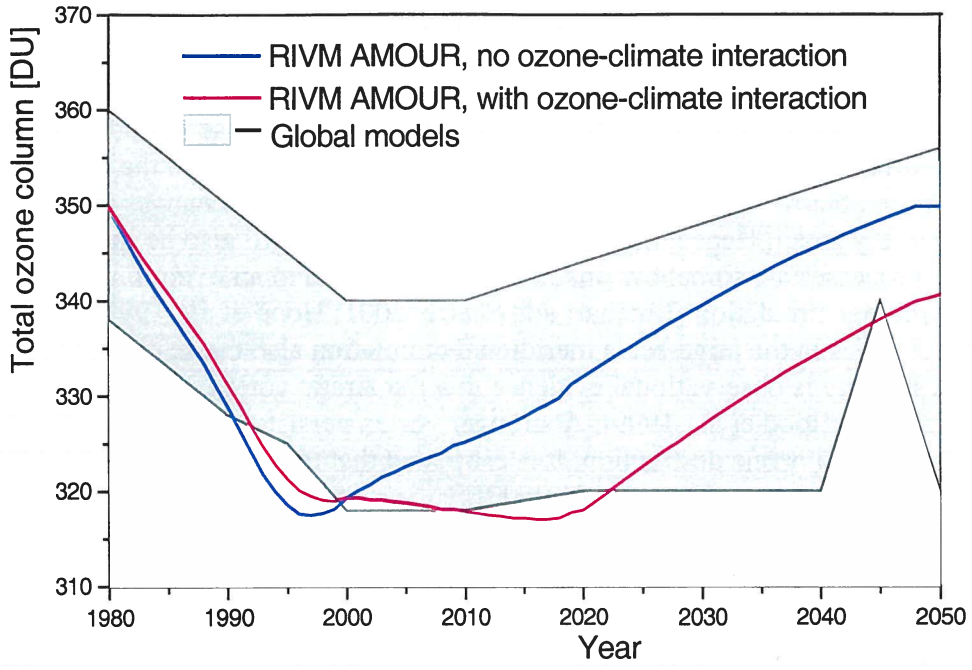

Figure 2.1 **Range in prognoses for the future development of the stratospheric ozone layer (hatched area) based on recent publications [Shindell et al., 1998; 1999; Austin et al., 2001, Austin et al., 2000; Dvortsov and Solomon, 2001]. The two drawn lines give the prognosis based on calculations with RIVM AMOUR. In blue without ozone-climate interaction and in red with ozone-climate interaction (see appendix 5, figure 17).**

From the results in figure 2.1 we can conclude that the calculated past trend obtained from the global models appears somewhat lower, than the trend obtained with the AMOUR-model. The latter, however appears to be in better agreement with the observations (illustrated in the calculated UV-trends in appendix 5, figure 18). The observed differences may point to an underestimation of the (historical) ozone depletion by the global models. The difference may also arise from regional differences in ozone depletion. The global model calculations are based on zonal averages, but the AMOUR-profiles represent regional observations representative for north west Europe (see figure 6, appendix 5).
A major uncertainty in all model calculations, however, is the crude representation of heterogeneous chemistry, as mentioned earlier. A few studies report on the importance of ice particles and their effect on ozone loss if the future temperature decline in the stratosphere is continued. [Waibel et al., 1999; Tabazadeh et al., 2000]. Waibel et al. calculated sustaining fast ozone loss rates, even considering reduced chlorine abundance's at 2070 levels. However, a weakness is that these studies have only been performed with a boxmodel. Currently, no global chemistry-transport model has included a realistic ice particle sedimentation scheme, not even the most sophisticated 3D models.
It is clear that future changes in dynamical processes and continued cooling of the stratosphere favours the conditions for strong chemical polar ozone loss. Most models predict some delay of the ozone recovery. However, it should be noted that the accuracy of the calculated transport processes is low, that the predicted temperature cooling shows large differences among the models, and that the chemical schemes representing polar ozone loss are too simple.

2.4 Conclusions

Figures 2.2 and 2.3 summarise the relative contribution of long-term mid-latitude trends in key parameters discussed in this section to changes in total ozone column.
Table 2.1 gives a brief explanation of the different variables.
During the past two decades the increasing chlorine loading and the development of strong isolated polar vortices, especially during the 1990s, were the major causes for the observed negative ozone trends. The world-wide moratorium on CFC emissions is expected to be the predominant cause of the recovery of the ozone layer. However, trends in other – climate change driven - processes, with the largest contribution from the strength of the polar vortex in combination with decreasing temperatures, will slow down the recovery speed. In figure 2.3 the assumed net recovery is shown in blue, which is approximately 70% in 2050 instead of the expected 100% if climate change is neglected. This difference can be translated in 15-20 years of delay, as discussed in this section.

Table 2.1. Explanation of the processes in figures 2.2 and 2.3

Processes	Description	Chemical mid- latitude	Dynamical mid-latitude	Chemical polar	Dynamical polar	Montreal protocol	Kyoto protocol
CFCs, halons	Catalytic ozone destruction in the stratosphere; decreased depletion is anticipated due to lower emissions of CFCs, halons, CCl_4, CH_3CCl_3, HCFCs.	x				x	
N_2O	Chemical destruction of ozone by NO_x-cycle; anticipated increase in N_2O emissions.	x					x
CH_4	Formation of reservoir species HCl decreases ozone destruction.	x					x
T(gas chem)	Temperature dependence of the Chapman cycle; anticipated decrease in temperature in the stratosphere.	x					x
Polar vortex	Additional polar ozone loss by cooling and a stronger vortex, combined with spread out of ozone depleted air into mid-latitudes		x	x	x		x
H_2O increase	Increase in stratospheric H_2O as a result of changes in dynamics and methane oxidation, and consequent chemical reactions that affect ozone	x	x				x
Dynamics	An increase of the stratospheric circulation intensity, leading to: - Increase of tropopause height - Accelerated removal of CFCs from the atmosphere - Increase transport subtropical air into mid-latitudes		x				?

Notes: Table 2. (and figures 2.2 and 2.3) assume full compliance with the Montreal Protocol and no control measures on the emission of greenhouse gases (no Kyoto protocol).

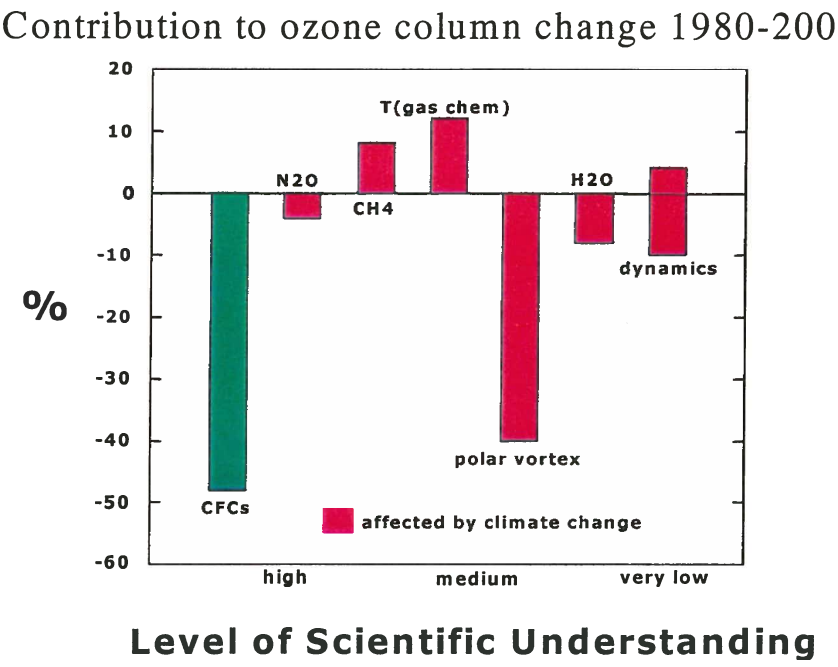

Figure 2.2 **Relative contribution (%) to the mid-latitude ozone column change between 1980 and 2000 by the processes considered in this study. The red coloured bars represent effects related to climate change. Horizontally an estimate of the level of scientific understanding is given.**

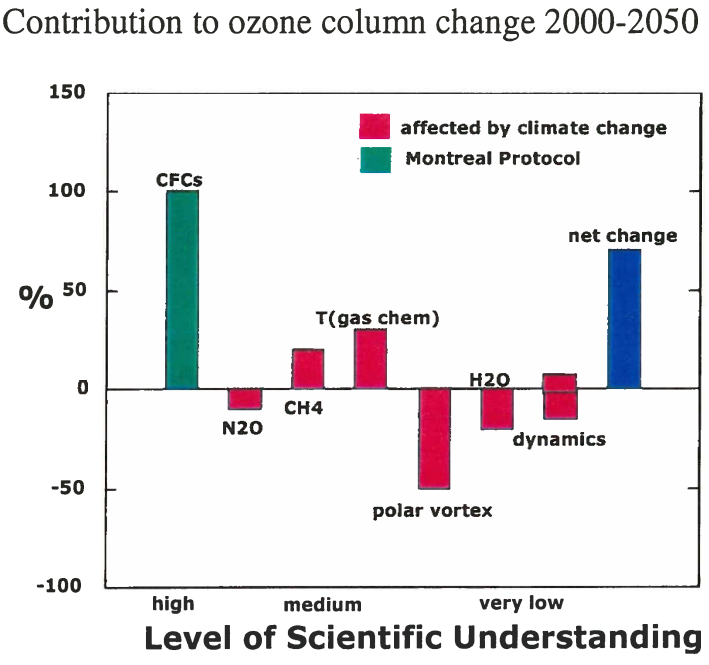

Figure 2.3 **Relative contribution (%) to the mid-latitude ozone column change between 2000 and 2050 by the processes considered in this study. The red coloured bars represent effects related to climate change. The blue bar represents the estimated net recovery in 2050. Horizontally an estimate of the level of scientific understanding is given.**

3. UV-climatology and trends

A changing UV-climate may have a wide range of effects on the population and on ecosystems (see section 1). To quantify the associated risks, information on the spectral changes in UV irradiance at the earth surface is needed. Most adverse effects from solar UV-exposure are primarily caused by UV-exposure from the UVB part (280-315 nm) of the solar spectrum at the earth's surface. Stratospheric ozone selectively absorbs these shortest wavelengths of the solar spectrum, i.e. the so-called UVB and UVC part of the spectrum, and thus provides an effective shield against part of the harmful UV. We will focus here on the UV-radiation which is relevant for adverse effects, therefor the UV-spectrum at the ground is weighted and summed according to its effectiveness. The effective UV-radiation received at the ground is primarily depending on the solar height, the total ozone column, clouds, aerosols and snow cover. Furthermore, the local environment like mountains, buildings, snow and trees can shade and reflect part of the UV sky and influence the radiation levels actually received.
The most direct way to assess changes in the UV-climate would be to use long-term data from highly accurate ground based UV-monitoring stations, however such long-term data are largely lacking at present [WMO, 1998]. An assessment of changes over prolonged periods of time is therefor based on modelled UV-transfer, using ozone and other atmospheric data from either ground based or satellite based sources. Such model approaches can be at least partly validated by a comparison with ground based measurements for shorter time periods (den Outer et. al 2000, Slaper et. al 2001).
The effect of an ozone change on the effective UV-dose received at the ground is illustrated in figure 3.1, which shows the clear anti-correlation between skin cancer weighted UV and ozone.

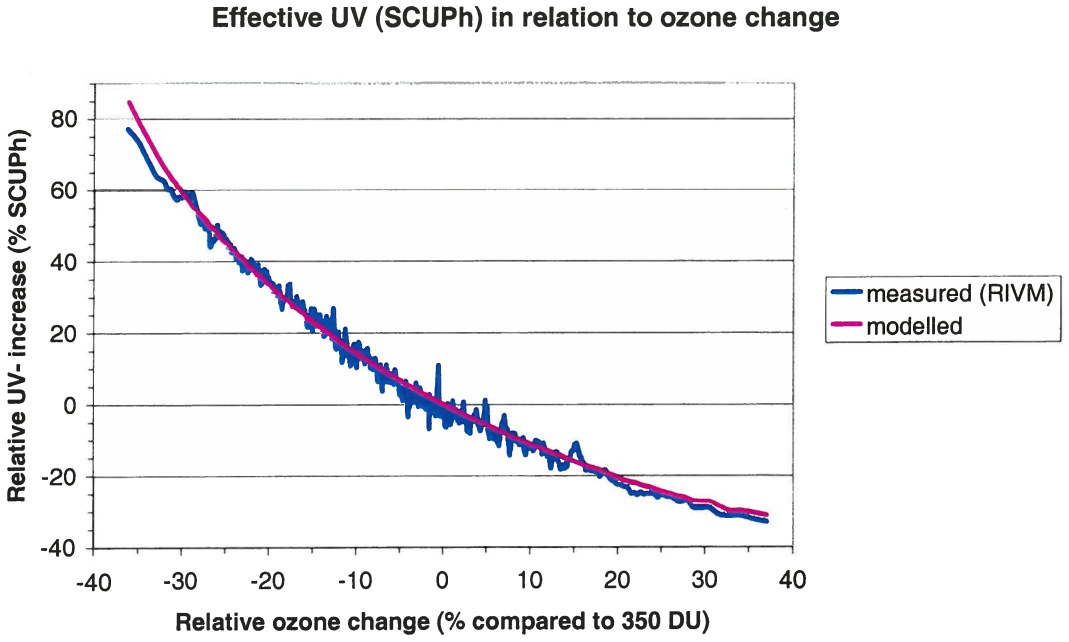

Figure 3.1 **Relative change in daily doses of effective UV (SCUP-h weighted) in relation to changes in ozone. Data obtained from the RIVM UV-monitoring system for Bilthoven (52 NL).**

The measured results, which are corrected for cloud effects, are obtained using daily integrated UV-measurements from the RIVM UV-monitoring system in Bilthoven for the period 1996-2000, and are compared with modelled results. Similar approaches for other locations are summarised in WHO (1998). In addition it has been shown that an upward trend in clear-sky UV-dose is correlated to a downward trend in ozone [Zerefos et. al.,1998; Mckenzie, 1999].
Figure 3.2 gives an example of a (UV) trend analysis – based on satellite data and ground measurements - for De Bilt over the period 1979-2000. The trend calculated from these data amount to an increase of around 5% per decade over the past two decades. A similar, albeit more uncertain increase is found if the cloud variability is included in the analysis.

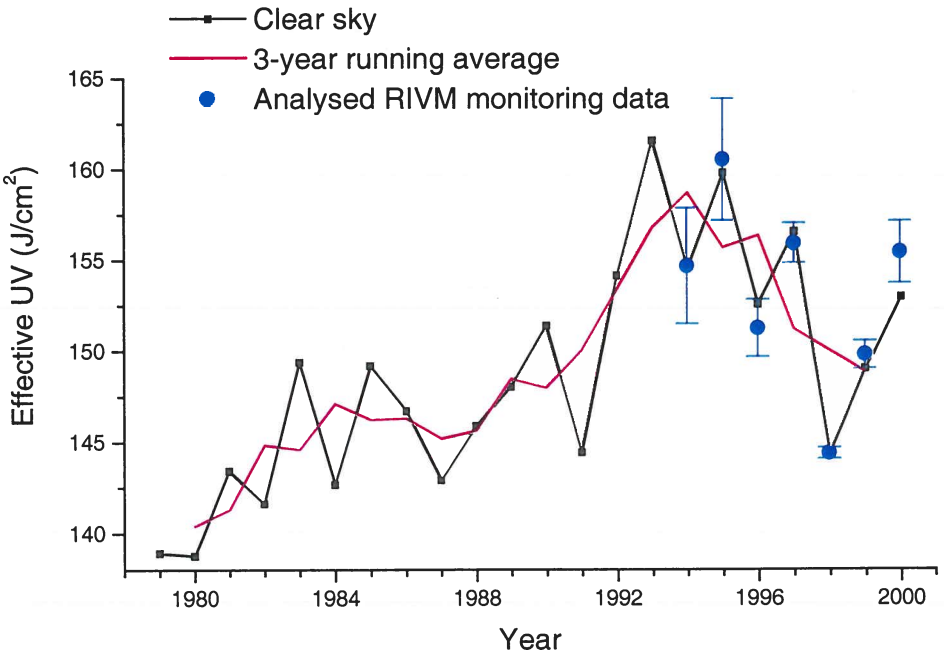

Figure 3.2 **Analysis of effective UV year-doses at De Bilt over the period 1979-2000. Black squares indicate satellite derived data and blue circles data from the RIVM measuring site. In red the three year running mean is plotted. Data from: 'Milieucompendium 2001 at the RIVM Worldwideweb: rivm.nl/milieucompendium/ section D 2.9**

Apart from direct measurements, ground-level UV doses can be calculated using remote sensing techniques. These satellite based methods have been validated to yield good estimates for UV doses at ground-level [Matthijsen et al., 2000, Slaper et al., 2001]. The way these UV budget maps changed over the last two decades can, in retrospect, be used to assess health and environmental risks. Figure 3.3 shows the change in effective UV over Europe over the period 1980-2000.

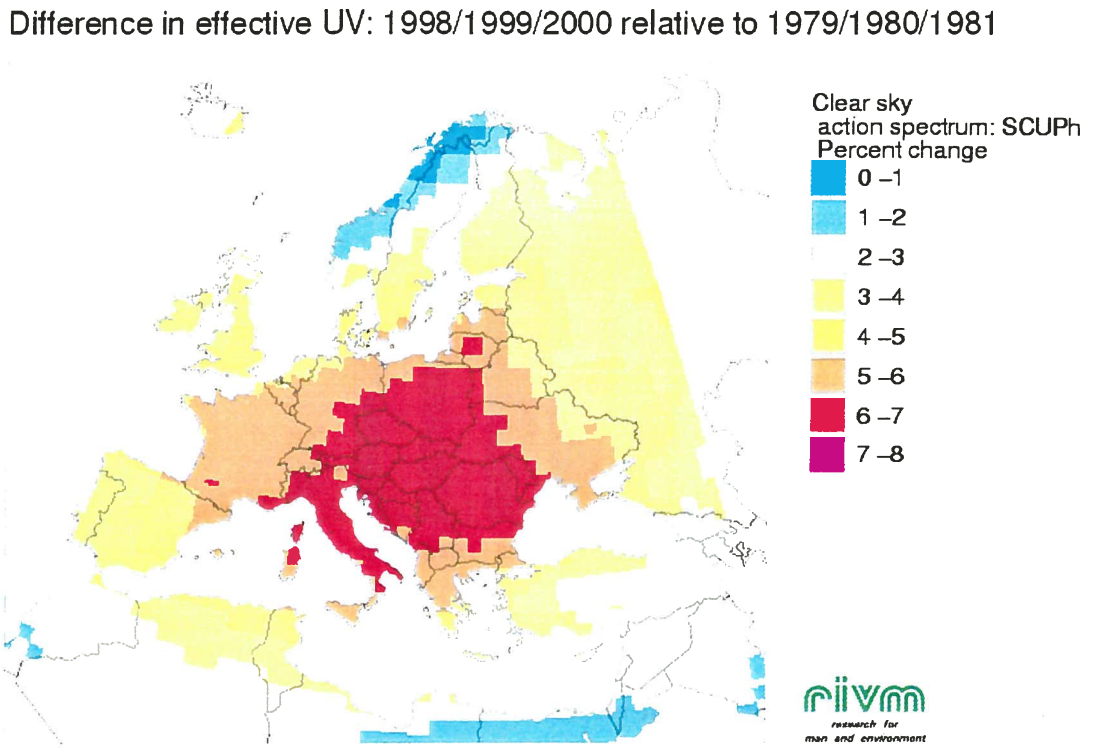

Figure 3.3 **Budget map showing the change in effective UV over Europe. The average effective UV over the period 1998-2000 is compared to the UV-budget over 1979-1981. Data from: 'Milieucompendium 2001 at the RIVM Worldwideweb: rivm.nl/milieucompendium/**

Apart from ozone clouds are a dominating and highly variable factor in determining the year-round UV-budget. The treatment of clouds in UV-climatology and risk assessments is still a challenge. Clouds are a decisive factor in the effective UV on the ground (see figure 3.4), and thus in the actual exposure of the population. But their high variability in time and place makes accounting for their effects in long-term risk assessments difficult.

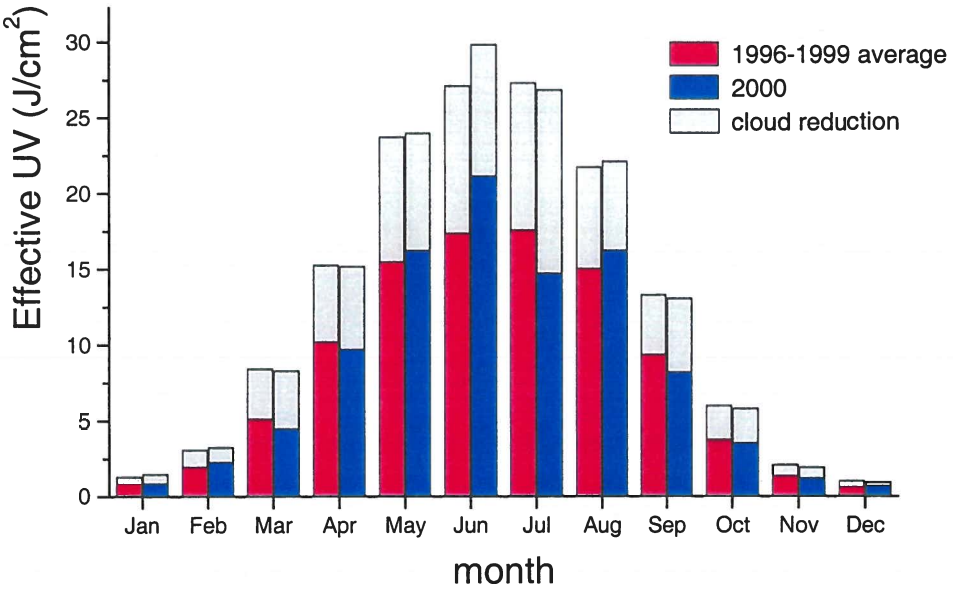

Figure 3.4 The reduction of the effective monthly UV-dose by clouds over the period 1996-2000.

The effects of clouds are also important with respect to climate change. Although no decisive evidence is available yet, climate change may well affect cloud cover and cloud optical thickness in a way dependent on season and location. A change in cloudiness and temperature will, in turn, influence (recreational) exposure with potential impacts on the overall risk of the population. At the moment, effects of structural change in cloudiness or a change in human behaviour due to climate change are not incorporated in our prognosis for (future) human risks.

Although there is a lack of direct observations of UV-trends in relation to ozone changes, it is highly likely that the yearly UV-doses received in large parts of Europe have increased by 5-10% over the past two decades. Further monitoring is required to substantiate the analysis and to establish how the climate-ozone changes influence the future UV-radiation levels at the ground. In addition to the climate-ozone interactions indicated in the previous chapter, clouds can also be influenced by climate change and thus lead to additional changes in the UV-doses received on the ground. In view of the high year to year variability of clouds and vortex effects, one might argue that a prolonged observation period will be required to fully establish UV-trends.

4. Overview of UV induced effects

4.1 Skin cancer

Skin cancer is a very common form of cancer among white Caucasians. The three main types are basal cell carcinomas (BCC), squamous cell carcinomas (SCC) and cutaneous melanomas (CM). SCC is most straightforwardly related to the total sun (UV) exposure: these tumours occur on skin areas that are most regularly exposed (face, neck and hands) and the risk goes up with the life-long accumulated UV dose. BCC and CM do not show these simple relations to UV exposure: these tumours appear to be more related to intermittent over-exposure (episodes of sunburn, especially on irregularly exposed skin) and sun exposure in childhood [Kricker et al., 1995, Holman and Armstrong, 1984]. BCC is the most common of the three. In NW Europe BCC occur in white Caucasians at a rate of about 90 cases per 10^5 people per year, followed by SCC with about 15 cases per 10^5 per year and CM with about 10 per 10^5 per year, summing up to 17.000 cases per year (in 1990) in the Netherlands [Health Council 1994). Recent brochures of the Dutch Cancer Society point to higher incidences; well over 20,000 cases of skin cancer per year in the Netherlands. Consequently, skin cancer forms a substantial pressure on the health system. Although the incidences are high, the mortality is generally low when compared to internal cancers.

UV radiation is known to be a very prominent environmental toxic agent. It is absorbed by a great variety of organic molecules in the skin and superficial layers of the eye. It can damage these molecules or neighbouring molecules through the release of 'radicals' (intermediate reactive chemicals). DNA is a very prominent absorber of UV radiation and mutations may subsequently occur. This implies that human skin exposed to sunlight is under continuous threat of accumulating oncogenic damage, which may result in skin cancer. The evidence that UV radiation is a major causal factor for skin cancer rests on three pillars: epidemiology, animal models and molecular genetics (de Gruijl, 1999).

1. Epidemiology

Epidemiological surveys show a clear correlation between ambient UV-dose and the incidence of skin cancer [Scotto and Fears, 1981, 1987].

2. Animal experiments

Animal experiments confirm that UV-induced genotoxicity indeed is the major driving force behind the induction of skin cancer. Dose-effect relationships from animal experiments combined with epidemiological data and data on ambient UV doses, yield the dose and age dependency for skin cancer induction in humans [de Gruijl et al.,1983]. On basis of the wavelength dependency for cancer induction derived from animal experiments, the action spectrum in humans has been estimated [de Gruijl et al., 1994].

3. Molecular genetics

Recently, the rapid advancements in the field of molecular genetics build the third pillar of evidence. It appears that skin tumours arise via a combination of an activated oncogenic pathway and an inactivated tumour suppressor gene (see appendix 1). The emerging fundamental understanding on which specific molecular changes are involved in the various types of skin cancer will enable us to pin point which steps in the process of carcinogenesis are affected by UV radiation.

The quantitative information on skin cancer outlined here (derived from appendix 1) is integrated in the RIVM risk assessment model AMOUR (appendix 5), which calculates extra UV-loads and excess skin cancer risks under a changing ozone layer. Results of the calculations are given in section 5.

4.2 Cataracts

The lens of the human eye changes with increasing age: it looses its brightness and it turns yellowish to brownish [Van Best et al., 1998]. In addition to this overall changes opaque spots may appear which grow in size and ultimately hamper vision. This lens opacity is referred to as a cataract and, as it is related to age, often as a 'senile cataract'. Cataract is world-wide a major cause of blindness. In developed countries cataract is adequately treated by an operation, but in developing countries it often leads to permanent blindness with grave social/economic consequences. Three main types of cataract can be distinguished: cortical cataract (CC), nuclear (sclerotic) cataract (NC) and posterior subcaspular cataract (PSCC).

In contrast to UV exposure and skin cancer the relationship between cataracts and UV is much less univocal, and an animal model for senile cataracts is missing. The literature survey in appendix 2 leads to the (prudent) conclusion that UV radiation appears to have impact on all types of cataract, albeit perhaps at different stages of life (early versus continuously) and to different degrees: CC appears to be most clearly related to UV exposure (especially in chronically exposed male outdoor workers), and NC the least clearly (perhaps related to early in life UVB exposure).

From this starting point a preliminary dose-response model for cataract has been formulated in appendix 2. The overall yield for cataract can be described by:

$$Y(a) = k_0 D^p (a-d)^6 \qquad (1)$$

Y	= yield, number of cataracts
K0	= UV-dose independent rate constant
D	= annual ambient cataractogenic UV-dose
a	= age
d	= a delay period, approximately 22 years for senile cataract
p	= exponent describing the dose dependency, p≈ 0.55 (all cataracts)

In appendix 2 it has been made plausible that the ambient cataractogenic dose may be quite well approximated by the erythemally weighted UV-dose. This effective erythema dose can be derived from routine UV-monitoring or calculated with a UV-transfer model. However, an additional complication arises from the fact that the exposure of the eye is strongly dependent on the orientation of the eye surface. This complicates the use of equation (1), especially when large differences in ground reflectance occur (e.g. snow compared to grassy surfaces). To complete the description of the onset of UV-induced cataracts we need basic data for cataract incidence (yield) at a given ambient effective dose. This information is derived from the Dutch general practitioners registry on cataracts recorded in the 'Nationaal Kompas Volksgezondheid'[1].

Table 4.1 gives the basic data for cataracts in the Dutch population in 1994. The ambient erythemally effective UV-dose for 1994 at De Bilt is approximately 165 J/cm².

