DOCUMENTS OF THE NRPB

Assessment of Skin Doses

VOLUME 8 NO 3 1997

National Radiological Protection Board
Chilton, Didcot, Oxon OX11 0RQ

The National Radiological Protection Board was created by the Radiological Protection Act 1970. The functions of the Board are to give advice, to conduct research, and to provide technical services in the field of protection against both ionising and non-ionising radiations.

In 1977 the Board received Directions under the Radiological Protection Act which require it to give advice on the acceptability to and the application in the UK, of standards recommended by international or intergovernmental bodies, and to specify emergency reference levels (ERLs) of dose for limiting radiation doses in accident situations.

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ABSTRACT

The 1990 recommendations of ICRP introduced the quantity 'effective dose' to replace 'effective dose equivalent'. The recommendations also included the skin in the computation for the first time. A tissue weighting factor of 0.01 was recommended for the skin by ICRP. This document reviews the biological basis for dose limitation in the skin and recommends a practical approach to the calculation of doses for a variety of exposure situations, including those involving partial exposure. The depth at which the skin dose should be evaluated is also addressed.

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INTRODUCTION

1 The aim of this document is to review the biological basis for dose limitation in the skin and to recommend a practical approach for the calculation of doses to the skin for a variety of exposure situations, in particular those where the skin is only partially exposed, in both occupational and environmental dose assessments. The depth at which the skin dose should be evaluated is also addressed and consideration given to the shielding effects of clothing.

BACKGROUND

2 Radiation damage to the skin, discovered at the turn of the century, was the first type of radiogenic health effect to be described. Since then radiological protection principles for the skin have gone through several changes as more information on both stochastic and deterministic effects of radiation has emerged. In 1977, the International Commission on Radiological Protection (ICRP)[1] considered that the skin was less susceptible to fatal cancer than were other tissues and organs and that deterministic effects were the primary concern. It was also recognised that unacceptable cosmetic effects could occur following absorbed doses of 20 Gy or more, delivered over weeks or months to limited areas of the skin. This value was adopted as the basis for the annual dose equivalent limit of 500 mSv for exposure over a working lifetime to prevent the occurrence of deterministic effects. No tissue weighting factor, w_T, was specified for the skin in the calculation of effective dose equivalent. In 1978 ICRP again considered the risk of fatal skin cancer caused by ionising radiation but maintained that deterministic effects should remain as the basis of skin dose limits[2]. However, ICRP did suggest that a small risk of fatal cancer resulting from exposure of the skin may need to be considered when assessing detriment in the context of population exposure. A weighting factor for the skin of 0.01 was suggested for use in such calculations. In Publication 42[3] ICRP further clarified its position on the skin, stating that the 'remainder' tissues did not include the skin and therefore that the skin should be excluded from the computation of the effective dose equivalent. However, it was stressed that this exclusion applied only to the assessment of the effective dose equivalent to individuals. It was suggested by ICRP that the weighted dose equivalent to the skin should be added to the collective effective dose equivalent and the resulting quantity be referred to as the 'collective effective dose equivalent (including skin)'[3]. Inconsistency between the manner in which the skin was treated in the assessment of the effective dose equivalent to individuals and populations was therefore introduced. Kocher and Eckermann[4] urged that the skin be included routinely in the calculation of effective dose equivalent both for individuals as well as for population groups. They gave the example of the exposure of the skin from immersion in a semi-infinite cloud of ^{85}Kr gas where the inclusion of the skin dose equivalent weighted by a tissue weighting factor of 0.01 more than doubles the effective dose equivalent.

3 Since the issue of ICRP Publication 26[1], much more information on both stochastic and deterministic effects in the skin has become available and this has improved the basis for recommendations of dose limits for that organ. ICRP Publication 59[5] addressed the biological basis for dose limitation in the skin and presented a review of the available data. The report focused on non-melanoma skin cancer (NMSC) and highlighted the apparent synergism between ultraviolet radiation (UVR) and ionising radiation. The whole body

skin cancer risk is dominated by the risk to areas of the skin which are normally exposed to sunlight, ie the face, neck and the outer aspects of the hands and arms. As a result of this, ICRP Publication 59 stated that the risk (or the effective dose) for areas of the skin that are some fraction of the total area of the skin normally exposed to sunlight can be estimated from the ratio of the exposed area to the total UVR-exposed skin area.

4 The 1990 recommendations of ICRP (Publication 60) introduced the quantity 'effective dose' to replace 'effective dose equivalent'[6]. Although the idea of the effective dose remained unchanged, ie the sum of the weighted tissue or organ doses, the weighting factors assigned to many of the tissues were altered to reflect improved information on risks to the different organs and tissues of the body. The skin was also included in the computation for the first time with a tissue weighting factor of 0.01. Furthermore, the 1990 recommendations (in paragraph 173) stated that 'For stochastic effects the equivalent dose can be averaged over the whole area of the skin'. This is inconsistent with ICRP Publication 59 which suggests that averaging for partial exposure of UVR-exposed skin should be over the area of UVR-exposed skin.

5 There are many situations where the dose to the whole skin is fairly uniform and in these cases the effective dose can be obtained by applying the appropriate tissue weighting factor to the equivalent dose. One example of this, already mentioned, is the dose due to immersion in a semi-infinite cloud of a β-emitting gas such as ^{85}Kr. However, there are also many practical situations, in both environmental and occupational dose assessment, where exposure of the skin to weakly penetrating β or low energy γ radiation will cause only partial irradiation of the skin. This may result from either non-uniform skin contamination with radionuclides or exposure to a more distant source.

6 Non-uniform skin contamination may arise when members of the public handle material contaminated with radionuclides discharged, either routinely or accidentally, from nuclear sites. For example, fishermen's hands may come into contact with contaminated mud during their work. In other cases, the exposure geometry is such that standing over, for example, a β-emitting source on the ground may lead to only partial exposure of the UVR-exposed areas. In the case of partial skin exposure, the question of averaging the equivalent dose over an area arises when comparing the dose with both stochastic and deterministic dose limits.

SKIN AS AN ORGAN

Structure of the skin

7 The skin is an organ which covers the surface of the body and in standard man has a mass of approximately 2 kg with a surface area of approximately 2 m^2. It is broadly divisible into two basic layers: the outer epidermis and the underlying dermis (see Figure 1), which together vary in thickness over the body from about 0.5 to 4.0 mm. The skin also contains 'appendages', ie hair, nerve receptors, sweat, apocrine and sebaceous glands, as discrete units arranged more or less perpendicularly to the layered plane of the skin.

8 The epidermis may be further subdivided into several zones. The outermost keratinised section comprises many layers of dead cells which in certain areas of the body, such as the soles of the feet and palms of the hands, can be especially thickened.

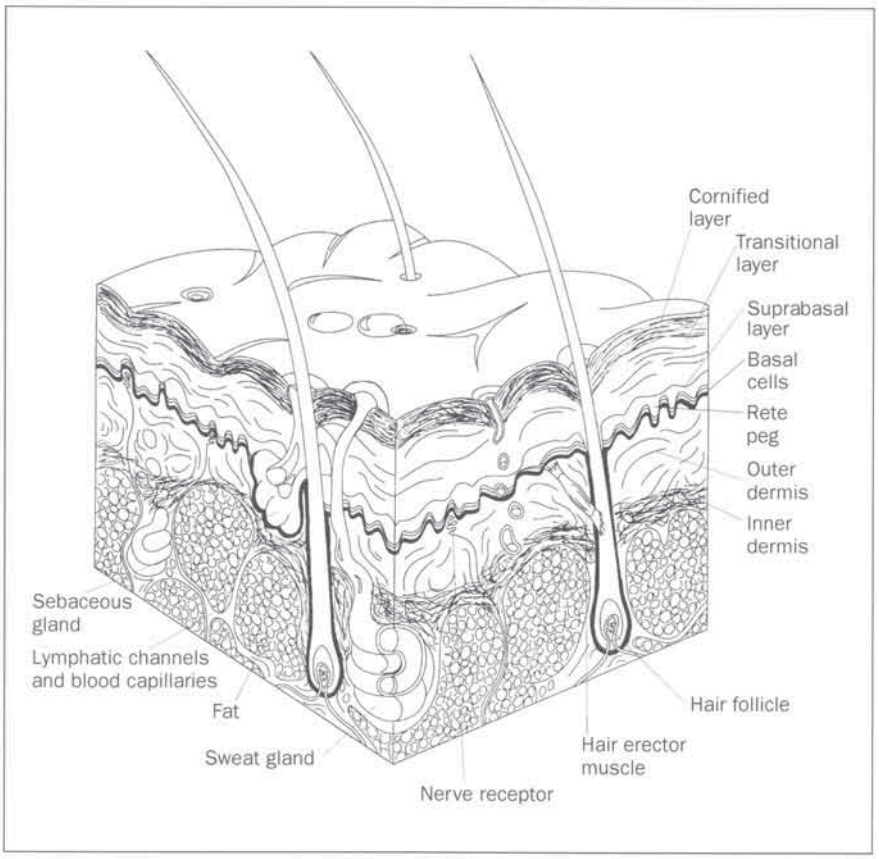


FIGURE 1 *Structure of the human skin*

Beneath this dead surface layer of cells is a transition layer, four or five cells thick, and beneath this is located the viable region of the epidermis. The viable region comprises a single basal layer of cells, which is the main site of the proliferating stem cells, overlain by several layers of suprabasal cells where possibly 20–30% of the cell divisions in the epidermis also occur.

9 The basal layer is separated from the dermis beneath by a basement membrane. This boundary is not flat but undulates and there are also discrete points known as 'rete pegs' where the epidermis projects down into the dermis. In addition, the basal layer extends around the skin appendages, notably the shaft and base of the hair follicles which project even deeper into the dermis. At some sites on the body, over 50% of the basal layer stem cells are associated with the hair follicles. Therefore, the depth of the basal layer is very variable. In most body areas it ranges from 20 to 100 μm deep in the interfollicular sites, but exceptionally, eg in the finger tips, it could be over 150 μm deep because of the enhanced outer cornification. The deeper projections associated with hair follicles result in basal cells being situated over 200 μm deep.

10 The dermis comprises two layers. The outer layer is approximately the same thickness as the epidermis and is composed of loosely arranged collagen bundles interspersed with elastin fibres. There are many blood capillaries present which supply the

metabolic needs of the epidermal basal cells and are also the main site for the body's thermoregulation. The deeper dermis is thicker, much more densely collagenous and has less vasculature. The principal role of this region is to provide the main structural strength of the skin. The inner surface of the dermis comprises loose connective tissue that forms an attachment to the body together with variable amounts of fat. There is a network of subcutaneous blood vessels from which the dermal vasculature arises. The dermis is also traversed by sensory and autonomic nerves and lymphatic vessels. The latter arise in the upper dermis, merge into more discrete vessels in the deeper dermis and these in turn link with major channels that connect with the regional lymph nodes.

Skin cancers

11 Cancers of the skin are relatively common and, in recent years, have been increasing in incidence in white Caucasian populations. They are believed to be induced predominantly by exposure to UVR from the sun, although the causative link has not been confirmed[7]. The commonest malignant tumours of the skin are the so-called non-melanoma skin cancers (NMSCs) whose incidence is thought to be related to cumulative solar radiation exposure. In 1989, 31 495 cases were reported in England and Wales[8]; however, only 362 deaths from NMSCs were recorded in this population in 1993[9]. These cancers are usually slow growing and are found predominantly in older people.

12 The two main types of NMSC are squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) or epithelioma (otherwise known as a rodent ulcer as it appears to erode the surrounding skin)[7]. Squamous cell carcinoma occurs as a result of the neoplastic transformation of cells in the epidermis, possibly those in the early stages of keratinisation – the suprabasal cells; this tumour may occasionally metastasise to other organs. Basal cell carcinoma is particularly slow growing and originates from the basal cells of the epidermis or hair follicles; this tumour does not usually metastasise.

13 Among white Caucasian populations the incidence rate of BCC is almost always greater than that for SCC. Scotto and colleagues[10] reported sex- and age-adjusted rates for SCC in eight regions of the USA as $4.1\ 10^{-4}\ y^{-1}$, compared with a rate of $1.9\ 10^{-3}\ y^{-1}$ for BCC. The BCC : SCC incidence rate ratio was about 4 : 1 in males and about 6 : 1 in females[10]. Very similar ratios have been reported in a number of other surveys[11–15]. However, because of the greater fatality rate for SCC than for BCC (due principally to the greater metastatic potential of SCC), the numbers of deaths due to SCC is generally rather higher than that for BCC. ICRP[5] reviewed a number of studies and concluded that the metastasis rate (and by implication the mortality rate) for BCC was very low, probably much less than 0.1%, while the rate for SCC was about 1%.

14 Malignant melanomas develop from the neoplastic transformation of melanocytes (melanin producing cells) which lie in the basal layer of the epidermis. Melanocytes are derived embryologically from neural crest tissue and have dendritic processes that stretch out among neighbouring cells. Malignant melanomas occur predominantly in white Caucasian populations and if not identified and treated promptly are frequently fatal. They are the major cause of skin cancer death. Exposure to UVR, particularly in the first decade of life, is considered to be a risk factor. In 1989, 3603 malignant melanomas were reported in England and Wales[8] and 1397 deaths from this condition were recorded in this population in 1993[9].

BIOLOGICAL BASIS FOR SKIN DOSE LIMITATION

Stochastic effects

15 The stochastic effects of ionising radiation that will be considered comprise the so-called non-melanoma skin cancers (NMSCs). ICRP Publication 59[5] indicated that there is substantial evidence linking the incidence of NMSC to exposure to ionising radiation; for malignant melanoma, the evidence is less compelling, although it is not possible to exclude a weak association. For example, in the Japanese atomic bomb survivor tumour incidence dataset[16] there are 13 cases of melanoma. The best estimate of the excess relative risk (ERR) is 0.13 Sv^{-1} (90% confidence interval, CI < 0–2.60). This is estimated using a shielded kerma dose and a neutron relative biological effectiveness (RBE) of 20. However, there is no significant trend with dose, nor is there strong evidence for an excess incidence of melanomas in other human data[17,18]. Therefore, melanoma will not be considered further.

