Radiat Environ Biophys (2001) 40:249–257 

ORIGINAL PAPER

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# On the conversion of solid cancer excess relative risk into lifetime attributable risk

Received: 5 April 2001 / Accepted: 1 July 2001

**Abstract** Risk coefficients representing the lifetime radiation-induced cancer mortality (or incidence) attributable to an exposure to ionizing radiation, have been published by major international scientific committees. The calculations involve observations in an exposed population and choices of a standard population (for risk transportation), of suitable numerical models, and of computational techniques. The present lack of a firm convention for these choices makes it difficult to inter-compare risk estimates presented by different scientific bodies. Some issues that relate to a necessary harmonization and standardization of risk estimates are explored here. Computational methods are discussed and, in line with the approach utilized by ICRP, conversion factors from *excess relative risk* (*ERR*) to *lifetime attributable risk* (*LAR*) are exemplified for exposures at all ages and for occupational exposures. A standard population is specified to illustrate the possibility of a simplified standard for risk transportation computations. It is suggested that a more realistic perception of lifetime risk could be gained by the use of coefficients scaled to the lifetime spontaneous cancer rates in the standard population. The resulting quantity *lifetime fractional risk* (*LFR*) is advantageous also because it depends much less on the choice of the reference population than the lifetime attributable risk (*LAR*).

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## Introduction

The derivation of nominal risk coefficients for ionizing radiation is a 2-step process. Epidemiological data from a *study population*, such as the observations of the solid cancer or the leukemia mortality (or incidence) rates among the A-bomb survivors, are first modeled to derive the excess absolute risk (*EAR*) or the excess relative risk (*ERR*) in their dependence on various parameters such as dose, *D*, sex, *s*, age at exposure, *e*, and/or age attained, *a*. The excess risk or excess relative risk is then, in a second step, "transported" to an idealized or real *reference population* and is expressed in terms of lifetime attributable risk per unit dose. This entails an integration over the ages at exposure that are considered and the periods at risk. The transport of *ERR* requires an integration also over the background cancer mortality (or incidence) rate, $m(a)$, in the reference population. Risk coefficients are, thus, dependent not only on the observation in an exposed population, but also on the background cancer rates and the life table data of the selected reference population.

The International Commission on Radiological Protection (ICRP) has introduced the notion of the nominal risk coefficient and has in the last general recommendations [1] presented risk estimates that were obtained from the observations on the A-bomb survivors and were then expressed, on the basis of computations by Land and Sinclair [2], in terms of average values for five reference populations, US, UK, Japan, China, and Puerto Rico. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) in a major new assessment [3] has invoked the same five reference populations and has presented new risk estimates that will serve as guideline for regulatory decisions in radiation protection; the results will also be used as bench marks for comparisons with other numerical exercises. However, such exercises will be impeded by the lack of a clear convention on the population data to be used in the risk transport and on the definitions that are to be employed.

Land and Sinclair [2] have, in fact, in their computations for ICRP documented the input data in terms of the *equilibrium* survival functions (*actuarial* survival functions) for the five reference populations and the age-specific solid cancer mortality rates, and they have used a computational procedure that offers itself as a convention. By invoking the same five reference populations, UNSCEAR [3] has given the impression that it accepted the convention. But somewhat different and more complex input data were used, which have not been published. In addition, the concepts and quantities that were employed were similar but not equal. A current reevaluation [4], which explores new modeling procedures, highlights the resulting difficulty of arriving at a meaningful comparison of risk estimates that are based on different and only partly documented procedures. The subsequent considerations are meant to clarify some of the issues and to contribute towards the necessary harmonization of input data and of concepts and computational details.

Radiation-risk estimates tend to be scrutinized to a level of precision that is out of balance with their inherent degree of uncertainty. While unnecessary precision can be misleading, it is nevertheless essential in an often controversial discussion on risk coefficients to work with numbers that can be traced precisely to their computational origin and that can be reliably compared. The transport of risk from the study population to the reference populations contains inherent uncertainties and requires unproven assumptions. But this unavoidable uncertainty does not justify lack of rigor. When different studies make different *ad hoc* choices in the selection of population data and in the details of rather complex computations, the choices need not have major overall impact, but they need to be clearly defined unless they obscure the results and their dependence on various aspects of the risk modeling.

## Concepts and quantities

The subsequent considerations can be kept on a fairly simple level. For a deeper analysis of the various concepts and quantities and their interrelation, the reader is referred to the treatment by Vaeth and Pierce [5], to the paper by Thomas et al. [6], and to the summaries in earlier UNSCEAR reports [7, 8].