[1] Hendrikse F. Hoe vaak komen gezichtsstoornissen voor? In: Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid Volksgezondheid, versie 1.3, 27 september 2001. © RIVM, Bilthoven. <http://www.nationaalkompas.nl>

Table 4.1 Basic data for prevalence, incidence and total numbers of cataracts for the Dutch population (1994)

	Men	Women	Population
Prevalence (per 1000)	7.35	16.69	12.07
Incidence (per 1000, per year)	1.47	2.75	2.12
Number of new cases ***(per year)***	11.200	21.400	32.600
Total number of cases (Dutch population 1994)	55.900	129.700	185.600

The quantitative information on UV induced cataracts outlined here (derived from appendix 2) and the information in table 4.1 can be integrated in the RIVM risk assessment model AMOUR (appendix 5). It provides a sufficient basis to assess the extra risk for cataracts under a changing ozone layer. At present, however, this new cataract risk module has not been implemented.

4.3 Effects on the immune system

Effects of UV radiation on the immune system have been shown to occur both in humans and in experimental animals. Modulation of the immune system occurs at relevant ambient doses, encountered in every day life. The experimental studies surveyed in appendix 3 provide evidence for a UV induced suppression of resistance to infections in humans. However, evidence is not unequivocal an the immune suppression is presumably moderate. In addition to genotoxic changes, the observed immunomodulation by UV radiation plays probably an important role in the formation of skin cancer.
The impact of the interaction of climate changes and ozone depletion on the expected levels of ambient UV exposure and resulting effects on neoplasms have been described elsewhere in this report (section 5). For an assessment of such impacts on the occurrence of infectious diseases, direct evaluations in humans cannot readily be made. As a consequence, risk assessments need to be based on dose-response studies in rodents, and the extrapolation of such studies to humans. Usually, animal experiments are performed using artificial UV-sources, and not with sunlight. Therefor, in such an extrapolation, the action spectrum for immune suppression should be taken into account. Although actionspectra for a number of immunological parameters have been described in the literature, action spectra for the reduction of resistance to infections are not yet available. Preliminary studies at RIVM however, indicate that such actionspectra may be different from known immunological and genotoxic actionspectra.
In addition to information on actionspectra, also information on adaptation of the immune system to higher ambient UV-levels is essentially missing. Finally, nature and magnitude of inter-individual variation in sensitivity to UV-induced immune effects are largely unknown, although preliminary information gained at RIVM indicates that such differences may be considerable.

In conclusion, appendix 3 suggests a lower resistance to infections at higher ambient UV-levels. But essential information for a full comprehension of the real risk of higher UV levels – caused by interaction of ozone depletion and climate change - for the occurrence of infectious diseases in the population is missing.

4.4 Effects on the marine environment

Marine phytoplankton in the world's oceans is at the basis of the marine food web and plays a major role in the global carbon cycle. The depletion of stratospheric ozone and subsequent increase in ultraviolet irradiance affects this 'primary production' negatively. An extra increase in UV radiation at sea level, caused by ozone-climate interaction, will enhance this negative effect. Other trophic levels have found to be directly and indirectly affected by UV radiation. Modelling studies estimate that a 5% reduction in primary production would translate to an equivalent or even higher reduction in fishery catches.
In the framework of the OCCUR-project, model calculations are presented that compare patterns of the potential global UV induced effect on primary production between 1978-1998 with the primary production over the period 1998-2018 (appendix 4). For the latter period, it is assumed that the trend in ozone column observed over the past decades will remain the same until 2018. This can be interpreted as a conservative 'worst-case' scenario for the development of the ozone layer.
The modelling results (figures 4.1 and 4.2) indicate that increased UV will reduce the world-wide microalgal primary production over the period 1978 - 2018. As a result the CO_2 uptake capacity of the oceans will be reduced. The percentage decrease in primary production is highest in the Antarctic Ocean under the ozone hole, max. 5.3% (see figure 4.1). Compared to the period 1978-1998, there is a stronger decrease in carbon fixation in the North Atlantic over the period 1998-2018. These results suggest that in the near future, ozone depletion above the highly productive North Atlantic Ocean might even play a more important role in reducing global primary production than the ozone depletion in the south pole region, around Antarctica. As a loss of primary production is usually accompanied by reduction of higher trophic levels, a serious impact on fish production in the North Atlantics may be possible.
Finally, ozone-climate interaction might activate a self-enforcing feedback loop; Higher CO_2 levels lead to extra cooling in the stratosphere. This cooling may result in enforced ozone depletion (see section 5). According to appendix 3, higher UV-levels give rise to a loss of primary production and CO_2 binding capacity of the oceans. This, in turn means higher CO_2-levels and stronger stratospheric cooling, and so on.
For future research on the effects of UV radiation on phytoplankton, it is therefore recommended not only to focus on the Antarctic situation. Further, more effort has to be put in estimating the indirect and direct effects of UV radiation on other trophic levels, especially fish production.

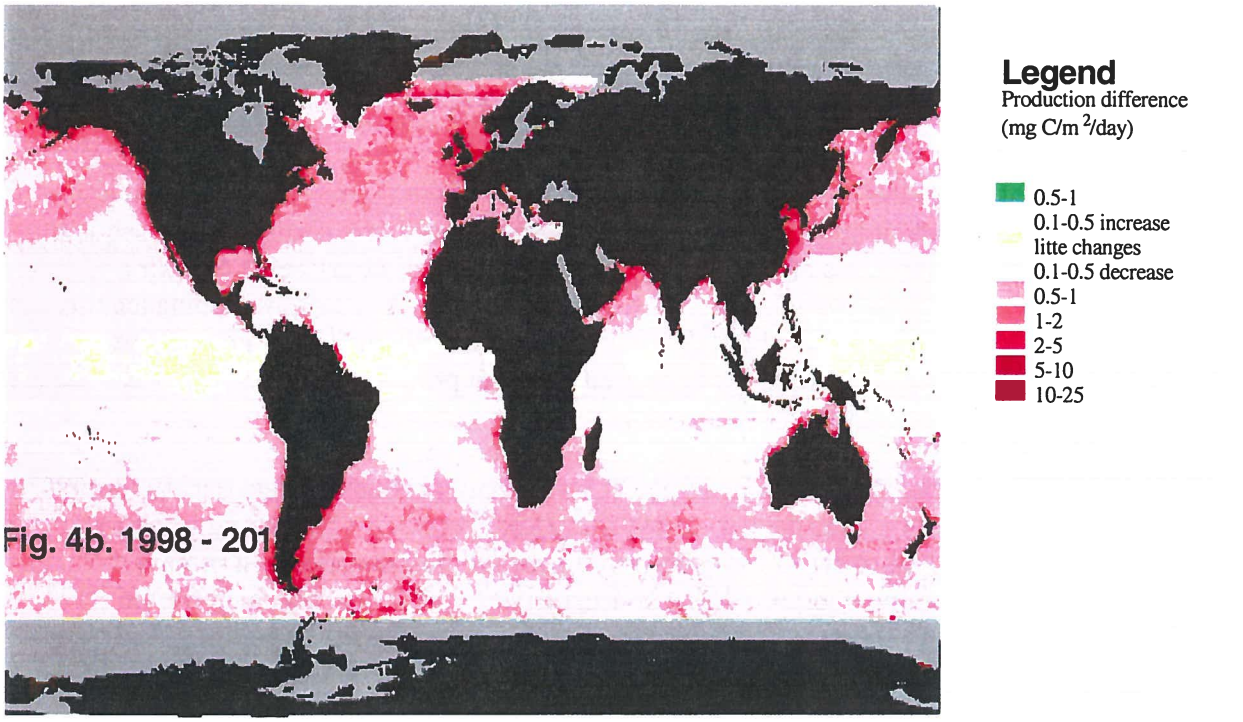

Figure 4.1 **Reduction in primary production resulting from increase ambient UV-levels Period: 1978 - 1998**

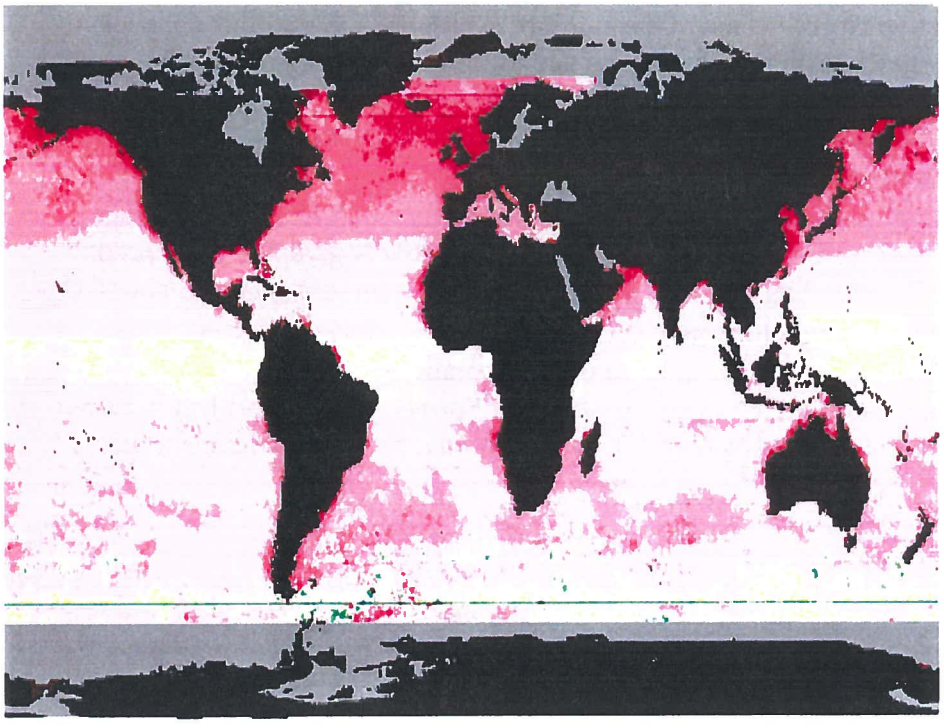

Figure 4.2 **Reduction in primary production resulting from increase ambient UV-levels. Period: 1998 - 2018**

5. Integrated risk assessments

Skin cancer is one of the best documented adverse effects of UV exposure. Ozone depletion will enhance ambient UV-levels, ultimately resulting in a higher incidence of skin cancer. To evaluate the consequence of ozone depletion - and of the possible stronger depletion induced by interaction between the ozone layer and climate change – the full source-risk chain has to be taken into account. The Assessment Model for UV Radiation and Risks (AMOUR) developed at RIVM gives such an overview; from production and emission scenario's for CFCs, through photochemical breakdown of these CFCs in the stratosphere and ozone depletion to increase in (effective) ambient UV-levels and corresponding increased skin cancer risks. The prognosis for the development of the ozone layer over Europe during the period 1980-2100 is based on a scenario for chlorine in the stratosphere and on the ozone trend over 1979-1991 observed by the NASA-TOMS satellite. Monthly ozone values enable us to calculate - with a UV-transfer model – the future effective UV-levels at the earth's surface. These future UV-levels yield via a dose-response model for skin cancer, eventually the increased skin cancer incidence.
In this report the baseline risk - determined by the situation with no ozone-climate interaction – is compared with a scenario including ozone-climate interaction. The magnitude of the interaction is based on a literature survey, 2D model calculations for the Arctic vortex and on expert judgement. For the ozone-climate interaction we formulate the following preconditions:

- Chlorine scenario A1 [Madronich et. al, 1998]
- Stratospheric temperature according to IPCC, IS92a [Velders, 1997]
- Stratospheric cooling results – via a shift in the chemical equilibrium for ozone production/destruction - in 0.9% extra ozone per one Kelvin drop in temperature.
- Splitting up of the arctic vortex induces a month and latitude dependent ozone depletion over the Northern hemisphere. The magnitude of the ozone loss is calculated by 2 D simulation [Velders, 1997].
- Of the observed ozone trend 25% can be attributed to non-vortex dynamical changes.

For details on the AMOUR model, the calculations and the interaction between the ozone layer and climate change, see appendix 5 and chapter 2.
The result of the AMOUR assessment can be given at a fixed location in terms of the increase in effective UV and skin cancer incidence with and without ozone-climate interaction. Finally AMOUR produces maps of the difference in effective UV and skin cancer incidence over Europe.
Figure 5.1 shows the increase in effective UV at De Bilt with and without ozone-climate interaction. Figure 5.2 depicts the extra cases of skin cancer at De Bilt with and without ozone climate interaction. AMOUR assessment yields similar information for all cells in the TOMS-grid. These data can be put together in UV and skin cancer difference maps for Europe in a certain year. These maps strongly depend on the year chosen. For UV the maximum difference between the situation with and without ozone-climate interaction is expected around 2020. For skin cancer incidence the maximum difference is much later due to the long latency period for skin tumours, and is detected around 2070. Figure 5.3 shows the difference in 2020 over Europe for the effective UV with and without ozone-climate interaction. Figure 5.4 gives the same data for the excess skin cancer cases.

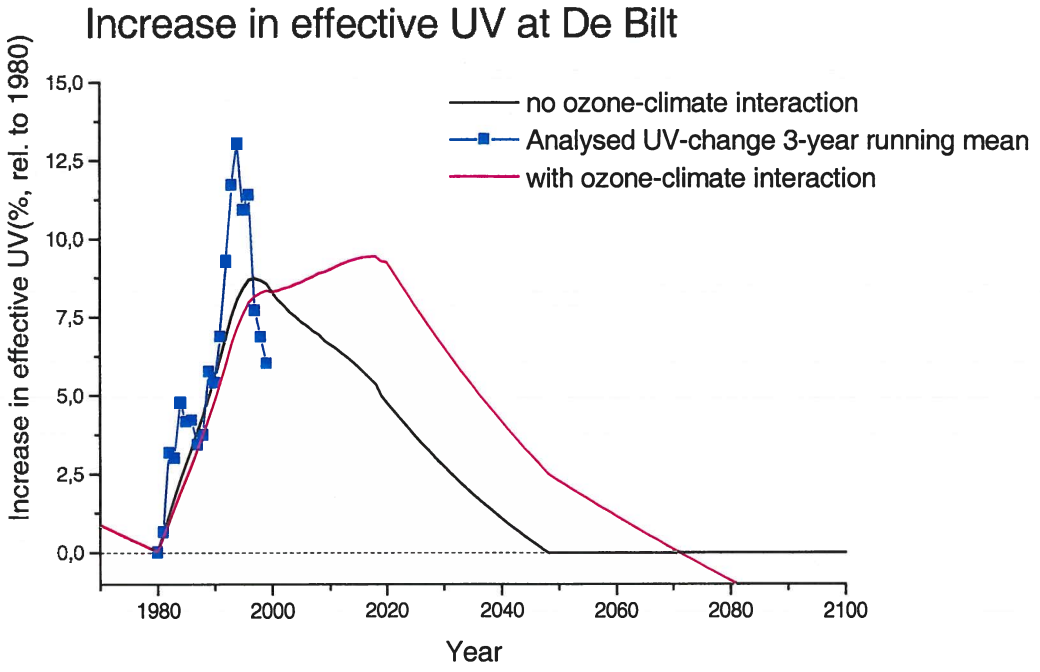

Figure 5.1 **Increase in effective UV with and without ozone climate interaction. Location De Bilt. As a comparison the analysed three year running mean, based on UV measurements included.**

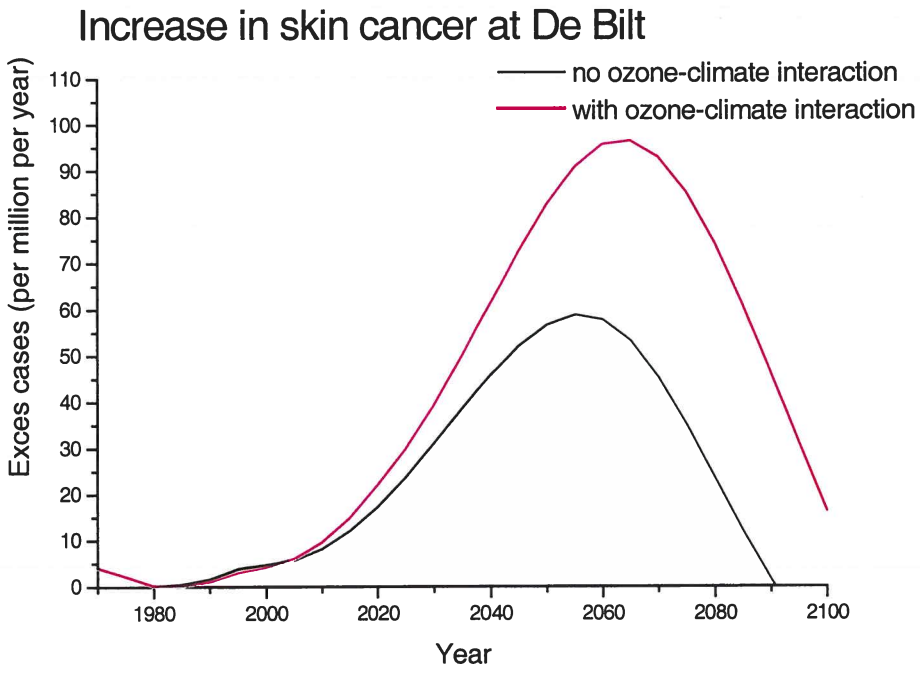

Figure 5.2 **Increase in skin cancer incidence at De Bilt, with ozone-climate interaction, and without ozone-climate interaction.**

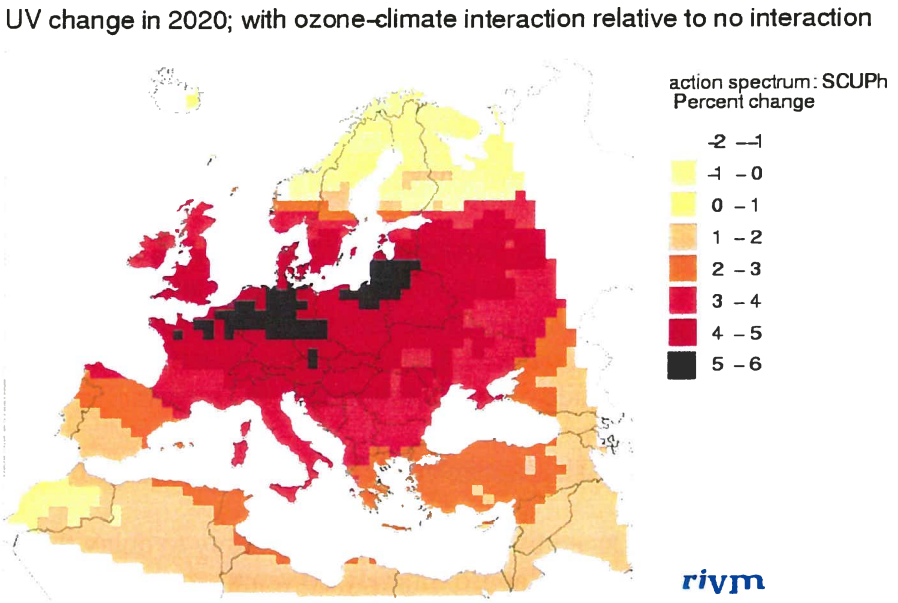

Figure 5.3 **Increase in effective UV. Prognosis with ozone-climate interaction compared to that without ozone-climate interaction The effective UV is expressed as the relative increase in UV compared to the effective UV without ozone-climate interaction**

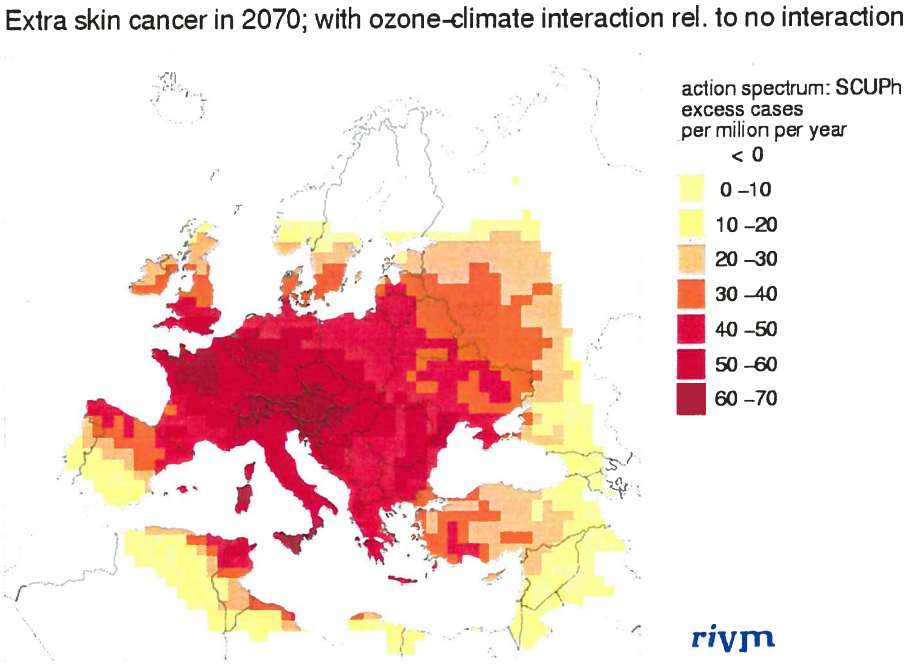

Figure 5.4 **Increase in skin cancer incidence. Prognosis with ozone-climate interaction compared to that without ozone-climate interaction. The change in risk is expressed as the number of extra cases (per million per year) in the situation with ozone-climate interaction compared to no ozone-climate interaction**

The result given have a large uncertainty because the stratospheric ozone concentration at mid-latitudes in our model is a subtle balance of chemical destruction of ozone, dilution by ozone poor air from the Arctic vortex, destruction/dilution by non-vortex dynamical effects and production of ozone due to chemical equilibrium shift. Scientific understanding of these processes, especially of the non-vortex dynamics and of the Arctic vortex itself, is far from perfect.
A preliminary analysis of the uncertainty introduced by the choice of the input parameters for the AMOUR model indicates that the fraction of the ozone trend attributed to the non-vortex dynamics introduces the largest uncertainty in the estimates of effective UV and corresponding risks (see appendix 5, table 4). Unfortunately, scientific understanding of this effect and consensus on the magnitude of its contribution is the lowest.

Under the uncertainties given the risk assessments leads to the following conclusions:

- Stratospheric cooling, induced by climate change, is likely to delay the recovery of the stratospheric ozone layer by approximately 20 years.
- Delay in recovery of the ozone layer induced by ozone-climate interaction, results in a higher and more persistent increase in (effective) UV levels over Europe.
- At De Bilt the maximum increase in UV-level (with ozone-climate interaction) is reached around 2020. At the maximum the increase in effective UV (with ozone climate interaction) is 9.4% (relative to the 1980 level) as compared to 8.7% extra UV (in 2000) with no ozone-climate interaction.
- Accounting for ozone-climate interaction, the effective UV-levels in 2020 for the mid-latitudes in Europe, are 4-6% higher compared to the situation with no climate interaction.
- Higher UV-levels due to ozone climate interaction lead to a higher and more persistent increase in skin cancer incidence.
- At De Bilt with ozone-climate interaction the maximum increase in skin cancer incidence is reached in 2065. In this year there are approximately 95 extra cases of skin cancer per million inhabitants per year. With no climate interaction a maximum excess number of about 60 cases per million per year is reached in 2055.
- Accounting for ozone-climate interaction, the excess skin cancer risk in 2070 for the mid-latitudes in Europe varies between 50 an 150 extra cases per million inhabitants per year, compared to the situation with no ozone climate interaction.

6. Conclusions

The result formulated in this quick scan of the impact of climate change on the recovery of the ozone layer and related effects on human health and environment bear a large uncertainty. This uncertainty arises from the fact that the stratospheric ozone concentration at mid-latitudes is a subtle balance of chemical destruction, dilution and production of ozone, and scientific understanding of the underlying processes, especially of the non-vortex dynamics and of the Arctic vortex itself, is far from perfect. With this in mind we conclude:

- The ozone layer is expected to recover as a result of the implementation of the Montreal protocol. Based on the expected decrease in chlorine and bromine a recovery is expected around 2050. The full recovery is probably delayed by increased concentrations of greenhouse gases.

- The delay calculated by Chemistry-Climate models show a large variation, ranging from about 10 years to more than 20 years.

- A stronger winter Arctic vortex - triggered by lower stratospheric temperatures – results in more efficient (chemical) ozone loss. Thus, the Arctic vortex contributes substantially to the delayed ozone recovery. The mechanism underlying this enhanced ozone depletion, however, is poorly understood.

- Dynamic changes in the climate system, not coupled to the Arctic vortex, may also contribute substantially to a delay in ozone recovery. But, at present there is little consensus on the magnitude and relative importance of this contribution.

- A delay in recovery of the ozone layer, induced by ozone layer - climate change interactions, leads to a higher and more persistent increase in effective UV-levels over Europe. In 2020 UV-levels over mid-Europe, accounting for ozone-climate interaction, are estimated to be 4-6% higher compared to the UV-levels without interaction..

- Elevated ambient UV-levels result in a higher and more persistent increase in skin cancer incidence. Under the assumption that other conditions, in particular cloudiness, are not affected and that climate change does not influence behaviour of the population, the risk at De Bilt increases from approximately 60 extra cases per million inhabitants per year (no ozone-climate interaction, 2055) to about 95 extra cases per million per year (ozone-climate interaction taken into account 2065).

- Increased UV at sea-level yields a reduction of microalgal primary production and carbon dioxide binding capacity in the oceans. Loss of primary production probably affects higher trophic levels in the food chain. This may lead to a serious impact on fish production, especially in the North Atlantic waters.

- A literature survey indicates a lower resistance to infections at higher ambient UV-levels. But essential information for a full comprehension of the real risk of elevated UV-levels for the occurrence of infectious diseases in the population is missing.

- A review of the causative factors for senile cataracts strongly indicates UV as a contributing factor, especially for cortical cataracts. This makes cataract formation sensitive to an increase in ambient UV-levels caused by ozone-climate interaction.

7. Future Research

The integrated risk-assessment provided in this study should be seen as a preliminary analysis of the consequences of climate-ozone interactions and further research is required to substantiate and improve the analysis. It should therefor be considered to initiate a broad integrative program, that further improves and integrates the knowledge of climate-ozone interactions, their consequences on UV-budgets, and the dose-time response relationship for a variety of health and environmental effects. Such a research program could and should serve as an integrative framework for the improvement of prognostic scenario assessments of the UV-related risk associated with atmospheric change.

More specifically, the following topics can be considered in such an integrative research program on the consequences of climate change and ozone depletion on UV-budgets and risks:

- Research on depletion of stratospheric ozone and research on climate change follow separate tracks. But the interactions between climate change and ozone layer depletion found in this report are so many-sided and may induce such (potentially) important effects that integration of these lines of research is required to get a full understanding of the impact on human health and environment. Internationally, this asks for a close co-operation of the Panels active under the Montreal protocol and the Intergovernmental Panel on Climate Change (IPCC).

- For a better understanding of ozone-climate interaction, development and validation of 3-dimensional models including the troposphere and the stratosphere, with an adequate description of (temperature) driven dynamical changes in the atmosphere and with a full coupling to ozone chemistry is required.

- To give the risk assessment for skin cancer induction with climate-ozone interaction a more solid basis, better information is required on the magnitude and nature of the interactions between climate change and ozone layer depletion, especially on the contribution of non-vortex dynamics.

- To better underpin the causes of the loss of primary production in the oceans and the effects on fish production further research on the contribution of North Atlantic Ocean is crucial. And more research effort is needed on influence on other trophic levels like fish production.

- The improved insight in the molecular and genetic background of the induction of skin cancer should initiate research to improve en validate the quantitative modelling of the development of skin cancer. In particular diagnosis and quantification of benign, pre-cancerous lesions may lead to improved models with a better prognostic capacity.

- The strong association between UV exposure and cataracts requires further study on the action spectrum for cataract formation and on the dose-effect relationship. The preliminary model presented in this report provides a sufficient basis to make a risk assessment for cataracts under varying ambient UV-levels.

- Better insight in the effects of UV on the immune system requires research on: action spectra for the reduction of resistance to infections, on adaptation of the immune system to higher UV-levels and on inter-individual differences in UV susceptibility.

- The present risk assessment study focussed on the three most substantial interactions between ozone layer and climate change. For a complete insight other contributions (N_2O, CH_4, water vapour, etc.) must be taken into account in the AMOUR-model.

