# From Hiroshima and Nagasaki to Fukushima 1

# Long-term effects of radiation exposure on health

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**Late-onset effects of exposure to ionising radiation on the human body have been identified by long-term, large-scale epidemiological studies. The cohort study of Japanese survivors of the atomic bombings of Hiroshima and Nagasaki (the Life Span Study) is thought to be the most reliable source of information about these health effects because of the size of the cohort, the exposure of a general population of both sexes and all ages, and the wide range of individually assessed doses. For this reason, the Life Span Study has become fundamental to risk assessment in the radiation protection system of the International Commission on Radiological Protection and other authorities. Radiation exposure increases the risk of cancer throughout life, so continued follow-up of survivors is essential. Overall, survivors have a clear radiation-related excess risk of cancer, and people exposed as children have a higher risk of radiation-induced cancer than those exposed at older ages. At high doses, and possibly at low doses, radiation might increase the risk of cardiovascular disease and some other non-cancer diseases. Hereditary effects in the children of atomic bomb survivors have not been detected. The dose–response relation for cancer at low doses is assumed, for purposes of radiological protection, to be linear without a threshold, but has not been shown definitively. This outstanding issue is not only a problem when dealing appropriately with potential health effects of nuclear accidents, such as at Fukushima and Chernobyl, but is of growing concern in occupational and medical exposure. Therefore, the appropriate dose–response relation for effects of low doses of radiation needs to be established.**

## Introduction

Adverse health effects of exposure to ionising radiation were identified soon after the discovery of x-rays in 1895. Epilation was reported as early as 1896, and skin burns were described soon after.[1,2] With the invention of high-voltage x-ray tubes in around 1930, and their implementation in medical procedures, substantial amounts of radiation started to penetrate tissues deep in the body, such as bone marrow. Injuries to highly exposed tissues, known as tissue reactions, are classified as deterministic effects because they will always occur once a particular threshold dose has been exceeded (panel 1)—for example, an acute dose of 0·5 Gy to the bone marrow will lead to symptomatic depression of haemopoiesis (panel 2). Tissue reactions are caused by cell death and increase in severity as radiation dose increases.[3] However, in 1928, x-rays were shown to induce germline mutations in drosophila, the frequency

### Search strategy and selection criteria

Results of studies of Japanese atomic bomb survivors and their children, based on well defined cohorts with satisfactorily validated individual radiation doses, have been done by the Atomic Bomb Casualty Commission (ABCC) and Radiation Effects Research Foundation (RERF), so we used representative articles reporting findings of these studies published in peer-reviewed international journals, or monographs or ABCC and RERF reports when appropriate papers were not available.

For studies of Chernobyl, we searched PubMed, CiNii, Medline, and Google Scholar with the keywords "Chernobyl disaster, thyroid cancer", "Chernobyl nuclear accident, health risk", and "Chernobyl accident, psychological consequences". We selected papers published in peer-reviewed international journals, and used some authoritative reviews of the literature published by the UN Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and WHO.

### Key messages

- Exposure to ionising radiation increases risk of cancer throughout the lifespan, so study of exposed individuals for an extended period of time is necessary; one such study is that of the Japanese atomic bomb survivors (the Life Span Study)
- Survivors have a dose–response relation that is linear for solid cancer, but that is still unclear at low doses; survivors who were children when exposed have a higher risk of cancer than those exposed at older ages; risk of cardiovascular diseases and some other non-cancer diseases is increased at higher doses
- In children exposed to high doses of atomic bomb radiation in the womb, development of the central nervous system and stature were affected, and the risk of cancer increased with maternal dose
- Risks of hereditary malformations, cancer, or other diseases in children of atomic bomb survivors did not increase detectably with paternal or maternal dose, based on follow-up so far; atomic bomb survivors exposed to high doses of radiation tend to show deterioration of the immune system similar to that observed with ageing, and many survivors exposed to high doses of radiation have minor inflammatory reactions
- Increased incidence of thyroid cancer several years after Chernobyl was reported in children who received high thyroid doses owing to internal exposure to radioactive iodine; results of Chernobyl studies additionally show substantial psychological effects
- Cancer risk increases after exposure to moderate and high doses of radiation (more than 0·1–0·2 Gy); however, whether cancer risk is increased by acute low doses (0·1 Gy or lower) or low dose rates is unclear

