ogy by serving as the president of International Association of Radiation Research from 2007 to 2011. His contribution extends to the radiation protection field, serving the ICRP since 2001 and as a member of its Committee 1 on radiation effects as well as a Main Commission member.

Professor Roy Shore, Hiroshima, Japan

Dr Roy Shore received a Ph.D. in psychology from Syracuse University (1967) and a DrPH in epidemiology from Columbia University in 1982. He served as Professor and Chief of the Epidemiology Division at the New York University School of Medicine before going to the Radiation Effects Research Foundation (RERF) in Hiroshima-Nagasaki as Vice Chairman and Chief of Research in 2006. He is an author on numerous radiation-related publications and currently supervises RERF investigators on studies of radiation risks for a variety of diseases. Dr Shore has served on many governmental and scholarly committees, including as a long-time member of the ICRP and NCRP, and has served on various committees or task groups for UNSCEAR, WHO, the US National Academy of Sciences, the US National Cancer Institute and the US Environmental Protection Agency, among others. His interests include the effects of radiation on both cancer and non-cancer disease incidence, and understanding the epidemiologic and biological modification of radiation effects by various environmental, genetic and host-susceptibility factors.

Professor Richard Wakeford, Manchester, United Kingdom

Dr Richard Wakeford worked for British Nuclear Fuels plc (BNFL) for almost 30 years before taking early retirement in 2006. For much of this time he specialized in the risks to health posed by exposure to ionizing radiation, particularly low-level exposure. He is now Visiting Professor in Epidemiology at the Dalton Nuclear Institute of The University of Manchester, and is a member of a number of national and international expert groups such as the UK Committee on Medical Aspects of Radiation in the Environment (COMARE) and Committee 1 of the ICRP. In 2011, he was a member of the UK Government's Scientific Advice Group for Emergencies (SAGE) for the Japan Nuclear Incident, and his statement to the Japanese people on the risks from the Fukushima accident is available at the website of the Japanese Government's Cabinet Secretariat. He has been Editor-in-Chief of the *Journal of Radiological Protection* since 1997. Dr Wakeford has extensively studied the risks of radiation exposure in infants and children, as well as the risks associated with prenatal exposure.

Dr Linda Walsh, Munich, Germany

Dr Linda Walsh obtained her Ph.D. in Physics from the University of Manchester, U.K. in 1985. She has worked in British, Australian, Dutch, German and European Universities and research institutions in the fields of data analysis, applied statistics, numerical analysis and radiation epidemiology. Dr Walsh is currently working as a senior scientist at the German Federal Office for Radiation Protection (BfS). Dr Walsh's extensive research in the field of radiation epidemiology has included papers on the Life Span Study of Japanese Atomic bomb survivors covering a range of topics from cancer risks related to neutron and X-ray doses, organ-specific doses and carcinogenesis. She has also worked on the analysis of the cohort of German "Wismut" uranium miners exposed to radon and other potential carcinogens, and developed epidemiological models for lung and extra-pulmonary cancers.

Other studies that Dr Walsh has been involved with have considered the incidence of malignant diseases in humans injected with radium-224; the development of epidemiological models for thyroid cancer risk in areas affected by the 1986 Chernobyl accident; and analyses of data pertaining to cellular radiation damage relevant to the evaluation of both diagnostic radiation characteristics and the effects on cancer patients. Dr Walsh submitted her Doctor of Science thesis, based on 50 publications, entitled "Quantifications of the detrimental health effects of ionising radiation" to the Medical Faculty of Manchester University in December 2012. She has also been involved in various international research projects, most recently as a partner, task leader and project board member of an international research project started under the seventh framework programme of the European Union, FP-7-EU-ANDANTE (Multidisciplinary evaluation of the cancer risk from neutrons relative to photons using stem cells and the analysis of second malignant neoplasms following paediatric radiation therapy). As a WHO health risk assessment panel member, Dr Walsh made substantial contributions to the selection of risk assessment methodology, performed actual risk calculations and contributed to the writing of some major sections of the final report.