16 Studies on irradiated human populations only cover a limited period of the lives of the individuals and it is necessary, therefore, to use models to extrapolate over the lifetime of the exposed population in order to obtain risk estimates. The models that have been used by various scientific committees[6,19] can be broadly grouped into two types: absolute risk models where the excess risk is assumed to be constant and relative risk models where the excess risk is a constant multiple of the underlying spontaneous cancer risk. Both types of model can allow for the minimum time between irradiation and the appearance of a radiation-induced tumour – the latent period. For most tumours, the spontaneous cancer risk increases with age and, therefore, the time-constant relative risk model will predict an increasing incidence of radiation-induced cancer with increasing age. ICRP Publication 59 found that a relative risk model rather than an absolute risk model gave a better fit to the various datasets for NMSC. Thus, the relative risk model is to be preferred for projecting cancer risks over time. This point will be discussed at greater length below (see paragraphs 24–27 and Appendix B) in relation to the tumour incidence dataset for Japanese atomic bomb survivors. For this reason, most of the NMSC population risk calculations in this document are evaluated using relative risk projection models.

17 Most of the populations which have been studied for the purposes of deriving risk estimates resulting from exposure to ionising radiation, with the exception of the Japanese atomic bomb survivors, are white Caucasian. There is evidence, as will be discussed later, that NMSC risks resulting from exposure to ionising radiation on UVR-shielded skin, and also on heavily pigmented skin, are lower than NMSC risks for exposure on UVR-exposed non-pigmented skin. There may, therefore, be significant problems in estimating risks for non-Caucasian populations. However, as is discussed in paragraph 21, the risk estimates derived by ICRP[5] for UVR-exposed skin in Caucasian populations are similar to the risks which have been observed in the cohort of Japanese atomic bomb survivors[16].

Studies considered in ICRP Publication 59

18 The risks obtained from eight studies of skin cancer in UVR-exposed sites (head, neck and hands) are given in Table 1. These are reproduced from the paper by Shore[25] and ICRP Publication 59, with the exception of the tumour incidence dataset for Japanese atomic bomb survivors[16] and the dataset of Ron *et al*[18] for NMSC and melanoma skin cancers in an Israeli group followed up after radiation treatment for *tinea capitis* in childhood. The risk estimates given in Table 1, relating to the study by Ron *et al*,

TABLE 1 *Risk coefficients for NMSC incidence in UVR-exposed sites*

Study	Mean age at exposure (years)	Excess relative risk (Sv^{-1}) (and 90% CI)	Normalised absolute risk* (10^{-4} PY^{-1} Sv^{-1}) (and 90% CI)
Shore *et al*[17]	8	0.49 (0.37–0.63)	10.5 (8.1–13.5)
Hildreth *et al*[20]	0	1.05 (0.50–1.84)	15.9 (7.5–27.9)
Schneider *et al*[21]	9	0.11 (0.04–0.19)	10.2 (3.3–18.3)
van Vloten *et al*[22]	16	0.23 (0.13–0.59)	21.6 (12.3–55.5)
Ron *et al*[18]	7	0.70 (0.35–1.32)	1.31 (0.94–1.77)
Rowell[23]	≈50	0.12 (0.02–0.28)	54.6 (11.4–132)
Ševcova *et al*[24]	Adult	1.13 (0.75–1.62)	1.2 (0.6–1.5)
Thompson *et al*[16]	24	1.00 (0.50–1.75)	0.84 (0.47–1.27)†
Aggregate			
Excluding A-bomb[16]			
Person-year weighted		0.68 (0.43–1.11)	4.36 (3.28–5.84)
Variance weighted		0.22 (0.17–0.28)	1.41 (1.10–1.66)
Including A-bomb[16]			
Person-year weighted		0.89 (0.55–1.40)	2.06 (1.61–2.64)
Variance weighted		0.23 (0.18–0.29)	1.20 (0.96–1.42)

* Absolute risks normalised to 3000 cm^2 of UVR-exposed skin (with units of 10^{-4} per person-year per sievert).
† Absolute risks for whole body exposure.

supersede those given in ICRP Publication 59 which were derived from a previous analysis of the same dataset[26]. It should be noted that the first five studies listed in Table 1 relate to groups of irradiated children. The sixth study, by Rowell[23], is very small, representing the follow-up of 100 patients given x-ray treatment to the face for benign dermatoses. The seventh study relates to a cohort of Czech uranium miners[24] (the skin dose coming from α particles). The final study refers to the Japanese atomic bomb survivors[16].

19 The risks obtained in six studies of UVR-shielded skin (corresponding to those used in ICRP Publication 59) are shown in Table 2. All but one of the studies, by Shore *et al*[17], refer to groups irradiated for the most part in adulthood. The third study listed in Table 2 refers to the risks calculated for Negro children in the study by Shore *et al*, the corresponding entry in Table 1 being for white Caucasian children.

20 In all of the studies of irradiated children listed in Tables 1 and 2, and in most of the others[17,18,20–24,27,29], the risk estimates were calculated by restricting attention to those skin tumours which appeared in or near the actual irradiated sites[5]. This often required the use of supplementary (unpublished) information provided by the authors of the various studies[32]. The risk estimates shown in Table 2 for the study by Hay *et al*[28], of men followed-up after treatment for testicular cancer, are different from those presented in ICRP Publication 59. There are two difficulties in deriving risk estimates from the study by Hay *et al*. The first is that the expected number of tumours is calculated from national incidence rates, but as Hay *et al* commented, the excess incidence of these cancers is unremarkable given the greater surveillance to which these patients would have been subjected after their primary cancer. The more serious difficulty concerns the relationship between the dose in the irradiated skin area to the observed and expected number of cancers, which presumably occurred over the whole body. In fact, Hay *et al* reported that

TABLE 2 *Risk coefficients for NMSC incidence in UVR-shielded sites*

Study	Mean age at exposure (years)	Excess relative risk (Sv^{-1}) (and 90% CI)		Normalised absolute risk* (10^{-4} PY^{-1} Sv^{-1}) (and 90% CI)	
Veien *et al*[27]	≈ 18	< 0	(< 0–0.25)	< 0	(< 0–255)
Hay *et al*[28]	37	< 0	(< 0–32.12)	< 0	(< 0–17.5)
Shore *et al*[17]	8	< 0	(< 0–5.35)	< 0	(< 0–9)
Shore *et al*[29]	27	0.12	(< 0–0.38)	60	(< 0–193.5)
Boice *et al*[30]	≈ 55	< 0	(< 0–0.01)	< 0	(< 0–0.6)
Davis *et al*[31]	≈ 30	0.007	(< 0–0.03)	0.9	(< 0–4.5)
Aggregate					
Excluding Boice *et al*[30], Davis *et al*[31]					
Person-year weighted		< 0	(< 0–4.11)	10.36	(< 0–111.61)
Variance weighted		0.01	(< 0–0.25)	< 0	(< 0–8.02)
Including Boice *et al*[30], Davis *et al*[31]					
Person-year weighted		< 0	(< 0–0.32)	0.52	(< 0–8.56)
Variance weighted		< 0	(< 0–0.02)	< 0	(< 0–1.68)

* Absolute risks normalised to 15 000 cm^2 of UVR-shielded skin (with units of 10^{-4} per person-year per sievert).

all the skin tumours were outside the irradiated area. For this reason the risk estimates for this study given in Table 2 have been recalculated using the expected number of cancers in the irradiated area (derived by scaling from the expected number in the total area of UVR-shielded skin). For the last two studies listed in Table 2[30,31], no information was available on the location of the skin tumours in relation to the irradiated area[32] and thus the associated risk estimate from these two datasets should be treated with caution. For this reason, the combined NMSC risk estimates for UVR-shielded skin are given in Table 2 with these studies included or excluded. This makes little difference to the excess relative risk (ERR) coefficients, but the excess absolute risk (EAR) coefficients are increased substantially, from 0.52 10^{-4} PY^{-1} Sv^{-1} (90% CI < 0–8.56) when all the studies are analysed to 10.36 10^{-4} PY^{-1} Sv^{-1} (90% CI < 0–111.61) when the last two studies[30,31] were excluded.

21 Details of the incidence risks for NMSC in the cohort of Japanese atomic bomb survivors[16], information not available to ICRP[5], are also included in Table 1. The ERR for (uniform whole body) exposure for NMSC is 1.00 Sv^{-1} (95% CI 0.41–1.89). The EAR estimate is 0.84 10^{-4} PY^{-1} Sv^{-1} (95% CI 0.40–1.35). No separate risk coefficients for UVR-exposed or UVR-shielded skin were given in this study (but see the discussion in paragraph 28 and Appendix B). Little difference is made to the aggregate ERR coefficients by the inclusion of this study, although the change in the aggregate EAR coefficient is more pronounced.

Dose–response relationship for NMSC

22 The analysis of the cancer incidence dataset for the Japanese atomic bomb survivors reported in Appendix B shows strong evidence for a curvilinear dose–response relationship for NMSC. In particular, two possible forms of dose–response are suggested: the first, a simple (fourth) power of dose with an exponential sterilisation term resulting in a reduction in risk at higher doses (greater than 4 Sv); the second, in which a dose threshold at about 1 Sv is assumed, with significant curvature in the dose–response curve even above this value. Thompson *et al*[16] fitted a linear-spline model to

the NMSC data using a dose cutpoint of 1 Sv and found strong evidence ($p = 0.01$) that such a model provided a better fit than a linear model. The slope of the NMSC dose–response curve below 1 Sv estimated by Thompson *et al* was essentially zero. This reinforces the strong evidence of curvature in the dose–response curve in the analyses presented in Appendix B. The possible random and systematic errors in the DS86 skin dose estimates, used both in the analyses of Appendix B and in those of Thompson *et al*, together with certain methodological problems (discussed in Appendix B), imply that the findings of curvature in the dose–response curve should be treated with some caution. However, variant analyses in which each of the other 15 sets of DS86 organ dose estimates (supplied on the publicly available version of the solid cancer incidence dataset) are used, in place of the DS86 shielded kerma dose, yield broadly similar findings in relation to the significance of the curvature in the NMSC dose–response curve. Analyses in which account is taken of possible (random) errors in the estimated DS86 organ doses also result in similar findings[33].

23 There are limited epidemiological data on the shape of the dose–response curve for the incidence of NMSC, apart from the cohort of the Japanese atomic bomb survivors. Ron *et al*[18] found no evidence for curvilinearity in the dose–response relationship in a group of Israeli children who had been treated with large therapeutic doses of radiation for *tinea capitis*. However, the doses in this study were generally much higher than those in the Japanese dataset: no patients had received doses less than 5 Gy in the Israeli dataset. The only other information on the shape of the dose–response relationship comes from animal experiments and this was reviewed in ICRP Publication 59. The various sets of animal data suggest numerous possible dose–responses, including the linear-threshold and linear-exponential forms[5]. In particular, data on CBA/CaH mice after β irradiation[34,35] suggest the existence of a positive dose threshold, of at least 10 Gy. There is a substantial body of biological data indicating that single tracks of all types of ionising radiation can induce a variety of damage, including DNA double-strand breaks, which are believed to be the critical lesions in radiation-induced cancer[36]. There is also experimental evidence that argues against the operation of an error-free DNA repair system at low doses of ionising radiation that might result in a dose threshold for the induction of gene and chromosomal mutations[37,38]. However, given the indications from the human data, that relatively low doses (< 1 Gy) can lead to an excess incidence of NMSC[17], the plausibility of a threshold model is questionable. A further consideration is that NMSC incidence rates are critically dependent on the efficiency of the cancer registration system, so that it is possible that the 'true' shape of the dose–response curve in the Japanese dataset could be distorted by variations in the completeness of ascertainment between the various dose groups within the cohort. There are no grounds for supposing there to be such dose-dependent variations in ascertainment in the Hiroshima and Nagasaki tumour registries[39]. In particular, there is no evidence for differences between the NMSC rates in the members of the cohort who belong to the Adult Health Study (AHS) and the NMSC rates in the remainder of the cohort[16]. If there had been such differences, biases in the shape of the dose–response would have been introduced, because there are proportionally more survivors in the AHS in the higher dose groups[40]. In situations where there is curvilinearity in the dose–response relationship, a dose and dose rate effectiveness factor (DDREF) is used to extrapolate risks at high dose and dose rate to low dose and dose rates. ICRP Publication 60[6] recommended the general use

of a DDREF of two. However, the pronounced curvilinearity in the NMSC incidence data for the Japanese atomic bomb survivors makes it likely that the DDREF, relevant to NMSC, is considerably greater than two.

Time and age variations in radiation-induced NMSC risk

24 The analyses presented in Appendix B indicate that there is a highly significant reduction in ERR with increasing age at exposure, but no significant variation of ERR with time since exposure in the Japanese atomic bomb survivors. Both of these findings are consistent with the analysis of the same dataset by Thompson *et al*[16] and with the findings in various other human datasets[18,41,42]. The analyses presented in Appendix B demonstrate that the fit of a model using only an (exponential) adjustment for attained age is rather worse than that of a model incorporating (exponential) adjustments for age at exposure and time since exposure. Equally, the results of Appendix B indicate that the fit of the model incorporating exponential adjustments to the ERR for age at exposure (and time since exposure) is inferior to that of a model with adjustments to the ERR using powers of time since exposure and attained age.

25 It was the finding in various exposed groups that the solid cancer ERR decreases with increasing age at exposure[19], combined with the reduction in solid cancer ERR with increasing time since exposure in certain datasets, that led Kellerer and Barclay[43] to suggest that (an exponential function of) attained age was the factor principally determining the variation with time and age in solid cancer ERR. The finding that the rate of change of ERR for NMSC with age at exposure is significantly different from the rate of change of ERR with time since exposure implies that the attained-age model of Kellerer and Barclay fits the NMSC data rather less well than a model with separate adjustments for time since exposure and age at exposure. Kellerer and Barclay fitted their model to all solid cancers combined in the cancer mortality data for the Japanese atomic bomb survivors rather than to the NMSC incidence dataset, as used in Appendix B. They also employed a rather different statistical methodology, involving the fitting of a simple parametric function (a power of attained age) to model the background cancer mortality rates, rather than the essentially model-independent fitting of the background rates employed in Appendix B (at least for models 1–3). It is possible that either or both of these factors may contribute to the apparent discrepancy between their findings and those presented in Appendix B.