### Relative risk or absolute risk transportation

Before specific quantities are considered, one major issue needs to be determined. This is the choice whether the excess *relative* risk or the excess *absolute* risk is taken to be the same in the study population and in the reference population. When individual tumor sites are considered, the choice between *relative risk* (*RR*) *transportation* and *absolute risk* (*AR*) *transportation* will vary according to circumstances, and in some cases it may be necessary to employ intermediate procedures. However, when all solid tumors are combined, the choice between the *RR* and the *AR* transportation is not critical; UNSCEAR [3] obtained with the *AR* transportation risk coefficients that are about 10% less than those obtained by the *RR* transportation. In the interest of simplicity only *RR* transportation will be considered here.

### Lifetime attributable risk, *LAR*

The formal expression of the risk coefficient needs to be considered next. In radiation protection considerations the risk coefficient is usually taken to be the average of the coefficients for the two genders. However, to simplify the subsequent formulae, all quantities will be taken to be sex specific unless otherwise noted. Reference will here be made to the quantity *LAR* which is defined below. But more complicated quantities (*REID* and *ELR*) have been considered and while they may not be required in practice, their definitions and their relation to *LAR* are, nevertheless, explained in a subsequent section.

Most commonly, risk coefficients are expressed in terms of *lifetime attributable risk*, either for a specified age, *e*, at exposure (*LAR*(*e*)/Gy) or averaged over all ages at exposure (*LAR*/Gy). The quantity *LAR*(*e*) has earlier been termed *risk of untimely death* [*RUD*(*e*)], but this somewhat abstract name is here avoided in favor of the more familiar term. The equation for lifetime attributable risk has been given by Vaeth and Pierce [5]:

$$LAR(e) = \int_{e+L}^{a_{\max}} m_E(a)S(a)/S(e)\mathrm{d}a = \int_{e+L}^{a_{\max}} ERR(a)m(a)S(a)/S(e)\mathrm{d}a \qquad (1)$$

where $e$ and $a$ are age at exposure and attained age, respectively, $m_E(a)$ is the excess cancer mortality (due to an exposure at age, $e$) while $m(a)$ is the spontaneous cancer mortality rate and $L$ is the latent period. The *survival function*, i.e. the probability at birth to reach at least age $a$, is denoted by $S(a)$. The ratio $S(a)/S(e)$ is the conditional probability of a person alive at age $e$ to reach at least age $a$.

The terms $S(a)$ and $S(e)$ in Eq.(1) refer to the survival function not of the exposed, but of the unexposed population. This simplifies the concept and makes *LAR* proportional to *ERR* and independent of the non-cancer excess mortality which is difficult to quantify. Use of the unreduced survival function also implies that at higher doses where there is substantial life shortening, *LAR* is somewhat larger than the actual number of attributable cancer deaths per exposed person. However, this difference is of little or no practical concern, since no summary risk coefficient is sufficiently specific and precise to serve as an accurate quantitative parameter at high doses. Moreover, it might be perceived as awkward if risk coefficients were marked down because irradiation "prevents" some cancers by causing people to die at earlier ages.

Formulae for *LAR*

The excess relative risk, which has been written in the abbreviated form, $ERR(a)$, in Eq.(1), can be factorized in a dose ($D$) dependent, but gender-averaged reference value, $ERR_{\mathrm{ref}}$, and an age ($a$, $e$) and gender ($s$) dependent modifying function, μ:

$$ERR(D,s,a,e) = ERR_{\mathrm{ref}}(D)\cdot\mu(s,a,e). \qquad (2)$$

Omitting the argument $D$ in $ERR_{\mathrm{ref}}(D)$ and in $LAR(e)$, Eq.(1) then takes the form:

$$LAR(e) = ERR_{\mathrm{ref}}\int_{e+L}^{a_{\max}}\mu(s,a,e)m(a)S(a)/S(e)\mathrm{d}a. \qquad (3)$$

A more specific formulation invokes one of the two familiar projection models. The traditionally applied *age at exposure model* postulates a modifying function μ that depends only on age at exposure, $e$, and does not decrease in time after exposure. The parameter $ERR_{\mathrm{ref}}$ is, in this model, usually related to age 30 at exposure; $ERR_{\mathrm{ref}}$ is, therefore, written $ERR_{30}$:

$$\begin{aligned} ERR(D,s,a,e) &= ERR_{30}\cdot\mu(s,e) \\ &= ERR_{30}\cdot\exp(-g\cdot(e-30))\cdot(1\pm s) \end{aligned} \qquad (4)$$

(+ for females, – for males). In agreement with earlier analyses [9, 10, 11], typical parameter values are $g$=0.039/y and $s$=0.33 [4].