- An increase in methane in the atmosphere is expected to speed up the recovery of the ozone layer by the increased formation of chlorine reservoir species.

- For a comprehensive overview of UV induced changes, other environmental effects, e.g. effects on terrestrial ecosystems, should be evaluated.

- Further improvements of the integrative modelling frame to account for climate-ozone interactions and to integrate results from effect studies are required.

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Abbreviations

AMOUR	- Assessment MOdel for UV Radiation and Risks, Research model under development at the Netherlands National Institute of Public Health and the Environment (RIVM).
BCC	- Basal Cell Carcinoma
CA	- Copenhagen Amendment. A reduction scenario (under the Vienna convention) resulting in zero production of ozone depleting substances at the end of 1995.
CC	- Cortical cataract
CMM	- Cutaneous Malignant Melanoma
DU	- Dobson Unit, unit for ozone column thickness. An ozone column of 300 DU corresponds at standard pressure (1 atmosphere) and temperature (0°C) to a layer of ozone of 3 mm thickness.
CFC	- Chlorofluorocarbons
IPCC	- Intergovernmental Panel on Climate Change
LIDAR	- Light Detection and Ranging
MP	- Montreal protocol. A reduction scenario (under the Vienna convention) resulting in a reduction of 50% in the production of ozone depleting substances at the end of 1999 . The original Montreal protocol has been amended and adjusted several times, strongly limiting (or forbidding) the production and consumption of ozone depleting substances world-wide.
NASA	- National Aeronautics and Space Administration
NAO	- North Atlantic Oscillation
NC	- Nuclear (sclerotic) cataract
NR	- No Restriction scenario. A scenario (under the Vienna convention) assuming a yearly rise in the production of ozone depleting substances of 3% per year
OCCUR	- Ozone and Climate Change interaction effects for Ultraviolet radiation and Risks
ppbv	- parts per billion, volume
PSCC	- posterior subcaspular cataract
RIVM	- Netherlands National Institute of Public Health and the Environment
SCC	- Squamous Cell Carcinoma
TOMS	- Total Ozone Mapping Spectrometer on board of NIMBUS 7, METEOR3 and Earth Probe satellites; source for total ozone measurements
UV	- Ultraviolet radiation (wavelength range 100-400 nm)
UVB	- UV wavelengths ranging from 280-325 nm
UVC	- UV wavelengths ranging from 100-280 nm
WMO	- World Meteorological Organisation

Appendices

A.1 Skin cancers and ambient UV radiation

F. R. de Gruijl, J.C. van der Leun

A.2 Lens opacities and cataract

F.R. de Gruijl, J.C. van der Leun

A.3 The effects of UV radiation on the immune system and resistance to infections

H. Van Loveren

A.4 Effects of increased UV irradiance on the marine environment: controversial results, and perspectives

A. Piquet, T. van Oijen, W.W.C. Gieskes

A.5 Integrated risk assessments

G. Kelfkens, G.J.M. Velders, H. Slaper

A.1 Skin cancers and ambient UV radiation

Dr. F.R. de Gruijl, Dr. J.C. van der Leun

Contents

A.1.1 Introduction

Recent research on skin cancer is greatly benefiting from the rapid advancements in the field of molecular genetics: a fundamental understanding is emerging on which specific molecular changes are involved in the various types of skin cancer. This knowledge will also enable us to determine whether, and if so how exactly, UVB radiation contributes to the development of these skin cancers. Consequently, the impact of a stratospheric ozone depletion on the incidence of these skin cancers could be more reliably assessed.
Cell proliferation and terminal differentiation are regulated by signaling pathways in which cascades of chemical interactions ultimately lead to the activation or de-activation of certain cellular processes. Fundamental research is rapidly gaining ground in understanding how cancer is caused by disturbances in these growth-controlling pathways. Toxic agents, such as UV radiation, may disturb these pathways. The damage to proteins involved in the signal transduction will usually only have a temporary effect as proteins are broken down and synthesized in continuous renewal. Even damage to the mRNA from which the proteins are translated will have a temporary effect because the mRNA is also renewed. If these 'epi-genetic' interferences occur repeatedly, they may noticeably enhance or inhibit carcinogenic progression (i.e., the agent may act as a 'promotor' or 'anti-carcinogen', resp.). A permanent disturbance in a signaling pathway may be introduced by damaging the DNA of a gene that codes for a protein in the pathway. If the damage leads to an altered genetic code (mutation) or a complete loss of the gene, the altered protein or its complete absence can obviously corrupt the signal transduction in the pathway of a cell (an agent which causes these permanent oncogenic changes could be considered as a classical 'initiator'). This genetical defect will be passed along to daughter cells, and thus the corresponding defect in signal transduction will propagate. There are two categories of genes with direct relevance to cancer: oncogenes whose proteins contribute to cancer formation through a dominant gain of function, and tumor suppressor genes whose proteins suppress carcinogenic progression. The latter enable cancer growth through a recessive loss of function.
UV radiation is a very prominent environmental toxic agent, but it does not penetrate any deeper than the skin (and superficial layers of the eye). UV radiation is absorbed by a great variety of organic molecules, and can damage these molecules or other neighboring molecules through the release of intermediate reactive chemicals, 'radicals'. DNA is a very prominent absorber of UV radiation in cells. Genes in cells are, therefore, easily damaged upon UV irradiation, and mutations may subsequently occur. This implies that human skin exposed to sunlight is under continuous threat of accumulating oncogenic damage. Skin cancers are, however, not readily induced and mainly occur at old ages, which attests to an impressive adaptation of the human skin to this continuous environmental stress.

A.1.2 Types of skin cancers

Skin cancer is a very common form of cancer among white Caucasians, and by far the most frequent form in white Caucasians living in tropical and subtropical areas: e.g., in the USA over 30% of cancer cases concern skin cancer, with more than 1 million cases per year (*Miller and Weinstock, 1994*). The three main types are basal cell carcinomas (BCC), squamous cell carcinomas (SCC) and cutaneous melanomas (CM). All these types show a north-south gradient over the USA, i.e., a positive correlation with ambient UV radiation. BCC is the most common of the three, but the relative north-south increases are most

substantial in SCC. In NW Europe BCC occur in white Caucasians at a rate of about 90 cases per 10^5 people per year, followed by SCC with about 15 cases per 10^5 per year, and CM with about 10 per 10^5 per year (*Health Council 1994)*. Recent brochures of the Dutch Cancer Society state that there are well over 20,000 cases of skin cancer per year in the Netherlands, amounting to a substantial pressure on the health system. Although the incidences are high, the mortality is generally low when compared to internal cancers. The obvious advantage with skin cancers is that they become visible at a very early stage and are cosmetically undesirable, which implies that therapies are applied early with correspondingly more success.
People who sunburn easily and never tan run the highest risk of contracting all three types of skin cancer. SCC appears to be most straightforwardly related to the total sun (UV) exposure: these tumors occur on skin areas that are most regularly exposed (face, neck and hands) and the risk goes up with the life-long accumulated UV dose. BCC and CM do not show these simple relations to UV exposure: these tumors appear to be more related to intermittent over-exposure (episodes of sunburn, especially on irregularly exposed skin) and sun exposure in childhood (*Kricker et al., 1995, Holman and Armstrong, 1984).* A recent randomised prospective cohort study (*Green et al. 1999*) showed that 4.5 years use of sunscreen in adulthood lowered the development of SCC, but not of BCC. This would be in line with the finding that UV radiation contributes to the development of SCC at all stages during a lifetime, while UV radiation mostly affects the very early stages of BCC development. Also the number of nevi that a person contracts is determined by the level of ambient sun exposure in childhood (*Gallagher et al 1990.*), and the number of nevi is a well-established risk factor for CM. This is further confirms the importance of early life exposure to the risk of CM later in life.

A.1.3 Oncogenes and tumour suppressor genes

A.1.3.1 UV mutations in *P53* from BCC and SCC

The *P53* tumor suppressor gene is found to be mutated in a majority of human cancers. The p53 protein is therefore an apparent cellular "Achilles' heel", it plays a pivotal role in several signaling pathways related to DNA damage and expression of oncogenes (*Vogelstein et al., 2000*). Nuclear p53 expression is elevated after UV irradiation, and following a genotoxic insult p53 is involved in cell cycle arrest (late G1 and G2/M), apoptosis ('programmed cell death') and DNA repair. In SCC (about 90%) and BCC (>50%) from the US white population the *P53* gene appears to bear point mutations with the exact features of UVB-induced point mutations, i.e., associated with di-pyrimidinic sites, mostly C to T transitions and 5-10% CC to TT tandem mutations (*Brash et al., 1991, Ziegler et al., 1993*). Evidently, the *P53* gene is also a target in UV carcinogenesis, which has been extensively confirmed in mouse experiments (*Kress et al., 1992, Kanjilal et al., 1993, Van Kranen et al., 1995, Dumaz et al, 1997*) . In line with this finding, it is found that the wavelength dependency of the induction of SCC closely parallels that of the induction of UV-induced DNA damage (pyrimidine dimers) in the skin, especially over the UVB and UVA2 bands (*De Gruijl, 1999*); see fig. 1. Experiments with hairless mice show that clusters of epidermal cells with mutant p53 occur long before SCC become visible (*Berg et al., 1996*); such clusters of mutant p53 have also been found in human skin (*Jonason et al., 1996, Ren et al., 1996*). Dysfunctional p53 is likely to affect protective responses against DNA damage and oncogenic signaling. Hence, the early occurrence of *P53* mutations may cause genomic instability and thus facilitate further

carcinogenic progression. The frequency of p53-mutant cell clusters in the skin may be a direct indicator of skin cancer risk (*Rebel et al., 2001).*
A mutation in the *P53* gene is clearly not enough to cause BCC or SCC. At the very least some oncogenic pathway has to be activated; e.g., a growth-stimulating pathway which normally starts with the activation (oligomerization) of a receptor tyrosine kinase (RTK), e.g. EGF-R, at the cell membrane, and is further mediated through proteins like RAS into the cell cytoplasm from which transcription factors are finally activated. Activating *RAS* mutations have been reported in a minority of SCC and BCC to various percentages (*Pierceall et al., 1991, Cambell et al., 1993*). These activating mutations are restricted to the codons 12, 13 and 61, and are not specific of UV radiation. The RAS-pathway may be involved in SCC and BCC, but it is not usually effected through genetic changes in the *RAS* family of genes.

A.1.3.2 BCC and the *PTCH* gene

Patients with Gorlin syndrome, or basal cell nevus syndrome (BCNS), suffer from multiple, familial BCC. This genetic trait was traced to locus 9q22 and turned out to be carried by mutations in the *PTCH* gene (*Hahn et al., 1996*). Next to frequent loss of one of the parental genes (i.e. loss of heterozygosity, LOH) at this locus, many sporadic - non-familial - BCC showed mutations in the (remaining) *PTCH* allele (*Gailini et al., 1996*): 12 out of 37 tumors in SSCP screening, and 9 of these tumors showed LOH of *PTCH*. (The SSCP was apparently not sensitive enough as two tumors without variant SSCP or LOH were both found to have inactivating mutations.) Seven of 15 mutations occurred at di-pyrimidinic sites and were C to T transitions (among which 2 CC to TT tandem mutations), and could, therefore, have been caused by UVB radiation.
The *PTCH* gene is a human homolog of the *Patched* (*Ptc*) gene in *Drosophila melanogaster*, it is a serpentine-like receptor woven through the cell membrane. Extra-cellular 'Sonic Hedgehog' (SHH) protein couples to PTCH which triggers a pathway that ultimately activates the transcription factor GLI1, which induces epidermal hyperplasia (*Fan and Khavari, 1999*), and which is expressed in almost all BCC (*Dahmane et al. 1997*). Skin grafts of the SHH-transgenic keratinocytes onto immune-deficient mice show the specific histologic features of BCC (*Fan et al., 1997*). This indicates that activation of this Sonic Hedgehog pathway is essential to the formation of BCC. This has been confirmed in transgenic mouse strains.
Ptc heterozygous knockout mice have been reported to show BCNS-like developmental abnormalities and to develop medullablastomas and rhabdomyosarcomas, but no BCC (*Goodrich et al, 1997, Hahn et al., 1998*). These animals do develop microscopically detectable follicular neoplasms resembling human trichoblastomas and 40% develop BCC-like tumors after 9 months. Upon exposure to ionizing or UVB radiation the trichoblastomas and BCC occur earlier, and increase in size and numbers (*Aszterbaum et al., 1999*). Moreover, these exposures cause a clear shift in histological features toward BCC. The trichoblastomas and BCC show frequent loss of the wildtype *Ptc* allele, and all the ones tested (n=12) showed expression of Gli1 (SCC, n=2, did not). Two BCC out of 5 UV-induced trichoblastoma/BCC-like tumors carried *p53* mutations (3 in total, 2 C to T and 1 C to G). These experimental data show that UV radiation can play an important role in causing or enhancing the development of BCC. Next to the induction of *p53* mutations, UV radiation could exert a more direct effect on the Sonic Hedgehog pathway by enhanced loss of the wildtype *Ptc* gene and/or possible mutation of this gene.

A.1.3.3 Melanoma and *INK4a*

Some familial CM are linked to markers on chromosome 9p21, which led to the positional cloning of the 'multiple tumor suppressor' (*MTS1*) gene (*Kamb et al, 1994*) (designated *CDKN2A* in the human genome project). It is also named *INK4a* (*Ruas and Peters, 1998*) after the original finding that its product $p16^{INK4a}$ becomes associated with cyclin dependent kinases upon transformation of human fibroblasts by SV40 virus (*Xiong et al., 1993*), and acts as an inhibitor of CDK4 and CDK6 (*Serrano et al., 1993*). CDK4 is thus prevented from phosphorolating pRB and activating the E2F-1 transcription factor. An alternative reading frame in *INK4a* codes for the protein $p14^{ARF}$ ($p19^{ARF}$ in mice), which does not appear to inhibit any CDK but binds to MDM2 and thus interferes with the degradation of p53 (*Zhang et al., 1998*).

The loss of heterozygosity (LOH) at 9p21 is most compellingly linked to both familial and sporadic CM (*Healy et al., 1996*). Partial or complete homozygous loss of *INK4a* is observed in a majority (about 60%) of cell lines derived from sporadic CM, and most of the remaining cell lines (e.g., 8 out of 11) bear point mutations that are typical of UV radiation, i.e., C to T transitions at dipyrimidine sites (*Pollock et al., 1995*). Although 60-70% of sporadic melanomas (n=62) show a lack of $p16^{INK4a}$ expression and all (n=5) of the metastases (*Funk et al., 1998*), the high number of homozygous losses and mutations of *INK4a* found in cell lines is not reproduced in primary CM. Homozygous deletions are found in approximately 10% and reported mutation rates range from 0 to 25 % (*Ruas and Peters, 1998*). The reason for this discrepancy is not entirely clear but it could be due to a high selection for a loss or mutation of *INK4a* in generating the cell lines (*Flores et al., 1996*). It should, however, also be noted that LOH at 9p21-22 in CM is quite common, and is even frequently observed in microdissected dysplastic nevi (in 75%), potential precursors of CM, as is LOH at 17p13 (locus of *P53*) (in 60%) (*Lee et al., 1997*). *De novo* methylation in the promoter region of the remaining *INK4a* allele could potentially silence transcription, but such methylation has thusfar only been detected in 10% of primary CM (*Gonzalgo et al., 1997*). Alternatively, mutations in non-coding (5'UTR) regions could play a role, as was recently found in a CM-prone family (*Liu et al., 1999*).

Signaling pathways related to $p16^{INK4a}$ apparently play an important role in the pathogenesis of CM. And, although the *INK4a* locus often shows LOH and less frequently mutations in primary CM, it is not clear if and to what extent solar UV radiation is responsible for these pertinent genetic changes.

A.1.3.4 RTK growth-stimulating pathway and *INK4a* in CM

Another family of genes that is implicated in CM are the *RAS* oncogenes, more specifically *N-RAS*. 25-70% of CM from regularly sun-exposed sites have been reported to carry activating point mutations in *N-RAS*, whereas none of the CM from irregularly exposed sites carried such mutations (*Van Elsas et al., 1996, Van 't Veer et al., 1989*). In a comparative study the percentage of *N-RAS* mutated CM from sun-exposed sites was higher in an Australian population (24%) than in a European population (12%) (*Van Elsas et al,, 1996*). These mutations occur in the vicinity of dipyrimidine sites, the typical UV targets, but they are not dominated by C to T transitions.

As mentioned earlier, the RAS proteins function in mitogenic pathways which start by activation of RTK at the cell membrane, e.g. the receptor for epidermal growth factor, EGF-R. It is well known that oncogenic *RAS* will transform most immortal cell lines and make them tumorigenic upon transplantation into nude mice. Surprisingly, Serrano et al. (1997) found that expression of oncogenic *RAS* (producing an activated $H\text{-}RAS^{G12V}$) in primary human or rodent cells results in a state that is phenotypically characterized as 'senescence':

the cells are viable and metabolically active but remain in the G1-phase of the cell cycle. This oncogenic RAS-induced arrest in G1 is accompanied by an accumulation of both p16 and p53. The link between these pathways is likely to be mediated by $p14^{ARF}$ (*Sharpless and DePinho, 1999*). Inactivation of either p16 or p53 prevented this G1 arrest: the arrest did not occur in p53-/- cells, p16-/- cells, cells transfected with a dominant negative *p53* mutant ($p53^{175H}$) and cells with mutant $Cdk4^{R24C}$ insensitive to p16. Thus, cells immortalized by dysfunctional p16 or p53 will not go into senescence upon RAS activation, but may progress to a tumorigenic state.
In a fish model (with hybrids of *Xiphophorus maculatis* and *helleri*) an RTK gene (*Xmrk*) of EGF-R family and an *Ink4a* homolog (*CdknX* or *DIFF*) appear to important for hereditary CM (*Wittbrodt et al., 1989, Kazianis et al., 1998*). This provides experimental evidence for the cooperation of an RTK mitogenic pathway and dysfunctional *Ink4a* in melanomagenesis. In further evidence, Chin et al. demonstrated that $Ink4a^{-/-}$ mice in which expression of a human mutant $H\text{-}RAS^{G12V}$ transgene was restricted to melanocytes, developed melanomas. Although UV irradiation did not (yet) cause CM in this mouse model, UV irradiation of hybrid *Xiphophorus* fish did cause CM (*Setlow et al., 1989*). UVA radiation was surpisingly effective in this model, only about 10 fold less effective than UVB radiation per unit radiant energy (J/m^2). It is, however, as yet unclear how UV radiation affected *CdknX/Ink4a* or the *Xmrk*/RTK mitogenic pathway. In the opossum *Monodelphis domestica* UVB radiation appears to induce CM (*Ley et al 1989*), particularly when applied neonatally (*Robinson et al. 1998*). However, UVA radiation did not induce malignant CM in this model (*Robinson et al. 2000*), only benign melanocytic precursor lesions (*Ley 2001*). In a very recent study it was found that the UVB-induced CM from these opossums carried UVB-like mutations in the *CDKN2A* homolog, and that only the mutant allele was present and expressed in a metastatic cell line (*Chan et al. 2001*).

A.1.3.5 Oncogenes, suppressor genes and UVB radiation

From the data stated above it appears that at least a combination of an activated oncogenic pathway and an inactivated tumor suppressor gene is needed in order for a skin cancer to arise: in SCC it is possibly an activated RTK/RAS pathway in combination with dysfunctional P53 tumor suppression, in BCC the Hedgehog pathway with possibly dysfunctional P53, and in CM again possibly an activated RTK/RAS in combination with inactivation of the INK4a locus. These combinations may be required, but not necessarily sufficient for the development of a tumor. Additional oncogenic events may be necessary. Although the skin cancers appear to be related to UV radiation, the effect of UV radiation is only unambiguously clear in point mutations of *P53* in SCC and BCC. The mutations found in the other relevant genes are of a wider variety, which may (in part) be caused by solar UV radiation. Experiments are needed to clarify if and how UVB or UVA radiation can affect other relevant genes. Overall, the data presently weigh most heavily toward the carcinogenic effect of UVB radiation: the latest data on experimental induction of CM in the opossum *Monodelphis domestica* are not indicative of any important contribution of UVA radiation next to the dominant carcinogenicity of UVB radiation.

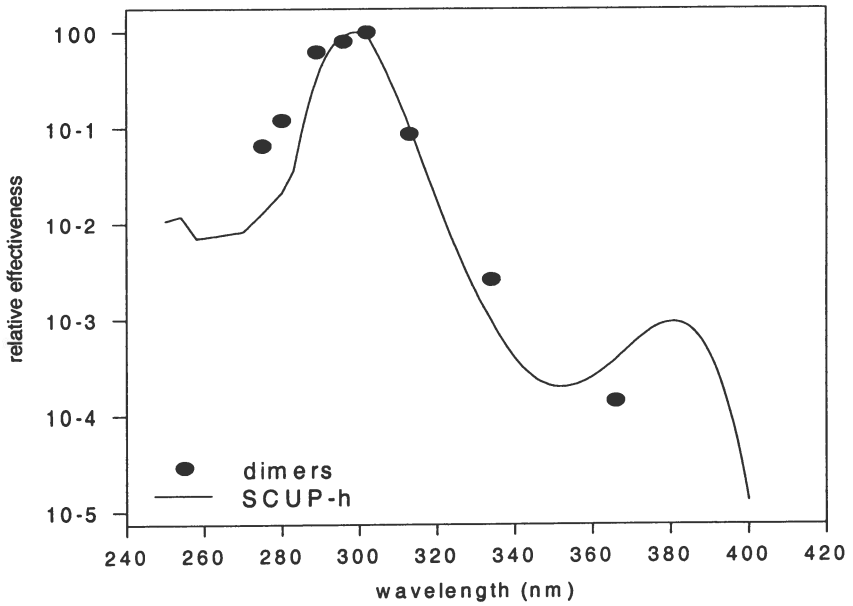
A.1.4 UV-Induced Tumour Formation

A.1.4.1 Relevant parameters

Tumor formation is a multi-step dynamic process in which one or more steps may be driven by external carcinogens (e.g. UV radiation). A risk assessment needs take the quality and quantity of the exogenous properly into the equation. In UV carcinogenesis the *wavelength* of the irradiation (spectrum), the *dose* (exposure regimen) and *time* (tumor latency) are the most important physical variables.

A.1.4.1 Wavelength

Shortwave UV radiation is directly absorbed by DNA and causes the formation of dimers at di-pyrimidine sites. Above 300 nm the efficiency of induction of these DNA adducts drops off steeply, and correspondingly, the mutation rate per J/m^2 drops off. A series of skin carcinogenesis experiments on hairless SKH-1 mice with various broadband UV sources has provided the data to establish the wavelength dependency of UV carcinogenes: the result was dubbed the SCUP-m action spectrum (*S*kin *C*ancer *U*trecht-*P*hiladelphia-*m*urine) (*De Gruijl et al 1993*). By correcting for differences in transmission of murine and human epidermisses the carcinogenic action spectrum for humans was estimated and dubbed the SCUP-h action spectrum (h stands for human) (*De Gruijl & Van der Leun 1994*); this correction shifted the maximum from 293 to 299 nm. The SCUP-h action spectrum is depicted in Fig. 1 together with the measured action spectrum for the induction of pyrimidine dimers in the human skin by Freeman et al. (1989). The two action spectra resemble each other remarkably well, especially in the UVB, which confirms that the UV-



induced genotoxicity is indeed the major driving force behind UV carcinogenesis.

Figure 1: Comparison of wavelength dependencies of Skin Carcinoma induction (SCUP-h, solid line (*De Gruijl & Van der Leun 1994*) and cyclobutane pyrimidine dimers (points (*Freeman et al. 1989*)) in human skin.

A.1.4.2 Time (age) versus dose

Tumor formation can be envisaged as a process with multiple rate limiting steps (mutations in oncogenes and tumor suppressor genes), some of which are UV driven and some of which are not (the latter may be caused by endogeneous metabolic processes which generate ROS). The likelihood of the occurrence of a UV-dependent step will increase with the accumulated UV dose, whereas the likelihood of a UV-independent step will simply increase with the lapse of time. Clearly, the UV-independent steps will render the whole process of carcinogenesis less dependent on the UV dose: in mouse experiments the tumor induction time will not be shortened by a factor of 2 if the daily dose is increased by a factor of 2, i.e. there will be no direct reciprocity between daily dose and tumor induction time. This reciprocity can also be modified by adaptive processes, e.g. epidermal hyperplasia which diminishes the penetration to the germanitive basal cells. This lack of reciprocity is indeed found in experiments of SCC induction in hairless mice by daily UV exposure. The average number of tumors per mouse, the yield Y (or tumor multiplicity) can be written as

$$Y = (H/H_o)^{p1} (t/t_o)^{p} \qquad (1)$$

where H is the daily UV exposure (in $J/m^2/d$), t is time (in days), and H_o, t_o, p1 and p are constants (when $H=H_o$ and $t=t_o$ then $Y=1$, i.e. an average of 1 tumor per mouse; note that if $H=2H_o$ then $t=t_o/2^{p1/p}$ for $Y=1$). In a straightforward interpretation, the power of time, p, is likely to be proportional (not necessarily equal to) the total number of rate limiting steps that occur in the course of time (including those steps that depend on the daily UV exposure). The power of the daily UV exposure, p1, is likely to be proportional the the number of UV driven steps; which implies that $p1 \leq p$ (*De Gruijl & Van der Leun 1991*).

If all mice in a group are comparable (in sensitivity and treatment) then in terms of the probability theory Y is a cumulative hazard function, more particularly, a cumulative *Weibull* hazard function with H and t as variates. The probability, P, for a mouse of contracting a first tumor then becomes

$$P = 1 - \exp(-Y) \qquad (2)$$

which, in absence of any intervening deaths, equals the prevalence of tumor bearing animals in a (large) group. These relationships hold rather well in the experiments with albino hairless mice, where $p = 7.2 \pm 0.8$ and $p1 = 4.3 \pm 0.5$ for early tumors of 1 mm in diameter (*De Gruijl & Van der Leun 1991, De Gruijl et al. 1983*), with pigmented hairless mice $p1 = 2.1 \pm 0.2$ ($p1/p = 0.3$ computed from data in (*Davies & Forbes 1988*); this lower dependency on the daily UV exposure is probably due to a better adaptation by pigmentation of the animals). When the daily exposure of the albino mice is discontinued after a couple of weeks, long before the appearance of tumors, then Y increases with t to the power 2.8 ± 0.2, which power equals p-p1 ($=2.9 \pm 0.3$), the power related to the UV-independent steps (*De Gruijl & Van der Leun 1991*)..
In human populations the age-specific incidences of cancers are measured, which equal the increase in Y per unit time (e.g. per year) if the fraction of patients with multiple tumors is small. The probability (calculated according to eq. 2) of SCC in the Dutch population follows a time-dependence which is quite comparable to that of albino hairless mice: $p = 6.6 \pm 0.4$ for males and 8.9 ± 0.7 for females (*De Gruijl 1997*). Under a level of daily exposure comparable to the estimated average among Dutch male, the tumors in the mice occur about

250 times faster. This appears to indicate that the tumor kinetics are very similar, but that the developmental rate of SCC (the mutation rate) is much higher in the mice. By combining measurements of ambient UV loads and epidemiological data from USA it can be inferred that p1 = 2.6 ± 0.8 for human SCC (*De Gruijl & Van der Leun 1993*); a value of p1 that is very similar to the one for pigmented hairless mice. For BCC p ranges between 4.5 and 5.5 and p1 = 1.4 ± 0.5 (*De Gruijl & Van der Leun 1993*).