26 The analyses presented in Appendix B indicate that the generalised relative risk model provides a more parsimonious description of the NMSC data than the generalised absolute risk model. Muirhead and Darby[44] analysed a subgroup of epithelial tumours in the UK ankylosing spondylitis patients and in the Life Span Study (LSS) mortality dataset in the Japanese atomic bomb survivors and found that in both datasets the fit of the time-constant absolute risk model was significantly worse than the fit of the time-constant relative risk model. Pierce *et al*[45] analysed all solid cancers combined in the Japanese LSS mortality data and found that both relative and absolute risk models with adjustments for the effects of age at exposure and time since exposure yielded equivalently good fits. The form of the hybrid model employed in Appendix B is arbitrary, and it should be stressed that its main function is to provide a nested family within which the generalised ERR and EAR models lie for the purposes of testing hypotheses. Clearly, in the presence of 'mixing', common parameters in both the ERR and EAR components would not be expected

(the terms inside the square brackets) in model 4 in Appendix B. However, fits of other sorts of hybrid ERR/EAR models, in which different parameters (and in particular different scale parameters α) are allowed in the ERR and EAR components of model 4, are subject to numerical instability. In large part this is because the parameters are poorly estimated in the region of $\mu = 0$ or $\mu = 1$, at which points these alternative hybrid ERR/EAR models become degenerate; the degeneracy of these models at $\mu = 0$ or $\mu = 1$ is also problematic theoretically, since then the asymptotic (χ^2) distribution of the deviance difference statistic is not guaranteed[46]. It is clear that, with enough adjustments for the relative and absolute excess risks, both generalised ERR and EAR models can be made to provide equivalent goodness of fit. The evidence presented here, that for NMSC the generalised relative risk model provides a more parsimonious description of the radiation-induced excess cancer risk, should be considered within the context of the relatively simple adjustments to the ERR and EAR (power and exponential functions of time and age) that are employed in Appendix B.

27 These adjustments are not entirely arbitrary, being motivated in part by mechanistic considerations. In particular, the multistage model of Armitage and Doll[47], in which it is assumed that the numbers of stem cells and the mutation rates are constant (apart from the mutation rate affected by radiation exposure), predicts an ERR following instantaneous radiation exposure proportional to a product of powers of time since exposure, age at exposure and attained age[42]. Similarly, the two-mutation model of Moolgavkar *et al*[48,49] predicts that, when the stem cell population and the mutation rates are eventually constant, at a sufficiently long time after an instantaneous radiation exposure the ERR and EAR decay exponentially[42]. This property is also true of various generalisations of the Armitage-Doll and two-mutation models[50].

28 There are some grounds for questioning the conclusion of ICRP Publication 59, as is discussed in Appendix B, that there is a supra-multiplicative interaction between the effects of UVR exposure and ionising radiation. In particular, there is evidence in the Japanese bomb survivor NMSC incidence dataset of higher relative risks on UVR-shielded skin than on UVR-exposed skin. However, as discussed in Appendix B, there are difficulties in interpreting UVR-exposure status in the Japanese cohort. There is also other evidence[17,51] to support the findings of ICRP Publication 59 in this respect. So, within this document the ICRP Publication 59 position has been taken, that the NMSC ERR is higher on UVR-exposed skin than on UVR-shielded skin.

Target depth for carcinogenesis

29 Information on the likely depth of target cells for carcinogenesis comes largely from animal experiments. Albert *et al*[52] concluded from experiments on rats that radiation had to penetrate at least 180 μm to induce tumours. Heimbach *et al*[53] found that accelerated α particles which penetrated to a depth of 120 μm were capable of inducing skin tumours in mice. The fact that an excess incidence of NMSC is observed in the Czech uranium miners[24] implies that the target depth in human beings must be less than 80 μm, this being the maximum track length of these α particles in human skin. These studies, and various others, were evaluated by ICRP[5], and it was concluded that for estimating the risk of carcinogenesis, dose should be evaluated to the basal layer of the skin (the deepest cell layer of the epidermis). The depth of this layer varies between individuals and from one body site to another. ICRP Publication 59 gave a range of depths of 20–100 μm, which is in

fact appropriate to those areas of skin which are usually exposed to UVR. Important exceptions to this generalisation are the palms of the hands, finger tips, sides of fingers and soles of the feet, which have a significantly deeper basal layer[54].

Population cancer risk methodology

30 An absolute risk coefficient for the risk of skin cancer, under the assumption of uniform irradiation of the 3000 cm^2 of UVR-exposed and 15 000 cm^2 of UVR-shielded skin in an adult, was given in ICRP Publication 59. The risk estimates for the incidence of NMSC calculated there for high dose rate exposure of UVR-exposed skin were an ERR of 0.611 Sv^{-1} and an EAR (normalised to 3000 cm^2 UVR-exposed skin) of 6.7 10^{-4} PY^{-1} Sv^{-1}. The corresponding risk estimates for UVR-shielded skin for high dose rate exposure were an ERR of 0.005 Sv^{-1} and an EAR (normalised to 15 000 cm^2 of UVR-shielded skin) of 2.0 10^{-4} PY^{-1} Sv^{-1}. The averaging used to derive these risk coefficients in ICRP Publication 59 was based on weighting the results by the number of person-years in each study. However, a statistically more defensible procedure might have been to weight each risk coefficient in inverse proportion to its variance. When this is done the aggregate ERR coefficient for UVR-exposed skin is 0.22 Sv^{-1} (90% CI 0.17–0.28) (Table 1), and for UVR-shielded skin the corresponding figure is less than 0 Sv^{-1} (90% CI < 0–0.02) (Table 2). ICRP Publication 59 adopted this non-standard weighting procedure because the canonical (variance) weighting assigned very high weights to a few, mostly small studies with (perhaps fortuitously) very narrow confidence intervals in the risk estimates. Most of the variance-weight for the ERR risk coefficients is attached to just four studies in Tables 1 and 2[17,21,30,31]. Most of the variance-weight for the EAR risk coefficients in Tables 1 and 2 is attached to two studies[16,30]. For this reason, although the variance-weighted risk coefficients are somewhat lower (by about a factor of three) than the person-year weighted risk coefficients, the preference of ICRP Publication 59 has been followed for the use of person-year weighted risk coefficients. As the person-year weighted risk coefficients derived for this document are not very different from those of ICRP Publication 59, and for consistency with ICRP, from now on the ICRP Publication 59 ERR and EAR coefficients will be used.

31 Although it is often reported that a significant excess risk of radiation-induced solid cancer is not seen until at least ten or more years after exposure[18,55], a radiation-related increase in solid cancer mortality is apparent in the cohort of Japanese atomic bomb survivors during the first five years of follow-up, five to ten years after the bombings (ERR = 0.24 shielded kerma Gy^{-1}, 90% CI 0.05–0.48)[56]. Carcinogenesis may be described by quasi-biological or mechanistic models, in which cancer is assumed to result from the accumulation of a sufficient number of critical mutations. Among the better known models of carcinogenesis that have been proposed are the so-called multistage model of Armitage and Doll[47] and the so-called two-mutation model of Moolgavkar *et al*[48,49]. Both of these mechanistic models, and various generalisations of them[50], predict that soon after exposure the excess risk of cancer would begin to increase[42,50]. Subject to the rapid development from a single malignant cell to a clinically detectable neoplasm, in an individual the latent period should not be regarded as a well-defined interval, in as much as given a sufficiently large group of people who are exposed to a sufficiently large dose of radiation, an arbitrarily small latent period might be detected. These theoretical considerations are supported by the observed rapid increase in thyroid cancer

incidence in the former USSR following the Chernobyl nuclear accident[57]. However, for consistency with the risk calculations in ICRP Publication 59 a latent period of ten years is taken for skin cancer. If a latent period of zero years is assumed, the risk estimates are not substantially inflated.

Population cancer risk calculations

32 The calculated lifetime risk for NMSC incidence for a current UK population and the analogous information for NMSC mortality are shown in Tables 3 and 4. The population is assumed to have the 1993 UK cancer and general mortality rates[9] and the 1989 UK cancer incidence rates[8]. Following the procedure adopted in ICRP Publication 59, the ERR coefficient used is a weighted sum of the UVR-exposed and UVR-shielded risk coefficients, $(0.611 \times 0.9) + (0.005 \times 0.1)\ Sv^{-1} = 0.55\ Sv^{-1}$, reflecting the fact that 90% of

TABLE 3 *Population risks for NMSC incidence* (Sv^{-1}) calculated for a current UK population (1993 mortality rates, 1989 cancer incidence rates) using a constant relative risk model †*

Age group (years)	Male	Female	Total
0–9	0.0310	0.0272	0.0291
10–19	0.0310	0.0272	0.0291
20–29	0.0310	0.0270	0.0290
30–39	0.0304	0.0262	0.0283
40–49	0.0283	0.0243	0.0263
50–59	0.0234	0.0208	0.0221
60–69	0.0152	0.0145	0.0148
70+	0.0049	0.0048	0.0049
18–64	0.0274	0.0239	0.0257
Total	0.0251	0.0212	0.0231

* Cancer risk is the low dose limit (test dose = 0.001 Sv) of the quality analogous to the risk of exposure-induced death (REID) for cancer incidence[58].

† Latent period ten years. ERR coefficient = $(0.611 \times 0.90) + (0.005 \times 0.10)\ Sv^{-1} = 0.5504\ Sv^{-1}$, equilibrium population.

TABLE 4 *Population risks for NMSC mortality* (Sv^{-1}) calculated for a current UK population (1993 mortality rates) using a constant relative risk model†*

Age group (years)	Male	Female	Total
0–9	0.000421	0.000286	0.000355
10–19	0.000419	0.000287	0.000355
20–29	0.000408	0.000288	0.000349
30–39	0.000393	0.000289	0.000342
40–49	0.000376	0.000285	0.000332
50–59	0.000353	0.000278	0.000316
60–69	0.000300	0.000255	0.000277
70+	0.000182	0.000156	0.000167
18–64	0.000379	0.000283	0.000332
Total	0.000362	0.000263	0.000312

* Cancer risk is the low dose limit (test dose = 0.001 Sv) of the risk of exposure-induced death (REID)[58].

† Latent period ten years. ERR coefficient = $(0.611 \times 0.90) + (0.005 \times 0.10)\ Sv^{-1} = 0.5504\ Sv^{-1}$, equilibrium population.

NMSCs occur on the head and upper extremities, compared with 10% on the trunk and lower extremities (see paragraphs 36 and 37, and Table 5). The overall incidence risk for a general UK population is $2.3\,10^{-2}\,Sv^{-1}$, with slightly higher risks for males ($2.5\,10^{-2}\,Sv^{-1}$) than for females ($2.1\,10^{-2}\,Sv^{-1}$). For a working population (aged 18–64 years) the overall risks are marginally higher than for a general population ($2.6\,10^{-2}\,Sv^{-1}$). The cancer mortality risks are very much lower than these: $3.1\,10^{-4}\,Sv^{-1}$, with again slightly higher risks for males ($3.6\,10^{-4}\,Sv^{-1}$) than for females ($2.6\,10^{-4}\,Sv^{-1}$) and slightly higher risks for a working population ($3.3\,10^{-4}\,Sv^{-1}$) compared with a general one.

33 Using the ICRP EAR coefficients ($6.7\,10^{-4}\,PY^{-1}\,Sv^{-1}$ for the 3000 cm^2 of UVR-exposed skin, $2.0\,10^{-4}\,PY^{-1}\,Sv^{-1}$ for the 15 000 cm^2 of UVR-shielded skin) to calculate population cancer risks, then the corresponding cancer incidence risks are about $2.6\,10^{-2}\,Sv^{-1}$ for a general population (cf $2.3\,10^{-2}\,Sv^{-1}$ using the relative risk model, from Table 3). For irradiation of a working population (aged 18–64 years at exposure) the cancer incidence risk is about $2.4\,10^{-2}\,Sv^{-1}$ (cf $2.6\,10^{-2}\,Sv^{-1}$ using the relative risk model, from Table 3). However, as has been discussed previously, there are compelling reasons for preferring to calculate risks using the relative risk model rather than using the absolute risk model.

34 ICRP Publication 59 calculated lifetime (uniform whole body) cancer incidence risks for a working population (18–64 years), having the mortality and incidence rates of the

TABLE 5 *Percentage distribution of NMSC incidence in UVR-exposed sites (head and neck and upper extremities) as a fraction of total NMSC incident cases*

Study	Ascertainment*	Gender	BCC percentage (cases)		SCC percentage (cases)	
Scotto *et al*[10]	MR	Male	86.0	(13 770)	92.4	(3 539)
		Female	87.4	(10 692)	85.3	(1 756)
Levi *et al*[59]	CR	Male	77.0	(1 970)	91.1	(685)
		Female	79.3	(1 841)	85.7	(491)
Østerlind *et al*[60]	CR	Male	82.6	(5 587)	91.7	(1 354)
		Female	80.1	(5 259)	83.7	(651)
Glass and Hoover[11]	CR/MR	Male	—		78.5†	(1 380)
		Female	—		70.7†	(496)
Karjalainen *et al*[61]	CR	Male	83.3†	(9 899)	78.2†	(1 481)
		Female	87.2†	(14 076)	77.2†	(1 446)
Gallagher *et al*[12]	CR	Male	83.5	(6 282)	92.1	(1 683)
		Female	84.4	(5 235)	85.4	(936)
Lloyd Roberts[13]	MR	Male	73.7	(114)	88.9	(27)
		Female	92.0	(87)	62.1	(29)
Magnus[14]	CR	Male	68.0	(8 058)	87.8	(2 204)
		Female	69.8	(8 400)	83.5	(1 518)
Serrano *et al*[15]	MR	Male	82.4	(1 022)	90.3	(202)
		Female	85.7	(739)	79.5	(75)
Marks *et al*[62]	Q/MR‡	Male	74.4	(272)	83.5	(113)
		Female	79.2	(186)	78.0	(53)

* CR = cancer registry; MR = medical records (doctors' notes, etc); Q = questionnaire.
† Head and neck only.
‡ Questionnaire administered to randomly selected sample of Australian dwellings, with medical record checks if indications given of ever having been treated for skin cancer.

population of the USA in 1983, to be $9.8\,10^{-2}\,Sv^{-1}$ using the (preferred) relative risk model and $2.4\,10^{-2}\,Sv^{-1}$ using an absolute risk model. The NMSC risk, calculated using the relative risk model, is somewhat higher than that calculated in this document using the same model applied to the population of the UK ($2.6\,10^{-2}\,Sv^{-1}$), and reflects the rather lower incidence rates of these cancer types in the UK compared with the USA. At least for the older age groups, skin cancer incidence rates are about three times higher in the USA as compared with the UK[5,8]. The corresponding cancer mortality risks are $2.0\,10^{-4}\,Sv^{-1}$ using the relative risk model and $4.6\,10^{-5}\,Sv^{-1}$ using an absolute risk model. ICRP calculated mortality risks by applying an average lethality of 0.2% to the incidence risk figures, death being assumed to occur at the time of incidence. The method of calculation employed in this document is rather different, using the national (UK) NMSC mortality rates directly. It is perhaps remarkable, in view of the different methodology, that the risks obtained for the UK population are not dissimilar ($3.3\,10^{-4}\,Sv^{-1}$) from those calculated by ICRP[5] for the population of the USA. ICRP Publication 59 acknowledges that there is some evidence for the relative risk of skin cancer decreasing many years after irradiation, particularly among those irradiated in childhood[18,41] so that the risks calculated by the relative risk model are expected to be conservative. Another reason for the risks probably being conservative is the fact that, as has been observed above (paragraphs 24 and 25), for NMSC, as for solid cancers generally, relative risks are higher for those exposed at younger ages[16,19,63]. Since cancer risks calculated by ICRP Publication 59 were driven by those for UVR-exposed skin, and these in turn were largely determined by the risk coefficients estimated for the five groups of irradiated children listed in Table 1, it is clear that the risks for those exposed in adulthood will be somewhat overestimated.