The more recent *attained age model* [12, 13] invokes a modifying function μ that depends only on age attained, $a$. In this model, the reference age 60 is a suitable choice; $ERR_{\mathrm{ref}}$ is, therefore, written $ERR_{60}$:

$$\begin{aligned} ERR(D,s,a,e) &= ERR_{60}\cdot\mu(s,a) \\ &= ERR_{60}\cdot\exp(-g\cdot(a-60))\cdot(1\pm s) \end{aligned} \qquad (5)$$

(+ for females, – for males). $ERR_{60}$ in the attained age model is numerically close to $ERR_{30}$ in the age at exposure model. Typical parameter estimates are $g$=0.025/y and $s$=0.34 [4].

The computations for UNSCEAR with the attained age model invoke (rescaled to reference age 60):

$$\mu(s,a) = (a/60)^{-1.5}\cdot(1\pm s) \qquad (6)$$

(+ for females, – for males; $s$=0.4). The power function leads to a rapid increase of *ERR* values at very young ages. A current reanalysis [4] retains, therefore, the somewhat more moderate exponential attained age modifier [Eq.(5)] that was used originally with the attained age model [12].

In subsequent formulae or statements, which apply both to $ERR_{30}$ and $ERR_{60}$, the symbol $ERR_{\mathrm{ref}}$ stands for either quantity.

For a specified model, i.e. a specified modifying function, it is straightforward to compute *LAR* from an exposure that occurs either acutely with a given probability per year or with constant low dose rate throughout life. The two scenarios lead to the same result, since a linear dose relation independent of dose rate is assumed in the concept of the nominal risk factor [1]. The lifetime attributable risk is then obtained as the average of $LAR(e)$ over life (see [5]). Using the abbreviation, $c$, for the life expectancy at birth,

$$c = \int_0^{a_{\max}} S(a)\mathrm{d}a \qquad (7)$$

one obtains:

$$LAR = \frac{1}{c}\cdot\int_0^{a_{\max}} LAR(e)S(e)\mathrm{d}e \qquad (8)$$

and the conversion factor between $ERR_{\mathrm{ref}}$ and *LAR* is:

$$LAR/ERR_{\mathrm{ref}} = \frac{1}{c}\cdot\int_0^{a_{\max}} LAR(e)/ERR_{\mathrm{ref}}\cdot S(e)\mathrm{d}e. \qquad (9)$$

Alternative quantities, *REID* and *ELR*

More complicated concepts than *LAR* are not actually required, but one such concept, the quantity *risk of exposure induced* (*cause specific*) *death*, *REID* [7], deserves consideration, because it is used in the most recent report by UNSCEAR [3]. *REID* for solid tumor mortality differs from *LAR* in being defined with reference to the actual survival function after the radiation exposure. The formula in Eq.(1) is then replaced by:

$$REID(e) = \int_{e+L}^{a_{\max}} ERR(a)m(a)S(a,D)/S(e,D)\mathrm{d}a \qquad (10)$$

where $S(a,D)$ and $S(e,D)$ represent the survival function of the population after exposure to dose $D$.

If *REID* were to be applied in radiation protection considerations, its values for different doses would be required. However, UNSCEAR has given only the values for 0.1 Sv, which do not differ appreciably from *LAR*, and the values for 1 Sv which are smaller than *LAR* at 1 Sv by about 10% for solid tumor mortality. Regardless of the question of practical applicability, it would be difficult to derive reliable values of *REID* because there is insufficient information to specify a dose-dependent survival function. Survival after a substantial radiation exposure is diminished due to radiation-induced cancer and non-cancer mortality. At doses of several Gy this also includes acute mortality. Recent studies among the A-bomb survivors show that there is late radiation-induced non-cancer mortality, but it remains difficult to quantify its dose dependence [14]. More is known about acute radiation mortality after high doses, but it is recognized to depend on the level of medical treatment which, in turn, varies with circumstances.

For these reasons it is unclear why UNSCEAR [3] refers, in spite of these various difficulties and limitations, to the quantity *REID*. There is an additional complication. In the absence of a specific statement on non-cancer mortality it seems likely that the calculations for UNSCEAR are actually directed not at *REID* but at an intermediate concept, *REID***(see Fig. 1) that disre-

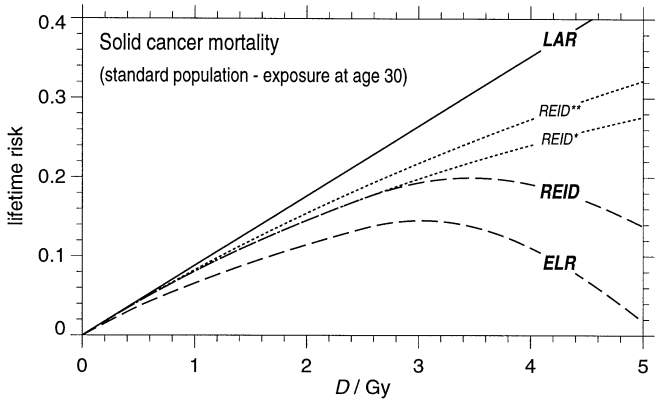


**Fig. 1** Lifetime attributable risk, *LAR*, (*upper solid line*), *risk of exposure induced* (*cause specific*) *death*, *REID* (*upper dashed line*), and the intermediate quantities *REID*** that disregards all non-cancer mortality and *REID** that disregards merely acute mortality (*dotted lines*). The (cause specific) *excess lifetime risk*, *ELR*, is also included (*lower dashed line*). The quantities are given for a linear dose dependence and the solid cancer mortality in the standard population [see Eq.s (15) and (16)]