A.1.4.3 Altered UV-exposure, incidences and risks

The easiest approach to quantify the effect of an increased UV exposure, such as caused by a depletion of the ozone layer, is to compare two stationary situations: one with a life-long low UV exposure and the other a life-long high UV exposure. Assuming that the White Caucasian populations in various locations in the USA are sufficiently comparable (in behavior and genetic composition) and in a stationary condition (in relation to UV exposure and skin tumor incidences), one can use the relationship between ambient UV loads and incidences for the assessment: for each percent of ozone depletion SCC would increase by 3%, BCC by 1.7%, and CMM by 0.5-1%, if the SCUP-h action spectrum is also applicable to CMM (*Longstreth et al. 1995, De Gruijl & Van der Leun 1993, Scotto & Fears 1987*). The complication here is that the incidences of BCC and CMM in particular are not stationary in the USA (*De Gruijl & Van der Leun 1993*).
Transitional changes in incidences due to changes in UV exposure are much harder to estimate. This requires much more detailed knowledge, e.g. on whether UV acts early, late or continuously in the process of skin carcinogenesis. From the above it appears that UV acts throughout the genesis of SCC, but mainly in an early stage of BCC and CMM development. For scenario studies on dynamic changes the tumor yield, Y, in eq. 1 may be factorized in a contribution from events driven by the *total* UV exposure, written as $(TH/H_o.t_o)^{p1}$, and a contribution from events purely dependent on time, taken as $(t/t_o)^{p-p1}$, where TH (= H.t) is the total UV exposure. For SCC these two factors are simply multiplied to calculate the yield, but for BCC and CMM the two factors need to be convoluted in time because the UV-dependent events are preceding the purely time dependent events (assuming that a small fraction of UV-initiated foci becomes tumors). Thus, scenario studies of changes in ozone can be made (*Slaper et al. 1996*): without restrictions the skin cancer incidence could quadruple by the end of the next century, and even initial restrictions under the Montreal Protocol would still yield a two-fold increase. With the Copenhagen amendments the incidence is projected to increase by a maximum of 10% around the year 2060. Clearly, the risk model needs to be refined further, but these calculations, despite their wide error margins, emphasize the disastrous potential of an uncontrolled increase of the ambient UVB load.
The impact presented above needs to be viewed on a population scale: in NW Europe the risk of contracting a BCC before the age of 75 is about 1 in 20, and about 1 in 100 for SCC and CMM (the risk of skin cancer is about 1 in 3 in Australia). Although the personal risk in a temperate climate is small, the impact on public health (and care) is very substantial, and worthwhile to curb by a simple moderation of our sun exposure.

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A.2 Lens Opacities and cataract

Dr. F. R. de Gruijl, Dr. J.C. van der Leun

Contents

A.2.1 Introduction

The lens of the human eye changes with increasing age: it looses its clearness, it turns yellowish to brownish, its fluorescence increases [Van Best et al., 1998], and its internal scattering of light increases [Sasaki et al., 1999]. In addition to these general changes in the bulk of the lens, localised changes may occur: opaque spots which can grow in size and ultimately hamper vision. Such an advanced stage of lens opacity forms a cataract, and as it appears to be related to age, it is referred to as 'senile cataract'. Cataract is world-wide a major cause of blindness. In developed countries cataract is adequately treated by an operation, but in developing countries it often leads to permanent blindness with grave social/economic consequences. Three main types of cataract can be distinguished: cortical cataract (CC) involving the surficial part at the front, nuclear (sclerotic) cataract (NC) at the centre of the lens, and posterior subcaspular cataract (PSCC) at the inwardly turned surface of the lens. Among 297 subjects with cataracts from a US health survey of 1971-72 104 (35%) had pure NC, 55 (18.5%) pure CC, 18 (6%) pure PSCC and 120 (40%) mixed forms of cataracts [Hiller et al. 1986]. Percentages from a hospital-based study (1008 cataract patients) in the region of Parma, Italy, are 49% CC, 11% NC, 3% PSCC and 38% mixed [Italian-American Cataract Study Group, 1991], with - according to the authors - an unexpectedly low number of NC. CC appears to be more abundant in populations living in temperate climates and NC in populations in more tropical climates, e.g. Iceland and Noto versus Singapore and Amami [Sasaki et al. 1999]. Of people older than 40 years in Victoria, Australia, 12% were found to have CC, 13% NC and 5% PSCC [McCarty et al 1999].

A.2.2 UV radiation and the etiology of cataracts

A.2.2.1 Literature survey

The mechanisms underlying all of these 'senile' changes are not fully established, but a general contention on ageing is that it is caused by (endogenous) oxidative processes (see for example [Berry and Truscott 2001, Fu et al. 1998]). As UV radiation can generate reactive oxygen species, it is also suspected to contribute to the deterioration of the lens [Eaton JW 1994, Dillon 1994, Sommerburg et al. 1998, Lee et al. 1999]. By comparing Portuguese and Dutch males, evidence was found that autofluorescence of the lens may indeed be related to sun (UV) exposure, and Van Best et al. (1998) reported that after a 15-year followup of a cohort of 15 people, the individual with the highest initial lentigular fluorescence developed a cataract.

Epidemiology shows that the etiology of cataract is complicated and involves many risk factors, among which some very prominent ones like alcohol abuse, heavy smoking, severe diarrhoea (dehydration), diabetics and chronic steriod use (odd ratios 2-6) [Harding and Van Heyningen, 1987, Clayton et al., 1984, Hodge et al. 1995]. In considering all risk factors Taylor (1999) concludes that the only effective preventive interventions seem to be to stop smoking and to reduce ocular UVB exposure.

In a thorough review of epidemiological studies Dolin (1994) concluded that there is limited evidence that UV exposure causes cortical and posterior subcapsular opacities in humans, but no evidence that UV-exposure causes NC. In a more recent review [West 1999] the conclusion is drawn that there is sufficient evidence of an increase in cortical opacities with

increasing UV exposure to warrant advising the public on measures to decrease their ocular exposure.

The reported risks from sun (UV) exposure in population-based studies are generally quite moderate, mostly odd ratios < 2 (e.g. 1.12, 95% CI 1.06-1.18, for women in [Hayashi et al. 1998]), and often not significantly different from 1 (e.g. 1.05, 95%CI 0.97-1.14, for men in [Hayashi et al. 1998]). However, the poor quality of retrospective assessments of exposure will inevitably lead to large errors and consequently to underestimation of the relative risk. Importantly, the potential impact of solar UV radiation is population-wide, and not - like the most prominent risk factors - limited to certain high risk groups. A majority of ecological studies show an increase in cataracts in geographical locations with high UV insolation [West 1999, Javitt and Taylor 1994, Hiller et al. 1986, Hollows and Moran 1981]. Despite the 'ecological fallacy' (i.e., importance of factors not considered), these studies are superior in assessing UV exposure, albeit an ambient instead of a true personal exposure, and they have an obvious direct relevance to assessments of the impact of increases in ambient UV radiation (on the merits of ecological studies for assessments of health impacts see [Soskolne et al. 2000]).
In a study on Chesapeake Bay watermen a special effort was made to assess retrospectively the individual solar UV exposures, and a relative risk of 3.3 (95% CI 0.9-10) was found for CC between the top and bottom quartiles of exposure [Taylor et al. 1988]. The lifetime exposure of individuals with CC was significantly higher than that of cataract-free controls, no association between UV exposure and NC was found (exposures before the age of 15 years were not included in the assessment). Using the same methodology of exposure assessment in a hospital-based study, Bochow et al. (1989) found a significant risk of PSCC associated with annual and cumulative ocular UV exposure. Most of the other studies found either no significant increase in risk [Collman et al. 1988, Dolezal et al. 1989] in relation to sun/UV exposure, or solely a significant increase in the risk of CC [Hiller et al. 1986, Italian-American Cataract Study Group 1991]. The latter result was also obtained in the 'Beaver Dam Study' of the various types of lens opacities in male patients with eye diseases, however, no association between sun exposure and lens opacities was found in female patients [Cruickshanks et al. 1992]. Cortical, nuclear and posterior subcapsular opacities were observed at similar frequencies in this population of patients, but the average age of the women was higher and they showed a significantly higher incidence of cortical and nuclear opacities than the men. The authors stress the point that despite the higher frequency of cortical opacities in females, these opacities do not show an increased risk with increases in UV exposure, like in the males. However, the percentages and numbers of persons that spend most of their professional and/or leisure time outdoors are dramatically smaller for females than for males. Thus, the numerical strength of testing any relation with UV exposure may be lost in the female population. The relation between CC and UV exposure was more broadly confirmed in a more recent population-based study in Salisbury, Maryland, by West et al. (1998). They found odd ratios just over 1 (1.10 , 95%CI 1.02-1.20, for males and 1.14, 95%CI 1.00-1.30, for females and 1.18, 95%CI 1.04-1.33, for African Americans). In a recent study in Iceland on people (n = 1045) older than 50 years odd ratios of 2.80 (1.01-7.80) and 2.91 (1.13-9.62) were found for grades II and III, respectively, of cortical opacification in people who spend more than 4 hours per day outside on weekdays [Katoh et al., 2001]. Although they found a substantial association with the time spend outdoors (a surrogate for UV exposure), these investigators stress - what has been found time and again - that 'age' appears to the main independent risk factor. Interestingly, cortical opacities appear to develop mainly in the lower (inferior) half of the lens [Mohan et al. 1989, Berliner 1949] or the nasal-inferior quadrant [Duke-Ehler 1926, Schein et al. 1994] which is taken as

evidence of the causal role of sun exposure (consider the convergence of oblique incoming UV light toward the equatorial region at the opposite side of the lens [Coroneo 1993]).

Although NC is commonly not found to be associated with UV exposure (mostly evaluated over the adult life), Wojno et al. (1983) intriguingly found a significant reduction in the risk of NC in people that wore (glass) spectacles for most of their lives. This would indicate a possible effect of blocking UVB radiation, perhaps most importantly, early in life before the onset of substantial brunescence of the lens. Such a significant reduction in risk was also found in the Beaver Dam Eye Study for men - but not for women -wearing glasses for distance before the age of 21 years when compared to those who started wearing glasses at ages over 40 years; a similar reduction in risk of CC was observed, but it did not reach statistical significance [Cruickshanks et al. 1992]. Myopia -short sightedness - has also been reported to be associated with a reduction in cataracts [Dolezal et al. 1989, Belkin et al. 1982], but other studies found myopia to be associated with an increase in cataract [Van Heyningen and Harding 1988, McCarty et al. 1999]. The reason for this discrepancy is unclear, and no dedicated study has yet been done to test the hypothesis that early-in-life solar UV exposure carries a risk of NC later in life.

A.2.2.2 Conclusions

Overall, the prudent conclusion on the potential impact of UV radiation appears to be that all types of cataract may be affected, albeit perhaps at different stages of life (early versus continuously) and to different degrees: CC appears to be most clearly related to UV exposure (especially in chronically exposed male outdoor workers), and NC the least clearly (perhaps related to early in life UVB exposure). This prudent conclusion is somewhat at odds with more rigorous epidemiological analyses that require consistent results over several studies, preferably 'proper' case-control studies; in that case, UV would only be considered a weak risk factor for CC. The impact of UV exposure on the relative risks in most case-control studies appears to be generally very moderate, but there is a general problem with assessments of lifetime personal exposures (mostly based on surrogates or crude estimates from recall). The inherent large errors are bound to yield underestimates of relative risks. Ecological studies appear to show a more substantial increase in prevalence of cataract with increasing ambient UV exposure (see below).

A.2.3 Cataract and UV: a Model

A.2.3.1 Dose-response relationship

A proper quantitative risk assessment needs to be based on a dose-response relationship. Such a relationship is not available for UV-induced cataracts in humans, and because of obvious ethical reasons, it cannot be determined directly by experimentation. Animal experiments on UV-induced lenticular opacification are not fully adequate in modelling senile cataracts observed in humans [Hockwin et al. 1999]. Because of the aforementioned inaccuracies in assessments of UV exposures, case-control studies and most other retrospective epidemiological studies are totally unsuitable to base a dose-response relationship on. Here, we will attempt to piece together a dose-response relationship from a combination of other epidemiological studies (ecological data and registries), animal and in vitro studies.

Burch and Chesters (1985) found that the age-dependency of the prevalences, P, of lenticular opacities and cataracts (from the Farmingham study [Podgor et al. 1983]) could be described

with a simple formula - similarly to incidences of skin cancer in accordance with Weibull statistics -

$$P(a) = 1 - \exp [-k(a - d)^6] \qquad (1),$$

where 'a' stands for age, 'k' a rate constant, and 'd' a delay time which equals 3.4 ± 2.5 year for 'senile lens changes' and 22.2 ± 1.9 year for 'senile cataract'. They interpret this formula in the framework of their theory on 'auto-aggressive diseases', among which they consider cancers. In case of cancers, a simple multiple (=6) hit interpretation would equate 'k' with 'm^6', where 'm' is an average mutation rate.

This analogy to the age-dependence of cancers invites the idea that the underlying process for cataracts may also involve a series of discrete (molecular) events, maybe even mutations in certain genes. This conjecture is not without substance: it is well known that certain inherited genetic defects cause cataract, e.g., specifically mutations in genes coding for crystallins. These proteins show homology to heatshock proteins and they serve as molecular 'chaparones' to prevent the aggregation of other proteins which could cause turbidity in the lens [Kumar et al. 1999]. Moreover, it would provide a natural explanation for the increasing risk with age, and why an opacity would increase in size: a clonal expansion of cells with a dysfunctional crystallin. As the proliferative cells are located in the equatorial region of the lens and the differentiating cells move inward, one would expect a similar course of development in expanding lens opacities; this appears to be particularly true for cortical opacities developing into cataracts. In connection with this, it is noteworthy that Burch and Chester (1985) already drew attention to the fact that cataract was "the first late effect to be recognised unequivocally among the survivors of the nuclear-bomb explosions at Hiroshima and Nagasaki". This clearly illustrates that a single exposure causes cataracts with a substantial delay, which calls for a mechanism of autonomous development and expansion of the opacity - analogous to the development of a cancer, but involving benign instead of malignant cells.

In this description according to eq. 1 it would appear that any effect from UV exposure will be expressed in the rate constant 'k' (in skin cancer, UV radiation would increase the rate of at least one of the mutations). Presently, the best way of establishing an appropriate dose dependency seems by considering latitudinal gradients in cataract as being caused by gradients in ambient UV exposure. Thus, we can look at published data on the latitudinal gradient in the Aboriginal population in Australia [Hollow and Moran 1981] or the registered cataract operations in the USA [Hiller et al. 1983]. Both of these data sets are related to the ambient UV in units from a Robertson-Berger meter with a spectral sensitivity that approximates the erythemal (sunburn) sensitivity of human skin. The first data set stretches from 1000 to 3000 UV units, and shows a corresponding 3 fold rise in prevalence in the age group of 40-59 years. The second data set goes from 2600 to 6000 UV units and shows a 1.58 fold rise in risk for people that have spent at least half of their life's at the location investigated, and with an increase in UV from 3000 to 4800 units a 1.28 fold rise in risk is observed. For prevalences <30% we can take the prevalence to equal the yield, i.e. $k(a-d)^6$. This in turn implies that these increases in risk are approximately equal to the increases in k. These data can be described by $k \propto (\text{UV dose})^p$ - in analogy with skin cancers - and we find that $p = 1$ for the first data set and $p = 0.55$ for the second. Thus, we find for the overall yield, Y, of cataract that

$$Y(a) = k_0 D^p (a-d)^6 \qquad (2),$$

where D is the annual ambient UV dose, k_0 is the rate constant independent of UV, and p varies from 0.55 to 1.0. In a later study Hiller et al (1986) studied CC and NC separately, and found the risk of the first to increase 3.6 fold going from 2600 to 6000 UV units while the risk of latter did not change. This means that p = 1.5 for CC and p = 0 for NC. With p=0.55 for all cataracts together and p=1.5 for CC, it could be inferred that about 1/3 of the total cataracts are UV-sensitive CC, and the remaining 2/3 are independent of UV (if the overall yield, $Y_{all} = Y_{cc} + Y_0 \propto D^{0.5}$, and the yield of CC, $Y_{cc} \propto D^{1.5}$, while the yield of other cataracts, Y_0, is constant, we find that $0.5 = (d \ln Y_{all} / d \ln D) = 1.5\ Y_{cc}/Y_{all}$ and hence $Y_{cc}/Y_{all} = 0.5/1.5 = 1/3$). Previously, Van der Leun and De Gruijl (1993) made a rough estimate of p = 0.7 for CC, based on the data from the watermen study [Taylor et al. 1988] in which it was reported that a doubling in UV exposure (assessed in retrospect form a person's professional history) increased the risk 1.6 fold. However, the UV exposure in this study was not as accurate as measurements of the ambient UV radiation.

A.2.3.2 Action spectrum

The remaining issue is whether an erythemally weighted UV dose is the appropriate dose for cataract formation. Much like erythema, the wavelength dependence of cataract formation in animals is found to peak in the UVB [Merriam et al. 2000, Pitts et al. 1977]. If genetical damage is really involved, like in skin cancer formation, then the carcinogenic or erythemal doses appear to be good approximations [De Gruijl and Van der Leun 1994, Young et al. 1998]. Even if next to direct dimer formation in the DNA, oxidation of DNA plays an important role the action spectrum will show a dominant peak in the UVB [Kielbassa et al. 1997]. Moreover, damage to the epithelial cells at the frontal surface and their release of prostaglandins appear to cause cortical cataract in underlying lens tissue [Li et al. 1995, Andley et al. 1996], and UVB radiation is particularly effective in inducing these cellular responses. If the oxidation of proteins is important in UV cataractogenesis [McCarty and Taylor 1996, Sommerberg et al. 1998], UVA could be relatively more important [Dillon et al. 1999] - depending on the endogeneous UV sentisizer - [Lee et al. 1999, Dillon 1994] and an erythemal spectral weighting may then underestimate the contribution from the UVA band. This would imply that the gradient in cataracts would be steeper with ambient UVA (as the latitudinal gradient in UVA is less than that in UVB), and that a change in UVB (such as with a thinning of the ozone layer) would affect the cataractogenic dose to a lesser extent.

Considering the experimental results and the good correlation between UVB and CC in the study Chesapeake Bay watermen (better than with UVA) [Taylor et al. 1988], the balance of evidence would presently favour that the main cataractogenic action in sunlight resides in the UVB, and the erythemal or carcinogenic dose would therefore be a good first approximation. Hence eq. 2 with p = 0.55 would appear an appropriate choice for the European population, and if the statistics for CC, NC and PSCC are known separately, p = 1.5 can be used for CC and p = 0 for the remaining cataracts (i.e. the latter would not respond to increases in ambient UVB radiation). With a 1% increase in ambient cataractogenic UV radiation for every 1% decrease in ozone, we find that the incidence of cataract would increase by 0.55% and that of CC by 1.5%. For a scenario study of the time course of changes in caratact incidences following a decline and a rise in ozone levels we could reasonably assume that UV radiation affects CC development continuously throughout life, similar to squamous cell carcinomas.

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A.3 The effects of UV radiation on the immune system and resistance to infections

Dr. H. van Loveren

Contents

A.3.1 Introduction

It is well known that exposure to ultraviolet radiation (UVR), especially the B-waveband (UV-B, 280-315nm) may cause skin cancer [1]. Studies on the mechanisms underlying the UVR induced carcinogenesis indicate that immunomodulating effects are initiated in addition to genotoxic (mutagenic) effects [2]. UVR has been shown to suppress both systemic and local immune responses to a variety of antigens, including several micro-organisms. The biological function of this change might be to prevent unnecessary inflammation in the skin in response to UVR-induced neo-antigens or common environmental antigens. If exposure to UVR occurs at the same time or just prior to infection or oncogenesis, then this immunosuppression may be harmful to the host [3].
A multistep process is induced by UVR, starting with the absorption of photons by chromophores (DNA, cis-UCA) in the skin. The following steps involve the production of several mediators by keratinocytes and other cutaneous cells, and phenotypic and functional cellular changes such as in Langerhans cells (LC), the major antigen presenting cells of the epidermis. As a consequence, the activity of T cells is modulated. There is evidence that UVR promotes production of the T helper-2 (Th-2) associated cytokines and reduces the production of T helper-1 (Th-1) associated cytokines [4]. The susceptibility to infections may be changed due to this differential effect on cytokine levels.
Influences of UVR on the resistance to viral, bacterial, and parasitic infections and resulting pathology have been noted [3 5 6 7 8]. In several animal models of infection UVR causes an increase in the microbial load and the severity of symptoms [3]. Although these models are helpful for elucidating how UVR may alter immune functions and hence impair the resistance to infections, the relevance in quantitative terms for humans remains unclear.

A.3.2 Mechanism of immunomodulation by UV radiation

A.3.2.1 Absorbing chromophores

As UVR wavelengths, particularly the B-waveband (UV-B), do not penetrate far into the skin, it is thought that cutaneous photoreceptors are needed to absorb the radiation, change as a result and initiate a complex cascade of responses ending in immunosuppression. Different photoreceptors have been suggested, including DNA and urocanic acid (UCA).

A.3.2.1.1 DNA

It is well known that UVR-induced DNA damage plays a pivotal role in UVR-induced carcinogenesis. In various studies Kripke and co-workers demonstrated that DNA damage is at least partially involved in local as well as systemic UVR-induced immunomodulation [9 10]. In transgenic mice that were deficient in genome repair systems it was shown that NER is crucial in the repair process of distant UVR-induced immunosuppression of CHS [11 12]. From these studies it was concluded that UVR-induced immune suppression involves both TCR and GGR. This implies that the mechanisms of UVR-induced erythema and immunosuppression are different, and that the sensitivity to acute sunburn effects of UVR

may not fully correlate to the sensitivity to the immunosuppressive effects of UVR, at least in mice [13]. On the other hand, Kelly and Young have shown in a study in human volunteers that the sensitivity to UVR-induced distant suppression of CHS and erythema are highly correlated [14].

A.3.2.1.2 Urocanic Acid (UCA)

A second photoreceptor involved in initiating UVR-induced immunosuppression, including reduced resistance to infections, is UCA [15]. The naturally occurring *trans*-UCA in the stratum corneum isomerises to *cis*-UCA after UVR exposure and *cis*-UCA has been shown to act as a down-regulator of immune responses in a variety of systems. For example, in a rat model of oral infection with the worm *Trichinella spiralis* it has been found that exposure to either UVR or cis-UCA led to lowered immune responses to infection and to a higher parasitic load [6]. Furthermore, if rats were injected with a monoclonal antibody with specificity for *cis*-UCA 2 hr prior to UVR exposure, the UVR-induced suppression of DTH to *T. spiralis* and the increase in larvae counts were significantly inhibited compared with rats that were similarly injected with a control antibody [6]. This result is of particular interest as there is no skin involvement at any stage during the infection and therefore the cis-UCA must be acting systemically. From these data it can be concluded that UCA is an important photoreceptor and that it plays a role in the mediation of the UVR-induced suppression of resistance to infections.

However, it was also demonstrated in rodent models that the DTH might be suppressed at UVR wavelengths that are very inefficient in the trans-to-cis isomerisation of UCA [16] and that the actionspectrum for the cis-UCA production in human volunteers appeared to be red-shifted from the action spectrum for suppression of CHS. These results indicate that other mechanisms, like DNA damage, also play a role in mediation of UVR-induced immunomodulation.

A.3.2.2 Microbial antigens in animal models

As indicated earlier, a wide array of infections in laboratory animals has been shown to be affected by UVR [3]. This effect may be mediated by the influence on different cytokines; a shift from a Th-1 to Th-2 cytokine profile has been reported [3 4]. Studies using the parasite infection model Trichinella Spiralis, however, indicated that the production of IgE, a Th-2 associated cytokine, is significantly suppressed by UVR [7].

A.3.2.3 Microbial antigens in humans

For extrapolation of laboratory animal data to the human situation, it is of importance to study whether effects as they have been observed in animals in fact occur in humans. It is obvious that experimental infections cannot be studied in humans. Although there are several published papers showing that UVR may cause recrudescences of Herpes Simplex Virus infection (HSV) in some people, the importance of exposure to solar UVR for viral and other infections has still to be substantiated [3]. Effects of controlled UVR exposure on a variety of immune responses that reflect the capacity of the host to react to infectious agents can readily be studied in humans and may shed light on this issue.

A.3.2.4 Immune response after hepatitis B vaccination

Measurement of vaccine responses has been recommended as an opportunity for monitoring immune function in humans [17]. Antibody levels evoked during vaccination indicate the

functioning of the integral immune system and may be subject to different modulating factors. Studying of antibody responses after vaccination is relevant from a public health point of view [18]. Furthermore, we may evaluate the effect of UVR on the protection to an infection without the need to induce the infection experimentally or to wait for natural infections to develop [18 19]. As there is a strong association between exposure to UVR and the season for people living in non-tropical countries, it has been examined whether there was a seasonal difference in antibody titers after hepatitis B virus (HBV) vaccination. Anti-HBs levels were monitored during a standard immunisation protocol (0, 1, 6 months, 20μg Engerix-B, SB) given to health care students (n=522) in Utrecht in the course of the years 1994-2000. During the immunisation procedure a tendency to a lower mean antibody titer was observed in those who received their first vaccine in summer in comparison with students who had their first immunisation in winter. However, at the end of the immunisation procedure (a few weeks after the administration of the third vaccine) no statistically significant differences between summer- and winter-groups could be established. These results may indicate that exposure to ambient UVR influences the antibody responses after vaccination immediately, but the level of clinical protection eventually achieved appears to be unaffected.

A.3.2.5 HSV T cell immunity

There is a lot of evidence that exposure to UVR is a common triggering factor for recrudescence of HSV ("cold soars") [20 21]. The mechanism underlying this phenomenon is still unknown. UVR may suppress the local immune response to HSV to allow the cytopathic effects of the virus [3]. The role of UVR-induced down-regulation of systemic HSV T cell immunity is controversial. UVR exposure given to HSV positive subjects undergoing phototherapy as used in the treatment of psoriasis did not cause an alteration neither in the *in vitro* lymphoproliferation in response to HSV nor in the HSV-specific cytotoxic T cell activity [3 22 23]. In contrast, the NK-cell activity was significantly reduced shortly after the initiation of the phototherapy [23].

A.3.2.6 Granulocyte activity

The systemic effects of whole body UVR irradiation on human peripheral blood phagocytes was studied at different time points, up to 24 hr after a single erythemal dose of UVR radiation. Two phagocyte functions were tested, i.e. adhesion and phagocytosis, and both were found to be reduced by 50%. This functional suppression was accompanied by a decrease in the expression of complement- (CR1 and CR3) and IgG Fc- (FcRII and FcRIII) receptors. These data suggest that UVR irradiation may suppress some important functions of circulating phagocytic cells that may have consequences for resistance to infections [24].

A.3.2.7 Conclusions on immunomodulation

In conclusion, some host defence mechanisms in human subjects can be affected by UVR exposure. We found clear effects of UVR on T-cell dependent immune responses in humans such as CHS and on non-specific immune responses. On the other hand, we did not observe effects on specific HSV T cell immune responses and only very marginal, and most likely clinically irrelevant effects on HBV vaccination. Therefore, it remains unsettled whether host resistance to infections in humans is affected by UVR.

A.3.3 Risk assessment in humans

For quantitative risk assessment, information on the dose response relationships between of the infectious disease parameters (microbial load, clinical symptoms) with exposure to UVR in humans is required. As such information is not available in humans, but is available from laboratory animal studies, we have attempted to extrapolate from the models to the human situation. This assumes that the difference in sensitivity for UV-induced modulation of *in vitro* or ex vivo *situ* immunological parameters between rodents and humans reflects the difference in sensitivity for UV-induced impairment of the resistance to infections between rodents and humans. For example, dose response studies in rats infected intravenously with *Listeria monocytogenes* indicated that 6.8 kJ/m² UVR (FS40 lamps) inhibited the specific cellular immune response by 50%. The suppression corresponded with he delay in clearance of the bacteria from the spleen. In order to extrapolate from the rat to the human situation, this dose was multiplied by a factor representing the interspecies difference in sensitivity for the effect of UVR as assessed in the MLRS, which is an *in situ* test.

Humans are less sensitive to UVR-induced induced suppression of the MLRS by a factor 3.85 than rats [25]. This means that humans have to be exposed to 3.85 times more UVR in order to induce suppression of the MLRS by the same order as rats (i.e. 50%). For natural killer (NK) cell function the difference was 3.24, which is approximately the same as for MSLR species differences [26]. Furthermore, a factor for individual differences in sensitivity to UVR, as was assessed in our study group of 17 human volunteers all with skin type II (intraspecies factor=0.5), was applied. For extrapolation from artificial to solar UVR we used four different actionspectra, as it is still unknown what action spectrum is the most relevant for the immunosuppression. Starting from these data and the biologically effective doses of sunlight as calculated by De Fabo et al.[27], i.e. the CHS action spectrum was applied, it could be estimated that exposure for 92 minutes (cumulative dose received during 7 consecutive days) at 40^0N in July at local noon could lead to 50% suppression of specific T-cell-mediated responses to *L. monocytogenes* in humans [25 27] . By applying the alternative action spectra, the numbers of minutes exposed to cause the same effect could be calculated. The effect of ozone decreases on the level of ambient UVR and hence on the possible immunosuppression during outdoor exposure could be estimated [26].