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### Panel 1: Deterministic effects, stochastic effects, and risk

**Deterministic effects**

Deterministic effects result from radiation-induced cell death, which, when it occurs at a high enough rate, can impair the integrity, and compromise the function, of organs and tissues. A threshold dose is needed for damage to become clinically observable, and the extent of damage depends on the absorbed dose, dose rate, and radiation quality. Thus, the severity of the effect increases with increasing absorbed dose.[3] Early tissue reactions include gastrointestinal symptoms (eg, haemorrhagic diarrhoea), bone marrow failure (eg, anaemia and leucocytopenia), skin disturbance (eg, erythema and epilation), and various other symptoms. Among late tissue reactions are cataracts, cardiovascular disorders, and necrosis.

**Stochastic effects**

Exposure to ionising radiation, even at low doses, can cause damage to the genetic material in cells, which might result in radiation-induced cancer years later, or in heritable disease in the descendants of the exposed individual, and possibly to some developmental effects under specific conditions. These effects are known as stochastic effects. For both radiation-induced cancer and heritable disease, the probability of the occurrence of the effect—but not severity—depends on the dose. The risk of stochastic effects increases with dose, with no threshold.[3]

**Excess relative risk and excess absolute risk**

Excess relative risk or rate (ERR) is an indicator of the proportional increase in risk or rate over background—eg, ERR of 0·5 means a 50% increase in risk or rate over the background risk or rate. Excess absolute risk or rate (EAR) is the additional risk or rate above the background risk or rate that exists in the absence of the specific exposure under consideration.

of which increased linearly with radiation dose to the gonads. This discovery led to the definition of stochastic effects of radiation and formed the foundation for the linear no-threshold (LNT) model.[4] Stochastic effects arise as a result of mutations, and mutations are thought to be induced proportionally to the extent of DNA damage, which is related to radiation dose. In addition to hereditary effects, which originate in germline mutations, cancer is classified as a stochastic effect since it originates in somatic mutations.[5] The probability—but not the severity—of stochastic effects increases with radiation dose.

70 years ago, on Aug 6, 1945, for the first time in human history, an atomic bomb was dropped on the Japanese city of Hiroshima; another was dropped on Nagasaki 3 days later. The atomic bomb used at Hiroshima was a uranium-235 device, whereas the bomb at Nagasaki was a plutonium-239 device. The explosions generated shock waves, thermal energy, and

ionising radiation. According to local authorities, roughly 140 000 people died in Hiroshima and 74 000 died in Nagasaki.[6,7] In addition to injuries produced by the blast and heat from the bombs, high doses of radiation caused acute deterministic effects, including death from severe gastrointestinal and bone marrow damage and non-fatal symptoms such as epilation. Survivors of the bombings have had delayed health outcomes owing to late-onset deterministic and stochastic effects of radiation.

Humanity has experienced these atomic bombs and other nuclear disasters as an example of the negative side of the progress of science and technology. The most recent example—the Fukushima Daiichi nuclear power plant accident—occurred in March, 2011.

Health effects of large-scale nuclear disasters persist for many years, so long-term epidemiological studies are needed to reliably show any cause-and-effect relation between irradiation and effects on health. We focus mainly on late-onset health effects of the largest nuclear disasters in history—the atomic bombings of Hiroshima and Nagasaki and the Chernobyl nuclear power plant accident (Ukraine [then USSR], 1986).