Dr Wei Zhang, Chilton, United Kingdom

Dr Wei Zhang received his Ph.D. in Plasma Physics and Controlled Nuclear Fusion from the University of Saskatchewan, Canada in 1993. He subsequently worked as a research scientist at the Centre Canadien de Fusion Magnétique in Quebec, Canada, and the Joint European Torus (JET) in the UK. In 1997, Dr Zhang started his career in Medical Statistics and Epidemiology at the University of Oxford. He joined the National Radiological Protection Board (now part of the Health Protection Agency) in 2002 and currently is a principal scientist at the Health Protection Agency. His interests cover health risk assessment, epidemiological studies of radiation workers and radiotherapy patients.

Annex B. Declaration of interests statement

All experts who participated in the meetings of the Health Risk Assessment Expert Group on the initial evaluation of radiation exposure from the nuclear accident after the 2011 Great East Japan Earthquake and Tsunami were asked to complete a WHO Declaration of Interest form. In some cases, the experts were asked to provide additional information on the form submitted by them.

At the start of the meetings of this Group, all participants were asked to confirm their interests and to provide any additional information relevant to the subject matter of the work.

Certain experts declared interests of a non-commercial nature, having worked for organizations such as UNSCEAR, the US National Cancer Institute (NCI), NCRP, and governmental radiation protection agencies. These interests were not deemed to give rise to a conflict. In addition, two of the experts declared having a potential conflict of interest of a commercial nature, as follows:

Dr Richard Wakeford: He is currently and has over the last 2 years performed consultancies (on the health effects arising from exposure to ionizing radiation) for EDF Energy plc, Augean plc, British Nuclear Fuels plc and Sellafield Ltd.

Dr Dominique Laurier: His unit at IRSN has received research support from Areva and EDF (for research projects on workers).

Dr Ohtsura Niwa later disclosed that, as a member of the International Commission on Radiological Protection (ICRP), he has (over the last 11 years) received travel support from the Radiation Effect Association using funds provided by several sources, one of which is the Federation of Electric Power Companies (an umbrella association of electricity companies). WHO brought this information to the attention of the other experts.

As noted in the section describing the background of each of the experts, Dr Wakeford has a unique expertise on radiation effects in infants and children, particularly on childhood leukaemia. Dr Laurier belongs to a WHO Collaborating Centre which includes in its terms of reference the provision of technical support on radiation risk assessment. He has particular expertise in the field of radiation epidemiology. Dr Niwa has particular expertise in molecular biology and radiation biology.

Considering these experts' unique knowledge and expertise in the fields described above, and bearing in mind that the remaining experts did not disclose any interests of a commercial nature, it was decided that their declared interests did not merit their exclusion from this Group, provided that these interests be publicly disclosed.

Annex C. Overview of radiation epidemiology

Available scientific data on the biological effects of ionizing radiation are based on experimental and epidemiological studies. The most informative source of epidemiological data about human exposure to radiation is the Life Span Study (LSS) of the Japanese survivors of the atomic bombings of Hiroshima and Nagasaki. In addition, several other sources have provided useful epidemiological data, including past accidents (e.g. Chernobyl), medical exposures, occupational exposures and natural radiation exposures, as described below.

C.1 Atomic bombings of Hiroshima and Nagasaki

The strongest evidence for cancer risk from ionizing radiation in humans has been obtained from the Life Span Study (LSS) of individuals exposed from the atomic bombs of Hiroshima and Nagasaki. Although cancer is the main late effect demonstrated in the LSS, it has also provided information about other health outcomes such as benign tumours and non-cancer diseases (*5,16,19,21,55,56,70,105*). There are reports showing excess cancer risk associated with in *utero* radiation exposures on the order of a few tens of mGy among children exposed to radiation *in utero* due to maternal X-ray pelvimetry as well as in various other populations prenatally exposed to radiation, including the LSS (*34,36,122,160*).

C.2 The Chernobyl accident

The follow-up of people exposed as a result of the nuclear power plant accident that occurred in 1986 at Chernobyl (Ukraine) provided information about radiation risks, particularly thyroid cancer, from internal exposure to radioactive iodine. A significant increase in the incidence of thyroid cancer was observed in residents of affected areas of Ukraine, Belarus and the Russian Federation, with higher risks among those exposed at a young age (i.e. infants, children and adolescents) compared with adults. Some increase in the risk of leukaemia among emergency workers was also reported (*22,82*).