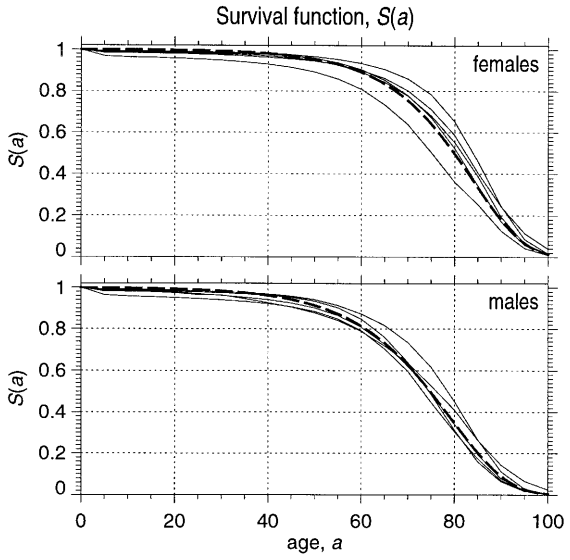


**Fig. 2** The survival functions of the five reference populations chosen by ICRP (*light lines*) and, for comparison, the survival function for the tentative standard (*dashed lines*) discussed in the subsequent section [see Eq.(15)]

gards both late and acute radiation-induced non-cancer mortality. To give a feeling for the different quantities, Fig. 1 presents the quantities *LAR* and *REID* (upper solid line and upper dashed line) for the standard population that is specified in a subsequent section. The intermediate quantities *REID*** that disregards all non-cancer mortality and *REID** that disregards merely acute mortality are indicated by the dotted lines. In this example an exposure at age 30 is assumed, and a linear dose-dependence with a gender-averaged *ERR*=0.5/Gy for solid cancer mortality. The dose dependence is taken not to bend downwards at high doses, which amounts to an overestimation. The late non-cancer mortality is – in the absence of better information – taken to have a threshold at 0.5 Gy and beyond this postulated threshold a slope of *ERR*=0.1/Gy is assumed. The acute radiation induced mortality is represented – again with unavoidable degree of arbitrariness – by a median lethal dose ($LD_{50}$) of 5 Gy and a half width of the distribution of lethal doses of 2.5 Gy. The main point is that *REID*, in its original definition [7], decreases rapidly at high doses and that the modification of the definition makes a considerable difference. It is also seen that the various quantities are not substantially different from *LAR* at low and intermediate doses.

The *(cause specific) excess lifetime risk*, *ELR*, is another quantity that has been adduced to express lifetime risk [15, 16]. It is the difference between the probability to die of cancer after the irradiation and the probability to die of cancer if unexposed. At high doses, i.e. when lifetime is considerably reduced, *ELR* assumes negative values. While there is little reason to invoke *ELR* in radiation protection considerations, it is included in Fig. 1 (lower dashed line) to show – as has been done with *REID* – its relation to the simpler and more suitable quantity *LAR*.

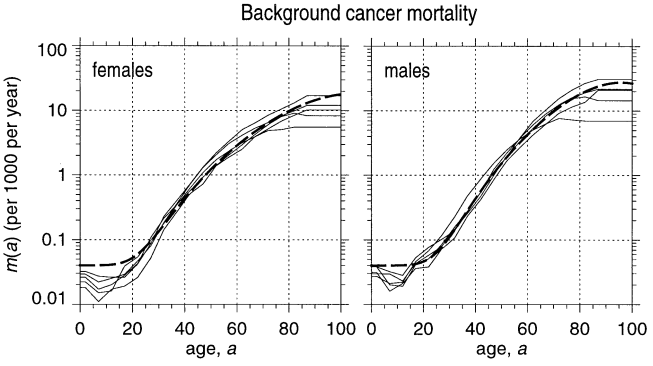


**Fig. 3** The age-specific solid cancer mortality rates of the five reference populations chosen by ICRP (*light lines*) and, for comparison, the rates for the tentative standard (*dashed lines*) discussed in the subsequent section [see Eq.(16)]. The cancer death rate in the five reference populations is taken to be constant after age 87

## Conversion factors

### ICRP data for the reference populations

In their risk computations [2] for ICRP [1] Land and Sinclair have chosen five reference populations. They have documented the input population data in terms of the actuarial survival curves, $S(a)$, and the age-dependent solid cancer mortality rates, $m(a)$, for each population and the two genders. These same data are summarily represented in Figs. 2 and 3. The heavy dashed lines represent a surrogate data set which will be discussed in the subsequent section; it can serve as an *ad hoc* substitute for the five ICRP reference populations to simplify risk transport calculations.

