A Framework for Estimating Radiation-Related Cancer Risks in Japan from the 2011 Fukushima Nuclear Accident

Author(s): L. Walsh, W. Zhang, R. E. Shore, A. Auvinen, D. Laurier, R. Wakeford, P. Jacob, N. Gent, L. R. Anspaugh, J. Schüz, A. Kesminiene, E. van Deventer, A. Tritscher, and M. del Rosarion Pérez
Source: Radiation Research, 182(5):556-572. 2014.
Published By: Radiation Research Society
DOI: http://dx.doi.org/10.1667/RR13779.1
URL: http://www.bioone.org/doi/full/10.1667/RR13779.1

RADIATION RESEARCH **182**, 556–572 (2014)
0033-7587/14 $15.00

DOI: 10.1667/RR13779.1

A Framework for Estimating Radiation-Related Cancer Risks in Japan from the 2011 Fukushima Nuclear Accident

L. Walsh,[a,1] W. Zhang,[b] R. E. Shore,[c] A. Auvinen,[d] D. Laurier,[e] R. Wakeford,[f] P. Jacob,[g] N. Gent,[b] L. R. Anspaugh,[h] J. Schüz,[i] A. Kesminiene,[i] E. van Deventer,[j] A. Tritscher[j] and M. del Rosario Pérez[j]

[a] *BfS – Federal Office for Radiation Protection, Radiation Protection and Health, Neuherberg, Germany;* [b] *Public Health England, United Kingdom;* [c] *Radiation Effects Research Foundation, Hiroshima and Nagasaki, Japan;* [d] *Radiation and Nuclear Safety Authority and University of Tampere, Finland;* [e] *Institut de Radioprotection et de Sûreté Nucléaire, Fontenay-aux-Roses, France;* [f] *The University of Manchester, Centre for Occupational and Environmental Health, Institute of Population Health, Manchester, United Kingdom;* [g] *Helmholtz Zentrum München – German Research Center for Environmental Health and Institute of Radiation Protection, Neuherberg, Germany;* [h] *Radiobiology Division, University of Utah, Salt Lake City, Utah;* [i] *International Agency for Research on Cancer, Section of Environment and Radiation, Lyon, France; and* [j] *World Health Organization, Geneva, Switzerland*

Walsh, L., Zhang, W., Shore, R. E., Auvinen, A., Laurier, D., Wakeford, R., Jacob, P., Gent, N., Anspaugh, L. R., Schüz, J., Kesminiene, A., van Deventer, E., Tritscher, A. and del Rosario Pérez, M. A Framework for Estimating Radiation-Related Cancer Risks in Japan from the 2011 Fukushima Nuclear Accident. *Radiat. Res*. 182, 556–572 (2014).

We present here a methodology for health risk assessment adopted by the World Health Organization that provides a framework for estimating risks from the Fukushima nuclear accident after the March 11, 2011 Japanese major earthquake and tsunami. Substantial attention has been given to the possible health risks associated with human exposure to radiation from damaged reactors at the Fukushima Daiichi nuclear power station. Cumulative doses were estimated and applied for each post-accident year of life, based on a reference level of exposure during the first year after the earthquake. A lifetime cumulative dose of twice the first year dose was estimated for the primary radionuclide contaminants (^{134}Cs and ^{137}Cs) and are based on Chernobyl data, relative abundances of cesium isotopes, and cleanup efforts. Risks for particularly radiosensitive cancer sites (leukemia, thyroid and breast cancer), as well as the combined risk for all solid cancers were considered. The male and female cumulative risks of cancer incidence attributed to radiation doses from the accident, for those exposed at various ages, were estimated in terms of the lifetime attributable risk (LAR). Calculations of LAR were based on recent Japanese population statistics for cancer incidence and current radiation risk models from the Life Span Study of Japanese A-bomb survivors. Cancer risks over an initial period of 15 years after first exposure were also considered. LAR results were also given as a percentage of the lifetime baseline risk (i.e., the cancer risk in the absence of radiation exposure from the accident). The LAR results were based on either a reference first year dose (10 mGy) or a reference lifetime dose (20 mGy) so that risk assessment may be applied for relocated and non-relocated members of the public, as well as for adult male emergency workers. The results show that the major contribution to LAR from the reference lifetime dose comes from the first year dose. For a dose of 10 mGy in the first year and continuing exposure, the lifetime radiation-related cancer risks based on lifetime dose (which are highest for children under 5 years of age at initial exposure), are small, and much smaller than the lifetime baseline cancer risks. For example, after initial exposure at age 1 year, the lifetime excess radiation risk and baseline risk of all solid cancers in females were estimated to be $0.7 \cdot 10^{-2}$ and $29.0 \cdot 10^{-2}$, respectively. The 15 year risks based on the lifetime reference dose are very small. However, for initial exposure in childhood, the 15 year risks based on the lifetime reference dose are up to 33 and 88% as large as the 15 year baseline risks for leukemia and thyroid cancer, respectively. The results may be scaled to particular dose estimates after consideration of caveats. One caveat is related to the lack of epidemiological evidence defining risks at low doses, because the predicted risks come from cancer risk models fitted to a wide dose range (0–4 Gy), which assume that the solid cancer and leukemia lifetime risks for doses less than about 0.5 Gy and 0.2 Gy, respectively, are proportional to organ/tissue doses: this is unlikely to seriously underestimate risks, but may overestimate risks. This WHO-HRA framework may be used to update the risk estimates, when new population health statistics data, dosimetry information and radiation risk models become available.

INTRODUCTION

The earthquake and tsunami in Japan on March 11, 2011 caused serious damage to the reactors at the Fukushima Daiichi nuclear power station (NPS), resulting in major releases of radioactive materials into the environment over an extended period (*1*, *2*). Since the beginning of this nuclear accident, the assessment of potential health risks to

Editor's note. The online version of this article (DOI: 10.1667/RR13779.1) contains supplementary information that is available to all authorized users.

[1] Address for correspondence: BfS – Federal Office for Radiation Protection, Ingolstaedter Landstrasse 1, D-85764 Oberschleissheim, Germany; e-mail: lwalsh@bfs.de.

humans from the Fukushima radiation exposure has received substantial worldwide attention. Such assessment requires knowledge of the magnitude of the radiation doses received by populations within Japan and beyond. The World Health Organization (WHO) convened an expert group to perform a health risk assessment (HRA) after the Fukushima accident (*3*) to fulfill its mandate in providing public health advice and assistance during radiation emergencies (*4*).

Available scientific data on the biological and health effects of ionizing radiation are based on experimental and epidemiological studies. The most informative epidemiological data on human exposure to radiation comes from the Life Span Study (LSS) of Japanese survivors of the Hiroshima and Nagasaki atomic bombings [e.g., see ref. (*5*)]. Several other studies have also provided useful epidemiological data, including those of past accidents [e.g., Chernobyl (*6*)], medical exposures, occupational exposures and naturally occurring radiation exposures (*7–9*). Despite the differences among types of exposure from the atomic bombings (largely external exposure) and nuclear accidents (external plus internal exposures), LSS models were applied here because they are based on the largest body of epidemiological data on cancer (and noncancer) radiation risks.

The purpose of this article is to describe the methodological framework of the WHO-HRA for estimating the radiation-related cancer risks in Japan from the Fukushima nuclear accident (*3*). Whereas the WHO-HRA (*3*) reported risks based on preliminary dose estimates (*10*) for groupings of geographical locations affected by the Fukushima accident, this article reports risks based on reference doses, which may be adapted for application to any affected region. The framework is based on the assumption that the solid cancer and leukemia lifetime risks for doses less than about 0.5 Gy and 0.2 Gy, respectively, are essentially proportional to organ/tissue doses. This proportionality could be used to perform risk estimations by scaling risk values linearly using actual dose estimates, as improvements in dosimetry beyond the WHO preliminary dose assessment (*10*), become available (e.g., *11–15*). There is, however, a caveat for scaling risks in that there is no direct epidemiological evidence for applying linear risks to very low doses, or even doses below 50 mGy: low-dose risks are generated by cancer risk models fitted to a wide dose range of 0–4 Gy, but risks are not significantly increased if just the range of 0–50 mGy is considered (which suggests that the assumption of linearity does not seriously underestimate risk at low doses). In this article, radiation-related risks are estimated for all solid cancers as well as for several radiosensitive sites.

MATERIALS AND METHODS

Radiation-related cancer risks were estimated for both males and females initially exposed as infants (age 1 year), children (ages 5 and 10 years) or adults (ages 20, 40 and 60 years). Models for specific cancer sites were applied to calculate risks attributable to radiation exposure over a lifetime and over the initial 15 years after the nuclear accident, based on a reference yearly organ/tissue dose, and using health statistics data from the current Japanese population.

Use of Yearly Organ/Tissue Doses

Reference doses are to be taken as organ/tissue doses for each of the target organs for the types of cancers evaluated (i.e., colon, red bone marrow, thyroid and breast organ/tissue doses for all solid cancers, leukemia, thyroid and breast cancer, respectively). Reference lifetime doses were calculated as cumulative annual doses and applied for the remaining lifetime up to age 89 years, starting with the doses received during the first year after the accident and ending up to the seventieth year after the accident. A lifetime cumulative dose of twice the first year dose was assumed, based on a reference first year dose for all organs/tissues. This ratio was considered appropriate for the primary longer lived radionuclide contaminants (^{134}Cs and ^{137}Cs), based on the experience from the Chernobyl accident (*6*), with further adjustments for the relative abundance of the two cesium radioisotopes and information on the promptness and intensity of cleanup efforts [further details are given in section 4.1.4 of the WHO report (*3*) as well as other published material (*16–19*)]. In the absence of evacuation shortly after plume passage, the relative contribution to dose of shorter lived radionuclides was minor for organs/tissues other than the thyroid. For all organ/tissue doses, the reference lifetime dose was chosen as 20 mGy with a first year dose of 10 mGy to represent a situation of no relocation after the accident. However, a reference first year dose of 10 mGy was chosen to represent a situation either of relocation after the accident or that appropriate for emergency workers[2] (*3, 20, 21*).

Doses to the thyroid gland require special consideration because contributions to the total dose from exposures to short-lived (mainly ^{131}I) and longer-lived (mainly ^{134}Cs and ^{137}Cs) radionuclides need to be accounted for. Within the first year after the accident, the internal thyroid exposure (mainly from ^{131}I) was the major contributor to the total thyroid dose and an assumption of a ratio of two is only applicable to the external and internal lifetime dose from longer-lived radionuclides (mainly ^{134}Cs and ^{137}Cs) to the thyroid.

In calculating the lifetime risks, the same reference dose was used for all ages at exposure and all organs/tissues considered. Although this dose level is significantly higher than the organ/tissue dose estimates for the majority of the Japanese subpopulations affected by the accident, it falls within the organ/tissue dose ranges considered in the WHO report [see Tables 5 and 6 in ref. (*3*)], where the colon dose is used for the calculation of all solid cancer risks.