C.3 Medical exposures

The carcinogenic effects (leukaemia and liver cancer) of long-term internal exposure were first reported beginning in the 1930s, among patients who had received thorium-containing Thorotrast as a contrast medium for radiological imaging procedures (*161*). Since the 1960s, long-term adverse consequences of radiotherapy from benign disease were documented in studies showing an increased risk of cancer after X-ray treatment for ankylosing spondylitis (*162*). These findings were confirmed during the 1970s, when analyses of cancer among children treated for enlarged thymus, enlarged tonsils and scalp ringworm showed an increased risk of thyroid cancer. Increased breast cancer risk

has been observed among young women who were repeatedly examined with fluoroscopy for tuberculosis (*162*). Recently, increased risks for leukaemia and brain tumours were reported in children undergoing repeated computed tomography scans that had cumulative doses in the range of around 50 mSv (*146*).

C.4 Occupational exposures

There have been a number of studies on workers exposed to radiation. The earliest cases of radiation-induced neoplasms were skin cancers, reported by pioneering researchers working with X-rays in the first years of the 20th century. Large doses of highly localized exposures resulting in excess risks of specific cancer types were demonstrated when bone cancers were reported among radium dial painters in the 1920s. Further evidence was reported in the 1950s, showing excess deaths from leukaemia among radiologists who began working in the early period with scanty radiation protection procedures (*163*). Excess cancer risks were observed among workers at the Mayak Plant in the Southern Urals after high-dose, low-dose-rate radiation exposure (*164*). A comprehensive review of 12 recent epidemiological studies on occupational exposures, including the 15-country study compiled by the International Agency for Research on Cancer (IARC) (*165*), concluded that there is evidence for an excess cancer risk among the populations occupationally exposed to moderate radiation doses at a low dose rate, and that there is no indication that such excess is smaller than for the atomic bomb survivors (*74,166*).

C.5 Environmental exposures

Excess cancer risks were reported in local residents after high-dose, low-dose-rate exposure to radiation from the Semipalatinsk nuclear test site (*167*). Epidemiological studies on cancer incidence or mortality conducted in residents of regions with some of the highest levels of background radiation in the world did not show excess cancer risk (*168,169,170,171*). Those studies have major methodological limitations and it is uncertain whether the studies conducted up to now were able to detect small excess risks (*172*). By applying recent risk models it was estimated that around one fifth of childhood leukaemia in Great Britain may be caused by exposure to natural background radiation in childhood. Authors acknowledged the uncertainties associated with such predictions, particularly concerning the nature of the risk transfer between populations (*173*). Indeed, a significant association between dose and red bone marrow owing to background radiation and childhood leukaemia risk was recently observed in a national case–control study (*174*).

Annex D. Survival curves

The probability of developing a cancer induced by radiation depends on the probability of being alive at that time. To calculate lifetime incidence cancer risks it is therefore necessary to know, for each age interval, the probability of the person being alive. This information is presented in "survival curves" or "survival functions". $S(a)$, the survival function, represents the probability of surviving to age a. $S(a)$ can be calculated from the age-specific all-cause mortality rates from $S(a) = exp\{-Mc(a)\}$, where $Mc(a)$ is the cumulative death rate up to attained age a. A summary of basic survival analysis concepts can be found in the appendix of a paper published by Thomas et al. in 1992 (*78*).

Deriving the survival function from all-cause mortality rates is appropriate where the lifetime risks of radiation-induced cancer death are concerned. However, it would be inadequate if the lifetime risks of radiation-induced cancer incidence are calculated, as many cancers have a high rate of cure and therefore the cancer incidence rate is higher than the cancer mortality rate. Thus, for calculating the lifetime attributable risk (LAR) pertaining to cancer incidence, an "adjusted" survival curve, $S_{aj}(a)$, which represents the probability of cancer-free survival, is preferable to the unadjusted curve $S(a)$. To calculate $S_{aj}(a)$, suitable data that relate to the same population are required. For the present assessment, "adjusted" survival curves $S_{aj}(a)$ were derived on the basis of all-cause mortality plus the difference between all-cancer incidence and all-cancer mortality (see Figures 26 and 27).