Systematic epidemiological study of the Japanese atomic bomb survivors started in 1950 with establishment of the Life Span Study (LSS), which has made a substantial contribution to understanding of radiation effects on human health.[8,9] This contribution was made possible by the size of the cohort, length of observation period, accurate dose assessment, wide dose range, inclusion of all people without selection, individual follow-up, and the power of sophisticated statistical analysis. The information generated by the LSS has provided a reliable foundation for assessment of radiation risks by internationally recognised authorities such as the International Commission on Radiological Protection (ICRP).[3]

In addition to damage to physical health, atomic bomb survivors had psychological disorders such as post-traumatic stress disorder (PTSD) and anxiety symptoms caused by concerns about their health and experiences not only of losing family members and collapse of the community, but also of social discrimination in marriage and employment.[10–13]

In 1957, the Japanese Government started to provide support to atomic bomb survivors with establishment of the A-bomb Survivors Medical Care Law, which is designed to develop health management, medical care, and welfare of survivors.[14] Under this law, people certified as atomic bomb survivors ("hibakusha") were issued an A-bomb Survivor Health Book enabling them to receive medical care and financial support. In 1994, by integration of previous laws and ordinances, the Atomic Bomb Survivors' Support Law was established to implement comprehensive support measures for survivors.[14] In March, 2014, 192 719 atomic bomb survivors lived in Japan, and 4440 were living abroad.[14]

## Panel 2: Radiation terms

Various concepts, terms, and their associated quantitative units are specific to radiation science. The becquerel (Bq) is the SI unit of radioactivity and is defined as the number of radioactive transformations per second. When used to measure activity in soil, food, and water, it is typically expressed as Bq/kg or Bq/m$^3$.

Different types of radiation emitted during radioactive disintegration, such as α-particles, β-particles, and gamma rays, deposit energy on their passage through matter. The basic quantity used for scientific purposes is the absorbed dose, which is the amount of energy deposited by radiation in a unit mass of matter. The SI unit of absorbed dose is the gray (Gy), which equals 1 joule of energy absorbed by one kilogram of matter (J/kg).

The extent of biological damage done by radiation at the cellular level depends on ionisation density of the type of radiation, with more densely ionising radiation (such as α-particles) causing more damage per unit absorbed dose than sparsely ionising radiation (such as gamma rays). For radiological protection, the International Commission on Radiological Protection has defined two dose concepts: the equivalent dose and the effective dose, for which the SI unit is the sievert (Sv). These doses are weighted absorbed doses, and are used within the system of radiological protection to broadly account for the extent of microscopic damage in different organs and tissues relevant to the detriment-weighted risk of stochastic health effects caused by low-level radiation exposure.

The equivalent dose is the sum of the absorbed doses to an organ or tissue, each multiplied by the radiation weighting factor for the type of radiation, showing the detriment-weighted risk of stochastic effects resulting from low-level exposure to that radiation. The value for the radiation weighting factor is defined as 1 for gamma rays and other sparsely ionising radiation, whereas for densely ionising radiation with high biological effectiveness, the factor is more than 1, and for α-particles, the weighting factor is 20.

The effective dose is the sum of equivalent doses to various organs or tissues, each multiplied by the tissue weighting factor for the specific tissue or organ. The tissue weighting factor accounts for different sensitivities of tissues to radiation-induced stochastic effects resulting from low-level exposure to radiation. The effective dose is the radiological protection quantity showing the detriment-weighted risk of stochastic health effects posed by a uniform whole-body low dose of reference gamma radiation. We summarise the main units used to quantify radiation doses in the table.[3]

Scientific knowledge obtained from epidemiological studies of atomic bomb survivors forms the basis of these laws, and so has an important role in enhancement of heath management, medical care, and welfare of survivors. Experience gained from the LSS and from medical care of atomic bomb survivors contributed to establishment of the Fukushima Health Management Survey and the medical care of local residents after the Fukushima Daiichi nuclear power plant accident in 2011.[15]

After Chernobyl, dose assessment was extremely difficult since information was not disclosed immediately and exposure conditions were complicated by the combination of external and internal exposures by various routes. Health effects of internal exposure to radioactive iodine and caesium became a major concern, and a high incidence of thyroid cancer among children with high intakes of radioactive iodine was reported.[16] In terms of internal exposure to radioactive materials released into the environment, Chernobyl differs substantially from Hiroshima and Nagasaki, where the exposure was predominantly to external radiation from explosion of the bombs. In both cases long-term health studies are needed to assess the resultant risks. After Chernobyl, as with the atomic bombings, the effect of psychological and social factors is important,[17] and these problems need to be addressed with great care in the aftermath of Fukushima.