**Table 1** Conversion factors, $LAR/ERR_{ref}$, for the five populations chosen by ICRP, and the averages of these factors. The results are given both for the attained age model [Eq.(5)] and the age at exposure model [Eq.(4)]. Using a power function in $a$ with the attained age model [Eq.(6)] leads to average conversion factors that are larger by about 6%. The last column gives conversion factors that result for the tentative standard population defined in the subsequent section. Note that $ERR_{ref}$ (i.e. $ERR_{60}$ or $ERR_{30}$) is a gender-averaged value that depends only on dose

| All ages at exposure | US | UK | Japan | China | Puerto Rico | **Average** | **Standard** |
|---|---|---|---|---|---|---|---|
| Mean lifetime | | | | | | | |
| Males | 71.7 | 72.5 | 75.9 | 69.6 | 72.6 | 72.5 | 72.8 |
| Females | 78.5 | 78.3 | 81.8 | 71.9 | 79.6 | 78.0 | 78.1 |
| Lifetime cancer mortality | | | | | | | |
| Males | 0.21 | 0.25 | 0.23 | 0.13 | 0.18 | 0.20 | 0.20 |
| Females | 0.18 | 0.22 | 0.17 | 0.10 | 0.15 | 0.16 | 0.16 |
| Both genders | 0.20 | 0.24 | 0.20 | 0.12 | 0.17 | 0.18 | 0.18 |
| Age attained model – $LAR/ERR_{60}$ | | | | | | | |
| Males | 0.099 | 0.115 | 0.100 | 0.066 | 0.082 | 0.092 | 0.092 |
| Females | 0.155 | 0.188 | 0.135 | 0.095 | 0.123 | 0.139 | 0.139 |
| Both genders | 0.127 | 0.151 | 0.118 | 0.081 | 0.102 | **0.116** | **0.115** |
| Age at exposure model – $LAR/ERR_{30}$ | | | | | | | |
| Males | 0.153 | 0.179 | 0.155 | 0.095 | 0.132 | 0.143 | 0.145 |
| Females | 0.237 | 0.289 | 0.209 | 0.138 | 0.193 | 0.213 | 0.216 |
| Both genders | 0.195 | 0.234 | 0.182 | 0.116 | 0.163 | **0.178** | **0.180** |

**Table 2** Conversion factors, $LAR/ERR_{ref}$, for the five populations chosen by ICRP, and the averages of these factors. The results are analogous to those in Table 1, but they refer to a working population (exposure ages 25 to 65 years)

| Working population (ages at exposure 25 to 65) | US | UK | Japan | China | Puerto Rico | **Average** | **Standard** |
|---|---|---|---|---|---|---|---|
| Age attained model – $LAR/ERR_{60}$ | | | | | | | |
| Males | 0.104 | 0.120 | 0.108 | 0.067 | 0.088 | 0.097 | 0.096 |
| Females | 0.167 | 0.201 | 0.149 | 0.098 | 0.134 | 0.150 | 0.147 |
| Both genders | 0.136 | 0.161 | 0.128 | 0.083 | 0.111 | **0.124** | **0.122** |
| Age at exposure model – $LAR/ERR_{30}$ | | | | | | | |
| Males | 0.091 | 0.106 | 0.095 | 0.054 | 0.081 | 0.086 | 0.086 |
| Females | 0.146 | 0.177 | 0.132 | 0.080 | 0.122 | 0.131 | 0.132 |
| Both genders | 0.119 | 0.141 | 0.113 | 0.067 | 0.102 | **0.108** | **0.109** |

## Results in terms of the conversion factor *LAR/ERR*

### *Values for members of the public*

The conversion factors obtained for the five reference populations of ICRP with the unchanged population data of ICRP [2] and their averages are listed in the first six columns of Table 1. Also included are the mean duration of life in each population and the lifetime cancer mortality. The conversion factors are given for the attained age model [Eq.(5)] and the age at exposure model [Eq.(4)]. The last column gives the conversion factors that result for a standard population that will be considered in the subsequent section. As explained, the conversion factors refer to a constant low dose rate exposure throughout life or to acute low dose exposures, at a random age.