For this HRA, the HRA Expert Group agreed to calculate the LAR using adjusted survival curves $S_{aj}(a,g)$ as a function of age-attained a, describing the probability of surviving cancer-free of a person of sex g. The ratio used in the LAR equation $(S_{aj}(a,g))/(S_{aj}(e,g))$ is the conditional probability of a person of sex g, alive at age e, reaching at least age a.

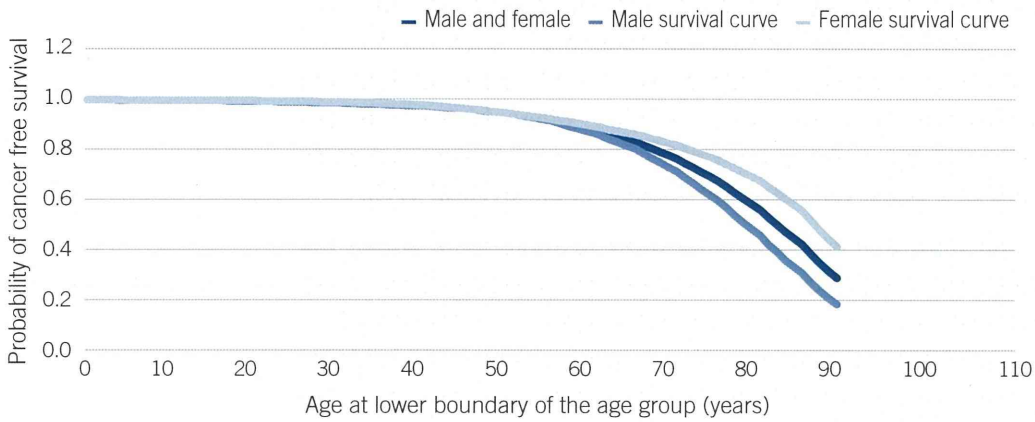
For the general population, the adjusted survival curves $S_{aj}(a,g)$ shown in Figure 26 were applied in the LAR calculations, and calculated from the all-cause mortality rates and all cancer mortality rates for 2010 obtained from the Portal Site of Official Statistics of Japan (*175*) and the all-cancer incidence rates for 2004 obtained from Table 3 of Matsuda et al. (*104*).

The healthy worker effect (HWE) is a bias found in occupational studies when rates of disease among employed people are compared with disease rates for the general population[1]. The so-called standardized mortality ratio (SMR) quantifies the difference in the mortality of workers with respect to the general population. If the SMR does not deviate much from 1, it indicates that the HWE is not very strong. The HRA Expert Group noted that this potential HWE might require care in the selection of a comparative population

1. The general population includes both employed and unemployed people and may therefore have a greater incidence, prevalence or mortality of disease than those who are employed. The strength of the HWE may vary from one occupational cohort to another and it is modified by a number of factors such as gender, age, length of employment and health monitoring status, among others.

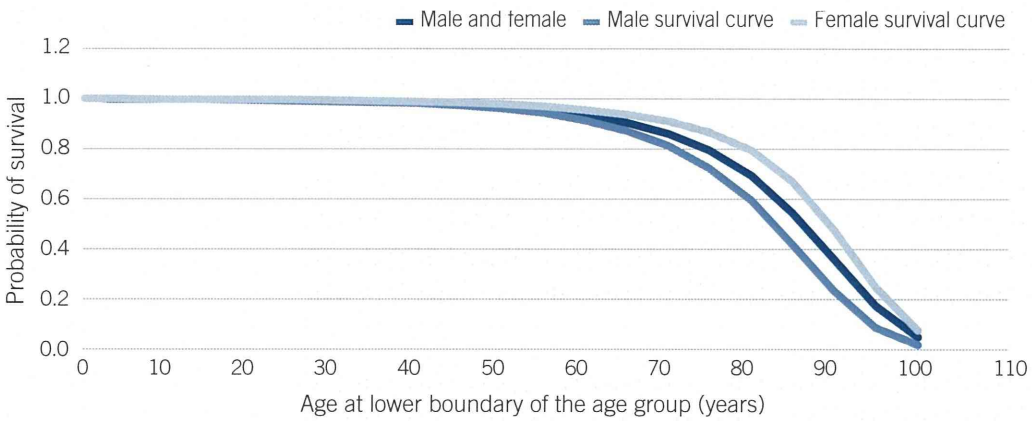
to calculate the LAR values for emergency workers in the present HRA. Two studies conducted in Japan were analysed. A study conducted in 2003 (*176*) showed a small deviation from one of the standardized mortality ratios (SMR). A recent study of Japanese nuclear workers does not give SMR values (*166*). The HRA Expert Group agreed to use for emergency workers the same adjusted survival curve (males) and the same baseline mortality and incidence rates as for the Japanese general population.