Health Statistics Data

Japanese population cancer incidence rates, given by sex, cancer site and 5 year age group, for 2004, are available from the Japan Cancer Surveillance Research Group compilation of 31 population-based cancer registries in Japan (*22*) [and for calendar years 1975–2008, from an electronic database (*23*)]. Japanese all cause mortality rates for 2010 are available from the Website of Official Statistics of Japan (*24*).

Risk Models for Specific Cancer Sites

The cancer types studied separately were leukemia (ICD10: C91–95), thyroid cancer (C73) and female breast cancer (C50). This was

[2] Although there is no precise date when the emergency phase ended, it is a reasonable approach to consider only the first year exposure in the case of emergency workers.

TABLE 1
Adopted Weights for the Transfer of Excess Relative Risk (ERR) and Excess Absolute Risk (EAR) Models in the Calculation of Lifetime Attributable Risk (LAR)

Cancer site	Main weights applied	Evidence for choice of main weights (see refs.)	Alternative weights
All solid cancers	50% ERR, 50% EAR ($w = 0.5$)	(*26*)	100% ERR ($w = 0$) and 100% EAR ($w = 1$)
Leukemia	50% ERR, 50% EAR ($w = 0.5$)	(*26–29*)	100% ERR ($w = 0$) and 100% EAR ($w = 1$)
Thyroid	50% ERR, 50% EAR ($w = 0.5$)	(*30–32*)	100% ERR ($w = 0$) and 100% EAR ($w = 1$)
Breast	100% EAR ($w = 1$)	(*33*)	100% ERR ($w = 0$)[a]

[a] This weight was not considered in the WHO report (*3*) but is given here so that uncertainties associated with the choice of different weights may be evaluated.

done because of the known radiosensitivity of these cancers and the demonstrated dependence of their risk on the age at exposure (*9*). In addition, the grouping of ''all solid cancers'' (C00–C89, all cancers except leukemia, lymphoma and multiple myeloma) was assessed because pooling many types of cancers can: 1. Provide information on the overall cancer risk from radiation exposure, which is widely used for radiation risk assessment and radiation protection purposes; 2. Reflect the fact that radiation exposure can cause cancer in most organs/tissues of the body; and 3. Provide more statistically stable risk estimates that are particularly relevant when assessing small risks at low doses (*25*).

Specific excess relative risk (ERR) and excess absolute risk (EAR) models were used to obtain the risk as a function of dose (d) for the different cancer sites considered. These models have the form of a linear dose-response function for all solid cancers, thyroid cancer and female breast cancer, as well as a linear-quadratic dose-response function for leukemia, and they include risk effect modification by age at exposure (e), sex (s) and attained age (a). The combined excess risk (ER) model, ER (d, e, a, s), is given by

$$\mathrm{ER}(d,e,a,s) = w\,\mathrm{EAR}(d,e,a,s) + (1-w)\mathrm{ERR}(d,e,a,s)m(a,s), \quad (1)$$

where: w is the weighting factor between an absolute (EAR) and a relative (ERR) transfer of risk, with $w = 0.5$ for all solid cancers, thyroid cancer and leukemia, and $w = 1.0$ for breast cancer [see Table 1 (*26–33*)]. EAR and ERR are models based on LSS cancer incidence data (*5*), with the exception of leukemia for which LSS mortality data were used (*27*) [full details of these models and fit parameters are given in Supplementary Table S1 (http://dx.doi.org/10.1667/RR13779.1.S1)], and $m(a, s)$ are the Japanese age- and sex-specific baseline cancer incidence rates in 2004 (*22*).

Risk Quantities

The lifetime attributable risk (LAR) (*34*) was selected as an appropriate and relatively simple risk quantity for assessments of long-term risks associated with an environmental exposure. At the low doses after the Fukushima Daiichi nuclear accident, LAR is equivalent to other similar measures (*35*) including the more complex risk of exposure-induced death (REID) from, or incidence of, cancer.

The lifetime attributable risk from one yearly dose, LAR (d, e, s), specifies the sex (s) and age-at-exposure (e) specific cumulative probability of a specific cancer attributable to radiation exposure over a period up to a maximum age ($a_{\max}$).

$$\mathrm{LAR}\,(d,e,s) = \int_{e+L}^{a_{max}} \mathrm{ER}\,(d,e,a,s)\,\mathrm{S_{aj}}(a,s)/\mathrm{S_{aj}}(e,s)\,\mathrm{d}a, \quad (2)$$

where d is the dose delivered to the organ/tissue during one year of exposure for age at exposure e, and L is the minimum latency period between the delivery of the dose to the organ and the expression of the radiation-induced risk. The minimum latency L was assumed to be 2 years for leukemia (*9*), 3 years for thyroid cancer (*36*) and 5 years for all solid cancers (*27*, *28*). For female breast cancer, the minimum latency period was assumed to be 5 years or until an attained age of 20 years, whichever was longer (the Discussion section gives the reasons for these choices). $a_{\max}$ was taken to be 89 years and LAR was obtained from Eq. (2) by numerical integration over age, a, in one year intervals.

The survival curve, $\mathrm{S_{aj}}(a/a_{min}, s) = \mathrm{S_{aj}}(a, s)/\mathrm{S_{aj}}(e, s)$, is the probability of surviving to age a, adjusted for cancer-free survival, with the condition that the probability equals 1 at age at beginning of risk (a_{min}), corresponding to age at exposure for exposed people. $S_{aj}(a/a_{min}, s)$ was calculated from Japanese all cause mortality rates for 2010 (*24*) (see Supplementary Fig. S1; http://dx.doi.org/10.1667/RR13779.1.S1).

The lifetime attributable risk based on lifetime organ/tissue dose, D, LAR (D, e, s) is a summation of integral terms from Eq. (2), i.e.,

$$\mathrm{LAR}\,(D,e,s) \sum_{i=1}^{70} \mathrm{LAR}\,(d_i,e,s) \quad (3)$$

where d_i is the yearly dose during the ith year and e is the age at exposure in year i (i.e., the doses were treated as age-at-exposure dependent in conferring the risk).

To put radiation-related cancer risks into perspective LAR was also considered as a percentage of the lifetime baseline risk (LBR) of cancer in Japan (i.e., the risk in the absence of radiation exposure from the accident). Applying the same notation for the definition of LAR, the LBR is calculated as:

$$\mathrm{LBR}(a_{\min},s) = \int_{a_{min}}^{a_{max}} m(a,s)\mathrm{S_{aj}}(a|a_{min},s)\mathrm{d}a, \quad (4)$$

The lifetime fractional risk (LFR) is calculated as the ratio of the LAR to the LBR [given in percentage (%) here] and is assumed to be more invariant to secular trends in the population cancer rates applied in the calculations of LAR or LBR than either of the individual quantities (LAR or LBR).

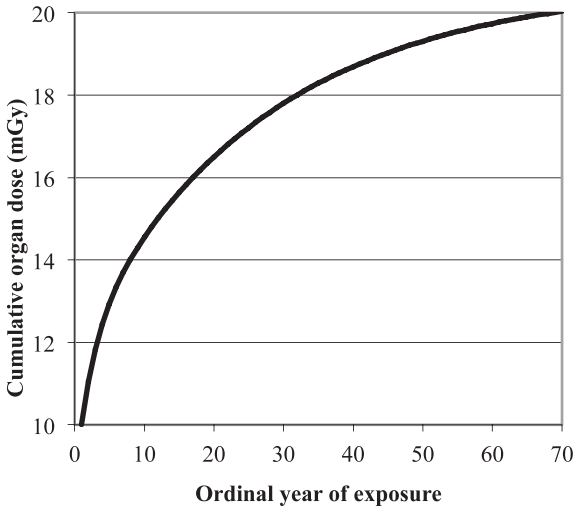

FIG. 1. Cumulative organ/tissue doses as a function of ordinal year of exposure from the model applied for calculating lifetime dose (over 70 years) from the first year dose of 10 mGy. The ratio of lifetime dose to the first dose is a factor of two.

$$\mathrm{LFR}(\%) = 100 \cdot \mathrm{LAR}/\mathrm{LBR} \tag{5}$$

These lifetime risk estimates are associated with large uncertainties. It should also be noted that the duration of the considered lifetime segment depends on the age at exposure (i.e., the higher the ages at initial exposure the shorter the lifetime segment up to age 89 years). This limits the comparison of results among different ages at exposure. Therefore, the cumulative risks over 15 years after the initial exposure (AR_{15}, BR_{15} and FR_{15}) were also calculated. AR_{15} is more pertinent for comparisons between the results presented here and those that will be provided by ongoing epidemiological studies, and because of interest in early risks of cancer from a short-term public health perspective. AR_{15} is especially pertinent for cancer types such as leukemia or thyroid cancer for which the relative increase in risk is expected to be stronger during the first few decades after exposure during childhood. Further, these risks are associated with smaller uncertainties because they are projected over a generally much shorter period than LAR and LBR.

The radiation-attributable risk for the 15 year period of life after an age at initial exposure, AR_{15}, was calculated from the LAR equation with the upper limit of integration a_{max} set to $e + 15$. The baseline risk for the 15 year period of life after a_{min}, BR_{15} was calculated from the LBR equation, with the upper limit of integration a_{max} set to $a_{min} + 15$. The fractional risk for the 15 year period of life after age at exposure, FR_{15}, was calculated as $FR_{15}\ (\%) = 100 \cdot AR_{15}/BR_{15}$.

RESULTS

Lifetime Dose Distribution

Figure 1 shows the cumulative annual organ/tissue doses delivered over a lifetime, used as input data for calculating the radiation-related risks, starting from a first year reference organ/tissue dose of 10 mGy. The total organ/tissue dose accumulated over lifetime[3] is 20 mGy and over a 15 year period is 15.6 mGy. The organ/tissue yearly dose levels are reduced drastically after the first year, with annual contributions to the lifetime doses in the second, third and fourth year being 10.5%, 7.8% and 6.05% of the first year dose, respectively (with the 1% level being reached in the 32nd year).

Lifetime Risks

The LAR for a reference lifetime dose of 20 mGy calculated with the weights from Table 1, and the LBR and LFR for both sexes and six different ages at exposure for all solid cancers, leukemia, thyroid and breast cancer incidence are shown in Table 2. Results from Table 2 are shown in Fig. 2A–D for all solid cancers, leukemia, thyroid and female breast cancer, respectively. Figure 3 compares the male and female LAR results for each cancer site for the age group most at risk, i.e., infants aged 1 year at exposure.

For all solid cancers, the LAR in females ranged from $0.1 \cdot 10^{-2}$ to $0.7 \cdot 10^{-2}$ depending on age group. This corresponds to a 2% lifetime fractional risk for childhood exposure (i.e., the LFR), but 0.5–1.5% for adult exposures. For males, the LAR estimates were lower ($0.06 \cdot 10^{-2}$ to $0.5 \cdot 10^{-2}$), while the baseline risks were higher, and therefore the LFR was lower than for females.