The age at exposure model predicts – at the present stage of the follow-up of the A-bomb survivors – a substantially larger lifetime attributable risk from childhood exposures than from exposures at later age. This is reflected in the large difference of the conversion factors for the two projection models.

For considerations that relate specifically to occupational exposure, somewhat different values of conversion factors result which correspond to the exposure of a working population represented – in line with the choice of ICRP [1] – by an exposure period from age 25 to 65. The computations are changed only by the choice of the integration limits to 25 and 65 in Eq.(9). Table 2 gives the results.

The choice of the projection model is uncritical for occupational exposures; the conversion factors for the two models are similar in this case.

### *Reference to lifetime fractional risk, LFR*

LAR specifies for a person exposed to a low dose the radiation-related excess probability for a fatal cancer. If, as is usual, the concept is applied to an exposed population, it specifies the expected number of fatalities, and such numbers – when they are not linked to the number of spontaneous cases – can be misleading. It is then more conducive for a realistic perception of risk to refer to a relative number. Such a number is obtained if *LAR* is scaled to the lifetime spontaneous cancer mortality (or incidence) in the reference population:

$$B = \int_0^{a_{max}} m(a) \cdot S(a) \mathrm{d}a. \qquad (11)$$

The resulting overall excess relative risk is here termed *lifetime fractional risk*[1]

$$LFR = LAR / B. \quad (12)$$

The *LFR* per unit dose can serve as an alternative form of the nominal risk coefficient. Numerical values are not given since they can easily be derived from Tables 1 and 2 for a specified $ERR_{ref}$. Apart from being more suggestive of the actual level of a radiation risk than the *LAR* per unit dose, *LFR* has the added advantage that it is more stable with regard to changing population data.

*LAR* increases substantially with the longevity of a population. The risk coefficient, as now expressed in terms of *LAR*, is thus substantially larger for developed countries than developing countries. The largest value of *LAR* among the five ICRP reference populations exceeds the smallest value by a factor 2 for either of the projection models and equally for a population of all ages or a working population (see Tables 1 and 2). In fact, *LAR* would nearly vanish for the population in an underdeveloped country, and while this expresses, of course, the fact that other hazards are of dominant concern in such populations, it would still convey a wrong message with regard to radiation protection.

In contrast, *LFR* is the ratio of two quantities that increase both with the longevity of a population, which explains why the value of *LFR* for a specified $ERR_{ref}$ does not vary greatly between the ICRP reference populations (either of all ages or of working ages). For a given projection model, *LFR* differs not by more than 20% between any of the ICRP reference populations. The lifetime relative risk coefficient, *LFR*, is thus a stable and meaningful parameter.

Expressed in terms of Eq.(12) and the average *LAR* and the average *B* for the five ICRP reference populations, *LFR* is:

$$LFR = 5.5 \cdot LAR. \quad (13)$$

Essentially the same relationship pertains if *LFR* is computed as an average of the *LFR* values of the five individual reference populations.

## Divergent concepts: *collective risk* versus *individual risk*

The definition of *LAR* or of the more complicated quantity *REID* invokes – as presented here [see Eqs.(1), (8), (10)] and previously [2, 5] the survival function $S(a)$. The resulting risk coefficient expresses the probability of harm for an *individual*, whether exposed at a specified age ($LAR(e)$) or

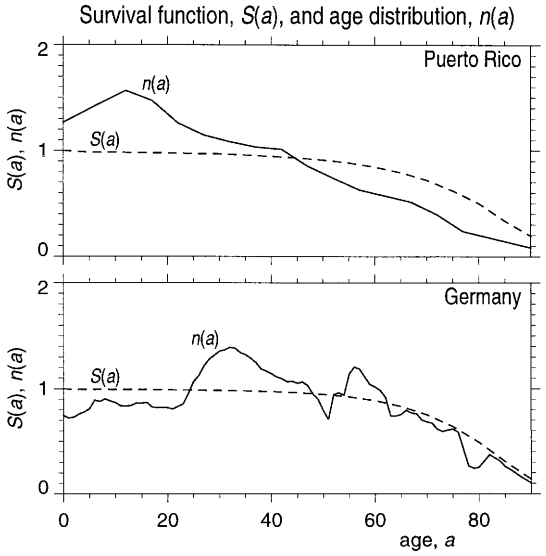


**Fig. 4** Comparison of the equilibrium age distribution, $S(a)$, for two populations with the actual age distributions, $n(a)$. The data refer to both genders combined. The distributions for Puerto Rico are from [2, 17]. The data for Germany are from the national statistical office [18]. The distributions, $n(a)$, are normalized to the area under $S(a)$ [the life expectancy, see Eq.(7)] of the two populations

throughout life (*LAR*). The risk coefficient *LAR* can, for example, be invoked to express the presumed risk for an individual from lifelong exposure to natural background radiation or to a lasting elevated radiation level. Similarly the *LAR* can express the risk to a worker from exposures during his working life from age 25 to 65.