Figure 26. The adjusted survival curves, $S_{aj}(a)$, applied in the LAR calculations.



Note: adjusted survival curves cannot be plotted to age 100, as for S(a) – because the population cancer incidence and mortality data are not available for the 5-year age intervals beyond 90 years of age.

Figure 27. The unadjusted survival curves $S(a)$ are presented for comparison purposes.



Note: they were not applied for LAR calculation in this HRA.

Annex E. Risk models for assessing cancer risks

This annex summarizes the risk models used to calculate the lifetime attributable risks for the difference cancer sites considered in the present assessment.

In the latest LSS solid cancer incidence analysis, a statistically significant dose-response was seen when analysis were limited to cohort members with doses of 0.15 Gy or less (*70*). The threshold model did not fit better than a linear non-threshold model (LNT). Within the latest LSS cancer mortality analysis, the estimated lowest dose range with a significant ERR for all solid cancers was 0–0.2 Gy, and the analysis indicated no threshold (*19*).This is consistent with the concept that there is weak evidence for a threshold at any dose meaningful to radiological protection.

For leukaemia, the dose-response is better described by a linear-quadratic than by a simple linear pattern (i.e. curving upwards with increasing dose). The dose response is often approximated by a purely linear model at doses less than 100 mGy (*22*).

Studies of thyroid cancer following radiation exposure in childhood have provided evidence of excess risk at dose levels down to 0.1-0.5 Gy (100-500 mGy). The risk decreased significantly with increasing age-at-exposure, with little risk apparent after age 20 years (*6*). Studies of thyroid cancer following exposure to radioiodine from the Chernobyl accident have shown substantially elevated risks at organ doses around 0.5. The largest study covered more than 1000 cases and showed an excess relative risk of 19 per Gy, with a negative quadratic term (indicating a flattening of the dose-response at high doses) (*107*). This latter observation is consistent with findings reported at very high doses (>10 Gy), associated with cancer therapy, where it seems to be a decrease or leveling of thyroid cancer risk (*6*). A pool analysis of 4 high-dose studies also shows a flattening effect above 10 Gy (*24*). A large study of thyroid cancer risk among 12 500 survivors of childhood cancer treated with radiotherapy showed a downward bend of the dose response curve at approximately 20 Gy (*120*). In a case-control study of 276 thyroid cancer cases, the odds ratio was approximately 5 at 1 Gy but there was little further increase at doses exceeding 2 Gy (*177*). Subsequent studies with longer follow-up times (and higher attained ages and time since exposure) have shown lower risk estimates (around 2 per Gy) (*76,127*). One of these studies reported a flattening of the risk above 5 Gy (*127*). A study conducted in Bryansk, Russia, reported a very high risk estimate, though with a wide confidence interval (ERR 49 per GY, 95% CI 5-1150) (*108*). Also, an increased incidence of childhood thyroid cancer has been reported by the US from atmospheric atomic bomb testing with thyroid doses below 0.3 Gy and a relative risk of approximately 1.2 at dose 0.1 mGy, but only for exposure before the age of 1 year (*109*). The latest LSS thyroid cancer incidence analysis (*21*) indicated excess risks persisting for more than 50 years for those exposed as children and "little" evidence of increased thyroid cancer rates for those exposed after 20 years old. This latter finding is consistent

with the conclusion of Ivanov et al., based on populations affected by the Chernobyl accident (*23*).