In the exercise so far we predicted the UVR dose that might lead to a suppression of antigen specific immune responses in humans. A next step is to predict the clinical outcome of such effects. For this reason a model for systemic HSV infection in the rat was recently developed. HSV is neurotropic and intranasal infection may cause neurological symptoms (paralysis, nervousness), that are aggravated by exposure to UVR. In this infection model both the viral load, the clinical outcome and the exposure to UVR prior to infection and their interrelationships could be properly quantified. Applying the action spectrum for suppression of CHS it was estimated that exposure to ambient UVR at 40^0N in July at clear sky and at local noon during 302 minutes (cumulative dose received during 7 consecutive days) leads to a 10% increase of neurological symptoms due to systemic infection with HSV in humans. Applying other action spectra in the extrapolation yielded alternative estimated number of minutes. The effect of ozone depletion on the ambient UVR levels and as a consequence the percentage of infections leading to clinical symptoms was also estimated.

In conclusion we may say that extrapolation of animal data enabled us to provide an estimate of the immunosuppressive effects of UVR in human populations. UVR at doses relevant for

outdoor exposure impairs the human immune system. As the extrapolation described relies on many assumptions, and data on real day-to-day exposure to ambient UVR have not been incorporated yet, experimental studies with human volunteers and observational epidemiology are needed to verify these results.

A.3.4 Observational studies

A series of epidemiological studies have been performed. The first study concerned a cohort of post-renal transplantation patients, who were monitored for the incidence of skin cancer. The association between the occurrence of skin infections and exposure to sunlight among other immune modulating factors like diabetes and dose of immune suppressive medication (azathioprine, prednison) were examined[[28]]. No consistent correlation was found between the incidences of infection and the estimate of lifetime cumulative exposure to sunlight. On the other hand, associations with the short-term estimate of exposure ('season') were found. Spring and summer were associated with the highest rates of respectively herpes simplex and herpes zoster ('shingles'). This finding is in accordance with the hypothesis of seasonal differences in ambient UVR that trigger a circannual rhythm in immune responses and hence in the resistance to certain infections in human populations [[29]]. Sunny season was also associated with the highest incidence of fungal skin infections, in contrast to the lowest incidence of bacterial skin infections found in such periods [28].

Another study was conducted among healthy 1-year-old children who had been recruited from the general Dutch population for a cohort study regarding the determinants of asthma and allergy. It was examined whether short-term exposure to sunlight in the spring and summer of 1998 was associated with a higher incidence of upper respiratory tract infections. In the children's study it was found that children with low exposure to sunlight showed a statistically significantly higher incidence of symptoms that indicate upper respiratory tract infections in the 4 weeks preceding the filling out of the questionnaire than children with high exposure to sunlight. This correlation was not confounded by other possible determinants of respiratory tract infections as seasonal differences, gender, smoking, atopy of the one of the parents, visits to day care centres etc. Furthermore, this correlation was still found when restricting the analyses to mild respiratory complaints only. This was done in view of the possibility that more severe respiratory complaints may imply that the child stayed indoor and as a consequence received a lower dose of solar UVR. The results of the children's study suggest a protective effect of sunlight on the occurrence of upper respiratory tract symptoms, a result that was not anticipated. However, children that suffered sunburn in the study period showed increased incidences of upper respiratory tract symptoms, supporting the notion of decreased resistance after higher doses of sunlight.

A.3.5 Concluding remarks

Immunomodulating effects of UVR on the immune system were observed in both animals and humans. In different infection models in the rodent a clear suppressive effect of UVR exposure on the host resistance could be established, leading to both impairment of specific immune response and an increase of microbial load and clinical symptoms. It is hypothesised that this effect is also relevant for human populations, leading to higher incidences of infection and/ or a more severe clinical course after infection.
In an extrapolation model (the 'parallellogram-approach') data from animal experiments were extrapolated to humans. This exercise shows that at relevant UV exposures decreased resistance to infections may be encountered. The dose needed to give an increase of clinical symptoms due to HSV was 2 - 3 times higher than the dose needed to give an effect on immune responses to Listeria model. This may reflect differences between these types of infections.
The experimental studies carried out in humans, and the epidemiological studies provide evidence to support adverse effects of UV exposure on resistance to infections, yet these indications are not unequivocal and in any case do not reveal dramatic effects.

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A.4 Effects of increased ultraviolet irradiance on the marine environment: controversial results, and perspectives

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Contents

A.4.1 The aquatic environment: distinct characteristics.

The solar radiance spectrum ranges from 100 nm to 1 mm, which includes infrared radiation, visible light and ultraviolet radiation. The latter can be subdivided into UV-A (400-315nm), UV-B (315–280nm) and UV-C (280–100nm) (10). Organisms that are directly exposed to UV-C and UV-B radiation suffer a wide range of damages, affecting molecular and organismal functions and structures. Fortunately atmospheric gases, especially ozone and oxygen, absorb all UV-C and part of the UV-B (figure 1). This protects the biosphere from the most dangerous types of UV radiation (10, 7).

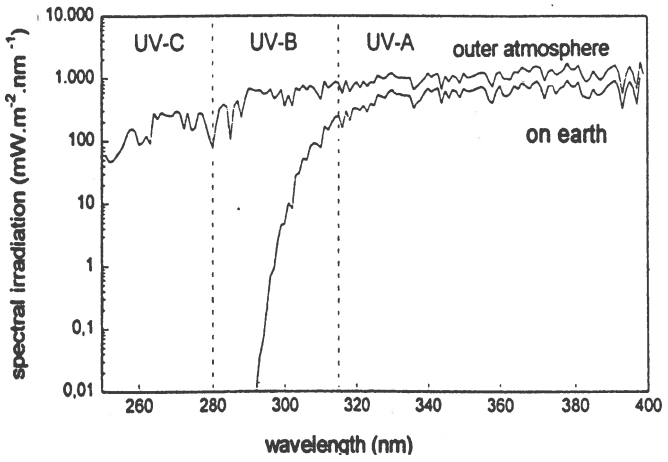

Figure 1. Solar spectrum reaching the outside layer of the atmosphere and the earth's surface, on a sunny day with a sun position at 28 degrees (ref. 7)

Since the beginning of the industrial period, increasing amounts of chemical compounds have been emitted into the atmosphere. Chemical compounds such as chlorofluorocarbons (CFCs) have proven to deregulate the natural ozone balance. These gases are very inert and accumulate in the atmosphere. Long-lived chlorine reservoir species (HCl, $ClNO_2$) are converted into the reactive form as soon as the temperatures high up in the atmosphere drop below 195K: the threshold to the formation of polar stratospheric clouds (PSC's). The long-lived chlorine reservoirs are then photolysed into species involved in stratospheric ozone destruction (Cl, ClO, ClO_2, Cl_2O_2, NO, HO, Br...) (11). The first observations made of decreasing ozone concentrations in the stratosphere were made in the 1950's. Concentrations above the Antarctic had dropped to 320 DU, whereas values above the Arctic still averaged 400 to 450 DU (33). Since then, ozone concentrations have dropped further, and recent modelling studies have predicted that ozone would reach a minimum around 2020 (11). The ozone decrease is correlated to an increasing amount of short-wavelength UV-R reaching the earth's surface; these short UV-B wavelengths are known to interfere with biological systems, both on the level of cells and of whole organisms and parts thereof, both algae, plants, and animals (1, 10, 13, 18).

The increasing UV-B radiation reaching the earth surface has proven to affect many biological processes and is by and large detrimental to individual organisms (34). The increase of skin cancers, eye damage and other health effects on humans and animals has lead

to much political and scientific concern. This resulted in the decision to stop ozone breakdown process. Agreements have been made at several world climate conferences such as in Montreal in 1987 to forbid emissions of chlorinated fluorocarbons (CFCs). Unfortunately, ongoing emissions of greenhouse gases such as methane and carbon dioxide are responsible for cooling down the stratosphere, which consequently triggers the conversion of long-lived chlorinated compounds into the reactive species. Cooling of the stratosphere is expected to cause more ozone breakdown than was originally expected, especially on the northern hemisphere (9). As a consequence more damaging UV-R will be able to reach northern latitudes.
The damaging effects of UV-R on terrestrial organisms have been studied extensively, but effects on aquatic organisms are less well known. It was long believed that UV-R did not penetrate in water, and would therefore not have any effects on freshwater or marine organisms. Recently, measurements of penetration of UV-R into the water column have demonstrated that UV-R penetrates to significant depths of the upper part, in which most primary production takes place (8). Primary production, the basis of the food chain in lakes, rivers, seas and oceans in the ocean, is mainly performed by microalgae. Marine microalgae are responsible for 40% of CO_2 fixation of the Earth, and much of this carbon, fixed in organic matter, is transported to the deep ocean, through a process referred to as the "biological pump" (9). Thus, detrimental effects of UV-R on microalgae might trigger a reduced CO_2 uptake capacity of the ocean, which would eventually have consequences for the CO_2 concentration in the atmosphere. Other trophic levels of the marine ecosystem are also affected by UV-R: bacterioplankton, viruses, zooplankton and even fishes (8). The impact of UV-R on the various levels of the marine ecosystem will be reviewed in this report. New modelling results will be integrated in the report in order to estimate the effects of ongoing ozone decreases on the primary production and its impact on the ocean's CO_2 uptake capacity. Effects of UV-R on nutrients will not be reviewed, e.g., UV's influence on iron speciation or on dissolved organic matter breakdown to components available to heterotrophs; both effects enhance food chain efficiency (6, 8, 9, 13).

A.4.2 Previous research

Measurements of UV-R penetration have been made at several oceanic and coastal locations. UV-R proved to reach different depths depending on particulate matter suspended in the water and on the amount of DOC (Dissolved Organic Carbon) and DOM (Dissolved Organic Material), all strongly absorbing UV-R (8, 9, 27). In the productive waters of Chesapeake Bay (Western North Atlantic Ocean) UV-R did not penetrate more than 0.5m from the surface (3). In the St. Lawrence Gulf, on the other hand, 10% UV-R reaches 50% of the summer mixing layer, which comprises the upper 3 - 4m of the water body (25, 27). Ocean waters usually allow much more UV-R to penetrate than more productive coastal waters, which contain more plankton, detritus, DOC and DOM (13, 16). The attenuation of the down-dwelling ultraviolet irradiance is wavelength dependent: the shorter wavelengths are more rapidly absorbed, which means that little damaging UV-B penetrates to significant depths of the water column (16, 20). The biological damage potential, which can be estimated from the DNA damage action spectrum, proved to have an even faster attenuation with depth than UVB-R. However, damaged DNA can be found to depths up to 50m: photoproducts developed near the surface are mixed downwards where winds and tides result in vertical mixing (2).

The upper water layer, the mixing layer, is the most productive (8). It contains the microalgae that require visible light to perform photosynthesis. The microalgae are not only exposed to visible light (PAR, Photosynthetically Active Radiation) but to UV-R as well. Phytoplankton exposed to UV-R suffer a wide range of damage at different levels: molecular, cellular, population and community (1, 8, 9, 13). Solar UV-R has proven to affect growth, reproduction, photosynthetic enzymes, pigments and other cellular proteins (1, 8, 19, 24). Especially irradiation by short UV wavelengths triggers structural changes in DNA mainly in the form of cyclobutane dimers (CPDs) and pyrimidine (6-4) pyrimidone dimers (1, 8, 24). Setlow's DNA action spectrum demonstrates the potential for UV-R damage to DNA, which increases exponentially with decreasing wavelengths (figure 2) (8).

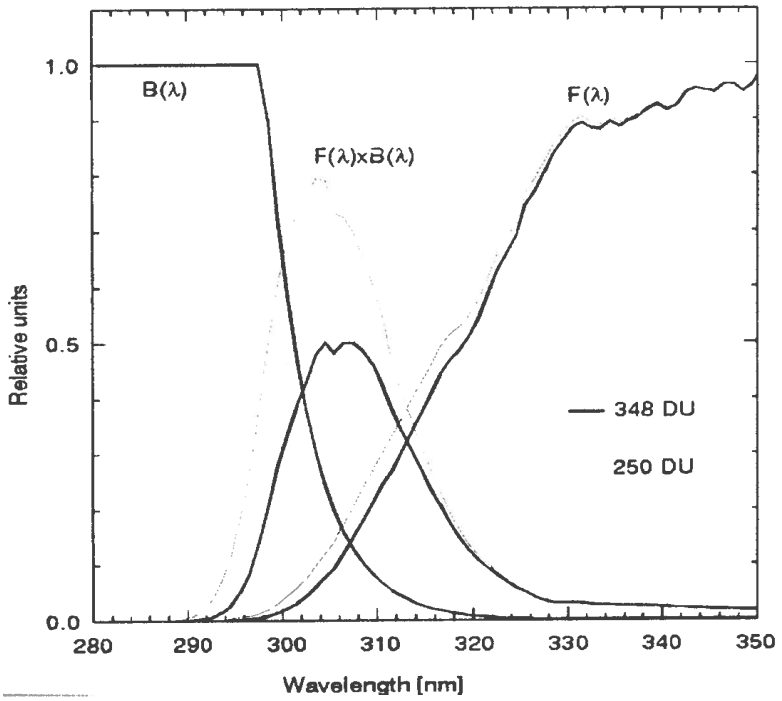

Figure 2. **Biologically active UV-R under full column atmospheric ozone values of 348 and 250 DU. Spectral irradiance F(λ), erythemal action spectrum B(λ), and the spectrum of biologically active radiation F(λ)B(λ). (ref. 10)**

Microalgae generally dispose of repair mechanisms that enable them to cope with these UV induced structural hiatus. The repair mechanisms consist of a photoenzymatic ("light") repair mechanism, and a nucleotide excision ("dark") repair mechanism (2). Diel patterns of DNA damage and repair have been observed in microalgae exposed to natural UV-radiation in the marine environment (2). The amount of CPDs accumulated during the day and decreased overnight, but some residual DNA damage was still present at the end of the night, which indicated that dark repair processes could not remove all CPDs (2). The UV induced damage reduces the microalgae's photosynthetic and growth rate and inorganic carbon uptake (4, 9, 15, 24). The latter is important for carbon dioxide sequestration by the ocean, as mentioned already. Production measurements indicated that CO_2 uptake decreases by 50% under UV-R stress (5). In Antarctic and temperate phytoplankton UVB irradiation reduced the inorganic uptake by 25 to 50%, compared to phytoplankton shielded from UVB (8).
Microalgae are the driving motor of marine food webs on which zooplankton and all other components of the ecosystem depend (9, 13). A reduced primary production is likely to be

reflected in the production of the higher trophic levels of the food chain, first affecting the grazers, zooplankton such as ciliates and flagellates, and eventually secondary consumers and fishes (8, 15, 18, 31). Modelling studies have resulted in estimates of the effect of reduced primary production on fish production: a 5% primary production reduction would translate to a 6 to 9% reduction in fishery catches (13). A 7% loss of fish yield represents 10 million tonnes of fish and shellfish per year, which equals the total amount of yearly aquaculture production (13).

A few studies have assessed the direct effects of UV irradiation on zooplankton and fishes (8). Zooplankton is often present in the mixing water layer and is consequently also exposed to UV-R. Adult zooplankton generally dispose of UV absorbing compounds such MAAs (Mycosporine-like Amino Acids) and blue pigments that prevent or at least limit the amount of UV irradiating the DNA (3, 8, 21). Adult fishes can avoid exposure to damaging solar UV-R by active migration and also dispose of a protective layer: the skin and its silver scales, which reflect UV-R. Fish and zooplankton larvae and eggs on the other hand are often located in the uppermost water layer or float passively at the very surface (1, 26, 31). As a consequence the eggs and larvae may become exposed to intense UV radiation. Several studies on commercial fish species such as Northern Anchovy (*Engraulis mordax*) and Atlantic Cod (*Gadus morhua*) have demonstrated that eggs, which had been irradiated by UV-B, suffered DNA damage (13, 18, 25, 32). They often developed into misformed fish larvae and had a higher mortality rate (8, 13, 25, 29). Larvae also may be affected by deleterious effects of UV-R, especially young larvae which haven't developed any UV protection mechanisms (s.a. UV absorbing compounds) (13). Young fishes (fingerlings) exposed to high UV-R underwent epidermis damage (sunburn), which was often associated to opportunistic fungal infection (8, 13). The latter suggests a damaged immune system. Several fish species inhabiting shallow waters proved to suffer of eye lens damage (8). These observations clearly demonstrate that the higher trophic levels of the marine ecosystem also undergo the direct effects of UV radiation. UV-B impact on Northern Anchovy (*Engraulis mordax*) lead to a 13% decrease in its annual production (25). Such UVB induced production reduction is not negligible and has large implications in fish species of commercial importance.

More recently research has also been directed to the impact of UV-B on bacterioplankton that occupy the central role in the microbial food web and are essential for the carbon cycle (1, 8, 28). Bacterioplankton is responsible for breaking down dead organic material and recycle organic carbon and essential nutrients (phosphate, silica, nitrate, etc), making them available for microalgae and consequently for higher trophic levels (8, 28). Bacterioplankton located in the upper mixed layer proved to suffer of UV-R induced damage, including DNA damage and reduced triated amino acid uptake, which translates into reduced bacterial production (8, 12, 18, 28).

In the marine ecosystem bacteria, viruses and phytoplankton are closely linked to one another (8). As a consequence the effects of UV-R on one group affect the other groups. Viruses are also subject to UV induced damage which translates to a reduced infective capacity, therewith reducing the effect of viruses on phytoplankton, which plays a central role in phytoplankton mortality (8, 18). Reduced microalgal primary production has been suggested to make more inorganic carbon available for the microbial food web, enhancing its production and its importance in the carbon cycle (8, 30). Since both bacterioplankton and phytoplankton are sensitive to UV-R, the overall reduced productivity might have implications for the ocean's CO_2 uptake capacity (13). Next to a possible reduction in the "biological pump", UV directly photolyses DOM into CO and CO_2 which means that UV-R might be responsible for the reduced ocean's CO_2 uptake capacity and an increased CO_2

emission from the ocean (8, 12, 13). An overview of the UV-R induced effects on the marine ecosystem is illustrated in figure 3.

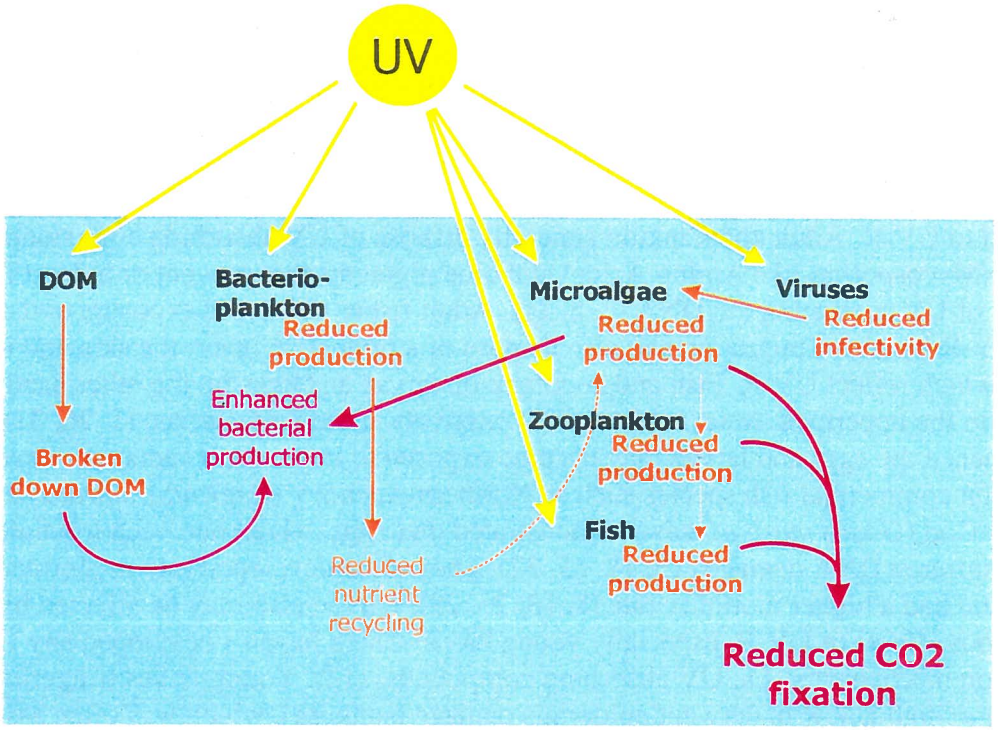

Figure 3. Overview of the UV-R induced effects on the marine ecosystem

One important aspect is studied since very recently. This is the influence of UV radiation on OH radicals (6, 8). These hydroxyl radicals are a major sink of gases in the atmosphere, and affect biocell structures and inorganic matter under water (8). OH radical formation is hard to quantify because of their ephemeral nature.

A.4.3 Modelling

It is clear that UV-R affects the marine ecosystem at different trophic levels in direct and indirect ways. In a model developed by Van Oijen (1998; ref. 9) the direct UV-R effect on global primary production is estimated for recent (1998) and past (1978) ozone layer conditions. The ocean's reduced carbon fixation capacity due to ozone depletion proves to be an ocean wide phenomenon. As expected, the primary production reduction is highest in the polar regions and especially in the Antarctic Ocean during the appearance of the ozone hole. The strongest reduction is detected for the month October: carbon fixation is reduced by max. 2.2%. Between 30° N and 30°S there are hardly any changes in primary production. In the Arctic a decrease of max. 0.6 percent is estimated for the period March-May, during the appearance of the 'northern ozone hole'. However, the absolute decrease in primary production in an ocean province depends not only on the increase in UV-R, but also on the amount of biomass it affects. In absolute numbers, the decrease in primary production in the Atlantic Ocean contributes as much to the total decrease in carbon fixation as the decrease in

the Antarctic. According to the model, the global decrease in primary production due to enhanced UV-R is only tenths of percents over the past decades (see table 1).

Table 1. Primary production reduction in percents for the different oceans from 1978 to 1998.

Ocean province	*Total primary production Reduction 1978-1998 (%)*
Pacific	0.15
Atlantic	0.18
Mediterranean	0.21
Indian	0.14
Antarctic	0.26
Arctic	0.14

In this study, the model of Van Oijen (1998) is used to calculate the expected decrease in primary production (CO_2 fixation) from 1998 to 2018. It is assumed that the trend in ozone concentrations over the past decades will remain the same for the coming 20 years. The modelling results indicate that increased UV-R will reduce the world-wide microalgal primary production from 1978 to 2018 (figures 4a, 4b and 4c). Over this period, the percentage decrease in primary production due to ozone depletion is highest for the Antarctic Ocean, max. 5.3%. Due to some problems with processing of the maps, this cannot be viewed on figures 4a,b and c.
Because the relationship between ozone depletion and reduction of primary production is not linear, changes in the global patterns in reduction can be observed. Compared to the period 1978-1998 (figure 4a), there is a stronger decrease in carbon fixation in the North Atlantic over the period 1998-2018 (figure 4b). As already pointed out above, between 1978 and 1998 the effect of ozone depletion on the northern hemisphere affects global

Fig. 4a. 1978 - 1998

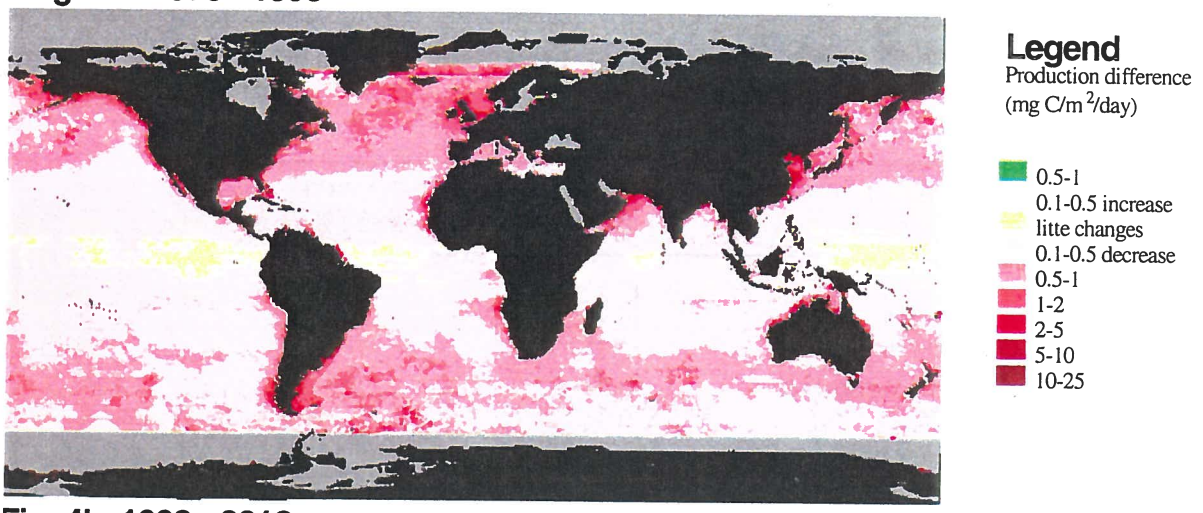

Fig. 4b. 1998 - 2018

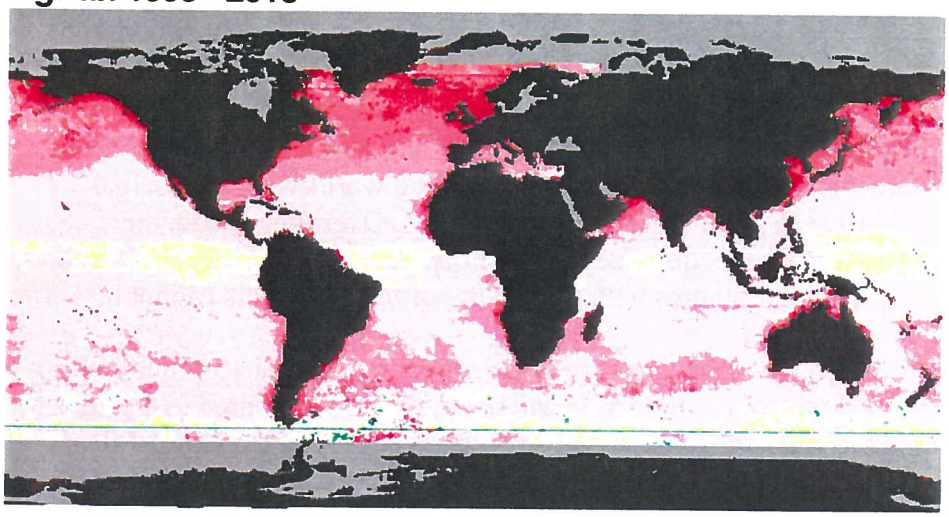

Fig. 4c. 1978 - 2018

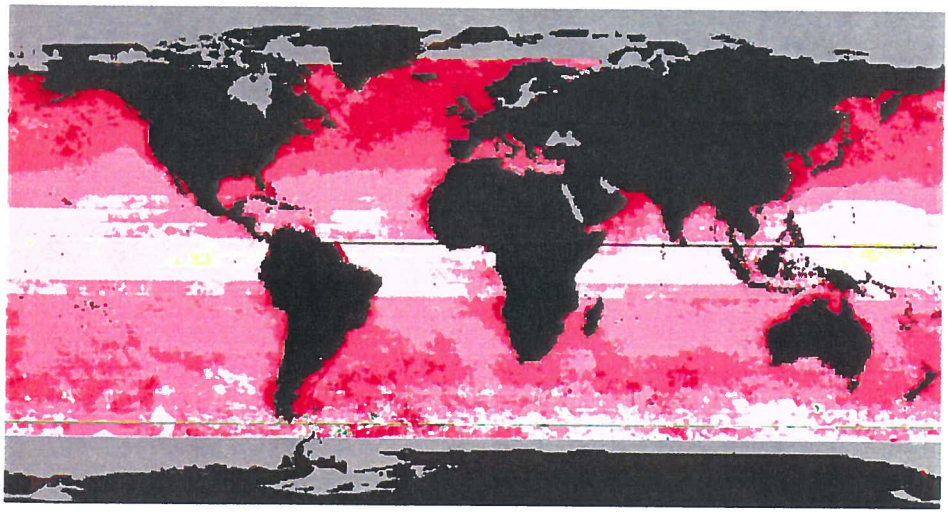

Figure 4. **Expected UV-R induced primary production for the period: a) 1978 to 1998; b) 1998-2018; c) 1978 to 2018.**

primary production as much as the appearance of the Antarctic ozone hole. The new modelling results suggest that in the near future, ozone depletion on the northern hemisphere might even play a more important role in reducing global primary production than the Antarctic ozone hole.
Between 30°S and 60°S, there is a lower in carbon fixation over the period 1998-2018 compared to 1978-1998. This observation can be explained by a slightly positive effect of ozone depletion because not only UV-R but also PAR (photosynthetically active radiation) increases. In some situations, this positive effect of ozone depletion is larger than the negative effect.