For leukemia, the LBR was generally smaller for females ($\approx 0.4 \cdot 10^{-2}$) than for males ($\approx 0.6 \cdot 10^{-2}$) and the LAR per reference lifetime dose for females was generally about 70% of the LAR for males. The LFR was rather small (a maximum of 3.5% for females and 3.7% for males who were 1 year old at initial exposure).

In the special case of thyroid cancer the LAR for a reference lifetime dose of 20 mGy is only applicable for exposure to long-lived radionuclide. The LBR for females ($\approx 0.8 \cdot 10^{-2}$) was about four times higher than for males ($\approx 0.2 \cdot 10^{-2}$), and the LAR for females was approximately five times higher than for males. The LFR was small with a maximum of 8.4% for females and 6.8% for males (age of 1 year at initial exposure). However to construct risks for thyroid cancers based on total dose, it is possible to combine the risks in Table 2, assuming that they apply to the thyroid doses from longer-lived radionuclides, with the risks in Table 3 (based on just the first year doses, i.e., from mainly short-lived radionuclides), assuming that they apply to the mainly internal doses (see Discussion section for an example).

Both for leukemia risk and the mainly external dose contribution to the thyroid cancer risk from longer-lived radionuclides, more than half of the yearly contributions to LAR resulted from the first year dose indicating that the first year doses had a much higher impact on the overall risk than a cumulative dose received in the subsequent years (this may be seen by comparing the results in Table 2 to those in Table 3).

For female breast cancer, the LAR was greatest after exposure at 1 year of age and became progressively smaller with increasing age at initial exposure. The LAR

[3] To calculate lifetime organ/tissue doses in the current study the dose was integrated up to 70 years after initial exposure. Any residual doses after a 70 year period were extremely small and therefore were assumed to be zero.

TABLE 2
Results Applicable to Risk Assessment for Members of the General Public Who Were Not Relocated after the Accident

Age at exposure (years)	Cancer site			
	All solid cancers	Leukemia	Thyroid	Female breast
Female risks per reference lifetime organ/tissue dose of 20 mGy				
	Lifetime attributable risk (LAR · 10^{-2})			
1	0.70	0.02	0.06	0.20
5	0.63	0.01	0.05	0.17
10	0.55	0.01	0.04	0.13
20	0.42	0.01	0.02	0.08
40	0.22	0.01	0.01	0.03
60	0.08	0.00	0.00	0.01
	Lifetime baseline risk (LBR · 10^{-2})			
1	29.04	0.43	0.77	5.53
5	29.09	0.42	0.77	5.54
10	29.09	0.41	0.77	5.54
20	29.07	0.40	0.76	5.55
40	28.17	0.37	0.66	5.13
60	22.98	0.32	0.38	2.69
	Lifetime fractional risk (LFR in percentages)			
1	2.4	3.5	8.4	3.6
5	2.2	2.4	6.6	3.0
10	1.9	2.2	4.9	2.4
20	1.5	1.9	2.7	1.5
40	0.8	1.5	0.8	0.5
60	0.4	1.1	0.2	0.3
Male risks per reference lifetime organ/tissue dose of 20 mGy				
	Lifetime attributable risk (LAR · 10^{-2})			
1	0.46	0.02	0.01	
5	0.42	0.02	0.01	
10	0.37	0.01	0.01	
20	0.28	0.01	0.00	
40	0.16	0.01	0.00	
60	0.06	0.00	0.00	
	Lifetime baseline risk (LBR · 10^{-2})			
1	40.60	0.60	0.21	
5	40.70	0.59	0.21	
10	40.71	0.58	0.21	
20	40.75	0.57	0.21	
40	40.90	0.52	0.19	
60	38.10	0.44	0.14	
	Lifetime fractional risk (LFR in percentages)			
1	1.1	3.7	6.8	
5	1.0	2.6	5.3	
10	0.9	2.3	3.9	
20	0.7	2.0	2.1	
40	0.4	1.6	0.6	
60	0.2	1.1	0.2	

Notes. Lifetime attributable risk [LAR from Eqs. (1–3)] calculated with the main weights from Table 1, lifetime baseline risk [LBR from Eq. (4)] and lifetime fractional risk [LFR from Eq. (5)] up to attained age 89 years for a lifetime dose of 20 mGy (both sexes and six different ages at exposure) for all solid cancers, breast cancer, thyroid cancer (applicable only to the mainly external doses from longer-lived radionuclides) and leukemia incidence. LFR has been calculated from LAR and LBR with computer precision values before rounding all numbers to fewer decimal places for this table.

ranged from $0.20 \cdot 10^{-2}$ for age 1 year, $0.08 \cdot 10^{-2}$ for age 20 years and $0.007 \cdot 10^{-2}$ for age 60 years, with LFRs of 3.6%, 1.5% and 0.3%, respectively. Similarly to leukemia and thyroid cancer, half of the lifetime dose, but 65–70% of the risk was associated with the first year of exposure, indicating the overall impact of the first year. The LFR was small with a maximum of 3.6% (age at initial exposure of 1 year).

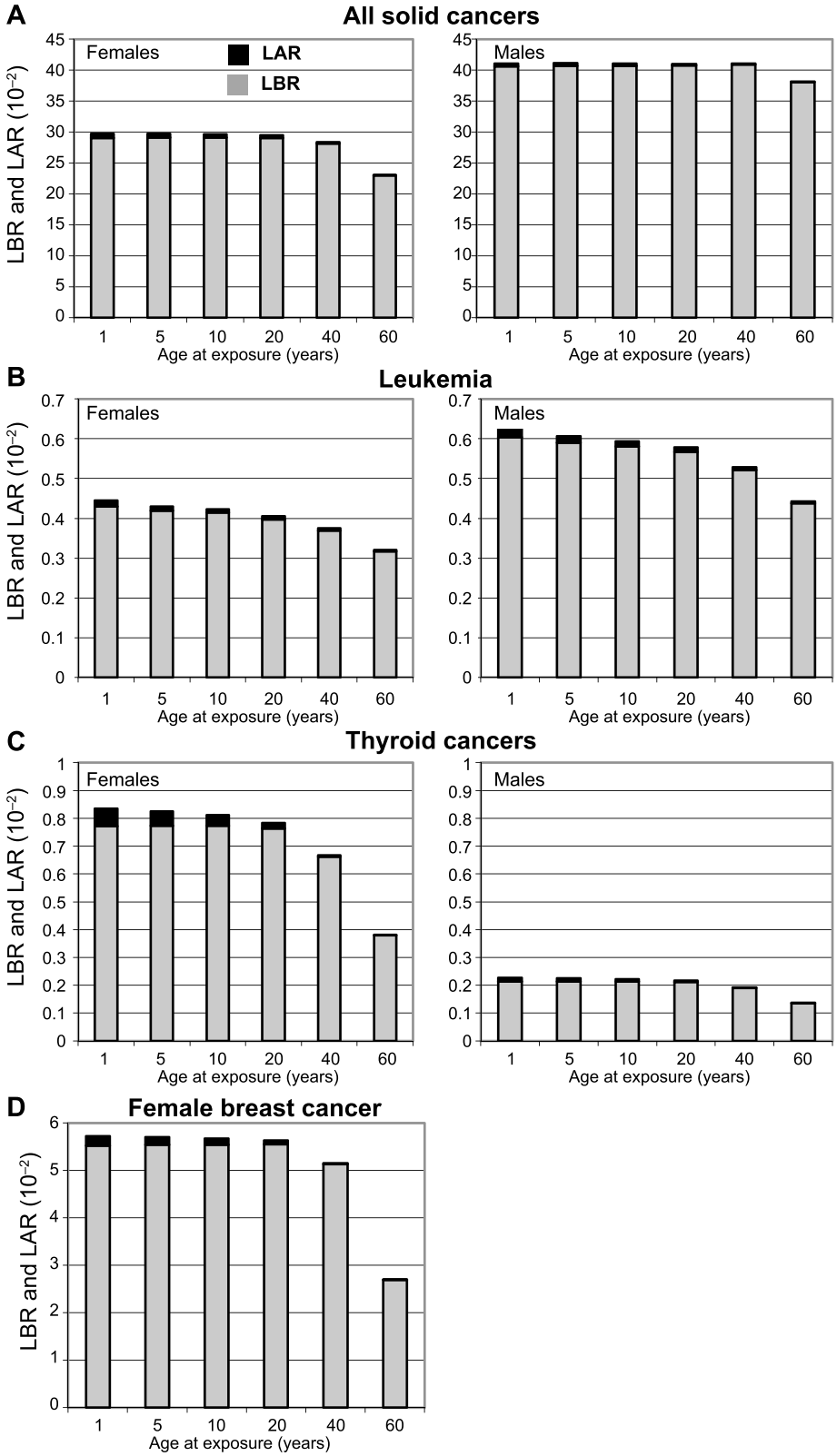

FIG. 2. Lifetime attributable risk (LAR) and lifetime baseline risk (LBR) for all solid cancer incidence (panel A), leukemia (panel B), thyroid cancer incidence (panel C) and female breast cancer incidence (panel D) at the reference lifetime organ/tissue dose of 20 mGy. Both quantities are given for females and males exposed at 1, 5, 10, 20, 40 and 60 years of age.

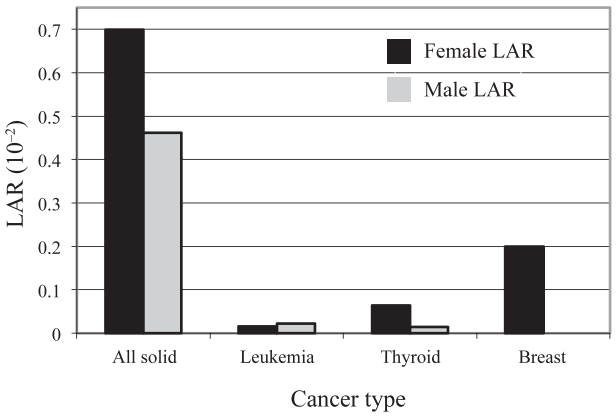

FIG. 3. Lifetime attributable risk (LAR) for the studied cancer types at the reference lifetime organ/tissue dose of 20 mGy, for females and males exposed at 1 year of age.

Risks over the First 15 Years after Exposure

Table 4 shows the AR_{15} based on a lifetime reference organ/tissue dose of 20 mGy[4] calculated with the main weights from Table 1 and the BR_{15} for both sexes and six different ages at exposure for incidence of all solid cancers, leukemia, thyroid and breast cancer. Table 4 also contains the FR_{15} for all of the ages at exposure considered. Results from Table 4 are shown in Fig. 4A–D for all solid cancers, leukemia, thyroid and breast cancer, respectively.