Derivation of weighting factors for the skin

35 Using the risks presented in Tables 3 and 4, values analogous to the ICRP tissue weighting factors can be calculated for NMSC in UVR-exposed skin and UVR-shielded skin. In order to do this, consideration must first be given to the proportion of NMSCs occurring naturally on UVR-exposed skin sites.

36 Estimates from various studies of the proportion (P) of BCC and SCC occurring naturally on UVR-exposed skin sites are set out in Table 5. The proportion of BCC on UVR-exposed sites ranges from 70 to 90%, with little apparent difference between the sexes. The proportion of SCC on UVR-exposed sites again generally falls within the range 70–90% and there are indications that the proportion of SCC on UVR-exposed sites might be greater for males than for females. Among the studies with a more thorough ascertainment of cases are those of Scotto *et al*[10] and Serrano *et al*[15], for which the proportions of cases of SCC and BCC on UVR-exposed sites are in the range 80–90%.

37 From the relative risk model the proportion of risk pertaining to the UVR-shielded areas should be $0.005(1-P)/[0.005(1-P)+0.611P]$, where P is the proportion of cancers on UVR-exposed skin. If P is taken[10,15] to be 0.9, then this proportion is $9.1\,10^{-4}$. Therefore the mortality risks predicted for UVR-shielded skin would be $3.1\,10^{-4} \times 9.1\,10^{-4}\,Sv^{-1}$ or $2.8\,10^{-7}\,Sv^{-1}$, while the mortality risks for UVR-exposed skin would be $3.1\,10^{-4} \times (1 - 9.1\,10^{-4})\,Sv^{-1}$ or $3.1\,10^{-4}\,Sv^{-1}$.

38 Following the methodology defined in ICRP Publication 60[6], the relative contribution of NMSC for UVR-shielded skin to the total radiation detriment is given by

$$2.8\,10^{-7}\ LL\ RNF/(7.253\,10^{-2}) = 7.8\,10^{-6}$$

where the relative length of life lost factor in the ICRP detriment is given by $LL = 1$, and where the relative contribution to the ICRP detriment to account for non-fatal cancers is given by the relative non-fatal contribution, $RNF = 2$, as shown in Table B-20 of ICRP Publication 60. The figure $7.253\ 10^{-2}$ is the total detriment for all cancers, again taken from Table B-20.

39 The relative contribution of NMSC for UVR-exposed skin to the total detriment is

$$3.1\ 10^{-4}\ LL\ RNF/(7.253\ 10^{-2}) = 8.6\ 10^{-3}$$

This last figure, which can be taken to correspond to the tissue weighting factor of the skin as a whole, w_{skin}, is very close to the (unrounded) contribution of the skin to the detriment of $6\ 10^{-3}$ calculated in ICRP Publication 60. Both of these organ weighting factors do not adjust for the effects of DDREF. Given the indications from the analysis presented in Appendix B of very substantial curvature in the NMSC dose–response, the corresponding values of the tissue weighting factors at low doses and dose rates are probably lower than these.

Summary of stochastic effects

40 There is evidence that exposure to ionising radiation causes non-melanoma skin cancers (NMSCs), of which squamous cell carcinoma and basal cell carcinoma are the two main types. However, evidence for radiation-induced malignant melanoma is much weaker. Radiation-induced NMSCs are largely concentrated in UVR-exposed skin, which is also where the majority of spontaneous NMSCs occur. The dose–response relationship for NMSC in the Japanese atomic bomb survivors shows strong indications of upward curvature with a possible threshold or a dose–response proportional to the fourth power of dose. This supports the application of a DDREF of at least two to obtain NMSC risks at low doses and low dose rates. The various human data on radiation-induced NMSC support the use of a modified relative risk model, which implies a marked decrease in relative risk with increasing age at exposure. A summary of the calculated risk factors for a UK population is given in Table 6.

Deterministic effects

41 Deterministic effects following irradiation of the skin have been extensively described and reviewed in ICRP Publication 59 and it is not the intention of this document to repeat that work. In summary, the earliest response of the skin occurs with acute x-ray doses in excess of 2 Gy. Erythema (skin reddening) occurs within a few hours and is thought to relate to the dilation of the blood capillaries. This response is transient and soon

Population group	Males	Females	Overall
General population			
Incidence	$2.5\ 10^{-2}$	$2.1\ 10^{-2}$	$2.3\ 10^{-2}$
Mortality	$3.6\ 10^{-4}$	$2.6\ 10^{-4}$	$3.1\ 10^{-4}$
Working population (18–64 years)			
Incidence	$2.7\ 10^{-2}$	$2.4\ 10^{-2}$	$2.6\ 10^{-2}$
Mortality	$3.8\ 10^{-4}$	$2.8\ 10^{-4}$	$3.3\ 10^{-4}$

TABLE 6 *Summary of calculated risk factors for NMSC for the UK population (Sv^{-1})*

disappears. A few weeks later erythema returns and may lead to dry desquamation (scaling of the skin), epilation (loss of hair) and via vesiculation (blistering) to moist desquamation (skin breakdown). When moist desquamation is slow to heal, secondary damage to the dermis may occur (ulceration). The extent of the ulceration depends on the ability of the skin to heal which in turn depends on the area affected; small areas heal more effectively. These reactions are caused by a failure of the basal cells to re-populate and the consequent failure to replace the surface cells. The reaction is more severe at higher doses. If healing occurs the repaired skin may be hairless and paler than normal skin.

42 Deterministic effects are characterised by a non-linear sigmoid-type relationship between dose and the proportion of people who show the effect. This sigmoid shape might reflect probabilistic effects within the same individual or a distribution of apparent thresholds among the population[64,65] and there is evidence to support both views. Several different mathematical functions have been used to describe this sigmoid shape. The cumulative normal distribution used in probit analysis has been preferred in ICRP Publication 59, while the Weibull function has been preferred by Evans *et al*[64] and the Board[65]. Both of these distributions are defined for positive values of dose and neither has a threshold. It is therefore common in calculations to insert a threshold to prevent meaningless calculations at low doses. Whether for deterministic effects there is a true threshold below which no clinical effect can occur or whether there is an apparent threshold where the probability of an effect is so small that it cannot be measured, is an open question which applies to all deterministic effects.

43 In ICRP Publication 59 (paragraph 130) it is suggested that moist desquamation is the reaction to be prevented following acute exposure to areas of 5 mm diameter or more, ie the limit should *not* be set to prevent erythema, epilation or dry desquamation which of themselves are not of lasting clinical significance. Based on doses evaluated at 16 μm depth, threshold doses of about 18 Gy have been measured using ^{90}Sr-^{90}Y β-plaques of 22.5 mm diameter or more placed on the skin of pigs. Higher threshold doses were measured with lower energy β-emitting nuclides and with smaller areas exposed. Data on pig skin from Moritz and Henriques[66] show that an acute dose of 10 Gy measured at a depth of 90 μm will not produce moist desquamation. The Board[65] recommends that the probability of occurrence of moist desquamation can be described by a Weibull function with ED_{50} (the dose giving the effect in 50% of cases) of 20 Gy and an arbitrarily imposed threshold of about 10 Gy determined at a depth of 70 μm.

44 Small, highly radioactive particles on the skin ('hot particles') produce spatially non-uniform acute doses to small areas of skin and can produce ulceration. Healing of an ulcer takes the form of scarring, which may be cosmetically disfiguring. In ICRP Publication 59 (paragraph 122) it is suggested that limiting the average dose to 1 Gy over 1 cm^2 at a depth of 100–150 μm is sufficient to prevent early ulceration. In reality, of course, the dose immediately below the particle may be very much higher.

45 ICRP[5] considers dermal thinning to be the late effect to be prevented following protracted exposures but there are no extensive published data to support this. An acute dose of 10 Gy to cells in the dermis produces a 10% reduction in the dermis of pig skin about one year after irradiation. In human beings, a 10% thinning is produced by a dose of 35–40 Gy, given in 2 Gy fractions spanning several weeks[5].

46 Recommending dose limits to ensure protection of the skin from deterministic effects is difficult because different cells within the skin are important for different effects. For erythema and desquamation it is the basal cells in the epidermis that lie generally 20–100 μm below the skin surface which are important. For dermal thinning the sensitive cells are believed to lie more than 500 μm below the skin surface[67].

47 ICRP[6] has synthesised these data to form recommended limits for workers and the public. It notes that the threshold for moist desquamation in large area irradiation ($> 1\ cm^2$) is about 20 Gy measured at a depth of 16 μm. Smaller areas, dose protraction and lower energy β-emitters increase the threshold dose. Cells at a depth of 20–100 μm are important and doses of up to 10 Gy to these cells do not produce moist desquamation. Late effects such as dermal atrophy and damage to the vasculature occur following acute doses above 10 Gy or chronic doses of 30–40 Gy given in 2 Gy fractions. ICRP[6] recommends a $0.5\ Sv\ y^{-1}$ individual organ dose limit for workers which, for low LET radiation, corresponds to 20 Gy over a 40 year working lifetime. This limit guarantees protection of the skin from any deterministic effects. However, the 30–40 Gy 'chronic' threshold comes from observations in radiotherapy patients who received the dose in acute fractions over a few weeks and so the recommendation of 0.5 Sv in a year for radiation workers probably contains a large measure of conservatism. Hot particles merit special attention and ICRP[5] suggests a threshold of 1 Gy averaged over $1\ cm^2$ at a depth of 100–150 μm. ICRP[6] does not recommend a special limit for hot particles but considers that its general limit of 0.5 Sv over any $1\ cm^2$ at a depth of 70 μm adequately protects against this damage. Thus, for hot particles there is a further element of conservatism.

48 For the public, ICRP[6] reduces the deterministic dose limit for workers by a further order of magnitude, ie to $50\ mSv\ y^{-1}$. This reduction is admitted to be arbitrary but could be justified on the basis that members of the public are exposed for about twice as long as workers (80 against 40 years on average) and because members of the public may show a wider range of sensitivity than workers (ICRP Publication 60, paragraph 194). There appears to be no scientific evidence for unacceptable deterministic effects on the skin at either of these dose levels. It could be argued that no special dose limit for members of the public is necessary because there is already sufficient conservatism in the chosen limit for workers.

Summary

49 **1** Exposure to ionising radiation appears to cause NMSCs, of which squamous cell carcinoma and basal cell carcinoma are the two main types. The (incidence) risk of malignant melanoma associated with ionising radiation exposure appears to be much lower than that for NMSC.

2 NMSCs resulting from exposure to ionising radiation are largely concentrated in UVR-exposed areas, which is also where the majority of these cancers occur normally.

3 The lifetime (high dose rate) NMSC incidence risk for a general UK population is estimated at $2.3\ 10^{-2}\ Sv^{-1}$, and $2.6\ 10^{-2}\ Sv^{-1}$ for a working population. The NMSC mortality risk for a general population is $3.1\ 10^{-4}\ Sv^{-1}$, and $3.3\ 10^{-4}\ Sv^{-1}$ for a working population. In both cases the dose is the weighted average evaluated over the whole body at a depth of between 20 and 100 μm below the skin surface, with most of the weight (99.91%) attached to the $3000\ cm^2$ of UVR-exposed skin area. A rounded value of $3.2\ 10^{-4}\ Sv^{-1}$ could be used in both situations.

4 There are strong indications of upward curvature in the NMSC dose–response relationship for the cohort of Japanese atomic bomb survivors, so that a DDREF of at least two should be applied to these figures to obtain NMSC risks at low doses and low dose rates.

5 Values analogous to the ICRP tissue weighting factors have been calculated. The value for UVR-shielded skin is $7.8\ 10^{-6}$ and the value for UVR-exposed skin is $8.6\ 10^{-3}$.

6 Most of the populations which have been studied for the purposes of deriving these risk estimates for ionising radiation exposure, with the exception of the Japanese atomic bomb survivors, are white Caucasian. The risks of NMSC resulting from ionising radiation exposure on UVR-shielded skin, and presumably therefore also on heavily pigmented skin, are lower than the risks of NMSC resulting from exposure on UVR-exposed skin. The risks that are derived, which are dominated by the risks to UVR-exposed skin, are therefore likely to be conservative for non-Caucasian populations.

7 The deterministic effect to be avoided following acute exposure of the skin is moist desquamation. The threshold for this is about 10 Gy evaluated at 70 μm depth below the skin surface.

8 For chronic or fractionated irradiation the deterministic effect of importance is dermal thinning. Annual doses of 0.5 Gy more than 500 μm below the skin surface to the same area of skin are insufficient to cause this effect.

9 Hot particles directly in contact with the skin will not cause significant ulceration provided that the dose averaged over 1 cm^2 is less than 1 Gy, determined at a depth of 100 μm.