A.4.4 Future research

The increasing UV irradiation levels following stratospheric ozone depletion have a wide range of deleterious effects on the marine ecosystem. Especially concerning is the impact on the "biological pump". Nevertheless some interpretations and calculations of UV-R impacts on organisms and food webs should be put in perspective.
First of all, the effects of UV-R on marine microorganisms are often evaluated for a continuous exposure to a fixed amount of UV irradiation. In reality, microalgae are subject to vertical mixing in the water column, which implies that the amount of UV irradiation and the spectral composition of UV-R to which they are exposed changes all the time (4, 8). In order to get a realistic evaluation of the impact of UV-R the vertical mixing component should be included in the evaluation of UV impact. Another important aspect is determining the actual biological impact of UV-R on the target organism (microalgae, zooplankton, fishes, bacterioplankton, and viruses). As mentioned before, short wavelength UV is much more damaging than the longer wavelengths (23), but is also more quickly absorbed in the water column. In order to be able to make accurate estimations of UV-R effects, one needs to measure the actual penetration of the different UV wavelengths into the water column and then calculate the action spectrum (with biological weighting functions) for the studied organism (5, 8, 13, 14, 22, 28). The action spectrum is calculated for each wavelength in the UV range and can be mapped onto the irradiance levels of the area and depth of interest (23). This alone would allow an accurate estimation of the deleterious effects of UV-R in the aquatic environment. At the same time, the repair capacity of organisms and their protective mechanisms, should be taken into account (17, 19, 22, 32).
Another aspect is often overlooked in the interpretation of the negative effects of UV on the marine ecosystem. The decreased primary production does not only affect the CO_2 uptake capacity but as mentioned before, it also affects other parts of the food chain, including fish production. The most productive waters are also the more turbid waters in which UV-R penetration is strongly limited. This implies that the effects of UV-R on the marine environment might be less than what has been thought in the past. In other words, estimations of the negative impact of UV on the marine ecosystem can easily be overestimated. However, experimental studies on the deleterious effects of UV-R on eggs and larvae of commercial fishes have demonstrated that there is a considerable reduction in production and that even a small decrease in primary production directly affects higher trophic levels. The expected further increase in UV-R for the coming years and the extension of ozone losses to lower latitudes are likely to have a serious impact on fish production.
Finally, as a consequence of global warming by increased atmospheric CO_2 concentration, more cooling is hypothesized in the stratosphere, which will be responsible for triggering

more ozone breakdown. This suggests that UV induced CO_2 uptake reduction might be at the basis of a vicious circle that will lead to more damaging UV-R reaching the earth surface. It is clear that the impact of a reduced carbon uptake capacity will have a positive feedback on the greenhouse gas CO_2 and the greenhouse effect.

A.4.5 Perspective

So far, studies performed on the effects of UV-R on the marine environment clearly indicate that UV has strong deleterious effects at all trophic levels. The most concerning impacts of UV are on the ocean's CO_2 uptake capacity mediated by microalgal primary production and the direct or indirect effects on fisheries production. Missing is an evaluation of UV-mediated radical formation. Radicals affect structures and essential components inside cells, and influence the cycling of elements. Especially the hydroxyl radical (OH) is highly reactive, but hard to quantify because of its rapid turnover.

Future studies need to assess the impact of UV-R on target organisms by using action spectra and accurate measurements of UV spectral irradiance in the water at different depths. A complicating factor here is vertical mixing so organisms tend to be exposed to a variable spectral irradiance climate. New action spectra have to be calculated for each studied organism in changing environments.

Obviously the effect of UVR on the ocean's CO_2 uptake capacity is concerning. Any decreased CO_2 fixation capacity will add up to the increased anthropogenic CO_2 emissions. The modelling effort presented here suggests a decreased efficiency of the "biological pump" of CO_2 if ozone depletion goes on in the next decades.

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A.5 Integrated risk assessments

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Contents

A.5.1 Introduction

Man made chlorofluorcarbons (CFCs) are one of the principal causes of depletion of the ozone layer, initially observed in the Antarctic 'ozone hole' and later on detected on a global scale [WMO, 1995, 1999]. Ozone depletion results in higher levels of solar ultraviolet at the Earth's surface, leading to harmful effects on environment and human health. The international policy on countermeasures started in the framework of the Vienna Convention (1985). Production of ozone depleting chemicals was not restricted in the Vienna convention. Such restrictions were formulated for the first time under the Montreal protocol (1987). Later on, these restrictions were made more stringent, e.g. in the Copenhagen amendments (1992). The first comparison of the future excess skin cancer risks under the restrictions of the Montreal protocol was published by Slaper [Slaper et al., 1996].

A.5.2 Risk assessment model: first version

The assessment model used by Slaper [Slaper et al., 1996] was based on the full source-risk chain: from the production and emission of CFCs through photochemical breakdown of the CFCs, ozone depletion and increase in carcinogenic ultraviolet to increased skin cancer incidence. Three scenario's for the production of CFCs were investigated [Madronich et. al. 1998]:

- no restrictions (NR)
  In this NR scenario a continuous 3% annual increase in the production of CFCs, halons and methyl chloroform is assumed
- Montreal protocol (MP)
  In the MP scenario, agreed upon internationally in 1987, a reduction in the production of the five most potent ozone depleting substances with 50% at the end of 1999 is assumed.
- Copenhagen Amendments (CA)
  Under the CA scenario (1992) a complete phase-out of 21 ozone depleting substances at the end of 1995 is assumed

Full global compliance with the MP or the CA scenario was assumed.

The emitted halocarbons eventually reach the stratosphere, where photochemical breakdown releases active chlorine and bromine atoms catalysing ozone destruction.
Analyses of stratospheric ozone levels suggest that the downward ozone trend started around 1975-1980, several years after the chlorine levels started to rise. This indicates that ozone depletion starts only after a certain elevated threshold value for the chlorine load (CL_0). For this threshold value we take 1.985 ppbv [Madronich et. al. 1998]. This chlorine level was exceeded for the first time in 1980. Above this threshold a linear relationship between the relative decrease in ozone column and chlorine level is assumed. The proportionality constant k_cl is calculated from the trend in yearly averaged ozone of -3.9 ± 0.7 % per decade (Northern hemisphere, mid-latitudes based on the Dobson network, WMO) and the increase in chlorine load. The k_cl-value is set by the ozone and chlorine values in two reference years (usually taken as 1980 and 1990).
The value of k_cl is approximately -4.6 ± 0.8 % per ppbv.
At a high chlorine load virtually all ozone in the lower stratosphere is destroyed and saturation of ozone depletion is assumed. Saturation is only relevant for the NR and MP scenarios towards 2100. In the CA protocol saturation of ozone depletion is never reached.

The saturation levels were obtained from model calculations [Slaper et al., 1996] and show a strong seasonal variation. For mid-latitudes saturation levels range from 140 DU in summer to 60 DU in winter. The yearly averaged saturation level is Oz_R. The assessment model accounts for natural variations in ozone over the year and for seasonal variations in ozone depletion. The actual ozone concentration in a certain year is calculated from:

$$Ozone(year) = Oz_0 + \Delta O_3(Cl\_gas) \qquad (1.1)$$

with:

$$\Delta O_3(Cl\_gas) = k\_cl * (Oz_0 - Oz_R) * ([chlorine] - Cl_0) \qquad (1.2)$$

Oz_0 = undisturbed ozone value

Oz_R = saturation value for ozone depletion at high chlorine loads

CL_0 = chlorine threshold above which ozone depletion starts

k_cl = proportionality constant

[chlorine] = actual chlorine concentration for year under consideration, if smaller than CL_0, CL_0 is taken for the actual chlorine concentration

To relate the changes in ozone concentration to the effective UV-dose we calculated a so called look-up table for mid-latitudes with the UV transfer model [Den Outer, 1999]. This look-up table contains the effective UV for every month of the year as a function of the ozone column thickness. On the basis of this look-up table and the actual ozone concentration, the monthly effective UV for the period 1900-2100 is calculated. These monthly UV-doses are summed up to effective yearly UV doses.
Results of these model-calculations under the three scenarios evaluated are given in figure 1 [Slaper et al., 1996]. The slightly rising effective UV under the Copenhagen amendments after 2075 is a result of the fact that the chlorine scenario used by Slaper et al.1996 shows a slight rise in chlorine concentration after 2075 (see figure 16).

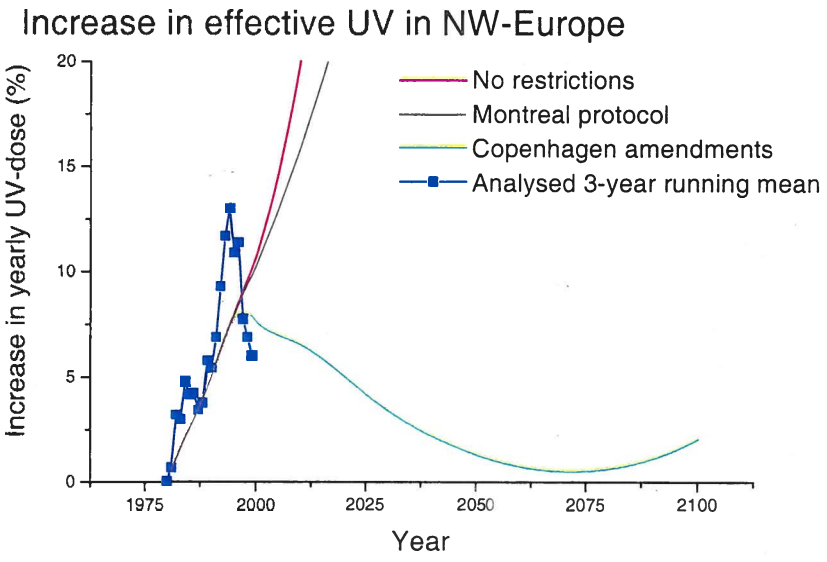

Fig. 1 **Relative increase in yearly effective UV at ground level at mid-latitudes, under the three scenarios evaluated: NR=no restrictions, MP=Montreal protocol, CA=Copenhagen Amendments.**

The increase in effective UV at ground level gives rise to a variety of effects on health and environment, amongst which the induction of skin cancer is best documented. Epidemiology indicates that three forms of skin cancer are associated with UV exposure: Squamous Cell Carcinoma (SCC), Basal Cell Carcinoma (BCC) and Cutaneous Malignant Melanoma (CMM). The incidence for SCC in humans is quite clearly related to the lifelong (cumulative) UV-dose, and animal experiments unambiguously point out UV as the causative factor in carcinogenesis. The yield of SCC in a birth cohort at age a can be described by:

$$Y_{SCC} \sim \phi(a)^c \times a^{d-c} \qquad (1.3)$$

Y_{SCC}	=	Yield for SCC
	~	means proportionality
$\Phi(a)$	=	the cumulative UV dose up to age a
a	=	age
d, c	=	constants describing age and dose dependency of Y

For BCC and CMM findings are different. The incidence (for BCC and CMM) is not related to lifelong exposure, but UV seems to act mainly in the early stages of tumour development (at a young age). Moreover, in absence of an animal model for the UV driven induction of BCC and CMM the role for UV as a causative factor is less unambiguous than for SCC. Incorporating the differences in timing for the UV driven processes leads to the following description for the yield of BCC and CMM:

$$Y_{BCC,CMM} \sim \sum_{allyears} D(x) \times \phi(x)^{c-1} \times (a-x)^{d-c} \qquad (1.4)$$

$Y_{BCC, CMM}$	=	Yield for BCC or CMM
	~	means proportionality
D(x)	=	The dose received in year x
Φ(x)	=	The cumulative dose at year x
a	=	age
d, c	=	constants describing age and dose dependency of Y

Table 1 **Parameters used in the skin cancer risk calculations. For SCC relation 1.1 is used, For BCC or CMM relation 1.2 is applied [Slaper et al., 1996].**

Type of cancer	C	d
SCC	2.5 ± 0.7	6.6 ± 0.4
BCC	1.4 ± 0.4	4.9 ± 0.6
CMM	0.6 ± 0.4	4.7 ± 1.0

Extrapolation of skin cancer incidences for non-melanoma (from the USA to the Netherlands) based on these description agrees quite well with the reported incidences, within 11%. For CMM the description is less accurate. Reported incidences deviate by 45% form the projected incidences, indicating a larger uncertainty in CMM prognosis.
Figure 2 depicts the excess incidences calculated for north western Europe for the three scenario's investigated.

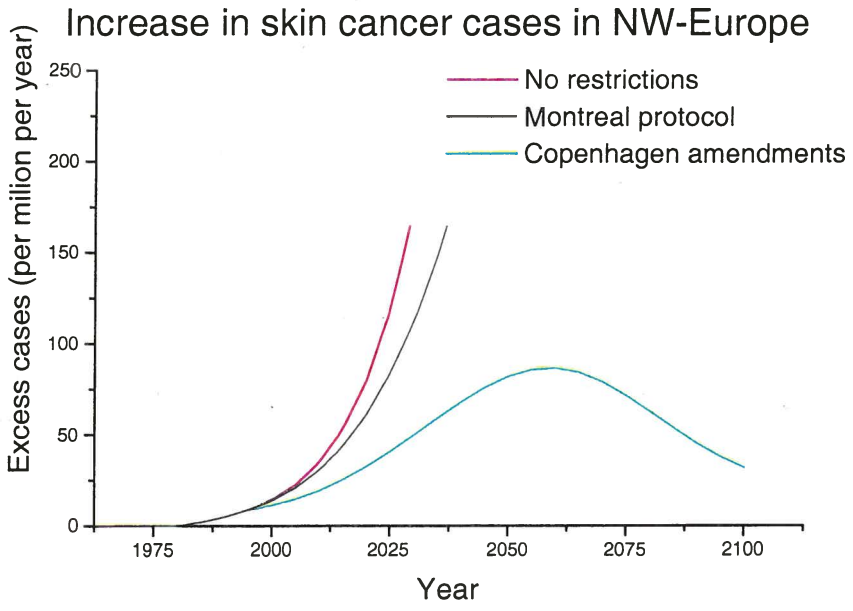

Figure 2. **Excess skin cancer incidences (all types of skin cancer summed up) calculated for north western Europe.**

Table 1.2 gives the excess number of skin cancers under the Vienna protocol scenario's, due to ozone depletion in the years 2050 and 2100. A population of 160 million for north-western Europe (including Belgium, the Netherlands, Luxembourg, Denmark, Germany and Great Britain) is assumed.

Tabel 2 Excess number of skin cancers [Slaper et al., 1996].

Scenario	Extra cases of skin cancer per year in 2050	Extra cases of skin cancer per year in 2100
No restrictions	55,680 (+35%)	550,000 (+315%)
Montreal protocol	36,960 (+21%)	170,000 (+95%)
Copenhagen amendments	14,240 (+7.5%)	4,000 (+2%)

A.5.3 Risk model: update

In the framework of the OCCUR project we improved the risk assessment model on two points. Originally risk assessments were based on the trend per decade calculated from yearly averaged ozone column values at mid-latitudes. The geographical differences in ozone trend were not accounted for and the total calculated ozone trend was attributed to the effect of the halocarbons alone. Interactions between the ozone layer and the climate system (at mid latitudes) were neglected. These two improvements have been implemented in our risk assessment model generally referred to as AMOUR: Assessment Model for UV Radiation and Risks.

A.5.3.1 Geographical differences in ozone trends

From the TOMS-satellite data record and ground based ozone measurements it is evident that ozone trends vary over the globe. Our risk assessments can be refined by using this location dependent ozone trend. For this purpose we calculated the ozone trends for every European grid cell in the TOMS data record. The results presented here are based on the TOMS record for the period 1979 – 1991. We chose this period because dust and aerosols from the Pinatubo eruption start to influence the TOMS measurements from 1992, and for the years 1993, 1994 and 1995 the TOMS record does not contain data for all months. Thus our ozone data record contains 13 full years of TOMS data.
In every grid cell we calculate - with a linear least square fit – the trend in ozone measurements over this period. This trend (in DU/year) is recalculated to a trend of % ozone change per decade relative to the average ozone value over the years 1979, 1980 and 1981. Ozone trend is based on year average ozone values. Additionally ozone month trends were calculated from TOMS monthly average ozone values. Zero ozone readings, common during December/January at northern latitudes, were excluded from the analysis. As a result ozone trend for northern grid cells during winter may be based on a smaller number of data-points, resulting in a higher uncertainty in the trend. Figure 4 and 5 give the ozone trends for Europe over the period 1979-1991 in the months April and October. Figure 6 gives the ozone trend based on year average ozone. As a comparison, figure 7 gives the year-based ozone trend for the period 1979-2000.

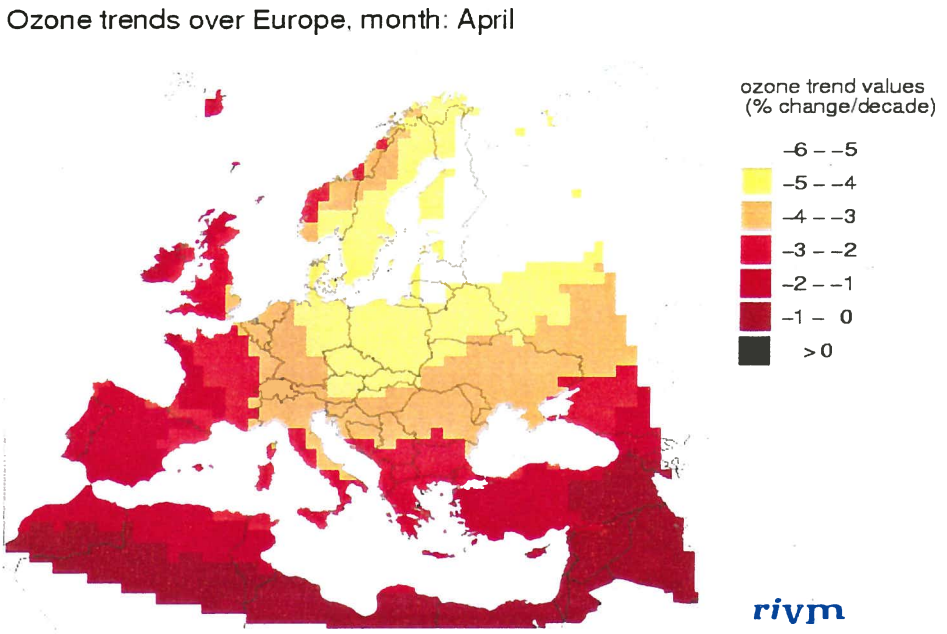

Figure 4 **Monthly ozone trends over Europe for the month of April, used as input for the risk assessment calculations. Period considered is 1979-1991.**

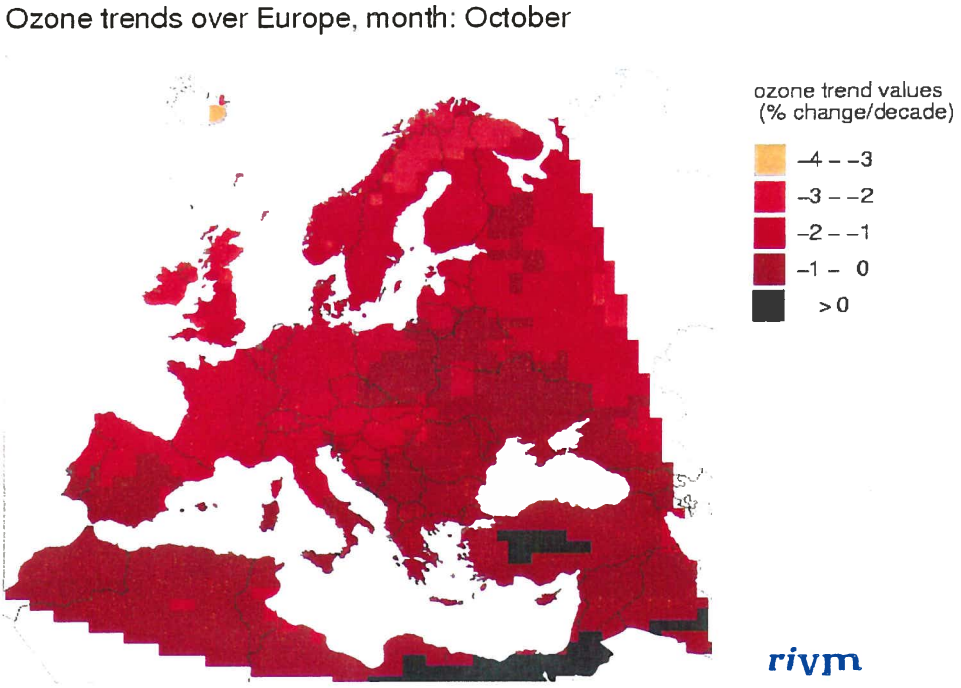

Figure 5 **Monthly ozone trends over Europe for the month of October, used as input for the risk assessment calculations**

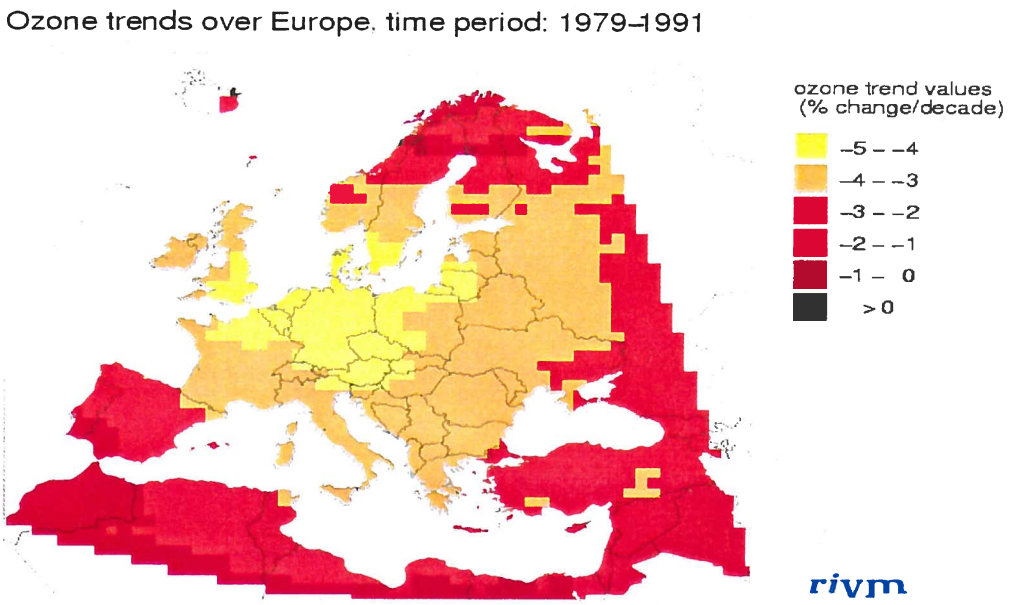

Figure 6 Ozone trends over Europe based on TOMS observation of year average ozone values for the period 1979-1991. Trends are expressed as percent change per decade, relative to the mean ozone value over the years 1979/1980/1981.

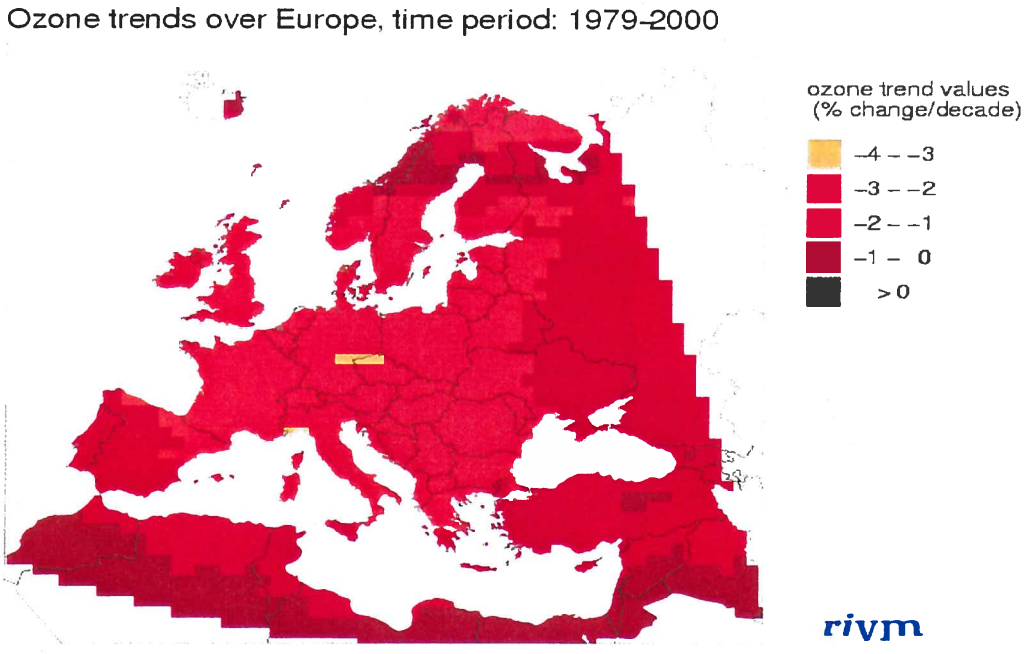

Figure 7 Ozone trends over Europe based on TOMS observation of year average ozone values for the period 1979-2000. Trends are expressed as percent change per decade, relative to the mean ozone value over the years 1979/1980/1981.

From figures 6 and 7 it is clear that the calculated ozone trends depend on the period chosen for the analysis. Ozone trends based on the period 1979-1991 yield a steeper decrease than those for the period 1979-2000.

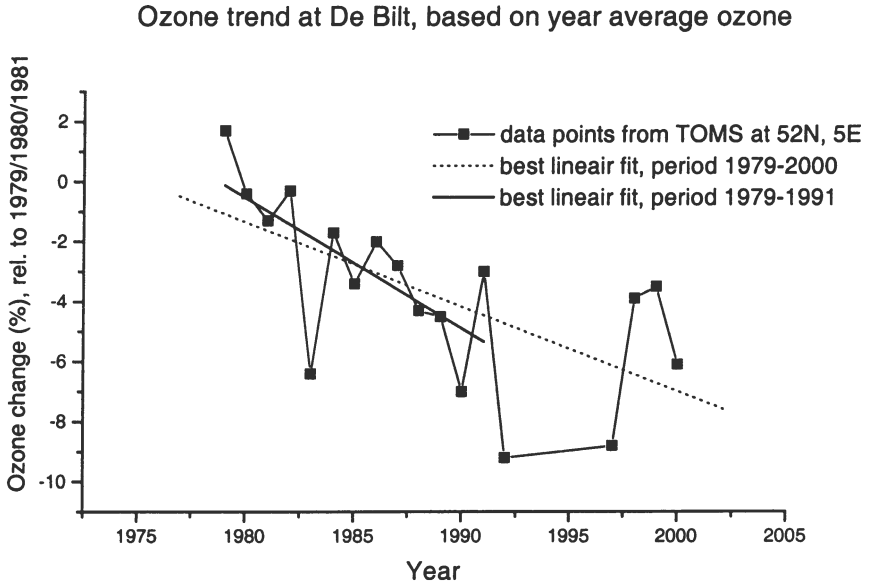

Figure 8 **Ozone data points and ozone trend for De Bilt. Trends lines are given for the periods 1979-1991 and 1979-2000. Trends are expressed as percent change in ozone relative to the average ozone value of 1979, 1980 and 1981.**
1979-1991 : ozone-trend (% per decade) = - 4.35 ± 1.4, R= - 0.69
1979-2000 : ozone trend (% per decade) = - 2.82 ± 0.9, R= - 0.64

Figure 8 illustrates this for De Bilt. This less steep decrease in ozone over the period 1979-2000 may be a genuine consequence of the reduction in CFC-emissions and subsequently a change in active chlorine levels during the second half of the nineties. However, it may also be due to the fact that the missing ozone values in the TOMS data gap (1993-1996) are expected to be relatively low (≈ -7%), as can be concluded from ground-based ozone measurements. Because these four, probably low data points, are not included in our trend analysis a less steep ozone decrease emerges.
At every location (TOMS grid cell) the monthly and yearly ozone trends (1979-1991) is fed into the risk assessment module, and the location and month dependent recovery of the ozone layer is calculated for the period 2000-2100. The actual ozone concentrations result – on basis of a latitude dependent look-up table for ozone column versus effective monthly UV dose – in effective monthly and yearly UV levels for the period 1900-2100. Risk calculation are completely analogous to those employed in the first version of the model (see A.6.2). Because we only have reliable data for the incidences of UV related skin cancer for the Dutch population (in 1990), we assume – as a first approximation – other European people to have the same susceptibility for skin cancer induction.