The highest radiation-related risks of all solid cancers were $0.03 \cdot 10^{-2}$ at ages 40 and 60 years. In contrast, AR_{15} in children aged 1 or 10 years was less than $0.01 \cdot 10^{-2}$ in females and roughly $0.005 \cdot 10^{-2}$ in males. The 15 year risk estimates were lower than lifetime risks (see above) by a factor of 60–80 for childhood exposure and 2–30 for adult exposure. The FR_{15} was 11% for females aged 1 year, but less than 1% for ages 40 and 60 years at exposure. These results are largely a reflection of the baseline risk at a young age.

For leukemia, the BR_{15} for females was between 60 and 94% smaller than for males and the AR_{15} per reference lifetime dose for females was between 60 and 71% of the AR_{15} for males, depending on the age at exposure. The FR_{15} showed a maximum of 29.5% for females and 33.2% for males, both values for age at initial exposure of 1 year. A substantial fraction of the LAR resulted from the AR_{15} for younger ages at first exposure (51% and 28% for ages at exposure 1 and 20 years, respectively).

In the special case of thyroid cancer, the AR_{15} is only applicable to the mainly external exposures from longer-lived radionuclides. For thyroid cancer, the BR_{15} for females ($\approx 0.8 \cdot 10^{-2}$) was between 2.9 and 5.2 times higher than for males, depending on age at exposure. The thyroid cancer AR_{15} for females was between 3.5 and 5.3 times higher than for males, depending on age at exposure. The FR_{15} had a maximum of 87.5% for females and 71.4% for males (see Fig. 4 and Table 4), both values for age at initial exposure of 1 year. A small fraction of the LAR, however, resulted from the AR_{15} for younger ages at first exposure (7% and 16% for ages at exposure 1 and 20 years, respectively).

The results for female breast cancer range from an effectively zero BR_{15} ($0.3 \cdot 10^{-5}$) at exposure age 1 year increasing up to 2% at the exposure age of 40 years. There was a trend of increasing AR_{15} with increasing age at first exposure up to 20 years, with AR_{15} decreasing after age 20 years at exposure. FR_{15} ranged from 0% (due to the minimum latent period) to 27% for initial exposure at age 10 years. Figure 5 details the male and female AR_{15} results for the age group most at risk, i.e., infants aged 1 year at exposure, illustrating the relationship between LAR/LBR and AR_{15}/BR_{15}, for the example of leukemia risk after exposure at 1 year. Figure 6 shows, for the specific case of leukemia in females exposed to the reference organ/tissue dose at 1 year of age, the impact of the applied risk quantities over different periods of life (i.e., a 15 year period compared to an 89 year period) and how the risks develop with increasing age attained. The minimum latency period is particularly visible in panel A.

DISCUSSION

This discussion will present the rationale for the choices made in the risk assessment, detail associated sources of uncertainties and give a brief review of other risk assessments. Several choices were made to perform the risk estimations in the current study both with respect to input data and to models and approaches. While a complete quantification of all uncertainties is beyond the scope of this article, the next few sections evaluate how different choices may have affected the LAR values reported here.

Choices of Specific Cancer Sites, with Emphasis on Thyroid

The estimates of all solid cancer risk together with leukemia risk essentially represent the overall impact of radiation exposure on cancer risk. Pooling all solid cancers together reflects the fact that radiation causes cancer in most body organs/tissues and enhances statistical power. However, in circumstances where the organ/tissue doses are highly heterogeneous, such as the dose to the thyroid after an intake of radioactive iodine, the risk of all solid cancers combined will not fully account for the risk of thyroid cancer. Thyroid cancer is especially relevant to the HRA because of the release of radioactive iodine from the Fukushima Daiichi NPS. Even though this study applies reference thyroid doses for performing the risk estimations, it must be noted that the doses to the thyroid are more uncertain than for other organs, since relatively few thyroid radioactivity measurements were made early after the

[4] Note that this reference lifetime dose of 20 mGy, which actually corresponds to a 15 year reference organ dose of 15.6 mGy, is applicable for members of the general public who were not relocated after the accident.

TABLE 3
Results Applicable to Risk Assessment for Either Relocated Members of the Public or Adult Male Emergency and Recovery Workers

Age at exposure (years)	Cancer site			
	All solid cancers	Leukemia	Thyroid	Female breast
Female risks per reference first year organ/tissue dose of 10 mGy				
		Lifetime attributable risk (LAR · 10^{-2})		
1	0.42	0.01	0.04	0.13
5	0.38	0.01	0.03	0.11
10	0.33	0.01	0.03	0.09
20	0.26	0.00	0.01	0.05
40	0.14	0.00	0.00	0.02
60	0.06	0.00	0.00	0.01
		Lifetime baseline risk (LBR · 10^{-2})		
1	29.04	0.43	0.77	5.53
5	29.09	0.42	0.77	5.54
10	29.09	0.41	0.77	5.54
20	29.07	0.40	0.76	5.55
40	28.17	0.37	0.66	5.13
60	22.98	0.32	0.38	2.69
		Lifetime fractional risk (LFR in percentages)		
1	1.4	2.4	5.6	2.4
5	1.3	1.4	4.4	2.0
10	1.1	1.2	3.3	1.6
20	0.9	1.1	1.8	1.0
40	0.5	0.9	0.5	0.4
60	0.3	0.7	0.2	0.2
Male risks per reference first year organ/tissue dose of 10 mGy				
		Lifetime attributable risk (LAR · 10^{-2})		
1	0.27	0.02	0.01	
5	0.25	0.01	0.01	
10	0.22	0.01	0.01	
20	0.17	0.01	0.00	
40	0.10	0.00	0.00	
60	0.05	0.00	0.00	
		Lifetime baseline risk (LBR · 10^{-2})		
1	40.60	0.60	0.21	
5	40.70	0.59	0.21	
10	40.71	0.58	0.21	
20	40.75	0.57	0.21	
40	40.90	0.52	0.19	
60	38.10	0.44	0.14	
		Lifetime fractional risk (LFR in percentages)		
1	0.7	2.5	4.6	
5	0.6	1.5	3.6	
10	0.5	1.3	2.6	
20	0.4	1.2	1.4	
40	0.3	0.9	0.4	
60	0.1	0.8	0.2	

Notes. Lifetime attributable risk [LAR from Eqs. (1–2)] calculated with the main weights from Table 1, lifetime baseline risk [LBR from Eq. (4)] and lifetime fractional risk [LFR from Eq. (5)] up to attained age 89 years for a first year dose of 10 mGy (both sexes and six different ages at exposure) for all solid cancers, breast cancer, thyroid cancer (applicable to the mainly internal doses from short-lived radionuclides and mainly external doses from longer-lived radionuclides) and leukemia incidence. LFR has been calculated from LAR and LBR with computer precision values before rounding all numbers to fewer decimal places for this table.

accident. ERR models for thyroid cancer incidence from the Japanese A-bomb survivors Life Span Study (*5*) yield an ERR per unit dose that decreases with age at exposure and age attained. The EAR per unit dose from the corresponding EAR models (*5*) also decreases with age at exposure, but increases with time since exposure. Comparisons with studies of people exposed to radioiodine after the Chernobyl accident have shown that the ERR per unit dose is quite

TABLE 4
Results Applicable to Risk Assessment for Members of the General Public Who Were Not Relocated after the Accident

Age at exposure (years)	Cancer site			
	All solid cancers	Leukemia	Thyroid	Female breast
Female risks per reference lifetime organ/tissue dose of 20 mGy				
	15 Year attributable risk ($AR_{15} \cdot 10^{-2}$)			
1	0.0091	0.0077	0.0035	~0
5	0.0080	0.0033	0.0039	~0
10	0.0093	0.0025	0.0041	0.0023
20	0.0183	0.0019	0.0032	0.0048
40	0.0350	0.0018	0.0016	0.0044
60	0.0343	0.0020	0.0005	0.0030
	15 Year baseline risk ($BR_{15} \cdot 10^{-2}$)			
1	0.0804	0.0261	0.0040	~0
5	0.0952	0.0231	0.0114	~0
10	0.1564	0.0228	0.0294	0.0085
20	0.6710	0.0221	0.0739	0.1927
40	4.8160	0.0521	0.2105	2.0033
60	10.6544	0.1470	0.2528	1.7844
	15 Year fractional risk (FR_{15} in percentages)			
1	11.3	29.5	87.5	~0
5	8.4	14.3	34.2	~0
10	6.0	11.0	14.0	27.1
20	2.7	8.6	4.3	2.5
40	0.7	3.5	0.8	0.2
60	0.3	1.4	0.2	0.2
Male risks per reference lifetime organ/tissue dose of 20 mGy				
	15 Year attributable risk ($AR_{15} \cdot 10^{-2}$)			
1	0.0053	0.0114	0.0010	
5	0.0048	0.0047	0.0010	
10	0.0055	0.0035	0.0009	
20	0.0087	0.0032	0.0007	
40	0.0208	0.0030	0.0003	
60	0.0324	0.0031	0.0001	
	15 Year baseline risk ($BR_{15} \cdot 10^{-2}$)			
1	0.0830	0.0343	0.0014	
5	0.0836	0.0254	0.0028	
10	0.1318	0.0243	0.0057	
20	0.3563	0.0370	0.0169	
40	3.7137	0.0802	0.0488	
60	21.0252	0.2256	0.0856	
	15 Year fractional risk (FR_{15} in percentages)			
1	6.4	33.2	71.4	
5	5.7	18.5	35.7	
10	4.2	14.4	15.8	
20	2.4	8.7	4.1	
40	0.6	3.7	0.6	
60	0.2	1.4	0.1	

Notes. Fifteen year attributable risk (AR_{15}) calculated with the main weights from Table 1, 15 year baseline risk (BR_{15}) and 15 year fractional risks (FR_{15}) for a lifetime dose of 20 mGy which, accumulated over a 15 year period, would be 15.6 mGy, (both sexes and six different ages at exposure) for all solid cancers, breast cancer, thyroid cancer (applicable only to the mainly external thyroid doses from longer-loved radionuclides) and leukemia incidence. FR_{15} has been calculated from AR_{15} and BR_{15} with computer precision values before rounding all numbers to fewer decimal places for this table.

similar to the risk observed in the LSS in the period of 13–18 years after exposure (*31*, *37*), although LSS incidence data are not available prior to that. Thyroid cancer risk information is available for Chernobyl accident studies beginning shortly after exposure, however, this information has substantial uncertainties (*30*, *31*).