IMPLICATIONS FOR DOSE LIMITATION TO THE SKIN

50 It is clear, from the description of biological effects on the skin, that the setting of limits for protection of this tissue is complicated. ICRP[6] points out that the limit on effective dose automatically limits the risk of skin cancer because the tissue weighting factor of 0.01 is based on carcinogenic effects. ICRP recommends that the dose should be calculated at the depth of the basal cell layer which generally lies between 20 and 100 μm over most of the body. There is no specific recommendation concerning the area over which the dose should be averaged but the scientific evidence suggests that the average should be over the 3000 cm^2 of UVR-exposed skin and the dose to the 15 000 cm^2 of covered skin can normally be ignored. However, there may be situations in which the skin dose is dominated by exposure to the UVR-shielded area of skin. Under these circumstances, application of the ICRP tissue weighting factor for skin of 0.01 will lead to a substantial overestimate of the contribution to effective dose and it may be appropriate to apply a modifying factor of 0.001 to this contribution before applying the tissue weighting factor of 0.01.

51 The individual limits for workers of 500 mSv y^{-1} and for the public of 50 mSv y^{-1} are adequate to ensure that no deterministic effects on the skin occur due to acute, chronic or hot particle irradiations. These doses are to be estimated over any 1 cm^2 of skin nominally at a depth of 70 μm[6]. For some radiations, however, such as lower energy β and α particles, where this nominal depth is not reasonable, averaging over 20–100 μm would be more appropriate.

GENERAL METHODOLOGY FOR ASSESSING SKIN DOSES

52 In paragraphs 52–62 a general methodology for calculating skin doses is presented, for both stochastic and deterministic effects, for situations where the equivalent dose either to the whole skin or to sections of the skin is known by measurement or by calculation. It is proposed that the mean depth at which doses should be evaluated is 70 μm (7 mg cm^{-2}). However, when assessing dose in cases of non-uniform exposure, it may be necessary to use thicknesses representative of the skin areas of interest; for example, the thickness of the palms of the hands is given by ICRP[54] as 400 μm (40 mg cm^{-2}).

Equivalent dose for comparison with deterministic dose limit

53 The dose limits for deterministic effects for workers and the public are 500 and 50 mSv y^{-1}, respectively, averaged over any 1 cm^2 area of skin. The maximum equivalent dose over any 1 cm^2 area is the dose to be compared with these limits. In addition, this dose can be used to predict the incidence of deterministic effects, following, say, an accidental release of radionuclides to atmosphere.

Uniform exposure

54 Where the equivalent dose is uniform over the total surface area of the skin then this is the dose to be compared with the deterministic limits since the dose to every square centimetre will be the same.

Non-uniform exposure

55 In cases where the exposure of the skin is non-uniform it is those areas which are most exposed which are relevant for comparison with the deterministic limits. It is the maximum dose averaged over any square centimetre which should be evaluated.

Effective dose for comparison with stochastic dose limit

56 The limits on effective dose for stochastic effects for workers and the public are 20 and 1 mSv y^{-1}, respectively. In the context of skin irradiation, this is largely relevant to situations where irradiation is due to weakly penetrating radiation and the skin is the dominant tissue exposed, eg as in the case of exposure to soft β radiation.

Uniform exposure

57 In this case the contribution of skin irradiation to effective dose is simply the product of the mean equivalent dose to the skin and the tissue weighting factor for skin of 0.01.

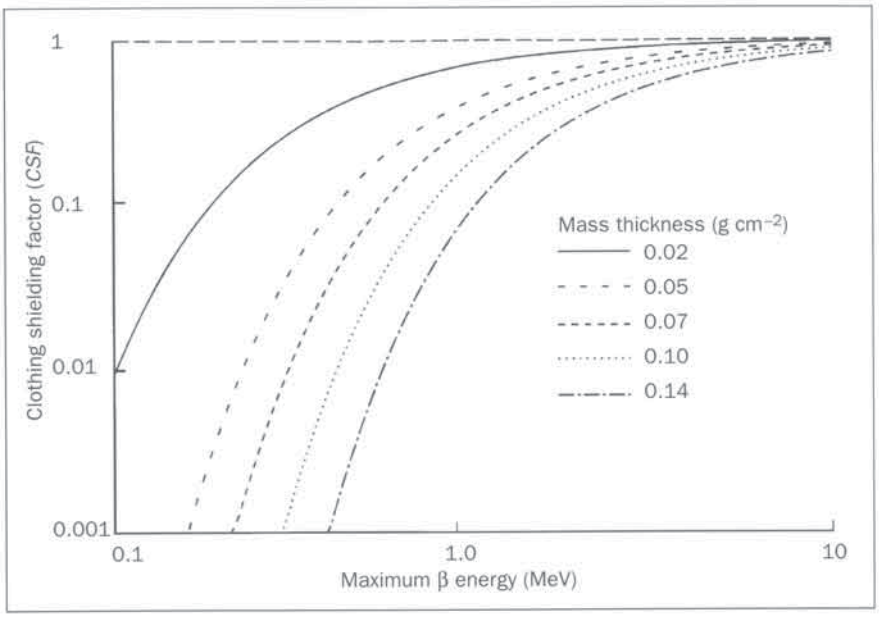
Non-uniform exposure

58 Where the skin is only partially irradiated and the exposed areas are in the UVR-exposed region then for the calculation of effective dose it is the mean dose over the UVR-exposed area which should be evaluated. The UVR-exposed area is taken as 3000 cm^2 and is defined as the face, neck and outer aspects of the hands and arms[5]. In the case of partial exposure of UVR-shielded skin, the mean dose over the UVR-shielded area (15 000 cm^2) should be evaluated and weighted by a factor of 0.001 before applying the tissue weighting factor of 0.01 in order to take account of the lower radiosensitivity (see paragraph 50).

Attenuation of β radiation by clothing

59 In the assessment of equivalent doses or effective doses for comparison with the dose limits for deterministic and stochastic effects, respectively, the attenuation of β radiation by clothing may be an important consideration. This may even be the case for UVR-exposed skin since the ICRP definition includes the outer aspect of the arms,

FIGURE 2 *Clothing shielding factor for β irradiation*[68]



which would normally be clothed out-of-doors in northern Europe. For β radiation the mass attenuation coefficient, μ_m ($cm^2 g^{-1}$), for materials of low atomic number can be calculated by[68]

$$\mu_m(E) \cong 17E^{-1.14}$$

where E is the maximum β energy (MeV).

60 The clothing shielding factor can then be calculated from

$$CSF(E, \chi_m) = e^{-\mu_m(E)\chi_m}$$

where *CSF* is the clothing shielding factor as a function of thickness and β energy and χ_m is the mass thickness of clothing ($g\,cm^{-2}$).

61 Figure 2 shows the clothing shielding factor as a function of maximum β energy and for five values of clothing thickness. Measurements carried out at the Fisheries Laboratory of the Ministry of Agriculture, Fisheries and Food[69], on a range of garments, resulted in thicknesses of 0.07 $g\,cm^{-2}$ for typical summer clothing and 0.14 $g\,cm^{-2}$ for typical winter clothing. Therefore, for a typical β energy of 0.5 MeV the dose reduction due to typical winter clothing is about 0.005 and for typical summer clothing about 0.07.

62 It should be noted that the above formulae apply to dry clothing and that wet clothing will increase the attenuation.

CONCLUSIONS

63 The 1990 recommendations of ICRP introduced the quantity 'effective dose' to replace effective dose equivalent. Skin was included in the computation for the first time with a tissue weighting factor of 0.01. There are some situations in both environmental and occupational dose assessment where partial irradiation of the skin may occur. This

document reviews the biological basis for limitation of doses to the skin and recommends a practical approach for the calculation of skin doses for a variety of exposure situations and, in particular, those where the skin is only partially exposed.

64 There is substantial evidence linking the incidence of non-melanoma skin cancers (NMSCs) to exposure to ionising radiation; for malignant melanoma, the evidence is less compelling and this type of cancer is not considered further. The two main types of NMSC are squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). In white Caucasian populations the incidence of BCC is around five times higher than that of SCC, but the SCC mortality rate is higher than that of BCC because of its greater metastatic potential. The mortality rates for both cancer types are low: the rate for SCC is around 1% and the rate for BCC is probably much less than 0.1%.

65 The sensitive cells for radiation-induced carcinogenesis are thought to be the basal cells of the epidermis. These cells generally lie between 20 and 100 μm below the surface of the skin, although some areas of the skin, eg the palms of the hands and the finger tips, have a significantly deeper basal layer. The dose–response relationship for the induction of NMSC by ionising radiation appears to be strongly curvilinear. Thus, the general dose and dose rate effectiveness factor (DDREF) of two recommended by ICRP is likely to overestimate the risks of NMSC at low doses and dose rates.

66 The available data indicate that the excess relative risk for the induction of NMSC by ionising radiation is considerably higher in skin exposed to ultraviolet radiation (UVR-exposed skin) than in skin shielded from ultraviolet radiation (UVR-shielded skin). This highly supra-multiplicative interaction is unusual.

67 The NMSC mortality risk at high dose rate for the general population of the UK is calculated to be $3.1\ 10^{-4}\ Sv^{-1}$, and for the working population $3.3\ 10^{-4}\ Sv^{-1}$. The majority of the risk, 99.9%, is associated with the 3000 cm^2 of UVR-exposed skin.

68 In calculating skin doses for inclusion in effective dose, the following recommendations are made.

(a) The skin dose should generally be evaluated at the mean basal cell depth of 70 μm. However, in the case of non-uniform exposure, it may be necessary to use the basal cell layer depth for the skin area of interest.

(b) Where the skin is uniformly irradiated, the contribution to effective dose is the product of the mean equivalent dose to skin and the tissue weighting factor for skin of 0.01. However, where skin is only partially irradiated and the exposed areas are in the UVR-exposed region, the mean dose over the UVR-exposed area (3000 cm^2) should be evaluated and multiplied by the tissue weighting factor. In the case of partial exposure of UVR-shielded skin, the mean dose over the UVR-shielded area (15 000 cm^2) should be evaluated and weighted by a factor of 0.001 before applying the tissue weighting factor of 0.01 in order to take account of the lower radiosensitivity.

69 Deterministic effects on the skin include erythema, dry desquamation and moist desquamation. The most significant of these effects from a clinical viewpoint is moist desquamation. The critical cells for this effect are the basal cells in the epidermis that generally lie between 20 and 100 μm below the surface of the skin. The ICRP deterministic dose limits for workers and members of the public of 500 and 50 mSv y^{-1}, respectively, provide more than adequate protection against moist desquamation. The maximum dose equivalent at the appropriate depth over any 1 cm^2 should be compared with these limits.

ACKNOWLEDGEMENTS

This document makes use of data obtained from the Radiation Effects Research Foundation (RERF) in Hiroshima, Japan. RERF is a private foundation funded equally by the Japanese Ministry of Health and Welfare and the United States Department of Energy through the National Academy of Sciences. The conclusions in this paper are those of the authors and do not necessarily reflect the scientific judgement of RERF or its funding agencies. The authors are grateful to Dr Dale Preston, Dr Elaine Ron, Professor Roy Shore, Professor Jack Schull, Dr George Kerr and Dr Michael Fry for many helpful comments.

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Appendix A

EXAMPLE CALCULATIONS OF EFFECTIVE DOSE FROM PARTIAL SKIN IRRADIATION

Skin contamination

A primary example of the need to calculate the effective dose due to skin irradiation may arise in the case of contamination of the hands with a β-emitting radionuclide. This may occur, for example, when a source is handled or following the contamination of the hands with radioactive materials.

In the case of contamination of the hands, the first step is to calculate the equivalent dose to the skin area exposed:

$$H_{skin} = A\,T\,\beta_{skin} \qquad (1)$$

where H_{skin} is the annual equivalent dose to skin ($Sv\,y^{-1}$), A is the activity per unit area of skin ($Bq\,cm^{-2}$), T is the exposure time ($h\,y^{-1}$), and β_{skin} is the skin equivalent dose rate to the basal layer of the skin epidermis for β irradiation[1] [$Sv\,h^{-1}/(Bq\,cm^{-2})$]. This quantity is dependent on skin thickness. The default value for skin thickness, and for comparison with the skin dose limits, is 70 μm (7 $mg\,cm^{-2}$) (see paragraph 51 of the main text). A greater value may be adopted for certain areas of the skin, eg the palms of the hands and finger tips[2] (400 μm).

To calculate the corresponding effective dose the area of the skin exposed is required:

$$E = H_{skin}\; m\; w_{skin}\; \frac{EXP_{area}}{TOTAL_{area}} \qquad (2)$$

where E is the effective dose ($Sv\,y^{-1}$), w_{skin} is the tissue weighting factor (rounded) (=0.01), m is a modifying factor to take account of the lower sensitivity of UVR-shielded skin (=1 for UVR-exposed skin and 10^{-3} for UVR-shielded skin), EXP_{area} is the exposed area (cm^2), and $TOTAL_{area}$ is the total area of either UVR-shielded skin (15 000 cm^2) or UVR-exposed skin (3000 cm^2).

It is recognised that the effective dose due to irradiation of UVR-exposed skin (defined by ICRP[3] as the face, neck and the outer aspect of the hands and arms) will dominate in the majority of situations. It is, therefore, rare that account will need to be taken of the exposure of any UVR-shielded areas when calculating the effective dose. Indeed for most practical exposure situations, involving a small fraction of the total UVR-shielded sites such as the palms of the hands, deterministic effects will be limiting. For example, exposure of the palms[2] (around 200 cm^2) at the skin equivalent dose limit for members of the public of 50 $mSv\,y^{-1}$ implies an effective dose of only $6.7\,10^{-6}$ $mSv\,y^{-1}$. If the whole of the UVR-shielded skin is exposed at the same rate then the effective dose is $5\,10^{-4}$ $mSv\,y^{-1}$. This type of calculation may be of interest when summing doses from a number of different exposure pathways.

Example

A nuclear plant discharges ^{234}Th in secular equilibrium with ^{234m}Pa into an estuary where it is adsorbed on to sediment. Local fishermen spend 2000 h y^{-1} working in the intertidal areas and it is assumed that the backs of their hands are contaminated with mud throughout this period. The activity concentration of ^{234}Th (+ ^{234m}Pa) in the mud is 0.50 MBq kg^{-1}.