A.5.3.2 Interaction between ozone and climate system

Initially ozone-climate interactions were not included in the risk assessment model, and the total observed ozone trend was attributed to the chemical (gas phase) destruction of halocarbons. In this report we include climate-ozone interactions in our model caluclations. Firstly, we restrict ourselves to those effects that are supposed to have the most substantial influence on the ozone layer. Secondly, we can only describe those aspects of ozone climate interaction for which scientific understanding is reasonable, and for which a quantitative description is feasible. Four aspects of climate-ozone interaction meet these criteria: the fraction of the ozone trend that can be attributed to atmospheric dynamics (exclusive of the Arctic vortex), the direct effect of temperature on the destruction/production equilibrium for gas phase ozone (Chapman cycle), the onset of the Arctic vortex and the effect of the vortex on ozone concentration at mid-latitudes throughout the year.

A.5.3.2.1 Atmospheric (non-vortex) dynamics

An increasing amount of greenhouse gases in the atmosphere may disturb the radiative balance and results in a change in dynamical processes [Shindell, 1998]. This directly affects the ozone layer for instance by changing the North Atlantic Oscillation, an increase in tropopause altitude, and a stronger and more persistent Arctic vortex (see chapter 2 for details). The fraction of the ozone attributed to dynamics is still a matter of debate. According to Madronich [Madronich et al., 1998] and the 2001 update of the report up to 50% of the observed negative ozone trend could be explained by dynamical processes in the atmosphere, inclusive the effects of the Arctic vortex. Here we discuss the effects not coupled to the Arctic vortex. For the influence of the Arctic vortex see A.6.3.2.3. In AMOUR a variable fraction of the observed TOMS ozone trend is attributed to non-vortex dynamics. These non-vortex dynamic effects include changes in the North Atlantic Oscillation, an altered tropopause altitude, intrusion of low-ozone subtropical air to mid-latitudes. Our starting point is a contribution of 0-25% of non-vortex dynamics to the ozone trend. The fraction of non-vortex dynamics is coupled to the atmospheric content of greenhouse gasses, and therefore time dependent. Literature suggests that the non-vortex contribution to dynamics started to gain importance in the period 1980-1990. From chemical models it is evident that the non-vortex dynamical contribution can not go on indefinitely, but will reach saturation at some point in the period 2010-2020. In our model this translates to a (relative) non-vortex dynamical contribution with: no effect on the ozone trend before the year 1980, a linear increasing contribution up to the maximum during the period 1980-2020, and saturation at the 2020 level. Figure 9 depicts this relation. As an alternative a steeper rise of the relative non-vortex fraction - used in non-standard calculations - is included in the picture.

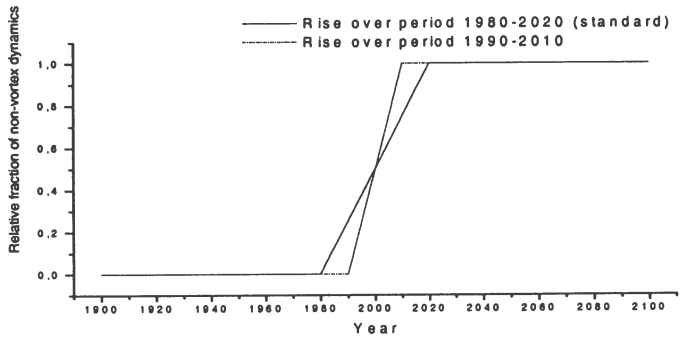

Figure 9 Time course of relative fraction attributed to non-vortex dynamics

Based on the time course of the non-vortex contribution dyn(year) depicted in figure 9, and the maximum contribution of non-vortex dynamics (f_dyn0) to the observed ozone trend, the actual contribution of non-vortex dynamics (f_dynact) in a given year is calculated by:

$$f\_dynact(year) = f\_dyn0 * dyn(year) \qquad (1.5)$$

This contribution of non-vortex dynamics to the ozone trend may depend on the season (month of the year). At present, we have no adequate data to describe this dependency. Therefor, the change in ozone caused by non-vortex dynamics (ΔO_3(non-vortex_dyn)) relative to the reference ozone depletion without climate-ozone interaction (ozone_reference_depletion) is given by:

$$\Delta O_3(non-vortex\_dyn) = f\_dynact(year) * ozone\_reference\_depletion * dynamics(year) / dynamics(refyear) \qquad (1.6)$$

A.5.3.2.2 Temperature effect Chapmancycle

The actual ozone concentration in the stratosphere is determined by the balance between destruction and production of gas phase ozone. This so called Chapmancycle is a chemical equilibrium and is affected by the temperature in the stratosphere. Greenhouse gases disturb the radiative balance in the atmosphere, resulting in a temperature rise in the troposphere, but in a cooling of the stratosphere. Figure 10 gives model calculations for the stratospheric temperature over the period 1900-2100, calculated with the OGI-1D model at RIVM, for the IPCC scenario IS92a (Velders, 1997).

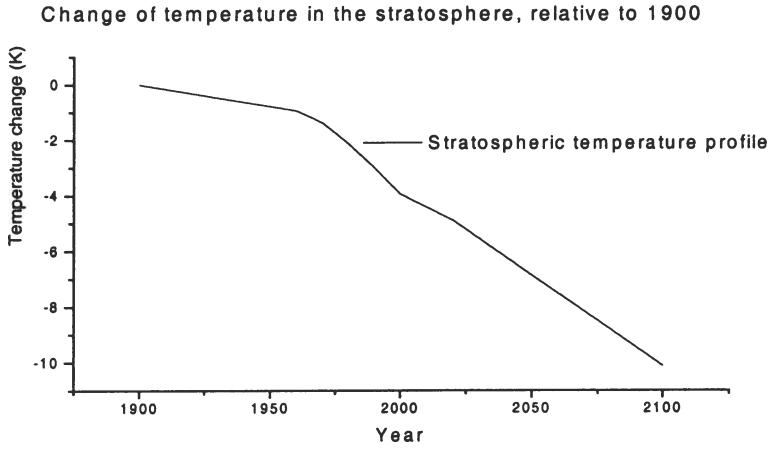

Figure 10 Temperature change in the stratosphere over the period 1900-2100. Data from Velders, 1997

The rate of ozone production increases with decreasing temperature, whilst the rate of ozone destruction decreases with decreasing temperature. So as a net effect stratospheric cooling result in an increased level of ozone. The change in ozone concentration (ΔO_3) is related to the temperature change (ΔT) by:

$$\Delta O_3(Chap) = k\_T * Oz0 * \Delta T \quad (1.7)$$

ΔO_3(Chap)	= change in O3 concentration due to equilibrium shift in Chapmancycle
Oz0	= ozone concentration at the start of the considered period
ΔT	= temperature change (K)
k_T	= proportionality constant

The value for the proportionality constant k_T is derived from Velders. Over the period 1990-2050 the ozone column is calculated to increase by 3.5% due this equilibrium shift [Velders, 1997, page 39]. Over the same period the expected temperature drop in the stratosphere is –3.87 [Velders, 1997, IS92 a scenario, page 58]. Consequently, the constant k_T = 3.5/-3.87 %O_3/K, approximately -0.9% O_3/K. The ozone change due to a change in stratospheric temperature is calculated from:

$$\Delta O_3(Chap) = -0.009 * Oz0 * \Delta T$$

A.5.3.2.3 Arctic vortex dynamics

The spring ozone hole in Antarctica was first detected in 1985 by Farman [Farman et al, 1985]. At present, it is generally accepted that this ozone hole is primarily caused by activation of chlorine containing molecules initiating heterogeneous reactions on the surface of ice crystals in polar stratospheric clouds. Starting from about 1990 the same mechanism is observed over the arctic too, probably as a result of a decrease in temperature in the stratosphere over the arctic region . But extent and profundity of the arctic 'ozone hole' are much smaller. Somewhere in spring with increasing stratospheric temperature the polar stratospheric clouds disappear and the ozone poor air from the arctic hole is transported to lower latitudes, there leading to a drop in actual ozone values. 3D modeling predicts a deepening of the arctic hole over the coming decade followed by a more or less stable phase and eventually gradually disappearing of the arctic hole around 2040 (Bregman, Velders personal communication). To calculate the effect of the arctic vortex on mid-latitude ozone (on the northern hemisphere), we enforce an arctic ozone hole on the RIVM 2D stratosphere model calculations (Velders, 1995). We introduced an arctic ozone hole extending from 71N to 90N. This arctic ozone hole splits up almost instantaneously at March 14. The arctic hole starts to develop in 1990, deepens (linear) until 2010. Eventually, a 200 DU lower ozone concentration in the hole is reached. Over the period 2010-2020 the drop in arctic ozone during winter remains the same. Thereafter the arctic hole starts to disappear (linearly) over the period 2020-2040. After 2040 the arctic hole no longer develops. Figure 11 depicts this development.

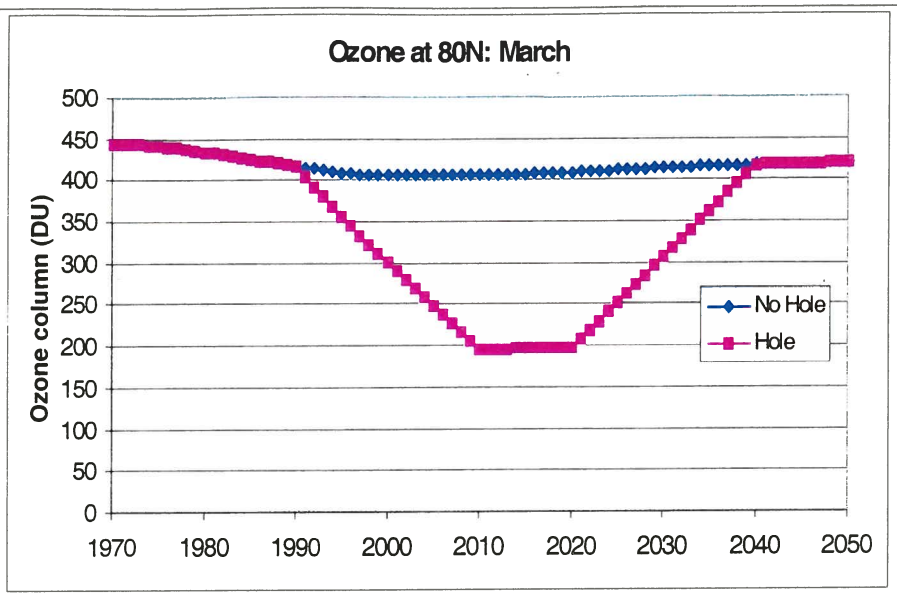

Figure 11. Time course of the modelled ozone hole over the arctic region

The effect of the arctic ozone hole on mid-latitude ozone after the split-up of the vortex is calculated with the 2D RIVM stratosphere model [Velders, 1995]. The drop in ozone column is largest in April and decreases gradually over the year and with decreasing latitude. Figure 12 gives the ozone drop at 50 N for April and figure 13 the year average ozone drop at 50 N.

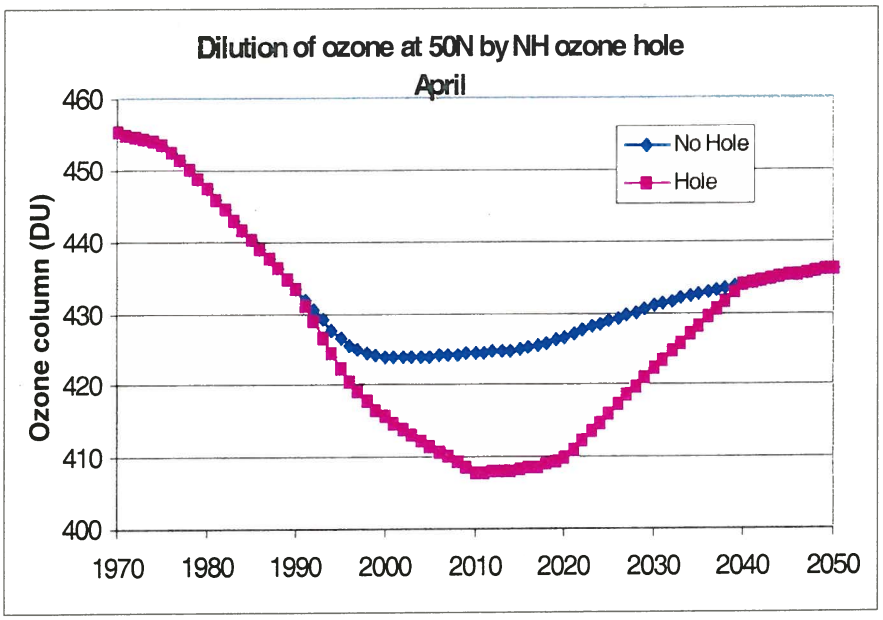

Figure 12 Dilution of ozone due to transport of ozone poor air from the arctic vortex to lower latitudes, for the month April.

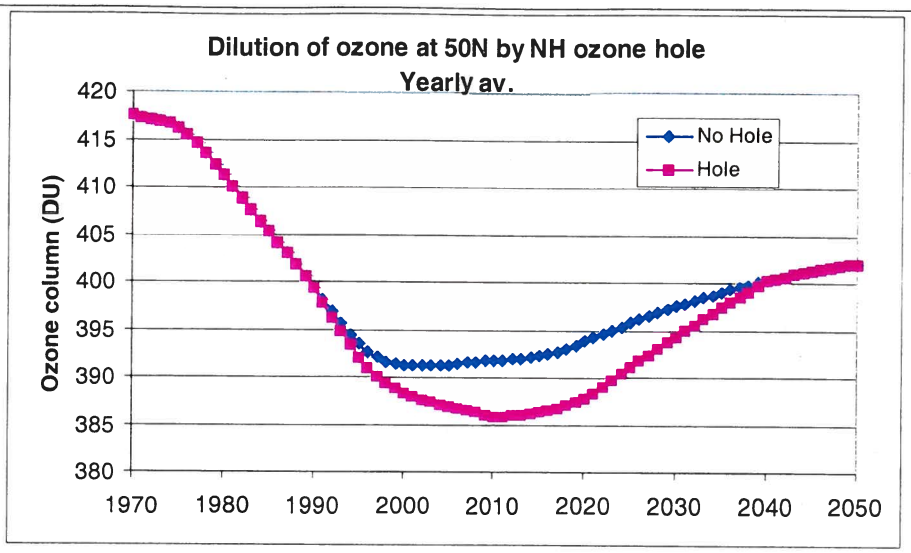

Figure 13 **Dilution of ozone due to transport of ozone poor air from the arctic vortex to lower latitudes, based on yearly averaged ozone.**

To assess the contribution of the arctic vortex to the ozone trend we calculate the Fp-factor defined as:

$$F_p\left(latitude, month\right) = \frac{\left(nonvortex\ ozone\ value - vortex\ ozone\ value\right)}{\left(ozone\ value\ in\ reference\ year - vortex\ ozone\ value\right)} \quad (1.8)$$

This Fp-factor gives the relative ozone depletion due to the Arctic vortex for a given month and latitude compare to a reference year. In our risk assessment model we calculate the Fp-factors for the year 2000 relative to 1980. Figure 14 depicts the latitude and seasonal dependency.

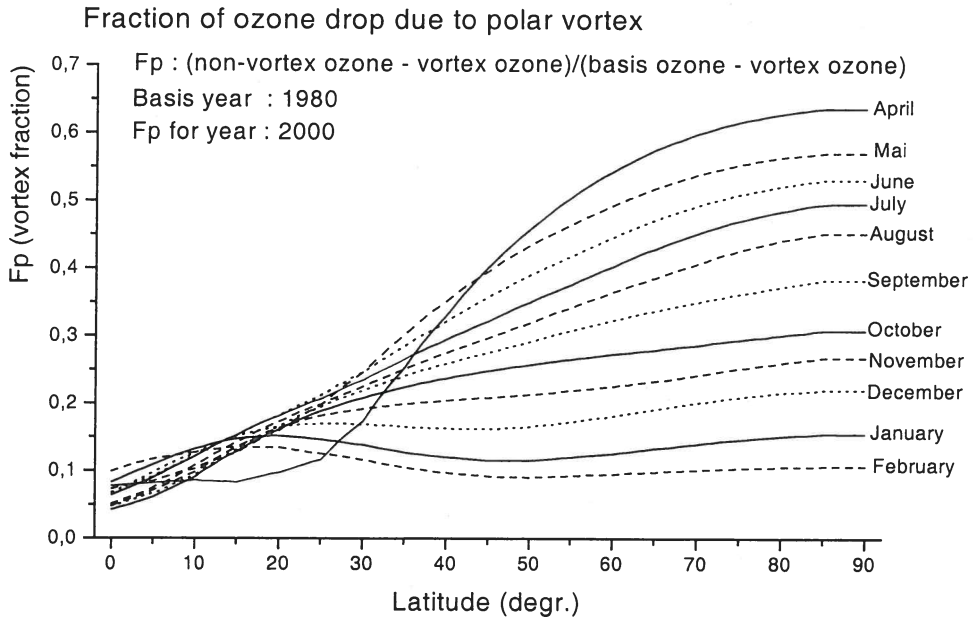

Figure 14 **Fp-factors caused by due to dilution of the polar vortex as a function of latitude and month.**

As an example, averaged over the summer months Mai-August (the most relevant period for the yearly outdoor UV dose) the Fp factor for De Bilt (52 N) amounts to 0.39. The year average Fp-factor for the Bilt is 0.27.

Eventually, the ozone depleting effect of the arctic vortex is taken proportional to the difference of the actual chlorine concentration and a baseline level (Chl0PV) below which no effect of the arctic vortex is expected. This threshold chlorine level is set at 0.8 ppb [Madronich et.al., 1998 page 11.18). Above a certain level of chlorine (ChlmaxPV) virtually all ozone in the arctic vortex is depleted and no further depletion can occur. For the Antarctic vortex this maximum level is about 3 ppb. For the arctic vortex we chose a value of 4 ppb for CHLmaxPV, because the temperature over the arctic is higher, resulting in a less efficient ozone depletion. For the chlorine values in between 0.8 ppm and 4 ppm we assume a linear relationship between the ozone depletion due to the arctic vortex (ΔO_3(arctic vortex)) and the difference of the actual chlorine concentration [chlorine] with Chl0PV.

$$\Delta O_3\left(arctic\,vortex\right) = K\_PV * polvort\left(year\right) * \left([chlorine] - ChloPV\right) \qquad (1.9)$$

K_PV is related to the reference ozone depletion without climate-ozone interaction (ozone_reference_depletion) and to the Fp-factor. The function polvort(year) accounts for the fact that the polar vortex starts somewhere around 1980 and reaches saturation around 2020. The polvort function has the same time course as the function used to describe the time behaviour of the non-vortex dynamics.

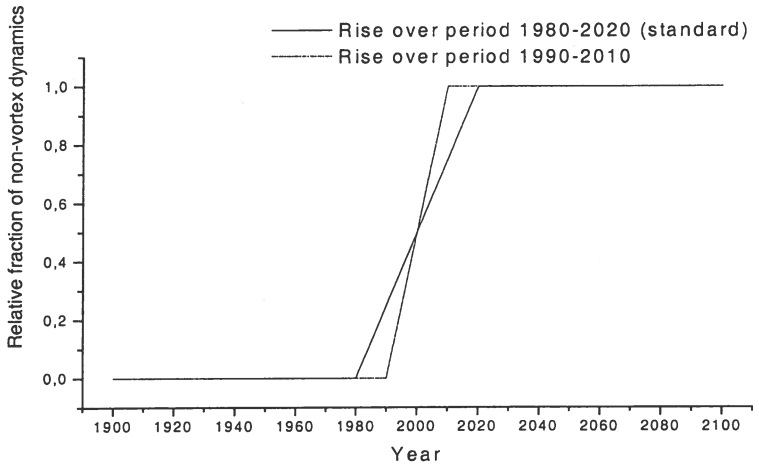

Figure 15 Time course of relative fraction attributed to the polar vortex dynamics

A.5.3.2.4 Ozone depletion by gas phase chemistry

The description of ozone depletion due to halocarbons is essentially the same as in the first version of the risk assessment. But now only part of the observed ozone trend is attributed to the gas phase chemistry. In other words, the constant k_cl from equation 1.2 is transformed to a k_cl_dyn by:

$$k\_cl\_dyn = k\_cl * (1 - f\_dynact) * (1 - K\_PV) \qquad (1.10)$$

A second difference with the first version of the risk assessment model is that we use the A1 scenario [Madronich et.al., 1998, page 11.15). as a more recent scenario for the chlorine concentration in the stratopshere. Figure 16 depicts the differences between the old scenario (referred to as Copenhagen amendments) and the A1-scenario.

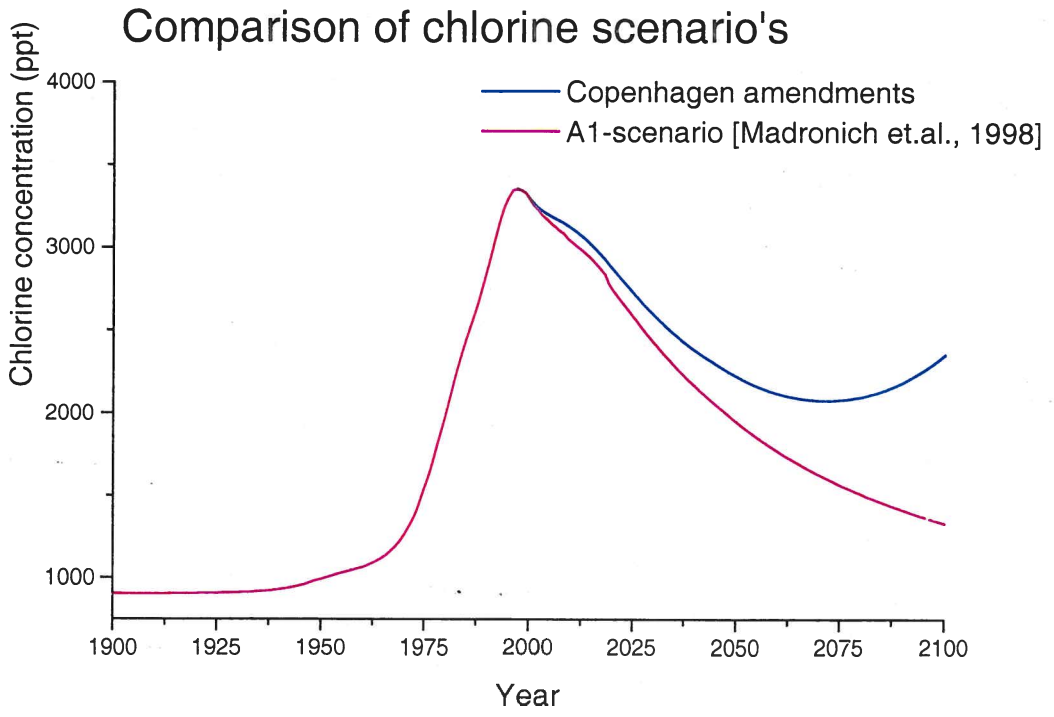

Figure 16 **Comparison of the chlorine scenario used in the first version of the risk assessment model (Copenhagen amendments) and the scenario used in the present calculations.**

A.5.3.3 Conclusions on the implementation of ozone-climate interaction

We have implemented ozone-climate interaction in the integrated risk assessment model for skin cancer by accounting for: gas-phase chlorine driven ozone depletion, ozone production in the stratosphere as a consequence of a drop in stratospheric temperature, non-vortex dynamics and the ozone depletion at mid-latitudes by intrusion of ozone poor air from the Arctic vortex. The latter three effects are likely to be influenced by climate change caused by an enhanced greenhouse effect. The total effect of these interactions on the ozone layer is given
by:

$$Ozone(year) = Oz_0 + \Delta O_3(Cl\_gas) + \Delta O_3(Chap) + \Delta O_3(non-vortex\_dyn) + \Delta O_3(arctic\_dyn) \qquad (1.11)$$

The parameter choice is summarised in table 3.

Table 3. Parameters for the description of the 'standard' ozone-climate interaction.

Chlorine scenario: [Madronich et.al., 1998]	A1
Stratospheric temperature: [Velders, 1997], figure 10	Extended IPCC, IS92a
Temperature constant (k_T) [recalculated from Velders,1997]	-0.009 O_3/K
Relative contribution of non-vortex dynamics	0.25
Arctic vortex Rising from 1980-2020, figure	Fp-factors, month and latitue depndent

In both situations – with and without climate interaction – the same historical development (1900-1980) for the temperature in the stratosphere is modelled. Decrease of stratospheric temperature over this period is approximately 2K [Velders, 1997].

A.5.4 Results

Results of the calculations can be expressed in terms of the effect on the ozone layer itself, on the UV levels and on the associated risks for skin cancer. Apart from the time course of UV levels and skin cancer we calculated UV-exposure maps and skin cancer risk maps over Europe for a given year.
Figure 17 depicts the development of the ozone layer with and without climate-ozone interaction.

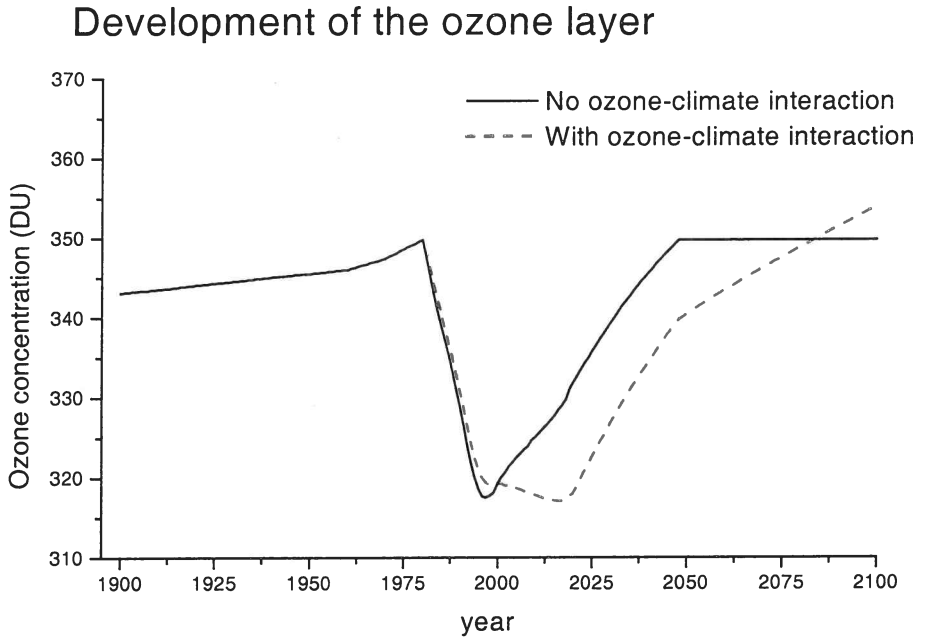

Figure 17 Ozone layer development with influence of ozone-climate interaction.

The differences in the development of the ozone layer are reflected in altered UV levels. Figure 18 gives the increase in effective UV at De Bilt, The Netherlands.

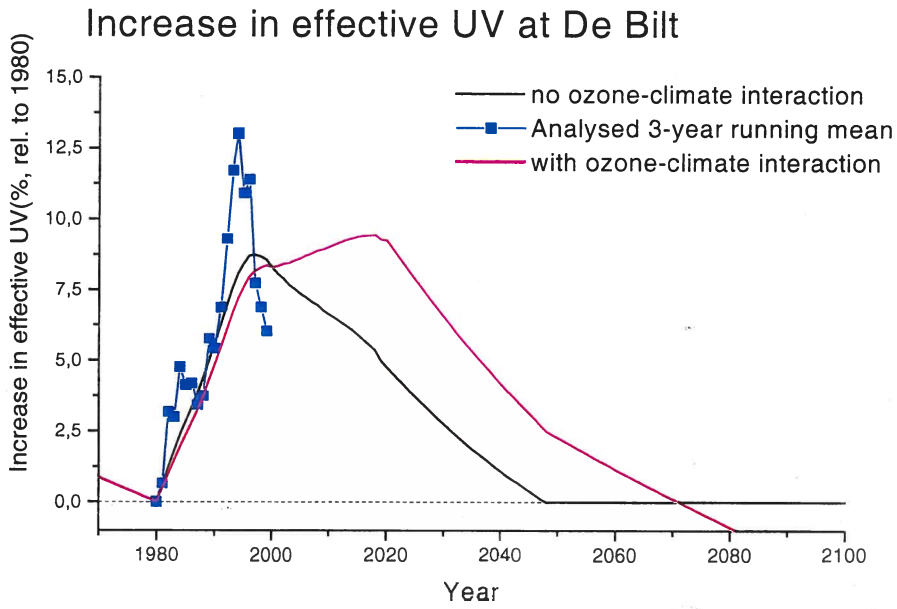

Figure 18. Increase in effective UV with and without ozone climate interaction. Location De Bilt

The increase in effective UV results eventually in an increase in skin cancer. Figure 19 gives this increase in skin cancer incidence for the location De Bilt, The Netherlands.