Since recently published thyroid cancer incidence rates in Japan for boys and girls under age 10 years were zero (*22*),

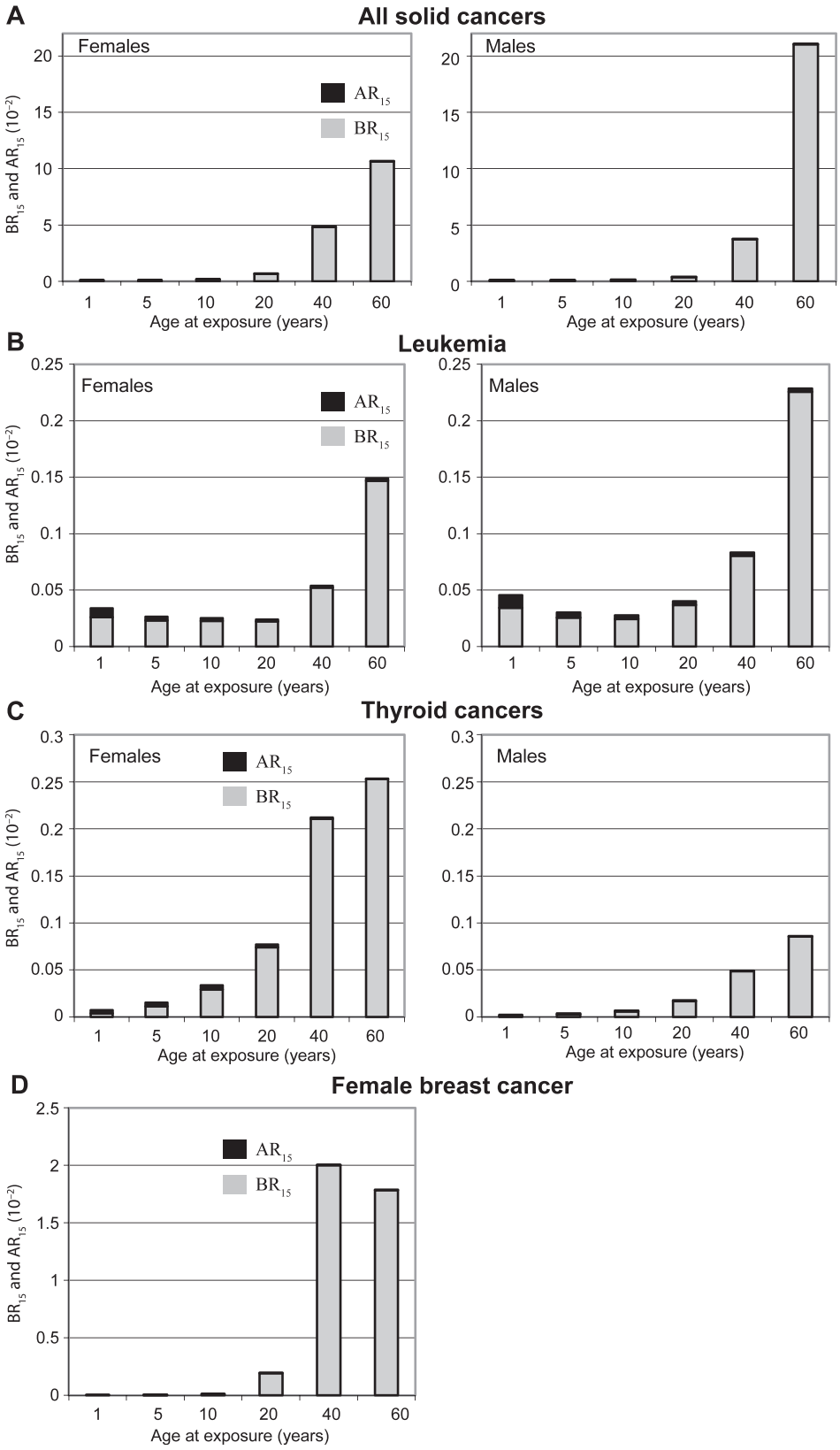

FIG. 4. Fifteen year attributable risk (AR_{15}) and baseline risk (BR_{15}) for all solid cancer incidence (panel A), leukemia (panel B), thyroid cancer incidence (panel C) and female breast cancer incidence (panel D) for the reference lifetime organ/tissue dose of 20 mGy. Both quantities are given for females and males exposed at 1, 5, 10, 20, 40 and 60 years of age.

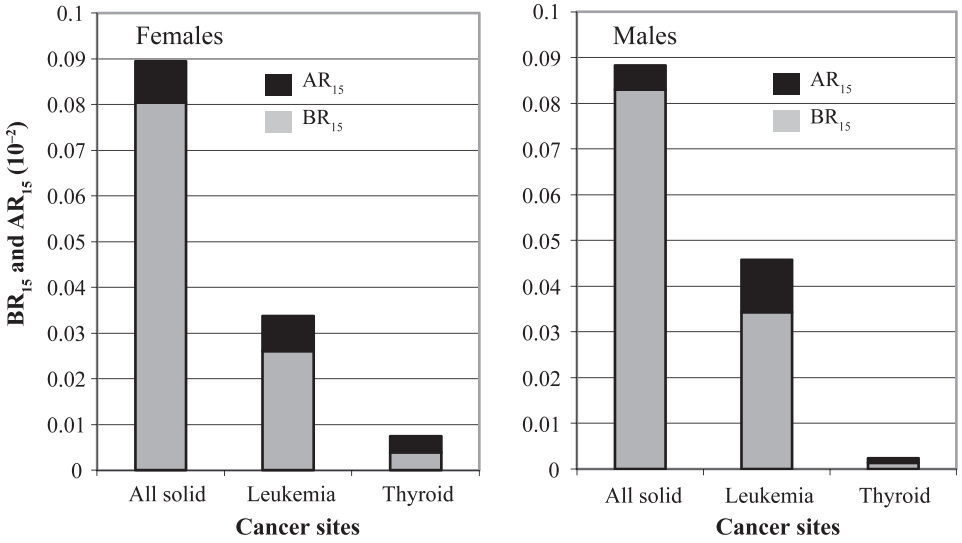

FIG. 5. Fifteen year attributable risk (AR_{15}) and baseline risk (BR_{15}) for the studied cancer types, at the reference lifetime organ/tissue dose of 20 mGy, for females and males exposed at 1 year of age. Only the nonzero AR_{15} values are shown, i.e., the risk for breast cancer is zero in this case.

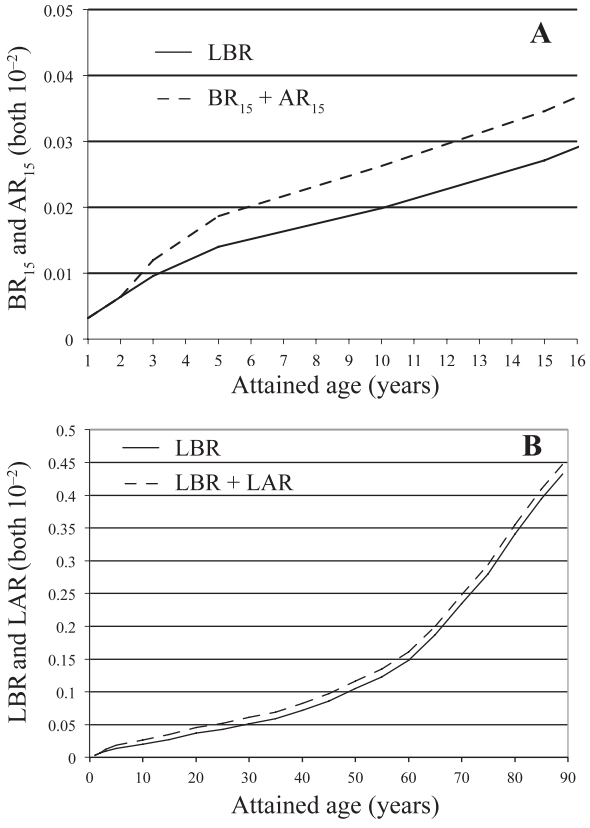

FIG. 6. Illustration of the evolution of attributable and baseline risks of leukemia according to attained age for an exposure at age 1 year to the reference dose of 10 mGy. Panel A shows the 15 year attributable risk (AR_{15}) and 15 year baseline risk (BR_{15}) (i.e., at attained age of 16 years). Panel B shows the lifetime attributable risk (LAR) and lifetime baseline risk (LBR) (at attained age of 89 years).

a pure transfer of the multiplicative excess relative risk model from the LSS to the current population of Fukushima Prefecture would lead to a prediction of zero excess thyroid cancer cases, clearly a potential underestimate. It was therefore decided to avoid such a zero risk prediction by adopting a 50% ERR and 50% EAR risk transfer (Table 1), especially since the assumption of a pure transfer of the excess relative risk per unit dose is debatable (*32, 37*).

Currently reported thyroid cancer prevalence rates, including background rates, will inevitably be influenced by the ultrasonographic surveys that are being performed in Fukushima Prefecture. During 1999–2010 the incidence rate of thyroid cancer in Korea rose by 24% per year in both sexes, and it has been proposed that this is a reflection of ''the identification of previously undetected disease with improved diagnostic techniques and increased screening rates'' (*38*), and a similar effect must be anticipated in Japan. It has been estimated that continued surveys in Fukushima will increase the thyroid cancer morbidity rate in the screened population by a factor of about 7, with a large uncertainty ranging from 1–17 (*37*). A reasonable assumption is that many of the thyroid cancer cases detected by these ultrasonographic surveys would not have become clinically relevant (*39*). This assertion is based on autopsy studies that indicate that such tumors are ordinarily prevalent in a proportion of the adult population as ''occult'' thyroid cancer (*40, 41*). In a study of Japanese atomic bomb survivors, 3.9% of the persons examined in the lowest dose group (<5 mGy thyroid dose) were found to have occult thyroid cancer (*42*). Therefore, it is particularly important to emphasize that effects of the screening measures on the natural evolution of thyroid disease in this population will result in an increased apparent ascertainment rate, which

might generate particular concern for health professionals and members of the general public near Fukushima.

Selection of a Reference Dose

As described above, reference lifetime doses were used to predict the risks resulting from the radiation exposure. The assumption of a ratio of lifetime dose to first year dose of two, used to produce the results in Table 2, does not hold for the persons relocated a few months after the accident, or for the emergency and recovery workers at the Fukushima Daiichi NPS. These groups would have received more than 90% of their lifetime dose in the first few months. In those cases where a factor of two may not be appropriate, the risks based only on a reference first year dose of 10 mGy, shown in Table 3, are considered more appropriate. A comparison shows that between 56 and 77% (depending on cancer site and age at exposure) of the total LAR based on lifetime doses (Table 2) is contributed by the LAR based on just the first year dose (Table 3).

Selection of Age at Exposure

To ensure representation of the younger, more radiosensitive (*9*) members of the general population, three ages at exposure in childhood were considered for this HRA with ages 1, 5 and 10 years to represent children. The selected adult ages at exposure of 20, 40 and 60 years were judged to be sufficient to represent adult members of the general public. Indeed, the Japanese population has been among those with the longest life expectancy in the world. The adult population characterized by these age groups is also well suited for male emergency workers. Epidemiological studies indicate that the thyroid cancer risk is higher for younger age-at-exposure groups and decreases substantially with increasing age at exposure, with little apparent risk for individuals exposed after 20 years of age (*43–46*). Therefore the selected groups allow for an appropriate estimation of thyroid cancer risks for different ages at exposure in both childhood and adulthood.