The activity concentration per unit area on the skin (Bq cm^{-2}) is given by

$$A_{skin} = \rho\, d\, A_{sed}$$

where ρ is the density of sediment (1.5 10^{-3} kg cm^{-3}), d is the thickness of sediment on the hand (cm) – assumed to be 0.01 cm – and A_{sed} is the activity concentration on sediment (Bq kg^{-1}). Therefore

$$A_{skin} = 7.5 \text{ Bq cm}^{-2}$$

Using equation 1,

$$H_{skin} = 7.5 \times 2000 \times 2.75\ 10^{-6} = \underline{0.04 \text{ Sv y}^{-1}}$$

where β_{skin} is 2.75 10^{-6} Sv h^{-1}/(Bq cm^{-2})[1] (assuming ^{234}Th and ^{234m}Pa in equilibrium and a skin depth of 7 mg cm^{-2}). Using equation 2,

$$E = 0.04 \times 0.01 \times \frac{300}{3000} = \underline{4.0\ 10^{-5} \text{ Sv y}^{-1}}$$

where EXP_{area} is 300 cm^2 (ICRP Publication 23[2]).

In this example the equivalent dose to the skin is just below the deterministic dose limit for members of the public. However, the effective dose is considerably below the relevant dose limit for the general public of 1 mSv y^{-1}.

Exposure to a non-contact source

Examples of this type of exposure occur both in the workplace and in the general environment, eg from a plane source of β-emitting radionuclides on the ground.

In this case it may be assumed, as an approximation, that the UVR-exposed skin area of a person standing upright is uniformly exposed. First an external dose rate measurement, or prediction, is required at a representative height above the ground. Parts of the UVR-exposed skin area may be clothed, for example, the arms. Therefore if a realistic estimate of the effective dose is required, allowance must be made for the dose reduction by clothing. The effective dose may be calculated as follows:

$$E = D\, T\, w_{skin}\, [(CSF \times F_{clothed}) + (F_{unclothed})] \qquad (3)$$

where E is the annual effective dose due to skin irradiation (Sv y^{-1}), D is the dose rate at reference height (Sv h^{-1}), T is the exposure time (h y^{-1}), w_{skin} is 0.01, CSF is the clothing shielding factor (see paragraph 60 of the main text), $F_{clothed}$ is the fraction of UVR-exposed skin covered by clothing, and $F_{unclothed}$ equals $1 - F_{clothed}$.

This approach may also be used for a volume source in air.

Example

A β dose rate measured above sediment contaminated with ^{234m}Pa is 10 μSv h^{-1}. It is known that some wildfowlers spend about 400 h y^{-1} in these intertidal areas.

Using equation 3,

$$E = 10 \times 400 \times 0.01\ [(0.5 \times 0.5) + 0.5] = \underline{30\ \mu Sv\ y^{-1}}$$

where T is 400 h y^{-1}, CSF is 0.5 (for ^{234m}Pa β radiation and a clothing thickness of 0.1 g cm^{-2}), and $F_{clothed}$ is 0.5 (ie half of the UVR-exposed area – arms and neck).

The effective dose calculated in this example is well below the dose limit for the general public.

Computer programs

For more detailed calculations of absorbed doses to skin from β radiation, there is a range of computer programs available. One example is the VARSKIN program for personal computers; this was developed in the USA for the assessment of doses from skin contamination, including hot particles. For more details on this and other computer programs the reader is referred to the ICRU report on dosimetry of external β radiation for radiological protection[4].

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Appendix B

MODEL FITTING TO THE NMSC INCIDENCE DATA FOR THE JAPANESE ATOMIC BOMB SURVIVORS

Methods

The following model is fitted to the non-melanoma skin cancer (NMSC) dataset of the Japanese atomic bomb survivors, analysed by Thompson *et al*[1]. The model assumes that the expected number of NMSC cases in stratum i with dose group d, sex s, average age at exposure a, and average time since exposure t is given by

$$PY_{id}\,\lambda_i \max\left[1 + 1_{d>d_t}[\alpha_s(d-d_t) + \beta(d-d_t)^2]\exp[\gamma(d-d_t)]\left(\frac{a}{25}\right)^{\delta}\left(\frac{t}{25}\right)^{\epsilon}\left(\frac{t+a}{50}\right)^{\phi}, 0\right] \quad (1)$$

where the PY_{id} are the number of (migration-adjusted) person-years of follow-up, the λ_i are the (estimated) baseline (zero dose) NMSC incidence rates, d_t is the (estimated) threshold dose and α_s, β and γ are the (estimated) linear, quadratic and exponential excess relative risk (ERR) coefficients. The variables of age at exposure (a), time since exposure (t) and attained age ($t + a$) are centred by dividing by their approximate average values in the Japanese incidence dataset (25, 25 and 50 years, respectively), thereby stabilising the parameter estimates. The stratification is very similar to that used by Thompson *et al*, the only significant difference being that Thompson *et al* also employed stratification by membership of the Adult Health Study (AHS)[2]. The dose d in sievert is shielded kerma dose, which was also used by Thompson *et al* as a surrogate for skin dose. The latest (DS86) dosimetry system employed in the analyses of Thompson *et al* and in those used in this document does not calculate skin dose, which is computationally difficult to evaluate[3]. For most analyses a neutron relative biological effectiveness (RBE) of 20 is assumed, as recommended by ICRP[4]. The coefficients δ, ϵ and ϕ determine the power adjustments to the ERR by age at exposure, time since exposure and attained age, respectively. The expression $\max[x, 0]$ takes the value x when $x > 0$ and is 0 otherwise. The expression $1_{d>d_t}$ takes the value 1 if $d > d_t$ and otherwise takes the value 0. The exponential adjustment in dose in expression 1, $\exp[\gamma(d - d_t)]$, allows for a possible sterilising effect of ionising radiation at high doses, such as has been observed in various human[5,6] and animal[7] datasets. Following the example of Thompson *et al*, in all the analyses presented here the survivors with a shielded kerma dose of more than 4 Gy are excluded, because of possible errors in the dose estimates at high doses. Additional analyses using all records were also carried out, but (with the exception of Figure B1) these are not reported further, since the conclusions reached were very similar to those from the more restricted analysis. The results of fitting this model to the Life Span Study (LSS) NMSC incidence dataset are presented in Table B1.

In view of the indications of curvilinearity in the dose–response curve, another model was fitted, in which the expected number of NMSC cases in stratum i with dose group d, is given by

$$PY_{id}\,\lambda_i \max\left[1 + 1_{d>d_t}\alpha_s(d-d_t)^k \exp[\gamma(d-d_t)^k]\left(\frac{a}{25}\right)^{\delta}\left(\frac{t}{25}\right)^{\epsilon}\left(\frac{t+a}{50}\right)^{\phi}, 0\right] \quad (2)$$

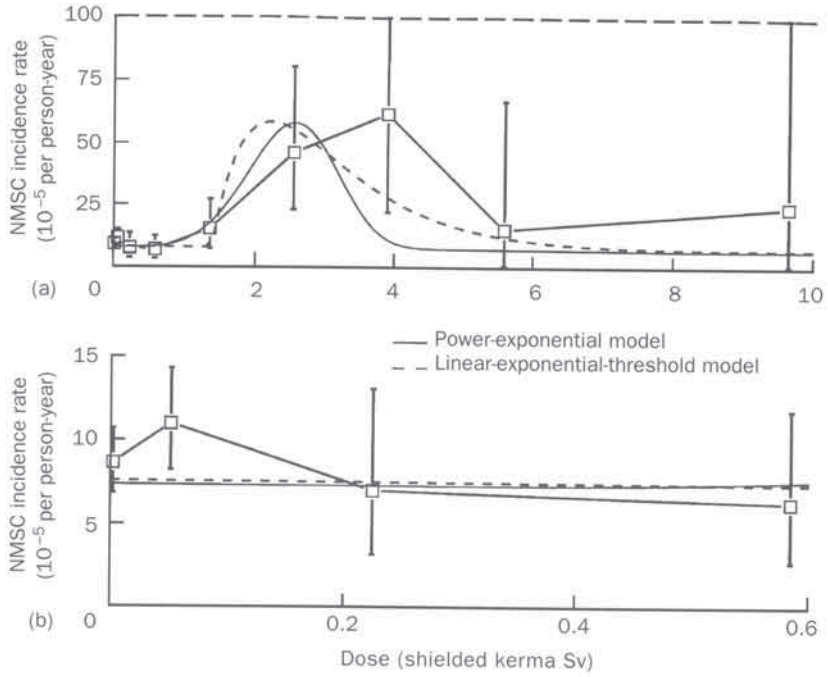


FIGURE B1 *Observed NMSC dose–response in the Japanese atomic bomb survivor cancer incidence dataset, with 95% CI*

Fitted dose–response implied by the two optimal models: power-exponential with fourth power of dose (Table B3) and linear-exponential-threshold (Table B1)

(a) all data (including > 4 Gy shielded kerma survivors),
(b) low dose region of part (a).

Models 1 and 2 incorporate power adjustments to the ERR for age at exposure, time since exposure and attained age. It is desirable also to explore the fit of models with exponential adjustments to the ERR for age at exposure, time since exposure and attained age. Therefore, the following model is also fitted to the Japanese LSS dataset, in which it is assumed that the expected number of NMSC cases in stratum i with dose group d is given by

$$PY_{id}\,\lambda_i \max[1 + \alpha\, d^4 \exp[\gamma\, d^4 + \omega\,(a - 25) + \rho\,(t - 25)], 0] \qquad (3)$$

A quartic-exponential dose–response is used in this model because of the indications from the fits of models 1 and 2 of a strongly curved dose–response relationship. (The fourth power of dose is assumed in model 3 because $k = 4$ is the smallest integral value that is reasonably statistically consistent with the data in fits of model 2, Table B1.) Details of the fits of this model to the Japanese NMSC dataset are presented in Table B2. It should be noted that by constraining the coefficients $\omega = \rho$ the adjustment to the ERR for the effects of age at exposure and time since exposure in expression 3 reduces to $\exp[\rho\,(a + t)]$, ie an exponential function of age attained. This sort of adjustment, as a function of attained age, to the solid cancer ERR has been proposed by Kellerer and Barclay[9].

There have been indications that the DS86 neutron dose estimates in Hiroshima may have been underestimated, particularly for those survivors beyond 1000 m from the

hypocentre[10]. For this reason additional analyses were carried out (reported in Table B3) in which the shielded kerma neutron doses in Hiroshima were multiplied by a factor $\max[0.57 d_{mn}^{-0.39}, 1]$, where d_{mn} is the bone marrow neutron dose in gray, this form of empirical adjustment being suggested by fits of a log-linear model to the data contained in a recent paper by Straume[8]. Table B3 also shows the effects of varying the neutron RBE, both for the unadjusted and for the dose-adjusted fits of the optimal model 2.

As well as fitting models 1–3, the main purpose of which is to elucidate the shape of the NMSC dose–response curve and the extent to which the excess relative risk is modified by the effects of time and age, it is desirable to compare the goodness of fit of the generalised excess relative risk (ERR) and generalised excess absolute risk (EAR) models. For these reasons, the results of fitting a hybrid generalised ERR/EAR risk model to the Japanese atomic bomb survivor cancer incidence dataset are presented in Table B4. The model assumes that the expected number of NMSC cases in stratum i with dose group d is given by

$$PY_{id}\left[\lambda(t,a,s,c)\left(1+\alpha d^4 \exp(\gamma d^4)\left(\frac{a}{25}\right)^{\delta}\left(\frac{t}{25}\right)^{\epsilon}\left(\frac{t+a}{50}\right)^{\phi}\right)\right]^{1-\mu} \times\left[\lambda(t,a,s,c)+\alpha d^4 \exp(\gamma d^4)\left(\frac{a}{25}\right)^{\delta}\left(\frac{t}{25}\right)^{\epsilon}\left(\frac{t+a}{50}\right)^{\phi}\right]^{\mu} \quad (4)$$

and where (in contrast to models 1–3) the background cancer rate $\lambda(t,a,s,c)$ is described by a smooth parametric function

$$\lambda(t,a,s,c) = \exp[\kappa + \pi s + \zeta c + \sigma \ln(t+a) + \tau \ln(t+a)\, s + \chi [\ln(t+a)]^2 + \theta [\ln(t+a)]^2 s + \eta \ln(t) + \Gamma \ln(t)\, s] \quad (5)$$

where $s = 1$ for females (= 0 for males) and $c = 1$ for Nagasaki (= 0 for Hiroshima). This form of model for the background cancer rate is very similar to that used by Thompson *et al*[1] in their analysis of these data. The only differences between the (background) model employed in this document and that used by Thompson *et al* are that they had an extra term adjusting for membership of the AHS and that they did not include the last two terms ($\eta \ln(t) + \Gamma \ln(t)\, s$) adjusting for possible time trends in the background incidence rates. Two special cases of model 4 should be noted, namely when $\mu = 0$, which corresponds to the generalised ERR model, and when $\mu = 1$, which corresponds to the generalised EAR model. Thompson *et al* only considered the generalised ERR model, ie $\mu = 0$.

All parameters in models 1–4 are determined by a maximum-likelihood fit to the data, whereby the numbers of cases in each cell is assumed to be Poisson with mean given by expressions 1–4. The details of the parameter estimates (and 95% profile-likelihood confidence intervals) and also the deviance statistics (= 2 [log(nonparametric maximum-likelihood) − log(maximum-likelihood for the model under consideration)], analogous to the χ^2 goodness-of-fit statistic[11]) are given in Tables B1–B4. It should be noted that for certain of the tests, and in particular those in which the presence of a dose threshold is being assessed, the asymptotic distribution of the deviance difference statistic employed for significance tests is not guaranteed, because of a lack of sufficient smoothness in the likelihood function[12]. This is a general problem with threshold models, which can be circumvented by the hazard-averaging techniques used to model the effects of dosimetric

errors in a recent analysis of this dataset[13]. Monte-Carlo simulations are therefore performed on all tests involving the threshold term, sampling 500 times from the more constrained of the fitted models in each case to assess the deviance difference distribution. The simulations tend to indicate a lower statistical significance than that predicted by the asymptotic distribution, ie the simulated $\mathbb{P}$-values are higher and so less statistically significant, so that for these (four) tests the simulation-based $\mathbb{P}$-values are given (indicated by $\mathbb{P}$-S below).