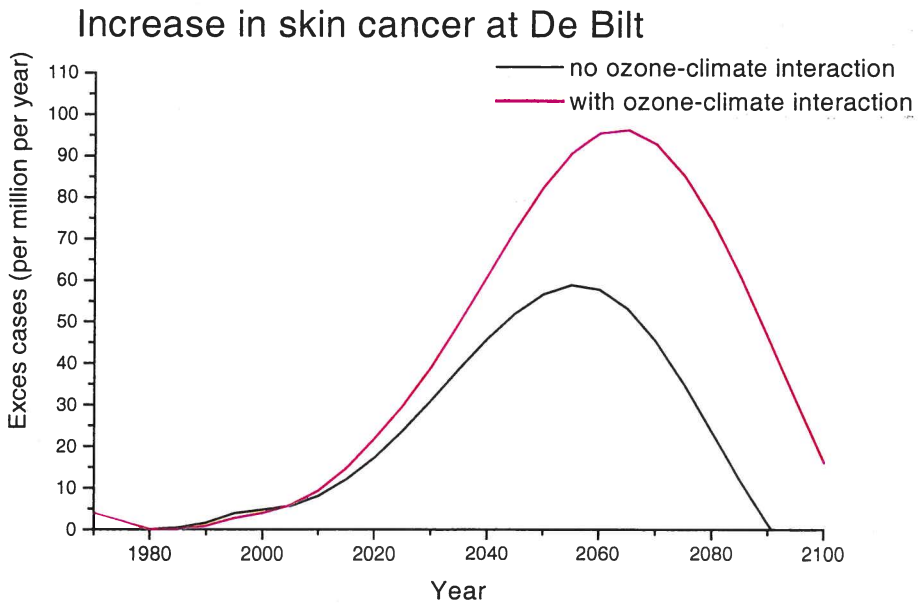

Figure 19 Increase in skin cancer incidence at De Bilt, with ozone climate interaction, and without ozone climate interaction.

The update of the risk assessment model yields maps for effective UV over Europe. Figure 20 gives the map for effective UV levels reached in the year 2020 (relative to the 1980-level) without ozone-climate interaction, and figure 21 gives the effective UV in 2020 with climate interaction.

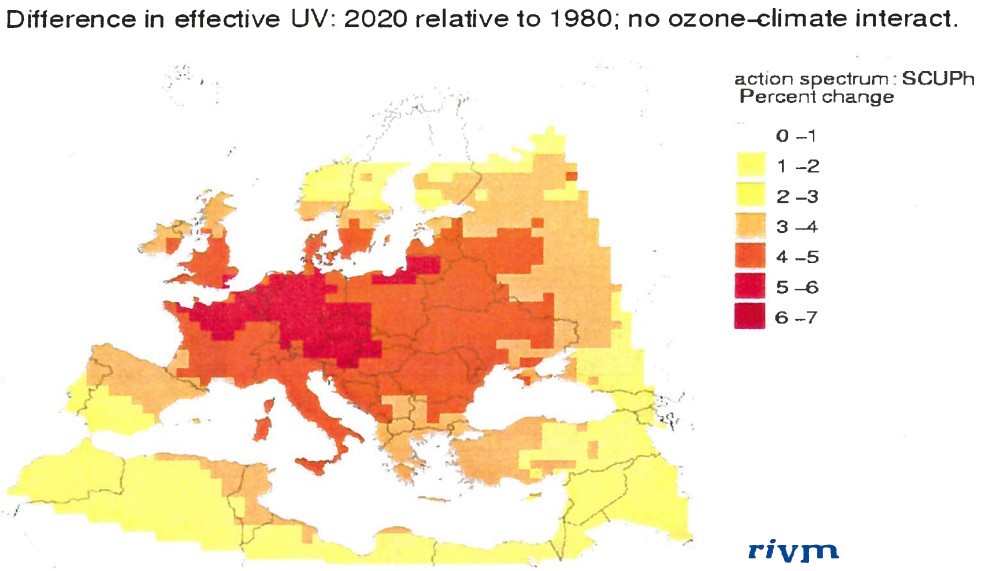

Figure 20 **Prognosis for the effective UV in 2020, without ozone-climate interaction. The effective UV is expressed as a percentage increase compared to the effective UV level in 1980.**

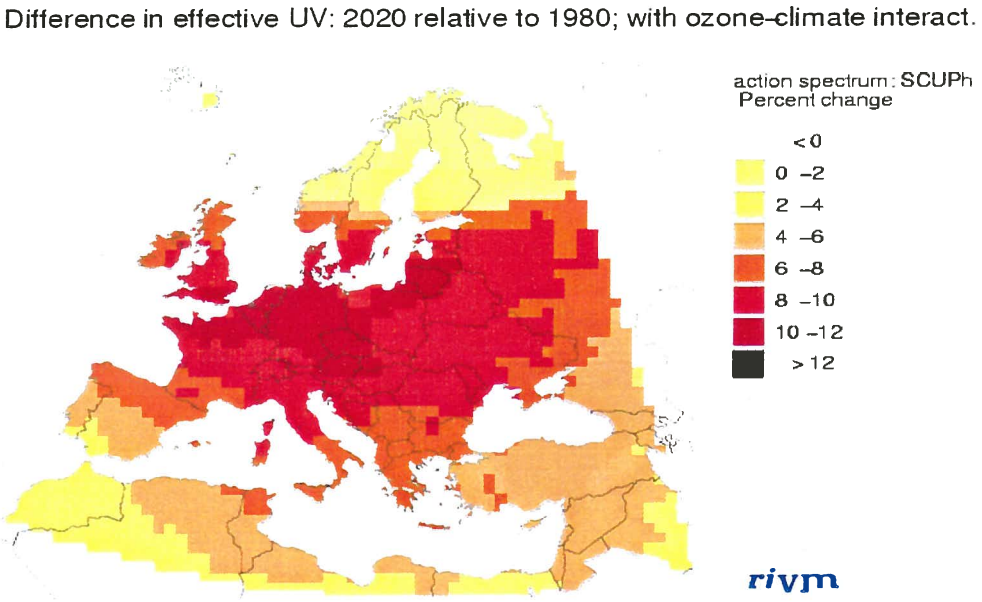

Figure 21 **Prognosis for the effective UV in 2020, with ozone-climate interaction . The effective UV is expressed as a percentage increase compared to the effective UV level in 1980. Note the two-fold difference in UV-scale as compared to figure 20.**

The increase in effective UV results in an increase in skin cancer incidence. Figures 18 and 19 show that the peak cancer incidence is expected about 50 years after the peak UV load. We therefore plot in figures 22 and 23 skin cancer incidence in 2070.

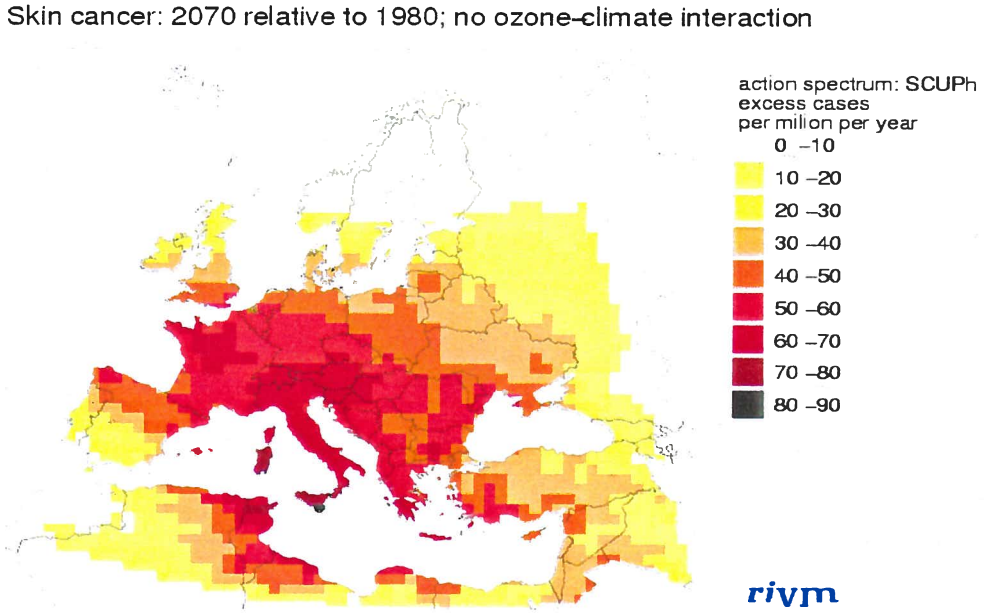

Figure 22 **Prognosis for the increase in skin cancer incidence in 2070, without ozone-climate interaction The increase in risk is expressed as the extra number of cases per million per year for the Dutch population.**

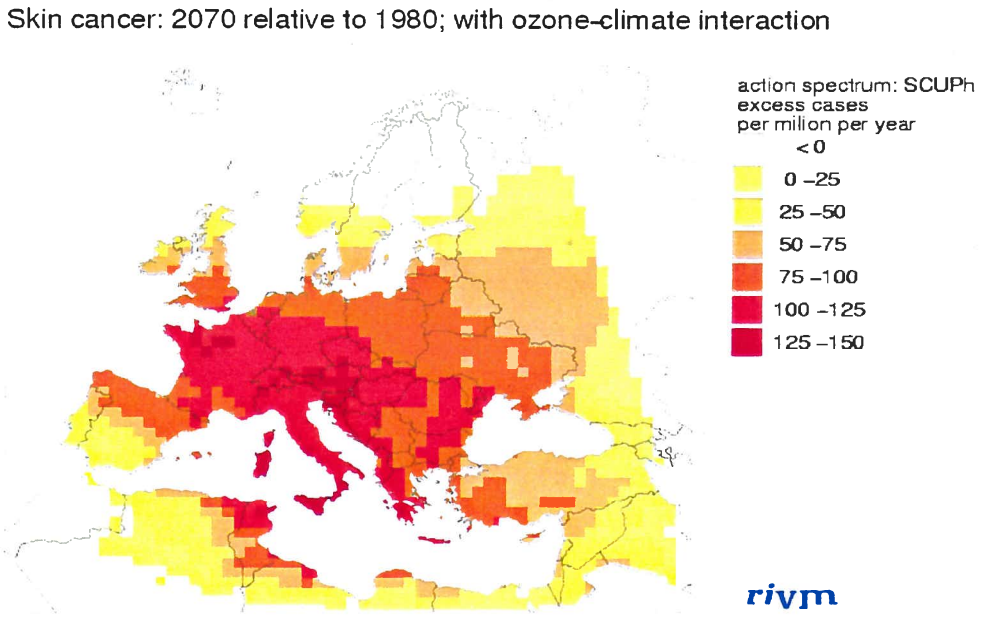

Figure 23 **Prognosis for the increase in skin cancer incidence in 2070, with ozone-climate interaction . The increase in risk is expressed as the extra number of cases per million per year for the Dutch population.**

The results can be summarized in two plots: the difference in effective UV in 2020 with and without ozone-climate interaction, and the difference in excess skin cancer cases in 2070 with and without ozone –climate interaction.

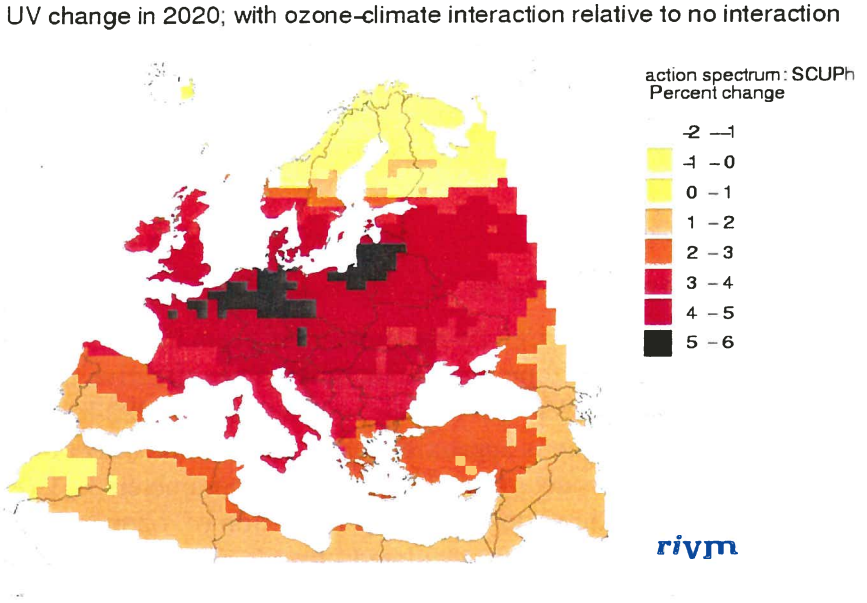

Figure 24 **Increase in effective UV. Prognosis with ozone-climate interaction compared to that without ozone-climate interaction The effective UV is expressed as the relative increase in UV compared to the effective UV without ozone-climate interaction.**

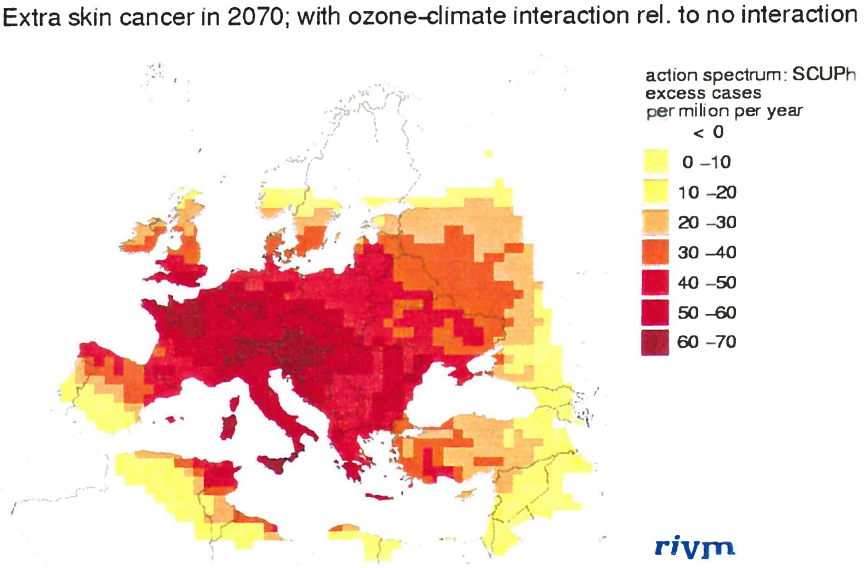

Figure 25 **Increase in skin cancer incidence. Prognosis with ozone-climate interaction compared to that without ozone-climate interaction. The change in risk is expressed as the number of extra cases (per million per year) in the situation with ozone-climate interaction compared to no ozone-climate interaction.**

A.5.5 Uncertainty analysis

It is important to estimate how the choice of the relevant parameters with respect to the climate interactions affects the ultimate result. A comprehensive uncertainty analysis is beyond the scope of this report. To get a first indication we estimate the inaccuracy introduced by the choice of the model parameters k_T (equilibrium shift), PV(Arctic vortex) and f_dyn (fraction of ozone trend explained by dynamics). Apart from this evaluation of the model parameters we add some remarks on the choice of CL_0 and the time-course of the onset of the dynamic contribution

A.5.5.1 Model parameters

Climate interaction can be characterised by the number of years it takes before the effective UV reaches the 1980 level. With ozone-climate interaction the effective UV reaches the 1980-level around the year 2071. Without climate interaction the 1980-level is reached already in 2048. So the actual delay is approximately 23 years. The effect of the three climate-interactions considered is determined by the model parameters k_T (equilibrium shift), PV(month, latitude) Arctic vortex) and f_dyn (fraction of ozone trend explained by dynamics). For all those three effects we calculated - from a series of model-runs - for what change of the relevant parameter the delay of UV recovery would be reduced by 10 years. Figure 26 gives an example of the run for the contribution of dynamics.

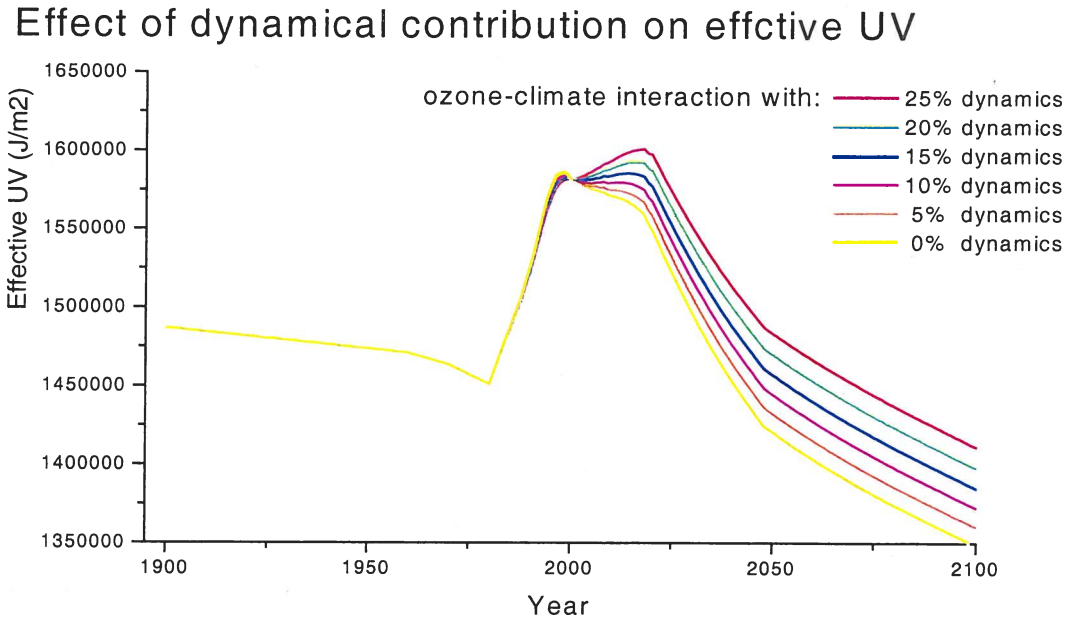

Figure 26 Effect of variations in dynamical contribution (f_dyn) on the time course of the effective ultraviolet. Location De Bilt.

The recovery of 10 years was measured starting from the standard interaction situation (k_T= -0.009, Arctic vortex according to 2D computations and 25% contribution of dynamics). From this situation one of the parameters was varied while the other two were kept constant. For k_T the range was between –0.012 and 0.0 (no effect of temperature on equilibrium shift). For the arctic vortex model runs were done with a vortex of 75%, 50%, 25% and 0% of

the LLO-calculations. The dynamical contribution to the ozone trend was varied between 25% and 0% . Table 4 givens the results for these calculations.

Table 4 **Change in model parameters needed to reduce the period it takes the effective UV to return to 1980-levels with 10 years.**

	Change needed for 10 year reduction of delay in UV recovery	Parameter change
k_T	-0.002	-0.009 -> - 0.011
Arctic vortex	Drop of 52%	100% -> 48%
Dynamics	Drop of 5.6%	25% -> 19.4%

From table 4 we conclude that our results are most sensitive to changes in the contribution of dynamics to the ozone trend, relatively sensitive to changes in the k_T parameter, and not very sensitive to changes in the magnitude of the Arctic vortex.

A.5.5.2 Role of threshold chlorine value CL_0

Analyses of stratospheric ozone levels suggest that the downward ozone trend started several years after the chlorine levels started to rise. In other words, ozone depletion started only after a certain elevated threshold value for the chlorine load (CL_0) was reached. At present, there is no full understanding of the causes of this threshold, which makes the choice of the value for CL_0 somewhat arbitrarily. In our model calculations we chose for a threshold chlorine value the concentration in 1980 (1.1985 ppb). However, the choice for CL_0 influences the ozone time-profiles (see figure 27). As a result, the effective UV-levels and the skin cancer risk may be (strongly) affected by the choice of CL_0. At present we have no information to make a better founded choice for CL_0. The incomplete understanding of the delay in ozone depletion introduces an extra uncertainty in our risk calculations.

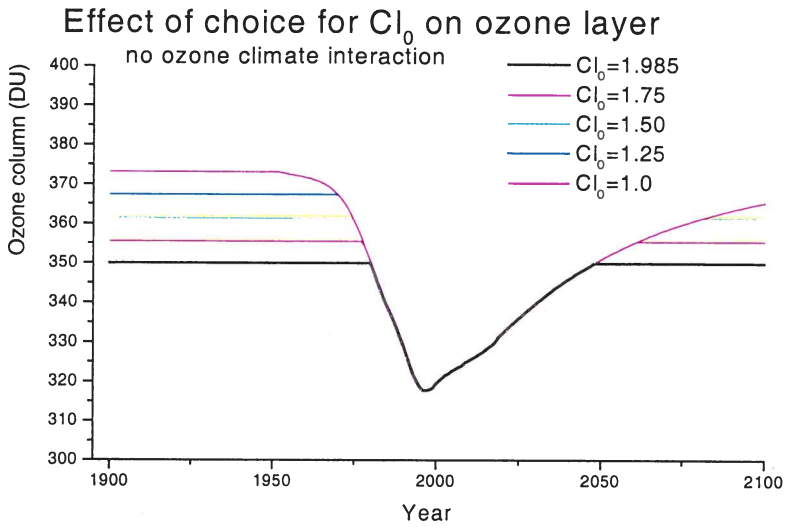

Figure 27 The influence of the choice for CL_0 on the ozone profiles.

A.5.5.3 Time course of dynamical contribution

Time course of the onset of the dynamic effects (arctic vortex and other dynamics) influences the model calculations. In the standard interaction we assume both effects to start in 1980 and evolve to a maximum in 2020. Figures 28 shows how the effective UV changes if we base the model calculation on steeper rising dynamics (over the period 1990-2010). The UV-profile and the maximum increase in UV both change, resulting in a different risk assessment. At present we have no a priori reason to prefer one of the periods. We chose the 1980-2020 period for our standard ozone-climate interaction, because the effective UV fits best with the Copenhagen amendments scenario and with the experimental data. The choice of the onset period thus introduces an extra uncertainty in the risk assessment.

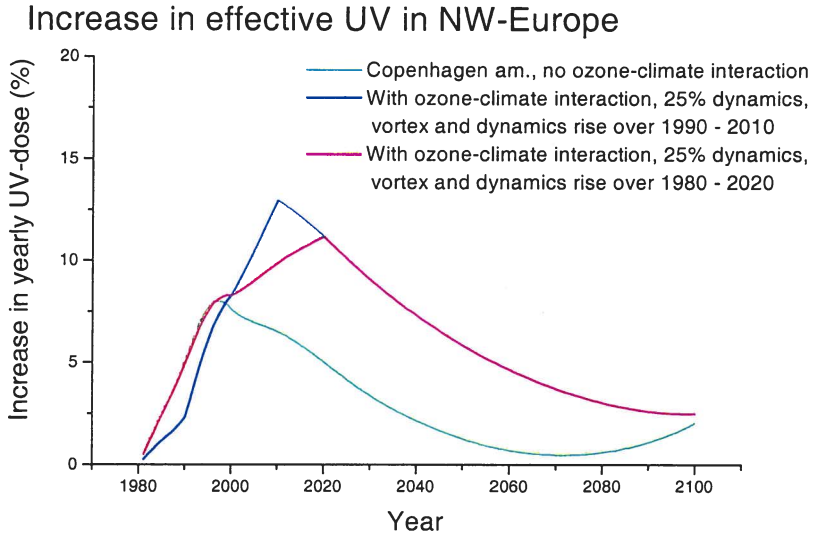

Figure 28 Effect of choice for onset period of the dynamic effects on the effective UV

A.5.6 Conclusions

The model calculations in this study lead us to the following conclusions:

- Stratospheric cooling, induced by climate change, is likely to delay the recovery of the stratospheric ozone layer by approximately 23 years.
- Delay in recovery of the ozone layer induced by ozone-climate interaction, results in a higher and more persistent increase in (effective) UV levels over Europe.
- At De Bilt the maximum increase in UV-level (with ozone-climate interaction) is reached around 2020. At the maximum the increase in effective UV (with ozone climate interaction) is 9.4% (relative to the 1980 level) as compared to 8.7% extra UV (in 2000) with no ozone-climate interaction.
- Accounting for ozone-climate interaction, the effective UV-levels in 2020 for the mid-latitudes in Europe, are 4-6% higher compared to the situation with no climate interaction.
- Higher UV-levels due to ozone climate interaction lead to a higher and more persistent increase in skin cancer incidence.
- At De Bilt with ozone-climate interaction the maximum increase in skin cancer incidence is reached in 2065. In this year there are 96 extra cases of skin cancer per million inhabitants per year. With no climate interaction a maximum excess number of 59 cases per million per year is reached in 2055.
- Accounting for ozone-climate interaction, the excess skin cancer risk in 2070 for the mid-latitudes in Europe varies between 50 an 150 extra cases per million inhabitants per year, compared to the situation with no ozone climate interaction.

These conclusions bear a large uncertainty for the following reasons:

- The stratospheric ozone concentration at mid-latitudes in our model is a subtle balance of chemical destruction of ozone, dilution by ozone poor air from the Arctic vortex, destruction/dilution by non-vortex dynamical effects and production of ozone due to chemical equilibrium shift. But scientific understanding of these processes, especially of the non-vortex dynamics and of the Arctic vortex itself, is far from perfect.
- Of the effects considered the fraction of the ozone trend attributed to the non-vortex dynamics introduces the largest uncertainty in the estimates of effective UV and corresponding risks. Unfortunately, scientific understanding of this effect and consensus on the magnitude of its contribution is the lowest.
- In our risk prognosis we are not able to account for a structural change in other climatological conditions, in particular cloudiness, or for the phenomenon that climate change may influence behaviour of the population.
- In the present version of out risk assessment model not all possible ozone-climate interactions are included.
- Understanding of the onset phase of ozone depletion, especially the existence of a threshold chlorine level below which no ozone depletion takes place, is not complete.

To improve the reliability of our prognoses further research is required on:

- Nature and magnitude of the (possible) interactions between climate change and ozone layer. To begin with the contribution of non-vortex dynamics.
- Details of the risk assessment model, especially with respect to the modeling of the onset phase of ozone depletion (1960-1980), and the modeling of skin cancer, and the inclusion of other interactions.
- 3-dimensional models with a full description of (temperature driven) dynamical changes in the atmosphere with a full coupling to ozone chemistry

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Abbreviations

AMOUR	- Assessment MOdel for UV Radiation and Risks, Research model under development at the Netherlands National Institute of Public Health and the Environment (RIVM).
BCC	- Basal Cell Carcinoma
CA	- Copenhagen Amendment. A reduction scenario (under the Vienna convention) resulting in zero production of ozone depleting substances at the end of 1995.
CMM	- Cutaneous Malignant Melanoma
DU	- Dobson Unit, unit for ozone column thickness. An ozone column of 300 DU corresponds at standard pressure (1 atmosphere) and temperature (0°C) to a layer of ozone of 3 mm thickness.
CFC	- ChloroFluorCarbons
MP	- Montreal protocol. A reduction scenario (under the Vienna convention) resulting in a reduction of 50% in the production of ozone depleting substances at the end of 1999
NR	- No Restriction scenario. A scenario (under the Vienna convention) assuming a yearly rise in the production of ozone depleting substances of 3% per year
ppbv	- parts per billion, volume
RIVM	- Netherlands National Institute of Public Health and the Environment
SCC	- Squamous Cell Carcinoma
UV	- Ultraviolet radiation (wavelength range 100-400 nm)
WMO	- World Meteorological Organisation

GLOBAL CHANGE

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