Selection and Availability of Health Statistics Data

Cancer incidence was considered to be more relevant than cancer mortality, from a public health perspective, because many cancers have an increasing prospect of cure and incidence can be less influenced than mortality by variables such as health system strength and access to early treatment. However, screening programs for thyroid and breast cancer may increase the apparent incidence (morbidity) much more than reduce the mortality. The current analysis applied ''cancer-free'' survival (adjusted survival, see Supplementary Fig. S1; http://dx.doi.org/10.1667/RR13779.1.S1), rather than overall survival, because the former is more appropriate for calculating the LAR and LBR of cancer incidence.

For leukemia, risk models based on LSS mortality data rather than incidence data were used because the most recent incidence data (*47*) were not available at the time of the WHO assessment (*3*). However, it is now possible to evaluate how the LAR values may be affected when the LSS mortality data models are substituted with the most recent LSS incidence data-based models (*47*). An evaluation was done by comparing some examples of the ERR and EAR (in cases per 10,000 person-years) at 10 mGy, for leukemia (Supplementary Table S2; http://dx.doi.org/10.1667/RR13779.1.S1), calculated with both models [i.e., with the adopted UNSCEAR model, based on mortality data (*27*), and with the most recent models (for leukemia, excluding chronic lymphocytic leukemia and adult T-cell leukemia) based on incidence data (*47*)]. The ERR and EAR results from the models based on either mortality or incidence data did not differ very much and so it may be concluded that use of the more recent incidence data (*47*) would not affect the LAR values. A similar conclusion may be drawn from calculating the ERR and EAR for both sets of models as functions of attained age for young ages at exposure (graphics not shown). In these instances the models fitted to incidence data (*47*) tend to predict higher risks at younger attained ages, but the reverse is true at higher attained ages. Therefore, in the integration over attained age in the calculation of LAR, such differences will tend to even out.

The choice of health statistics data applied in LAR calculations that project risks into the distant future represents one of the main sources of uncertainty in LAR, mainly because of the difficulty in predicting future cancer rates. Japanese rates were used because the Fukushima Prefecture Cancer Registry has only very recently introduced cancer registration. The most recent data available at the time of the risk calculations for the WHO report (*3*) were cancer incidence data for 2004 (*22*) and cancer mortality data and all cause mortality data for 2010 (*24*). A preliminary comparison of the survival curves calculated with the 2010 (Supplementary Fig. S1; http://dx.doi.org/10.1667/RR3779.1.S1) and the 2011 all cause mortality rates (*24*) did not show any statistically discernible differences. Age-specific population cancer incidence data for 2006 (*48*) were published (*3*), and show higher female breast and thyroid cancer incidence rates compared to the 2004 rates (for age ranges of 45–80 years and 25–55 years, respectively). Slightly higher LAR estimates for breast and thyroid cancer in adults may result if calculated using the 2006 cancer incidence rates (*48*). However, this would only minimally affect the estimates of lifetime fractional risk, which prove to be more invariant to secular trends in background cancer rates than LAR and LBR. For all solid cancers and leukemia, a comparison between the 2004 and 2006 rates merely showed apparently random variations.

A recent report on the analysis of trends in cancer incidence rates in Japan (*49*) showed that the incidence of all cancers continually increased from 1985–2007 with an

annual percentage change (APC) of 0.7% (95% CI: 0.6; 0.8). During the same time period, the APC for male and female leukemia were −0.4% (95% CI: −0.8; 0.0) and −0.2% (95% CI: −0.8; 0.3), respectively, while the APC for thyroid cancer was 3% (95% CI: 2.3; 3.7). The APC for female breast cancer based on data from 1996–2007 was 4.4% (95% CI: 3.9; 4.9) and the APC for female thyroid cancer based on data from 2002–2007 was 4.5% (95% CI: 1.0; 8.2). Given these trends, slightly higher LAR estimates for breast and thyroid cancer in adults may also result if calculated using 2007 incidence data (*50*) or 2008 incidence data (*23*), but again, the LFR values should only be minimally affected. Overall there are no major changes between the incidence data in 2004 and 2008, therefore it can be concluded that the LAR results would remain largely unchanged even if updated data were used.

International Classification of Diseases

There was an incomplete concordance in the LAR calculations of ICD-10 codes between the LSS data used to fit the adopted LSS ERR and EAR models and the Japanese health statistics data for all solid cancers [(LSS data was C00–C89 and Japanese health statistics data was C00–C90, which include multiple myeloma (C90)], and breast [(LSS data was C50 and Japanese health statistics data was C50 and D05, which include *in situ* breast cancer (D05) with invasive breast cancer (C50)]. However, these slight mismatches were not considered to substantially affect the LAR results for the following reasons. The potential inclusion of multiple myeloma in the all solid cancer ERR and ERR risk models for the followup period 1958–1998 would not be expected to influence the models based on 17,448 cancer incidences, for reasons of statistical power, because there were only 136 multiple myeloma cases eligible for the most recent analysis (based on the followup 1950–2001) and no evidence was found for a radiation-associated excess risk (*47*). In the Hiroshima and Nagasaki Prefecture Tumor Registries, 10.0% and 4.9% of breast cancer cases were *in situ*, respectively. However, these percentages are higher than in other Japanese registries because Hiroshima and Nagasaki registries both include a tissue registry that reports *in situ* cases, whereas none of the other prefecture registries have a tissue registry. Assuming a plausible hypothesis that radiation may be related to both *in situ* and invasive breast cancer (because studies on the radiation sensitivity of *in situ* breast cancer are unknown to the authors) then failure to include *in situ* breast cancers in the LSS could potentially result in a small underestimate of the EAR and LAR.

Choices of Latency Periods

Minimum latency periods were based on those reported in the literature [i.e., 2, 3 and 5 years for leukemia, thyroid cancer and all solid cancers (*9, 36, 27, 28*), respectively]. For female breast cancer, the assumed latency was 5 years after exposure or an attained age of 20 years, whichever was greater. The rationale for using a minimum age as part of the definition of latency was based on epidemiological evidence from a review of studies on populations with childhood radiation exposure that indicated the youngest age of disease onset was 20 years, regardless of the earlier age at exposure (*51–53*). Among Japanese atomic bomb survivors, none of the 68 breast cancers occurring among those who were 0–9 years old at the time of exposure were diagnosed before age 20 years (*54*). The Japanese population cancer incidence rates, used in the lifetime risk calculations (*22*), had zero age specific breast cancer rates for the four age groups under age 20 years. As a consequence, there was a trend of increasing AR_{15} with increasing age at first exposure from those exposed at age 5 years to those exposed at age 20 years; at older exposure ages the AR_{15} decreased. For thyroid cancer risk, studies done after the Chernobyl accident indicated a short minimum latency period for exposed children and this was taken into consideration here because early cases were missing from the LSS thyroid cancer incidence data. Small variations of minimum latency period by one year would only slightly affect the LAR results, at a level within the rounding errors given in the main results tables here.

Choices of Models

The choice of cancer risk models applied in LAR calculations represents another source of uncertainty. The preferred approach for assessing risks from low-dose radiation exposures relevant to the Fukushima Daiichi accident was considered to be the use of a linear no-threshold (LNT) model for solid cancers, and a linear-quadratic no-threshold model for leukemia. The relative risk transfer model assumes that the excess cancer risk induced by radiation is proportional to the underlying (baseline) risk, while the absolute risk transfer model assumes that the radiation-induced excess risk is independent of the baseline risk. Rates of incidence of cancer types vary among populations (*55*), but the risk models used in this assessment are based on the radiation-exposed Japanese population of atomic bomb survivors, so these variations in underlying risks are of less importance than, for example, the transfer of risk to a North American population. Nonetheless, there have been changes in cancer incidence rates in Japan over the past half-century, notably an increase in the breast cancer incidence rate, so the question of the weights used for ERR and EAR transfer remains pertinent.

The LAR may also be calculated with ERR/EAR weights other than those given in Table 1. Overall, the choices of the risk transfer weights were either consistent with the published literature (for all solid cancers, leukemia and breast cancer) or were more conservative (i.e., by including higher risks from the 50% EAR transfer for thyroid cancer) (see Table 1 for citations of articles containing evidence for the choice of the main weights applied here). The influence

of the choice of transfer weights (Table 1) on the LAR results can be seen by comparing Table 2 and Supplementary Table S3 (http://dx.doi.org/10.1667/RR13779.1.S1). In general, this choice did not substantially affect the LAR results. However, for breast cancer, higher LAR risks would result for persons aged 10 years or older at initial exposure, by an age-at-exposure-dependent factor of between 1 and 2.1, if a 50% EAR:50% ERR weighting had been applied instead of the 100% EAR weighting chosen here.

An important source of uncertainty in the LAR calculations includes the application of the ERR and EAR models at very low doses, very young ages at exposure and short times since exposure. These uncertainties associated with applications of the ERR and EAR models can be assessed with a sensitivity analysis by using the ERR and EAR models to calculate central risk estimates with 90% confidence intervals (CI) at 10 mGy for a selection of ages and short times since exposure (Supplementary Table S2; http://dx.doi.org/10.1667/RR13779.1.S1). The 90% confidence intervals for ERR and EAR estimates for all solid and female breast cancers all have lower limits above zero, so resulting 90% confidence intervals for LAR using any combination of ERR and EAR models would also be expected to have lower limits above zero. In contrast, the ERR and EAR estimates from leukemia models in Supplementary Table S2 all show very wide 90% CIs including zero risk, so the resulting LAR values would also be expected to have confidence intervals encompassing zero risk. The ERR and EAR estimates for thyroid cancer in Supplementary Table S2 show some very wide 90% CIs including zero risk and some excluding zero risk, making an overall estimation of the LAR lower confidence limits difficult. However, for ages at exposure greater than 40 years, the LAR confidence intervals would be expected to include zero risk.

Another source of uncertainty in the calculation of LAR relates to the dose and dose-rate effectiveness factor (DDREF) for extrapolating risks from moderate/high doses and dose rates to low doses and/or low dose rates. A DDREF of 2 is generally used for radiation protection purposes (*26*), however, a DDREF of 1 was assumed implicitly for this analysis, based on a review of the evidence (*56*, *57*).

Use of Colon Dose for Calculating All Solid Cancer Risk

As explained in the Materials and Methods section, the colon dose was used for the calculation of all solid cancer risks, an approach also used in the LSS. It should be noted that in circumstances where the organ/tissue doses are highly heterogeneous, e.g., when external exposure, mainly from radiocesium, is combined with internal thyroid exposure to radioactive iodine, the thyroid dose is greater than the colon dose. Therefore, the risk of all solid cancers combined based on colon dose will not fully account for the risk of thyroid cancer.