|  | SI unit | Definition |
|---|---|---|
| Absorbed dose | Gy (gray) | Energy deposited in a unit mass of matter (J/kg) |
| Equivalent dose* | Sv (sievert) | Absorbed dose multiplied by radiation weighting factor for the biological effectiveness of radiation type |
| Effective dose* | Sv (sievert) | Sum of equivalent doses, each multiplied by the tissue weighting factor for the sensitivity of different tissues to radiation-induced stochastic effects |

*Used only for purposes of radiological protection in the context of the risk of stochastic effects resulting from low-level exposure to radiation. When radioactive materials enter the body through inhalation, ingestion, or wounds, radionuclides accumulate in organs or tissues, and reside in the body for characteristic periods of time, during which they irradiate tissues internally. The equivalent or effective dose that will be received prospectively for a defined period of time from internal accumulation of radioactive material is the committed dose.

**Table:** Dose quantity

## Health effects of radiation from atomic bombs
### Assessment of radiation exposure

Radiation from atomic bombs is classified into two types: initial radiation emitted directly from explosions and from short-lived radionuclides in rising fireballs, which was composed mainly of gamma rays and neutrons; and residual radiation emitted from neutron-induced radionuclides in environmental materials and from radioactive fall-out containing radionuclides,

generated mainly as products of nuclear fission during explosions. Doses to exposed individuals were affected by the physical properties of the explosions, distance from explosion centre, shielding by buildings, and personal characteristics such as body size, posture, and orientation. The free-in-air dose of radiation, weighted by the relative biological effectiveness of the neutron component (ie, neutron dose × 10 + gamma ray dose) at a distance of 1 km at ground level from the hypocentre was estimated to be 7 Gy in Hiroshima and 10 Gy in Nagasaki. At a distance of 2·5 km from the hypocentre, this dose decreased to 13 mGy in Hiroshima and 23 mGy in Nagasaki.[18]

## Construction of cohorts

After investigations of somatic and hereditary effects of radiation in the atomic bomb survivors and their offspring during the 1940s, the Atomic Bomb Casualty Commission (ABCC) constructed some fixed cohorts that could be followed up for a prolonged period of time.[8,9] The LSS cohort is representative of the general population of atomic bomb survivors since participants were randomly selected from respondents to the National Census of Japan, 1950. This study was the first well organised large-scale epidemiological study of atomic bomb survivors in Japan, and initially consisted of about 94 000 people who had been within 10 km of the hypocentres, and another 26 000 people who had not been in either city at the time of the bombings as a control group.[8,9] Of the 94 000 survivors, around 86 500 (92%) have had doses successfully estimated. Of these, 2400 (2·8%) had an assessed weighted colon dose of 1 Gy or more, and about 68 500 (79%) had a dose of less

than 100 mGy, with around 48 000 (55%) non-trivially exposed (doses >5 mGy).[18] Tissue-specific doses have been assessed three times, with enlarged databases and increasingly sophisticated analyses. In 1958, 24 000 people from the LSS were invited to a biennial health examination programme, the Adult Health Study, at ABCC centres in Hiroshima and Nagasaki.[19] Participants have been followed up, with diagnoses carefully updated at every health check. LSS participants have been followed up for longer than any other cohort in radioepidemiological studies, which, in addition to detailed dose estimation and diagnosis, confirms that the LSS is the most reliable source of information about health effects of radiation exposure. However, the LSS has some inevitable limitations since its inception was 5 years after the bombings and information about solid cancer incidence has only been recorded since 1958. Additionally, studies of psychosocial aspects of the bombings were very limited. Although the time lag of observation might lead to selection bias, and bomb-related injuries not caused by radiation might increase mortality risks,[20,21] the results of the LSS are accepted by epidemiologists worldwide.[22,23]