Shape of the dose–response curve

Table B1 indicates that there is strong evidence for a curvilinear dose–response relationship. In particular, even among linear-quadratic models there are indications that the fit is improved by incorporation of a dose threshold ($\mathbb{P}$-S = 0.17). Above the estimated dose threshold value (of about 1 Sv) there is significant (exponential) curvature in the dose–response curve ($\mathbb{P}$-S = 0.01). Table B1 also demonstrates that the dose–response may be as well described by a simple power of dose ($k \approx 4$) with an exponential sterilisation term (as given by model 2). No further improvement in fit in this power-exponential model is provided by incorporation of a threshold ($\mathbb{P}$-S = 0.21), nor is there improvement in the fit of the threshold-exponential model by allowing a power of dose other than $k = 1$ ($\mathbb{P}$-S = 0.97). The non-linearity in the dose–response relationship for NMSC in this cohort, and in particular the bending over in the dose–response curve at higher doses (over 3 Sv), is easily seen in Figure B1. There are indications at borderline levels of statistical significance of a difference between the sexes ($\mathbb{P} = 0.10$) (Table B1), the ERR for males ($0.3\ \mathrm{Sv}^{-1}$, 95% CI < -0.1–1.2) being somewhat lower than that for females ($1.2\ \mathrm{Sv}^{-1}$, 95% CI 0.5–2.3). Table B3 demonstrates that, at least when a neutron RBE of 20 is assumed, the best estimate of the power of dose k in model 2 is somewhat reduced when the Hiroshima neutron doses are adjusted along the lines indicated above (dose-unadjusted $k = 5.4$, 95% CI 2.6–8.1, dose-adjusted $k = 4.2$, 95% CI 1.9–6.8). However, for values of the neutron RBE of 5 or less the magnitude and shape of the dose–response are much less sensitive to the Hiroshima neutron dose adjustments, as Table B3 also demonstrates (eg when RBE = 5, dose-unadjusted $k = 4.1$, 95% CI 2.8–6.1, dose-adjusted $k = 4.1$, 95% CI 2.8–9.7).

Additional analyses of the Japanese NMSC data demonstrate that after adjustments to the Hiroshima neutron doses along the lines discussed above, the best estimate of the neutron RBE using the optimal model (with quartic-exponential dose–response) is 1.3 (95% CI < 0–7.1)[14]. That possible upward revisions in neutron doses should have such importance for the skin is unremarkable, since the neutron to gamma dose ratio for the skin is generally higher than that for any other organ in the LSS data. Skin doses to the Hiroshima survivors are approximately doubled (when a neutron RBE of 20 is employed) after adjustments to the Hiroshima neutron dose estimates of the sort used here[14].

Time and age variations in relative risk

There is a highly significant reduction in ERR with increasing age at exposure ($\mathbb{P} < 0.001$) (Table B2). There is no significant improvement in fit if an additional (exponential) term adjusting for time since exposure variations in ERR is included in the model ($\mathbb{P} = 0.30$) (Table B2). The fit of a model using only an adjustment for attained age, which as noted above is equivalent to one in which the parameter constraint $\omega = \rho$ is imposed, is significantly worse than that of a model incorporating adjustments for age at exposure and time since exposure, ie in which ω and ρ are not constrained to be equal ($\mathbb{P} < 0.01$) (Table B2).

Text continues on page 38

TABLE B1 *Deviance statistics for fits of various generalised relative risk models (models 1 and 2) to all NMSC incident cancers in the Japanese atomic bomb survivors with shielded kerma dose < 4 Gy: parameter estimates and 95% CI*

Model*	Deviance (df)	Linear (Sv^{-1}) ($= \alpha_s$)	Quadratic (Sv^{-2}) ($= \beta$)	Power of dose ($= k$)	Exponential dose (Sv^{-1}) ($= \gamma$)	Dose threshold (Sv) ($= d_t$)	Power of attained age ($= \phi$)	Power of time since exposure ($= \epsilon$)
Model 1								
L	413.08 (2335)	0.8 (0.4 to 1.5)	—	—	—	—	—	—
L × Sex	410.37 (2334)	0.3 (<−0.1 to 1.2)† 1.2 (0.5 to 2.3)‡	—	—	—	—	—	—
L, A, Y	397.38 (2333)	0.6 (0.1 to 1.8)	—	—	—	—	−5.3 (−11.1 to −2.2)	5.2 (1.6 to 12.5)
Q, A, Y	399.14 (2333)	—	0.3 (0.05 to 0.6)	—	—	—	−4.7 (−8.2 to −2.0)	4.5 (1.5 to 9.1)
L, Q, A, Y	397.38 (2332)	0.6 (−0.3 to 2.6)	0.005 (−0.4 to 0.5)	—	—	—	−5.3 (−11.9 to −2.2)	5.2 (1.6 to 13.4)
L, T, A, Y	390.73 (2332)	1.3 (0.3 to 3.6)	—	—	—	0.6 (0.3 to 1.3)	−4.3 (−7.6 to −1.9)	4.1 (1.5 to 8.3)
L, Q, T, A, Y	377.64 (2331)	6.0 (1.7 to 13.3)	−1.6 (−3.8 to −0.4)	—	—	1.2 (0.8 to 1.4)	−4.2 (−7.2 to −2.0)	3.9 (1.4 to 7.8)
L, X, T, A, Y	377.40 (2331)	18.3 (3.5 to 62.6)	—	—	−1.2 (−2.3 to −0.4)	1.4 (1.0 to 1.6)	−4.2 (−7.3 to −2.0)	4.1 (1.5 to 8.1)
Model 2								
P, A, Y	396.83 (2332)	0.5 (0.1 to 1.9)	—	1.4 (0.3 to 2.2)	—	—	−4.6 (−63.2 to −1.9)	4.4 (1.4 to 67.8)
P, T, A, Y	381.11 (2331)	2.5 (0.04 to 8.6)	—	0.06 (0.04 to 0.5)	—	1.5 (1.2 to 1.5)	−6.4 (−27.2 to −2.5)	6.9 (2.0 to 29.9)
P, X, A, Y	380.64 (2331)	0.2 (0.01 to 1.0)	—	5.4 (2.6 to 8.1)	−0.007 (−0.06 to −0.0005)	—	−4.5 (−7.6 to −2.2)	3.8 (1.2 to 7.8)
P, X, T, A, Y	377.40 (2330)	18.4 (0.6 to 62.4)	—	1.0 (0.1 to 6.4)	−1.2 (−2.5 to −0.04)	1.4 (< 0 to 1.6)	−4.2 (−7.3 to −2.0)	4.1 (1.5 to 8.2)

* *L* = Linear; *Q* = Quadratic; *X* = Exponential; *T* = Threshold; *P* = Power; *A* = Attained age, power adjustment; *Y* = Years since exposure, power adjustment.
† ERR for males = α_m.
‡ ERR for females = α_f.

TABLE B2 *Deviance statistics for fits of generalised relative risk models (models 2 and 3 with exponential and power adjustments to the ERR, quartic-exponential dose–response) to NMSC incident cancers in the Japanese atomic bomb survivors with shielded kerma dose < 4 Gy: parameter estimates and 95% CI*

		Exponential adjustments to relative risk†			Power adjustments to relative risk		
Model*	Deviance (df)	Age at exposure	Time since exposure	Attained age	Age at exposure ($= \delta$)	Time since exposure ($= \epsilon$)	Attained age ($= \phi$)
Model 3 (exponential adjustments to ERR)							
—	399.88 (2334)	—	—	—	—	—	—
E_e	386.02 (2333)	−8.0 (−14.2 to −3.7)	—	—	—	—	—
Y_e	396.67 (2333)	—	6.9 (−0.6 to 17.9)	—	—	—	—
A_e	393.15 (2333)	—	—	−5.0 (−9.3 to −1.3)	—	—	—
A_e, Y_e	384.96 (2332)	−8.1 (−14.4 to −3.4)	4.2 (−3.5 to 14.9)	—	—	—	—
Model 2 with k = 4 (power adjustments to ERR)							
E_p	387.51 (2333)	—	—	—	−1.1 (−1.8 to −0.5)	—	—
Y_p	396.10 (2333)	—	—	—	—	2.0 (0.0 to 5.2)	—
A_p	391.80 (2333)	—	—	—	—	—	−2.6 (−4.6 to −0.9)
E_p, Y_p	385.73 (2332)	—	—	—	−1.1 (−1.9 to −0.5)	1.4 (−0.6 to 4.1)	—
E_p, A_p	387.50 (2332)	—	—	—	−1.2 (−2.5 to −0.1)	—	0.2 (−3.0 to 3.9)
Y_p, A_p	382.16 (2332)	—	—	—	—	3.8 (1.2 to 8.0)	−4.5 (−7.7 to −2.2)
E_p, Y_p, A_p	380.35 (2331)	—	—	—	2.2 (−0.8 to 6.3)	9.4 (1.6 to 23.2)	−13.0 (−31.3 to −1.5)
Model 2 with k = 4 and additional exponential adjustment for age at exposure (hybrid exponential/power adjustments to ERR)							
E_e, Y_p, A_p	381.17 (2331)	9.4 (−8.9 to 31.7)	—	—	—	6.5 (0.6 to 14.7)	−8.8 (−19.2 to 0.1)

* E_e = age at exposure, exponential adjustment; Y_e = years since exposure, exponential adjustment; A_e = attained age, exponential adjustment; E_p = age at exposure, power adjustment; Y_p = years since exposure, power adjustment; A_p = attained age, power adjustment.

† Figures shown are 100[exp (ω) − 1] for the age at exposure adjustment (ie the percentage change in ERR for each year of age at exposure), 100[exp (ρ) − 1] for the years since exposure/attained age adjustment (ie the percentage change in ERR for each year since exposure/year of attained age).

TABLE B3 *Parameters and 95% CI for optimal model (generalised ERR model 2 with power-exponential dose–response and with time since exposure and attained age power adjustments to the ERR) fitted to NMSC incident cancers in the Japanese atomic bomb survivors with shielded kerma dose < 4 Gy, and the effect of neutron RBE and adjustments to Hiroshima neutron doses*[a]

Model	RBE	Linear (Sv^{-1}) ($= \alpha$)	Power of dose ($= k$)	Exponential dose (Sv^{-1}) ($= \gamma$)	Power of attained age ($= \phi$)	Power of time since exposure ($= \epsilon$)
Power of dose unconstrained; unadjusted doses	20	0.2 (0.01 to 1.0)	5.4 (2.6 to 8.1)	−0.007 (−0.06 to −0.0005)	−4.5 (−7.6 to −2.2)	3.8 (1.2 to 7.8)
	10	0.5 (0.07 to 1.7)	3.9 (2.6 to 5.8)	−0.03 (−0.1 to −0.005)	−4.5 (−7.6 to −2.1)	4.1 (1.4 to 8.3)
	5	0.6 (0.08 to 2.0)	4.1 (2.8 to 6.1)	−0.03 (−0.1 to −0.005)	−4.7 (−7.8 to −2.3)	4.4 (1.6 to 8.6)
	1	0.7 (0.09 to 2.4)	4.4 (2.9 to 6.9)	−0.04 (−0.1 to −0.006)	−4.9 (−8.0 to −2.4)	4.6 (1.7 to 8.9)
Power of dose unconstrained; adjusted Hiroshima doses	20	0.05 (0.002 to 0.5)	4.2 (1.9 to 6.8)	−0.004 (−0.05 to −0.0008)	−4.2 (−7.7 to −1.7)	3.4 (0.8 to 8.6)
	10	0.07 (0.006 to 0.5)	5.9 (3.0 to 9.1)	−0.003 (−0.03 to −0.0001)	−3.8 (−6.8 to −1.5)	3.1 (0.8 to 6.8)
	5	0.4 (0.07 to 1.3)	4.1 (2.8 to 9.7)	−0.02 (−0.08 to −0.004)	−4.3 (−7.4 to −2.0)	3.9 (1.3 to 8.0)
	1	0.6 (0.09 to 2.2)	4.4 (2.9 to 6.6)	−0.04 (−0.1 to −0.006)	−4.8 (−7.9 to −2.4)	4.5 (1.6 to 8.7)
Power of dose constrained ($k = 4$); unadjusted doses	20	0.4 (0.06 to 1.0)	4	−0.02 (−0.04 to −0.006)	−4.5 (−7.7 to −2.2)	3.8 (1.2 to 8.0)
	10	0.4 (0.1 to 1.2)	4	−0.03 (−0.06 to −0.01)	−4.5 (−7.6 to −2.2)	4.1 (1.4 to 8.4)
	5	0.6 (0.2 to 1.6)	4	−0.04 (−0.07 to −0.02)	−4.6 (−7.7 to −2.3)	4.3 (1.6 to 8.6)
	1	0.8 (0.2 to 2.2)	4	−0.06 (−0.1 to −0.03)	−4.7 (−7.8 to −2.4)	4.5 (1.6 to 8.7)
Power of dose constrained ($k = 4$); adjusted Hiroshima doses	20	0.06 (0.008 to 0.2)	4	−0.005 (−0.01 to −0.001)	−4.2 (−7.7 to −1.8)	3.4 (0.8 to 7.6)
	10	0.3 (0.05 to 0.6)	4	−0.02 (−0.03 to −0.005)	−4.2 (−7.3 to −1.9)	3.5 (1.0 to 7.5)
	5	0.4 (0.1 to 1.1)	4	−0.03 (−0.06 to −0.01)	−4.3 (−7.3 to −2.0)	3.9 (1.3 to 7.9)
	1	0.8 (0.2 to 2.0)	4	−0.05 (−0.1 to −0.03)	−4.7 (−7.7 to −2.3)	4.4 (1.6 to 8.6)

TABLE B4 *Deviance statistics for fits of hybrid generalised relative/absolute risk model (model 4, with quartic-exponential dose–response) to NMSC incident cancers in the Japanese atomic bomb survivors with shielded kerma dose < 4 Gy: estimates of model mixing parameter (= μ) and 95% CI*

NMSC background term*	Dose modification*	Deviance (df)	Mixing parameter (= μ)†
Relative risk models			
Constant, Sex, City, ln A × Sex, ln A^2 × Sex, ln Y × Sex	Y, A	649.68 (2686)	0.0
Constant, City, ln A × Sex, ln A^2 × Sex, ln Y × Sex	Y, A	651.61 (2687)	0.0
Constant, Sex, ln A × Sex, ln A^2 × Sex, ln Y × Sex	Y, A	650.19 (2687)	0.0
Constant, Sex, City, ln A, ln A^2 × Sex, ln Y × Sex	Y, A	651.99 (2687)	0.0
Constant, Sex, City, ln A × Sex, ln A^2, ln Y × Sex	Y, A	652.27 (2687)	0.0
Constant, Sex, City, ln A × Sex, ln Y × Sex	Y, A	665.85 (2688)	0.0
Constant, Sex, City, ln A × Sex, ln A^2 × Sex, ln Y	Y, A	649.69 (2687)	0.0
Constant, Sex, City, ln A × Sex, ln A^2 × Sex	Y, A	650.44 (2688)	0.0
Constant, ln A, ln A^2	E	663.98 (2693)	0.0
Constant, ln A, ln A^2	Y	673.20 (2693)	0.0
Constant, ln A, ln A^2	A	670.61 (2693)	0.0
Constant, ln A, ln A^2	E, Y	661.34 (2692)	0.0
Constant, ln A, ln A^2	E, A	663.96 (2692)	0.0
Constant, ln A, ln A^2	Y, A	657.08 (2692)	0.0
Constant, ln A, ln A^2	E, Y, A	656.33 (2691)	0.0
Absolute risk models			
Constant, ln A, ln A^2	E	671.99 (2693)	1.0
Constant, ln A, ln A^2	Y	663.41 (2693)	1.0
Constant, ln A, ln A^2	A	673.86 (2693)	1.0
Constant, ln A, ln A^2	E, Y	663.25 (2692)	1.0
Constant, ln A, ln A^2	E, A	668.46 (2692)	1.0
Constant, ln A, ln A^2	Y, A	662.76 (2692)	1.0
Constant, ln A, ln A^2	E, Y, A	661.93 (2691)	1.0
Hybrid relative/absolute risk models			
Constant, ln A, ln A^2	E	662.46 (2692)	−0.06 (−0.18 to 0.04)
Constant, ln A, ln A^2	Y	663.21 (2692)	1.18 (0.36 to 2.41)
Constant, ln A, ln A^2	A	669.13 (2692)	−0.06 (−0.16 to 0.05)
Constant, ln A, ln A^2	E, Y	659.23 (2691)	−0.08 (−0.18 to 0.03)
Constant, ln A, ln A^2	E, A	662.44 (2691)	−0.06 (−0.18 to 0.04)
Constant, ln A, ln A^2	Y, A	655.64 (2691)	−0.06 (−0.16 to 0.05)
Constant, ln A, ln A^2	E, Y, A	655.12 (2690)	−0.06 (−0.16 to 0.06)

* E = age at exposure, power adjustment; Y = years since exposure, power adjustment; A = attained age, power adjustment.
† μ = 0 corresponds to a relative risk model; μ = 1 corresponds to an absolute risk model.