Scaling of Risk Estimates

In theory, the risk estimates provided here could be linearly scaled to other relevant organ/tissue doses. However, a caveat for scaling risks at low doses is that there is little direct epidemiological support for applying linear risks to very low doses, or even doses below 50 mGy. This is because low-dose risks are derived from cancer risk models fitted to a wide dose range (0–4 Gy) and the risks are not significantly increased if just the range of 0–50 mGy is considered. However, the LNT model is still accepted internationally as the most appropriate model for assessing solid cancer risks (*26–28*). Although epidemiological data are consistent with excess solid cancer risks that are proportional to the exposure, as predicted by the LNT model (*58*), such data do not allow for definitive statements about the shape of the dose-response at low doses. Therefore, scaling must be done cautiously with due consideration given to the large uncertainties in estimates of health risks from exposures to very low doses, at levels similar to or lower than natural background levels. Nonetheless, it is highly improbable that risks at low doses were seriously underestimated, since this would have been apparent in epidemiological studies of low-level exposure.

Another caveat applies to proportionality assumptions between solid cancer or leukemia lifetime risks and organ/tissue doses above 0.5 Gy and 0.2 Gy, respectively. Above these doses the assumption of linearity is no longer valid because the LAR for solid cancers diverges from other measures for lifetime risk (*35*) and the LAR for leukemia becomes nonlinear due to the linear-quadratic dose response in the ERR and EAR models applied in the LAR calculations (graphics not shown). To apply the LAR given in Table 2 (Figs. 2D and 3), or Table 3 to other doses, the age at exposure-, sex- and cancer site-specific LAR entries in Table 2 or Table 3 may be linearly scaled by dose, after taking into consideration the caveats just given. The same caveats apply for scaling the AR_{15} risks given in Table 4 (and Figs. 4A–D and 5) to other doses.

Scaling of risks for the thyroid gland to other doses requires a special consideration, because risk contributions from mainly internal and mainly external exposures due to short- and longer-lived radionuclides, respectively, may need to be accounted for. Results for a 10 mGy first year internal thyroid dose mainly due to ^{131}I (represented by Table 3 results) may be scaled and added to the scaled results based on a 20 mGy lifetime external thyroid dose mainly due to cesium (represented by Table 2 results), to create a composite lifetime risk from the two sources. For example, consider the exposure scenario of a 20 mGy internal first year thyroid dose mainly from ^{131}I plus an external 5 mGy first year thyroid dose (i.e., an external 10 mGy lifetime thyroid dose) mainly from cesium: the composite risk (LAR based on total lifetime thyroid dose) can be constructed with twice the LAR from Table 3 added to half the LAR from Table 2.

Review of Other HRA Studies

Excess lifetime cancer mortality and morbidity risks associated with both inhalation and external exposure due to the Fukushima accident have recently been published for each continent in the world (*59*). The U.S. EPA Dose and Risk Calculation (DCAL) software (*60*) was applied for this purpose. Risk coefficients were organ/tissue-, age- and sex-specific relative risk coefficients derived from the Japanese A-bomb LSS cohort. A DDREF of two was applied (except for breast cancer). The approach of Ten Hoeve and Jacobson (*59*) differs from the one used in this current study because DCAL estimates global numbers of attributable cancer cases or deaths (i.e., not sex- or cancer-site-specific). Another study (*61*) considered risk projections from radiocesium doses, calculated with an atmospheric transport model, in terms of local and global numbers of cases or deaths. While the LAR values reported appear generally consistent with those in the WHO-HRA (*3*), overall cancer risks were given rather than cancer site-specific risks. Another assessment has been based on lifetime doses integrated from dose rates measured within a 50 km radius of the Fukushima Daiichi NPS during a two-month period in 2012 (*62*). The risks provided in the published article by Harada *et al.* (*62*) were lower than those given here because the first year dose was not considered. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) has reported on the levels and effects of radiation exposure due to the 2011 Fukushima nuclear accident (*63*, *64*). The assumptions underpinning the UNSCEAR estimates of health implications and the UNSCEAR results for cancer risks due to the radiation from the accident are generally well aligned and consistent with assumptions and results presented here and in the WHO report (*3*).

Concluding Remarks

This article presents the methodological framework adopted by the WHO in a recent report (*3*) on health risk assessment of the Fukushima Daiichi NPS accident. The adopted framework has been used to provide sex- and age-at-exposure-specific radiation-related risk estimates for a reference organ/tissue dose for all solid cancer, leukemia, thyroid and female breast cancer incidence, in terms of LAR for groups of persons exposed as infants, children or adults. The main results show that even if the first year doses were of the order of 10 mGy, the lifetime radiation-induced cancer risks based on lifetime dose, even for children who were less than 5 years of age at initial exposure are small, and much smaller than the lifetime baseline cancer risks. The 15 year risks based on the lifetime reference dose are also very small. However, for initial exposure in childhood, the 15 year risks based on the lifetime reference dose are up to 33 and 88% as large as the 15 year baseline risks for leukemia and thyroid cancer, respectively. Half of the lifetime dose (assumed to be received in the first year of exposure) has a higher impact on the overall LAR than the doses accumulated in all subsequent years. The risk estimates given here may be applied to any revised dosimetry information pertaining to the Fukushima nuclear accident, because the risks for solid cancers and leukemia may theoretically be linearly scaled, with the caveats already given, to any organ/tissue doses under about 0.5 Gy and 0.2 Gy, respectively. The most recent population data on age-specific cancer incidence and mortality and all cause mortality available at the time of the risk calculations for the WHO report (*3*) were also applied here for consistency, even though there may have been some slight advantages in applying the population data most recently available at the time of writing this article. However, the framework described here may also be applied in the future to update the risk estimates when new data on population exposure and revised radiation risk models, such as those based on future followup LSS data of Japanese atomic bomb survivors or populations exposed after the Chernobyl accident, become available.

SUPPLEMENTARY INFORMATION

Table S1. Risk models for assessing cancer risks.

Table S2. ERR and EAR (in cases per 10,000 person-years) at the reference first year organ/tissue dose of 10 mGy with 90% confidence intervals (CIs).

Table S3. Results applicable to risk assessment for members of the general population who were not relocated after the accident.

Fig. S1. Adjusted survival curves (for males, females and both together), $S_{aj}(a)$, applied in the LAR calculations and calculated from the all cause Japanese mortality rates and all cancer Japanese mortality rates for 2010 obtained from http://www.mhlw.go.jp/english/database/index.html and the Japanese all cancer incidence rates for 2004 obtained from Table 3 of (*22*).

ACKNOWLEDGMENTS

The authors would like to thank Dr. A. Prüss-Ustün for useful discussions and Dr. Simon Bouffler for critically reading the manuscript. This article makes use of data (RP 1-75) obtained from the Radiation Effects Research Foundation (RERF) in Hiroshima and Nagasaki, Japan. RERF is a private, nonprofit foundation funded by the Japanese Ministry of Health, Labour and Welfare (MHLW) and the U.S. Department of Energy (DOE), the latter through the National Academy of Sciences. The data include information obtained from the Hiroshima and Nagasaki City Prefecture Tumor Registries and the Hiroshima and Nagasaki Tissue Registries. The conclusions in this report are those of the authors and do not necessarily reflect the scientific judgment of RERF or its funding agencies.

Received: April 23, 2014; accepted: July 21, 2014; published online: September 24, 2014

REFERENCES

1. Ohnishi, T. The disaster at Japan's Fukushima-Daiichi nuclear power plant after the March 11, 2011 earthquake and tsunami, and

the resulting spread of radioisotope contamination. Radiat Res 2012; 177:1–14.