E.1 Risk models for leukaemia mortality

The risk models chosen for the analysis for leukaemia mortality (ICD10 code: C91–C95) used a linear-quadratic dose response, from Table 46 of the UNSCEAR (*83*) report (see below E.1.1 and E.1.2) and Little et al. (*86*). In its 2006 report UNSCEAR (*83*) used excess absolute risk (EAR) and excess relative risk (ERR) models for leukaemia mortality for two conditions: quadratic response and linear-quadratic response. For the present assessment the EAR and ERR models with the linear-quadratic dose response were used. The coefficients of leukaemia mortality linear-quadratic models, fitted to current data for the survivors of the atomic bombings in Japan, are shown below. All models are fitted by Poisson maximum-likelihood, using adjustments for dosimetric error and assuming 35% geometric standard deviation errors.

E.1.1 Generalized ERR model

$$ERR = \lambda(a,e,D,g)[1+(\alpha D+\beta D^2)\exp[\kappa_1 \ln(a)]$$

where D is the radiation dose (Sv), a the attained age, e the age-at-exposure, g the sex, and the fit parameters are

$\alpha = 864.552\ Sv^{-1}$,

$\beta/\alpha = 1.180\ 92\ Sv^{-1}$,

$\kappa_1 = -1.647$

E.1.2 Generalized EAR model

$$EAR = \lambda(a,e,D,g)+(\alpha D+\beta D^2)\exp[\kappa_1 I_{female}+\kappa_2 \ln(a-e)]$$

where D is the radiation dose (Sv), a the attained age, e the age-at-exposure, g the sex, and the fit parameters are

$\alpha = 7.516\ 50\ X\ 10^{-4}\ Sv^{-1}\ a^{-1}$,

$\beta/\alpha = 1.034\ 55\ Sv^{-1}$,

$\kappa_1 = -525.26$,

$\kappa_2 = -614.1$

E.2 Risk models for all solid cancer incidence

Risk models and fit parameters for solid cancers (ICD-10 code: C00–C89) used in this assessment for calculating LAR were taken from Preston et al. (*70*) for all solid cancer incidence (1958–1998). The characteristics of the fit parameters are given in Preston et al. (*70*), Table 10. However the actual values of the fit parameters have been taken from the original EPICURE output on the RERF website and are given below.

E.2.1 ERR model

When use is made of a general rate (hazard) model of the form

$$\lambda(D,a,e,s) = \lambda_o(a,e,s)[1 + ERR(D,a,e,s)]$$

for the excess relative risk (ERR) where $\lambda_o(a,e,s)$ is the LSS baseline cancer death rate, a is age-attained and e is age-at-exposure, s is an indicator variable for sex (s=-1 for males, s=+1 for females) and D is the weighted colon dose (gamma colon dose plus ten times the neutron colon dose). The *ERR* is factorized into a linear function of dose and a modifying function that includes both age variables, *ERR(D, a, e)*. The functional form is exponential for age-at-exposure or a power function for age-attained where the modifying factors have been modelled as

$$ERR(D,a,e) = (1 + t.s).k_d D \exp[-g_e(e-30) + g_a \ln(a/70)]$$

where the fit parameters with standard errors are:

t= 0.2465±0.06762,

k_d = 0.4666±0.04413,

g_e = 0.01849±0.00636,

g_a = -1.621±0.3058

(fit parameters and deviance=14735.954, degrees of freedom, df=25551 values all from www.rerf:filename:-lss07sitemod.log).

E.2.2 EAR model

Similarly for EAR:

$$EAR(D,a,e) = (1 + t.s).k_d D \exp[-g_e(e-30) + g_a \ln(a/70)]$$

where the fit parameters with standard errors are:

t= 0.1622±0.06988,

k_d = 51.63±4.982,

g_e = 0.02805±0.006215,

g_a = 2.406±0.2731

(fit parameters and deviance =14739.933, df=25551, from www.rerf:filename:-lss-07sitemod.log).

E.3 Risk models for thyroid cancer incidence

The risk models for thyroid cancer incidence (ICD10 code: C73) are provided in this section. The ERR model is generally used in transfers of thyroid cancer risk from one population to another. However, the LSS cohort only provided data beginning 13 years after exposure. Extrapolation of the LSS results to shorter times after exposure was done on the basis of information from Chernobyl (*107,179*). For the period of 4–15 years after exposure, it can be seen from Figure 28 that an extrapolation of the EAR function for the LSS to periods shorter than 13 years shows good agreement with the Chernobyl experience. Therefore it was decided to present initial LAR results based on 50% EAR transfer and 50% ERR transfer (see section 3.5).