A somewhat different concept is related to the *collective* detriment, rather than the individual risk. One invokes in this case not the risk to a member of the population. Reference is, instead, made to the total detriment in an exposed population or a subgroup of a population. One uses, accordingly, in Eq.(8) the actual distribution of ages, $n(e)$, of the population or the subgroup of the population that is under scrutiny:

$$LAR = \int_0^{a_{max}} LAR(e)n(e)\mathrm{d}e \,/\, \int_0^{a_{max}} n(e)\mathrm{d}e. \quad (14)$$

Both concepts, the individual-related and the population-related measure of risk, are meaningful and have specific applications. But confusion must arise when the nature of the quantity is not spelled out. Thus, it is not sufficiently appreciated that ICRP [2] gives the individual-related risk quantity *LAR*, while UNSCEAR [3] has derived the population-related risk quantity *LAR*. Diverging definitions may not be entirely avoidable. However, it is necessary to state clearly the definitions and to bring out – at least in exemplary fashion – the general magnitude of the numerical differences between differently defined quantities.

Growing population numbers in most nations of the world imply that the actual age distributions, $n(a)$, differ substantially from the equilibrium age distributions,

[1] In computations that refer to specific cases it can be more appropriate to use in the definition of *LFR* as denominator the spontaneous cancer mortality (or incidence) over a specified period. For example if the radiation risk from screening by mammography is to be assessed, it is natural to refer to the time interval from beginning of screening onwards.

**Table 3** Conversion factors, $LAR/ERR_{ref}$, for Puerto Rico (an example of a young population with high birth rate) and Germany (an example of the opposite case). The results are given both, for the attained age model (*a*-model) [Eq.(5)] and the age at exposure model (*e*-model) [Eq.(4)]. The results refer to both age groups, i.e. all ages at exposure and a working population with exposure ages 25 to 65 years. The data for Puerto Rico are from [2, 17], the data for Germany from [18, 19]

| $LAR/ERR_{ref}$ | | All ages at exposure | | Working population (ages at exposure 25–65 years) | |
|---|---|---|---|---|---|
| | | *e*-model | *a*-model | *e*-model | *a*-model |
| Puerto Rico | Individual-related | 0.163 | 0.102 | 0.102 | 0.111 |
| | Population-related | 0.205 | 0.112 | 0.110 | 0.113 |
| Germany | Individual-related | 0.209 | 0.132 | 0.129 | 0.141 |
| | Population-related | 0.198 | 0.134 | 0.134 | 0.143 |

$S(a)$, with a significant shift towards younger ages. The age distribution that has been used in the UNSCEAR calculations for Puerto Rico can serve as an example. Figure 4 compares in the upper panel the distribution $n(a)$ with the equilibrium distribution $S(a)$ for Puerto Rico. An aging population with low birth rates is the opposite case; in the lower panel of Fig. 4, Germany is chosen as an example. For easier comparison with $S(a)$, $n(a)$ is normalized to the area under $S(a)$, i.e. to the life expectancy at birth [see Eq.(7)].

Table 3 gives the resulting conversion coefficients. The essential point is the substantial increase of *LAR* for a "young" population under the age at exposure model. In the example of Puerto Rico the conversion factor is $LAR/ERR_{30}$=0.163 in terms of the individual-related risk quantity, but $LAR/ERR_{30}$=0.205 in terms of the population-related risk quantity. For the attained age model the difference is substantially less: for the individual-related risk quantity the conversion factor is $LAR/ERR_{60}$=0.102, for the population-related risk quantity it is $LAR/ERR_{60}$= 0.112. For an "aged" population the differences are much smaller. In the example of Germany, for both risk models the individual-related risk quantity and the population-related risk quantity differ only slightly.

For occupational exposures, i.e. for exposures in the age range 25–65 the differences in the conversion factors are generally less. However, the population-related concept – if taken seriously – would require an even more detailed formulation in terms of gender-specific age distributions for the occupations in question. There appears to be little need for such exercises in accuracy. Generally speaking, the notion of the individual-related lifetime attributable risk as employed by ICRP appears to be more natural in relation to nominal risk coefficients than any concept that is sensitive to demographic variations.

## Specification of a standard population

The tabulated conversion factors can facilitate the comparison of risk coefficients in terms of the five reference populations selected by ICRP. In the interest of stable numerical values and meaningful comparisons it appears advisable to retain, for the time being, the reference populations and the cancer and survival data specified by ICRP [2]. Eventually, however, it will be desirable to define a standard population that can serve as a simpler, more practical reference. The choice of a suitable convention ought to be made by an official scientific body, such as the ICRP.