2. Wakeford R. And now, Fukushima. J Radiol Prot 2011; 31:167–76.
3. Health risk assessment from the nuclear accident after the 2011 Great East Japan Earthquake and Tsunami based on a preliminary dose estimation. World Health Organization; 2013. (http://www.who.int/ionizing_radiation/pub_meet/fukushima_risk_assessment_2013/en)
4. International Atomic Energy Agency. Emergency preparedness and response. In: Joint radiation emergency management plan of the international organizations. EPR-JPlan 2013. Vienna: IAEA. (http://www-pub.iaea.org/MTCD/publications/PDF/EPRJplan2013_web.pdf)
5. Preston DL, Ron E, Tokuoka S, Funamoto S, Nishi N, Soda M, et al. Solid cancer incidence in atomic bomb survivors: 1958–1998. Radiat Res 2007; 168:1–64.
6. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation (UNSCEAR 2008), Vol 2, Annex D: Health effects due to radiation from the Chernobyl accident. New York: United Nations; 2011. (http://www.unscear.org/docs/reports/2008/11–80076_Report_2008_Annex_D.pdf)
7. IARC Monographs on the evaluation of carcinogenic risks to humans. A review of human carcinogens: radiation (Vol. 100 D). Lyon: IARC Working Group on the Evaluation of Carcinogenic risks to Humans; 2012. (http://monographs.iarc.fr/ENG/Monographs/vol100D/mono100D.pdf)
8. Report of the United Nations Scientific Committee on the Effects of Ionizing Radiation (UNSCEAR 2010): Summary of low-dose radiation effects on health. New York: United Nations; 2010. (http://www.unscear.org/docs/reports/2010/UNSCEAR_2010_Report_M.pdf)
9. Report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR 2013), Vol. 2, Scientific Annex B: Effects of radiation exposure of children. New York: United Nations; 2013 (http://www.unscear.org/docs/reports/2013/UNSCEAR2013Report_AnnexB_Children_13–87320_Ebook_web.pdf)
10. Preliminary dose estimation from the nuclear accident after the 2011 Great East Japan Earthquake and Tsunami. World Health Organization; 2012. (http://www.who.int/ionizing_radiation/pub_meet/fukushima_dose_assessment/en)
11. Matsuda N, Kumagai A, Ohtsuru A, Morita N, Miura M, Yoshida M, et al. Assessment of internal exposure doses in Fukushima by a whole body counter within one month after the nuclear power plant accident. Radiat Res 2013; 179:663–8.
12. Endo S, Kimura S, Takatsuji T, Nanasawa K, Imanaka T, Shizuma K. Measurement of soil contamination by radionuclides due to the Fukushima Dai-ichi Nuclear Power Plant accident and associated estimated cumulative external dose estimation. J Environ Radioactivity 2012; 111:18–27.
13. Tsubokura M, Gilmour S, Takahashi K, Oikawa T, Kanazawa Y. Internal radiation exposure after the Fukushima Nuclear Power Plant disaster. JAMA 2012; 308:669–70.
14. Tokonami S, Hosoda M, Akiba S, Sorimachi A, Kashiwakura I, Balonov M. Thyroid doses for evacuees from the Fukushima nuclear accident. Sci Rep 2012; 2:507.
15. Kamada N, Saito O, Endo S, Kimura A, Shizuma K. Radiation doses among residents living 37 km northwest of the Fukushima Dai-ichi Nuclear Power Plant. J Environ Radioact 2012; 110:84–9.
16. Ministry of Education/Culture/Sports/Science/Technology. Reading of radioactivity level in fallout by prefecture. 2011. (In Japanese; http://radioactivity.mext.go.jp/en/)
17. Chino M, Nakayama H, Nagai H, Terada H, Katata G, Yamazawa H. Preliminary estimation of release amounts of 131I and 137Cs accidentally discharged from the Fukushima Daiichi nuclear power plant into the atmosphere. J Nucl Sci Technol 2011; 48:1129–34.
18. Masson O, Baeza A, Bieringer J, Brudecki K, Bucci S, Cappai M, et al. Tracking of airborne radionuclides from the damaged Fukushima Dai-ichi nuclear reactors by European networks. Environ Sci Technol 2011; 45:7670–7.
19. Final report of the international mission to support the remediation of large contaminated areas off-site of the Fukushima Daiichi Nuclear Power Plant. Document NE/NEFW/2011. Vienna: International Atomic Energy Agency; 2011 (http://www.iaea.org/newscenter/focus/fukushima/final_report151111.pdf).
20. Etherington G, Zhang W, Harrison J, Walsh L. Worker doses and potential health effect resulting from the accident at the Fukushima nuclear power plant in 2011. Int J Radiat Biol 2014; 16:1–24.
21. Tokyo Electric Power Company Press Release; November 2011. Evaluation status of internal exposure dose of emergency workers. (http://www.tepco.co.jp/en/press/corp-com/release/11113013-e.html)
22. Matsuda T, Marugame T, Kamo K, Katanoda K, Ajiki W, Sobue T. Cancer incidence and incidence rates in Japan in 2004: based on data from 14 population-based cancer registries in the monitoring of cancer incidence in Japan (MCIJ) Project. Jpn J Clin Oncol 2010; 40:1192–200.
23. Center for Cancer Control and Information Services. Cancer statistics in Japan; table download; Japanese cancer incidence data from 1975 to 2008. (http://ganjoho.jp/pro/statistics/en/table_download.html)
24. Official statistics of Japan, c2011. (in Japanese; http://www.e-stat.go.jp)
25. Douple EB, Mabuchi K, Cullings HM, Preston DL, Kodama K, ShimizuY, et al. Long-term radiation-related health effects in a unique human population: lessons learned from the atomic bomb survivors of Hiroshima and Nagasaki. Disaster Med Public Health Prep 2011; 5:S122–33.
26. International Commission on Radiological Protection. The 2007 recommendations of the International Commission on Radiological Protection. ICRP Publication 103. Ann ICRP 2007; 103:1–332.
27. Report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR 2006). Effects of ionizing radiation. Volume I. Annex A: Epidemiological studies of radiation and cancer. New York: United Nations; 2008 (http://www.unscear.org/docs/reports/2006/07–82087_Report_2006_Web.pdf).
28. National Research Council of the National Academies, Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation. Health risks from exposure to low levels of ionizing radiation: BEIR VII Phase 2. Washington DC: National Academies Press; 2006. (http://www.nap.edu/catalog/11340.html)
29. EPA radiogenic cancer risk models and projections for the US population. EPA Report No. 402-R−11-001. Washington, DC: US Environmental Protection Agency; 2011. http://www.epa.gov/radiation/docs/bluebook/bbfinalversion.pdf)
30. Jacob P, Bogdanova TL, Buglova E, Chepurniy M, Demidchik Y, Gavrilin Y, et al. Thyroid cancer risk in areas of Ukraine and Belarus affected by the Chernobyl accident. Radiat Res 2006; 165:1–8.
31. Walsh L, Jacob P, Kaiser J-C. Radiation risk modeling of the thyroid cancer with special emphasis on the Chernobyl epidemiological data. Radiat Res 2009; 172:509–18.
32. Walsh L, Schneider U. A method for determining weights for excess relative risk and excess absolute risk when applied in the calculation of lifetime risk of cancer from radiation exposure. Radiat Environ Biophys 2013; 52:135–45.
33. Preston DL, Mattsson A, Holmberg E, Shore R, Hildreth NG, Boice JD Jr, et al. Radiation effects on breast cancer risk: a pooled analysis of eight cohorts. Radiat Res 2002; 158:220–35.
34. Thomas D, Darby S, Fagnani F, Hubert P, Vaeth M, Weiss K. Definition and estimation of lifetime detriment from radiation exposures: principles and methods. Health Phys 1992; 63:259–72.

35. Kellerer AM, Nekolla E, Walsh L. On the conversion of solid cancer excess relative risk into lifetime attributable risk. Radiat Environ Biophys 2001; 40:249–57.
36. Heidenreich WF, Kenigsberg J, Jacob P, Buglova E, Goulko G, Paretzke HG, et al. Time trends of thyroid cancer incidence in Belarus after the Chernobyl accident. Radiat Res 1999; 151:617–25.
37. Jacob P, Kaiser JC, Ulanovsky A. Ultrasonographic surveys and thyroid cancer in the Fukushima Prefecture. Radiat Environ Biophys 2014; 53:291–401 (403, erratum).
38. Jung KW, Won YJ, Kong HJ, Oh CM, Seo HG, Lee JS. Cancer statistics in Korea: incidence, mortality, survival and prevalence in 2010. Cancer Res Treat 2013; 45:1–14.
39. Brito JP, Morris JC, Montori VM. Thyroid cancer*:* zealous imaging has increased detection and treatment of low risk tumours. BMJ 2013; 347:f4706.
40. Delides GS, Elemenoglou J, Lekkas J, Kittas C, Evthimiou C. Occult thyroid carcinoma in a Greek population. Neoplasma 1987; 34:119–25.
41. Harach HR, Franssila KO, Wasenius VM. Occult papillary carcinoma of the thyroid. A ''normal'' finding in Finland. A systematic autopsy study. Cancer 1985; 56:531–8.
42. Hayashi Y, Lagarde F, Tsuda N, Funamoto S, Preston DL, Koyama K, et al. Papillary microcarcinoma of the thyroid among atomic bomb survivors. Cancer 2010; 116:1646–55.
43. Furukawa K, Preston D, Funamoto S, Yonehara S, Ito M, Tokuoka S, et al. Long-term trend of thyroid cancer risk among Japanese atomic-bomb survivors: 60 years after exposure. Int J Cancer 2013; 132:1222–6.
44. Mabuchi K, Hatch M, Little MP, Linet MS, Simon SL. Risk of thyroid cancer after adult radiation exposure: time to re-assess? Radiat Res 2013; 179:254–6.
45. Dickman PW, Holm L-E, Lundell G, Boice JD, Hall, P. Thyroid cancer risk after thyroid examination with 131I: a population-based cohort study in Sweden. Int J Cancer 2003; 106:580–7.
46. Ron E, Lubin JH, Shore RE, Mabuchi K, Modan B, Pottern L, et al. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. Radiat Res 1995; 141:259–77.
47. Hsu WL, Preston DL, Soda M, Sugiyama H, Funamoto S, Kodama K, et al. The incidence of leukemia, lymphoma and multiple myeloma among atomic bomb survivors: 1950–2001. Radiat Res 2013; 179:361–82.
48. Matsuda T, Marugame T, Kamo K, Katanoda K, Ajiki W, Sobue T. Cancer incidence and incidence rates in Japan in 2006: based on data from 15 population-based cancer registries in the Monitoring of Cancer Incidence in Japan (MCIJ) project. Jpn J Clin Oncol 2012; 42:139–47.
49. Katanoda K, Matsuda T, Matsuda A, Shibata A, Nishino Y, Fujita M, et al. An updated report of the trends in cancer incidence and mortality in Japan. Jpn J Clin Oncol 2013; 43:492–507.
50. Matsuda A, Matsuda T, Shibata A, Katanoda K, Sobue T, Nishimoto H and The Japan Cancer Surveillance Research Group. Cancer Incidence and Incidence Rates in Japan in 2007: a Study of 21 population-based cancer registries for the Monitoring of Cancer Incidence in Japan (MCIJ) Project. Jpn J Clin Oncol 2013; 43:328–36.
51. Hildreth NG, Shore RE, Dvoretsky PM. The risk of breast cancer after irradiation of the thymus in infancy. N Engl J Med 1989; 321:1281–4.
52. Holmberg E, Holm LE, Lundell M, Mattsson A, Wallgren A, Karlsson P. Excess breast cancer risk and the role of parity, age at first childbirth and exposure to radiation in infancy. Br J Cancer 2001; 85:362–6.
53. Haddy N, Dondon M-G, Paoletti C, Rubino C, Mousannif A, Shamsaldin A, et al. Breast cancer following radiotherapy for a hemangioma during childhood. Cancer Causes Control 2010; 21:1807–16.
54. Tokunaga M, Land CE, Tokuoka S, Nishimori I, Soda M, Akiba S. Incidence of female breast cancer among atomic bomb survivors, 1950–1985. Radiat Res 1994; 138:209–23.
55. Forman D, Bray F, Brewster DH, Gombe Mbalawa C, Kohler B, et al, editors. Cancer incidence in five continents, Vol X (electronic version). Lyon: IARC; 2013. (http://ci5.iarc.fr)
56. Jacob P, Rühm W, Walsh L, Blettner M, Hammer G, Zeeb H. Is cancer risk of radiation workers larger than expected? Occup Environ Med 2009; 66:789–96.
57. Daniels RD, Schubauer-Berigan MK. A meta-analysis of leukemia risk from protracted exposure to low-dose gamma radiation. Occup Environ Med 2011: 68:457–64.
58. Wakeford R. Radiation effects: modulating factors and risk assessment – an overview. 2012 Ann ICRP 2012; 41:98–107.
59. Ten Hoeve JE, Jacobson MZ. Worldwide health effects of the Fukushima Daiichi nuclear accident. Energy Environ Sci 2012; 5:8743–57.
60. Dose and Risk Calculation (DCAL) Software. Oak Ridge National Laboratory/Environmental Protection Agency; 2006. (http://www.epa.gov/radiation/assessment/dcal.html)
61. Evangeliou N, Balkanski Y, Cozic A, Møller AP. Global and local cancer risks after the Fukushima Nuclear Power Plant accident as seen from Chernobyl: A modeling study for radiocaesium (^{134}Cs & ^{137}Cs). Environ Int 2014; 64:17–27.
62. Harada KH, Niisoe T, Imanaka M, Takahashi T, Amako K, Fujii Y, et al. Radiation dose rates now and in the future for residents neighboring restricted areas of the Fukushima Daiichi Nuclear Power Plant. Proc Natl Acad Sci U S A 2014; 111:E914–23.
63. Weiss W. Preparing a scientific report to the General Assembly on 'exposures due to the nuclear accident following the Great East-Japan earthquake and tsunami'. J Radiol Prot 2012; 32:N113–8.
64. Report of the United Nations Scientific Committee on the Effects of Ionizing Radiation. Effects of Atomic Radiation (UNSCEAR 2013). Volume 1: Levels and effects of radiation exposure due to the nuclear accident after the 2011 Great East-Japan earthquake and tsunami. New York: United Nations; 2014. (http://www.unscear.org/docs/reports/2013/13–85418_Report_2013_Annex_A.pdf)