The publicly available form of the RERF NMSC data that has been analysed in this document does not allow for separate analysis of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). The analysis of the same NMSC data by Thompson *et al*[1] and further analyses conducted by Mabuchi *et al*[15] indicate that the excess risk is confined to BCC. This confirms the weak indications (based on 2 controls and 0 cases) of an absence of risk for SCC in the Israeli *tinea capitis* case–control study[16]. However, in the Israeli study the irradiated areas were predominantly the head and neck, where BCC tends to predominate (over SCC)[17,18]. Excess SCC has been observed in various groups of early radiologists[19], who frequently received large doses of ionising radiation to the hands. On the hands, SCC occurs relatively more frequently than BCC[17,18].

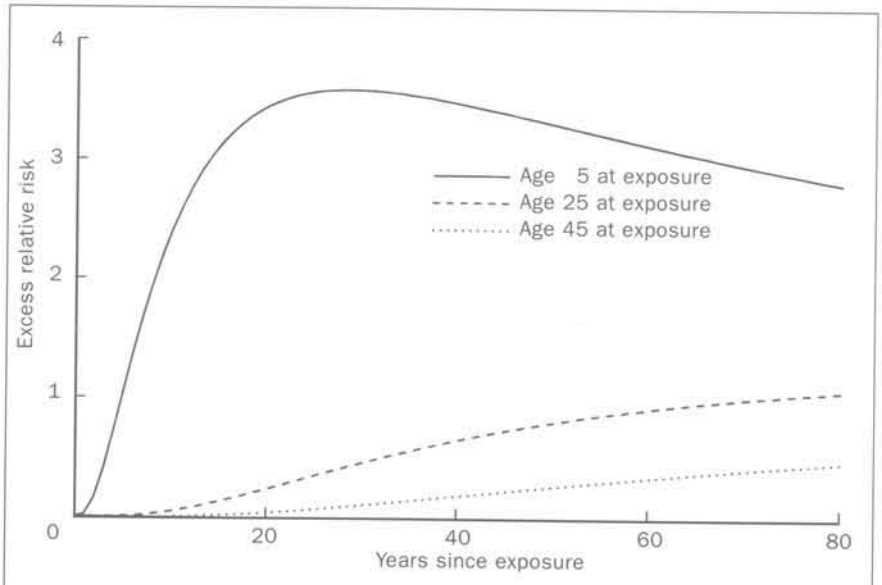
There are indications from recent RERF analyses[15] that the ERR is higher on UVR-shielded skin than on UVR-exposed skin, in apparent contradiction of the results of ICRP Publication 59[20]. However, all but one of the UVR-exposed-site studies considered in ICRP Publication 59 and listed in Table 1 of the main text were for exposures in childhood, while all but one of the UVR-shielded-site studies examined in ICRP Publication 59 and listed in Table 2 of the main text were for exposures in adulthood. Given the pronounced reduction of ERR with increasing age at exposure, it is possible that this variable confounded the comparison of the UVR-exposed and UVR-shielded studies considered in ICRP Publication 59. An approximate estimate of the impact of such a confounding factor can be made. On the assumption that the age at exposure of the groups considered in Table 2 is on average 30 years greater than that of the datasets of Table 1, and the assumption of an 8% reduction of ERR for each year of age at exposure (Table B2), the measure of ERR derived from the UVR-shielded studies listed in Table 2 that should be used for comparison with the ERR derived from the UVR-exposed studies listed in Table 1 is $-0.0085/0.92^{30}\,Sv^{-1} = -0.10\,Sv^{-1}$, the (person-year weighted) 90% CI for which (−0.27–3.85) is seen to include the best estimate ($0.68\,Sv^{-1}$) for the UVR-exposed ERR.

It should be noted that the patterns of solar radiation exposure in the Japanese population may be different from those in most Caucasian populations, which comprise the bulk of the studies considered by ICRP Publication 59. Present-day Japanese women are rarely exposed to UVR because they use parasols when outside even for short walks; Japanese men often use wide-brimmed hats when working in the sun[21]. However, it seems that the patterns of solar radiation exposure in the Japanese population four or five decades ago may have been appreciably different from the present pattern[22]. For example, 50 or so years ago it was common to see Japanese manual labourers clad only in a fundoshi, a simple breech cloth, particularly in summer when much of Japan can be quite humid[22].

Taken at face value the much higher relative risks for UVR-exposed skin compared with UVR-shielded skin calculated in ICRP Publication 59 imply a highly supra-multiplicative interaction between the relative risk arising from ionising radiation exposure and that due to UVR exposure. This hypothesis derives some support from the study of Modan *et al*[23], which suggests that summer sunbathing increased the relative risks of skin cancer in the Israeli group treated for *tinea capitis*. In general, the interactions between risk factors in epidemiological studies have been found to range between the additive and the multiplicative. For example, the interaction between smoking and radiation, as risk factors for lung cancer, is more additive than multiplicative in the LSS cohort of Japanese atomic bomb survivors[24], although the interaction in various groups of underground

miners is more multiplicative[25]. Breslow and Day[26] argued that a multiplicative interaction applies to many risk factors for a variety of cancers (eg asbestos and smoking for lung cancer), the combined effects of which have been investigated in epidemiological studies. Consequently, a supra-multiplicative interaction of the intensity implied by the ICRP Publication 59 analysis, would be a highly unusual phenomenon.

Table B2 indicates that, among generalised ERR models with a quartic-exponential dose–response and power adjustments for age at exposure, time since exposure and attained age, the optimal adjustments to the ERR are given by powers of time since exposure and attained age, rather than by exponential functions of these variables. The optimal model is shown in Figure B2. (A quartic-exponential dose–response is used because $k = 4$ is the minimum integral value of the power of dose in model 2 that is reasonably statistically consistent with the data, Table B1.) In particular, the fit of this model is significantly better than that of a model with a power adjustment to the ERR for time since exposure only ($\mathbb{P} < 0.001$) or one with adjustment for attained age only ($\mathbb{P} < 0.01$) (Table B2). No further significant improvement in fit is provided by a power adjustment of the ERR for age at exposure ($\mathbb{P} = 0.18$). As indicated above, among models with exponential adjustments to the ERR the optimal model is one with adjustment for age at exposure. There are indications at borderline levels of statistical significance that the fit of the model which incorporates an exponential adjustment to the ERR for age at exposure and power adjustments to the ERR for time since exposure and attained age is superior to that of the model with only an exponential age at exposure adjustment ($\mathbb{P} = 0.09$) (Table B2). There are no indications that this first model fits significantly better than the model with only power adjustments for time since exposure and attained age ($\mathbb{P} = 0.32$).



ERR predicted by the optimal model: power-exponential with fourth power of dose, power adjustments to ERR for time since exposure, attained age (Table B3), as a function of age at exposure and time since exposure.

FIGURE B2 *Excess relative risk (ERR) at 1 Sv in the Japanese atomic bomb survivor cancer incidence dataset*

It should be noted that the optimal ERR model, which indicates that the ERR is given by $\alpha\, d^4 \exp(\gamma\, d^4)\, t^{3.8}\, (t + a)^{-4.5}$ (Table B2 and Figure B2), predicts that the ERR will (for constant time since exposure) diminish with increasing age at exposure. Moreover, the rate of decrease of ERR with age at exposure will diminish with increasing time since exposure, ie the effect of age at exposure on ERR is proportionally greatest a short time after exposure, as demonstrated by Figure B2. Equally, for constant age at exposure the ERR will eventually (for $t > 5.7a$) diminish with increasing time since exposure, and this speed of reduction will be greatest for those at the youngest ages of exposure, as shown in Figure B2. This model therefore implies that lifetime NMSC risks would be somewhat lower than those predicted by models which assume that the ERR only varies with age at exposure.

Generalised relative risk model versus generalised absolute risk model

Table B4 indicates that, among generalised ERR models with a quartic-exponential dose–response and with adjustment to the ERR using powers of time since exposure and attained age, exponential adjustments in $\ln(t + a)$ and $[\ln(t + a)]^2$ adequately describe the background cancer rates. (A quartic-exponential dose–response and time since exposure and attained age adjustments to the ERR are used because of the findings of the analysis presented in Tables B1–B3.) The analysis presented in Table B4 reinforces the conclusions derived from the analysis presented in Table B2, namely that the optimal adjustments to the ERR are powers of time since exposure and attained age. The fits of all the generalised EAR models are unsatisfactory. The best fitting generalised EAR model is one with adjustment to the EAR for time since exposure, but the fit of this model is significantly worse than the hybrid ERR/EAR model with adjustment for time since exposure and attained age ($\mathbb{P} = 0.02$) (Table B4). Consequently, on grounds of parsimony, the optimal model is the generalised ERR model with power adjustments to the ERR for time since exposure and attained age.

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Glossary

Absolute risk projection model used for modelling radiation-induced cancer risk, in which the excess risk after some period of latency is assumed to be a constant.

Adult Health Study (AHS) subcohort of the LSS established in 1958 and subject to biennial medical examinations.

Basal cell attaching cell in lowest layer of stratified tissue.

Basal cell carcinoma (BCC) epithelial tumour of skin originating from basal cells of the epidermis or hair follicles – usually occurs as pearly nodule or plagued with central depression.

Case–control study an investigation into the extent to which a group of persons with a specific disease (the cases) and comparable persons who do not have the disease (the controls) differ with respect to exposure to putative risk factors.

Cohort study an investigation involving the identification of a group of individuals (the cohort) about whom certain exposure information is collected, and the ascertainment of the occurrence of diseases at later times. For each individual, information on prior exposure can be related to subsequent disease experience.

Confidence interval (CI) an interval calculated from data when making inferences about an unknown parameter. In hypothetical repetitions of the study, the interval will include the parameter in question on a specified percentage of occasions (eg 95% for a 95% confidence interval).

Dermis layer of the skin deep to the epidermis, comprising a dense bed of vascular connective tissue; also called the corium.

Desquamation shedding of surface layer of the skin.

Dose and dose rate effectiveness factor (DDREF) defined as the ratio D_L/D_H, where D_L is the dose of radiation delivered at low doses (<0.2 Gy) and low dose rates (<0.1 Gy per hour) which has the same biological effect as a dose D_H delivered at a high dose or high dose rate.

Dosimetry System 1986 (DS86) the most current set of dose estimates for the survivors of the atomic bombings in Hiroshima and Nagasaki, which superseded the older T65DR dosimetry system in the mid-1980s.

Epidermis the outermost and non-vascular layer of the skin.

Hot particle small radioactive particle of high specific activity.

Keratin simple insoluble protein with structural and protective functions. Present in skin, hair, and nails.

Keratinisation intracellular deposition of keratin.

Keratinocyte the skin cell which synthesises keratin.

Life Span Study (LSS) Cohort study of survivors of the atomic bombings of Hiroshima and Nagasaki, established in October 1950 and followed up for mortality and tumour incidence.

Melanin group of black, dark-brown, or reddish pigments present in the skin. Produced in melanocytes and stored in melanosomes.

Melanocyte dendritic clear cell of the epidermis that synthesises the pigment melanin.

Melanoma tumour arising from the melanocyte system of the skin and other organs. When used alone refers to malignant melanoma.

Metastasis process where cells break away from a tumour and spread around the body (verb: metastasise).

Non-melanoma skin cancer (NMSC) cancers that are not melanomous, eg squamous and basal cell carcinomas.

Squamous cell carcinoma (SCC) a tumour arising from neoplastic transformation of cells in the epidermis, possibly those in the early stages of keratinisation.

Radiation Effects Research Foundation (RERF) the binationally (US–Japanese) funded private foundation responsible for performing studies on the survivors of the atomic bombings in Hiroshima and Nagasaki.

Relative biological effectiveness (RBE) of a given dose D_q of some specified type q of radiation is defined as $RBE_q(D_q) = D_r/D_q$, where D_r is the dose of the reference radiation (usually x rays or γ rays) required to produce the same biological effect.

Relative risk (RR) the ratio of the disease rate in a group under study to that in a comparison group, with adjustment for confounding factors such as age, if necessary.

Relative risk projection model used for modelling radiation-induced cancer risk, in which the excess risk after some period of latency is assumed to be a constant multiple of the underlying spontaneous risk.

Ultraviolet radiation (UVR) electromagnetic radiation in the wavelength range 100 to 400 nm.

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