As an interim solution, analytical expressions for the sex-specific population survival functions and the cancer mortality rates can be invoked that provide nearly the same *LAR* as the utilization of the five ICRP reference populations. The survival functions are in this *ad hoc* "standard" represented by a *Gompertz* expression:

(15)

with $c_1$=0.0015, $c_2$=0.0820 for males and $c_1$=0.0005, $c_2$=0.0905 for females.

The solid cancer mortality rates are modeled by the familiar power functions with some bending over at high ages:

$$m(a) = k \cdot (a/60)^r \cdot \exp(-0.06 \cdot (a/60)^r) + 0.00004 \quad (16)$$

with $k$=0.0045, $r$=6 for males and $k$=0.0030, $r$=5 for females.

These dependencies are compared in Figs. 2 and 3 to the data for the five ICRP reference populations. To avoid unreadable diagrams the curves for the five reference populations have been indicated by light lines without identification of the countries. They are meant merely to indicate the bandwidth of the values and the rough agreement with the analytical expressions. The last columns in Tables 1 and 2 give the conversion factors that result for this tentative standard.

## Conclusion

Deriving nominal risk coefficients is one of the major aims of modeling computations with epidemiological data, such as the information from the follow-up of the A-bomb survivors [9, 10, 11]. While risk coefficients are subject to considerable uncertainties, they are nevertheless a critical input into regulatory decisions.

The new risk estimates recently reported by UNSCEAR [3] attest to the continued effort at extending the data and improving the modeling computations. The results need to be compared to the current ICRP risk estimates, and future estimates will, in turn, be compared to the values presented by UNSCEAR [3]. The numerical comparisons have not been the object of the present considerations. They are considered elsewhere [4], and it is seen that the difference of conventions can have substantial impact on the resulting risk estimates. The present discussion has, instead, been focused on the concepts and computations that are required in the derivation of risk estimates and on the population data that are used to convert excess relative risk (*ERR*) into lifetime attributable risk (*LAR*) or lifetime fractional risk (*LFR*).

ICRP has selected five reference populations and has specified the required population data. This selection is of necessity arbitrary, and if some degree of arbitrariness is accepted, there is little reason to keep updating the survival and cancer data for the reference populations. Instead, the reference needs to be seen as a standard that makes the nominal risk coefficients insensitive to changing parameters that are unrelated to new insights on radiation risk. In this sense it appears desirable to adopt a standard population that can serve as an agreed upon component in the definition of nominal risk coefficients. A tentative standard has here been considered that is largely equivalent to the five ICRP reference populations. However, this is meant to be at best an *ad hoc* surrogate for the combination of the five standard populations. An actual standard would have to be chosen and adopted by an official scientific body, such as ICRP.

Adopting a standard will, of course, not exclude specific efforts that might be directed towards the derivation of estimates for national populations or specific critical subgroups of a population. But even then the standard values will remain a useful guideline; they will help to judge whether detailed computations are warranted or whether they are insignificant in comparison to the inherent uncertainty of the risk estimates.

Being summary parameters, the nominal risk coefficients are meaningful when they are applied to a broad group of cancers, such as all solid tumors taken together. For certain considerations it can be of interest to work out the contribution of specific tumor entities to the total risk. This involves the same type of computations that have been discussed here, but the assessments would be directed at specific national or ethnic populations, and there is, accordingly, less need or possibility for standardized computations. Similarly, it would be complicated to extend the present considerations to leukemia. The required computational detail appears to be unjustified in view of the relatively minor contribution of leukemia to the total cancer risk coefficient and also in view of the fact that nominal risk coefficients are, as the term indicates, general guidelines rather than firm numbers. While precise modeling computations are required in cases such as the derivation of probabilities of causation, it is sufficient with regard to the overall nominal risk coefficient to account for leukemia in a summary fashion, as is the case in the current ICRP recommendations.

While the need for a standardization has been stated, it is perhaps equally important to emphasize the advantage that can be gained by moving away from stating risk coefficients (in terms of *LAR*) which specify the probability or the expected number of radiation-induced fatalities (or cases), and to turn, instead, towards the use of relative risk coefficients (in terms of *LFR*) which quantify the fractional increase of the cancer mortality. This quantity is – apart from being more suggestive of the factual impact of a risk – less dependent on the population data that enter the computation of the risk coefficients. But even risk coefficients expressed in relative terms, i.e. with reference to the lifetime fractional risk, will require a well defined computational convention to permit reliable comparisons and to ensure the necessary transparency of the underlying computations.

**Acknowledgements** The authors wish to thank Donald A. Pierce for valuable information and helpful discussions. This research was supported by the European Commission (Contract: NDISC-FIGD-CT-2000–0079) and the German Federal Ministry of Environment, Nature Conservation and Nuclear Safety (Contract: StSch 4175).

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