People exposed in utero to atomic bomb radiation were identified during the 1940s and 1950s, and about 3600 people were retrospectively selected for epidemiological studies and have been followed up since 1945; 1000 people have been invited to participate in the health examination programme, which began in 1978. Children born in 1946–84 with atomic bomb survivors as one or both parents were selected to form the F1 cohort, and about 77 000 of these people have been followed up. A health examination programme for the F1 cohort started in 2002, when the likelihood of cancer and other diseases was thought to be increasing owing to ageing, and about 12 000 people are participating. The research was taken over from ABCC by the Radiation Effects Research Foundation after its creation in 1975.[19] Hiroshima University, Nagasaki University, and other research organisations have formed their own cohorts and undertake their own studies of the health effects of atomic bombs.

## Malignancies in the LSS

Excess cases of leukaemia associated with close proximity to the hypocentres began to be reported about 3 years after the bombings, and the excess relative risk (ERR; the proportional increase of risk) peaked 6–8 years after exposure.[24,25] Among children aged around 10 years at exposure, the ERR for leukaemia at 1 Gy peaked at about 70 and then rapidly decreased with increasing time since exposure to an ERR of 1–3.[25] Among those exposed aged 30 years or older, the ERR was increased by only around a factor of 2 during the whole period since the bombings. The dose–response relation for the ERR of acute myeloid leukaemia was non-linear, with the slope increasing with increasing dose, whereas the

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**Panel 3: Radiation exposure in children**

On the basis of results from various epidemiological studies, including the Life Span Study (LSS), the UN Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) concluded that children are generally more sensitive than adults to radiation for 25% of cancer types, including leukaemia and cancers of the thyroid, skin, breast, and brain.[30] Results of studies suggest that children who undergo several CT examinations (which involve high-dose-rate, but low-dose x-ray exposure) are at increased risk of leukaemia and solid cancers,[31,32] although interpretation of these studies has some problems.[30,33] Exposure in utero to low doses at high dose rates can increase risks of leukaemia and solid cancers in childhood.[34–36] For chronic low-dose-rate exposure, initial results of a large British study[37] suggest an excess childhood leukaemia risk associated with natural background gamma radiation exposure in children at a level compatible with models based on the Life Span Study data. However, further studies are necessary to confirm this finding. Background radiation is discussed in the appendix.

dose–response was mostly linear for acute lymphoid and chronic myeloid leukaemia. For all forms of leukaemia for both sexes and all ages, the ERR was 3–5 at a dose of 1 Gy to the red bone marrow.[25,26] Risk of myelodysplastic syndrome likewise increased, and showed a linear dose–response relation.[27]

Increased risks of solid cancers have been reported since about 10 years after the bombings and continue at present.[19,28,29] The ERR of all solid cancers combined increased linearly with radiation dose, about 40–50% per Gy for both mortality and incidence for the sex-averaged risk at an attained age of 70 years after exposure at age 30 years.[28,29] The ERR was higher in those exposed in childhood (about 15–30% per 10 years), suggesting that children have a generally higher sensitivity to radiation-induced cancer than do adults (panel 3).[30–37] ERR decreased with attained age, but the excess absolute risk (EAR) of cancer increased, which is due to the increased background rate of cancer with older age.[28,29] The increased risk becomes statistically significant at a dose of 0·1–0·2 Gy, and the modelled dose–response relation (figure 1) suggests that the threshold is around 0, with an upper limit (95% CI) of about 0·15 Gy.[28] The risk of radiation-induced cancer at high doses (1 Gy or higher) is statistically significant, whereas at low doses (<100 mGy), the risk is uncertain. The effect of radiation is much smaller at low doses, leading to increased relative effects of statistical fluctuations and other risk factors and reducing statistical power.

The radiation-related risk of cancer varies between organs and tissues: the risks of cancer of the bladder, female breast, lung, brain, thyroid, colon, oesophagus, ovary, stomach, liver, and skin (excluding melanoma) increased significantly in atomic bomb survivors in the LSS, whereas risks of cancer of the pancreas, rectum, uterus, prostate, and kidney parenchyma did not (figure 2). ERR was higher in women than in men, but EAR was similar in men and women since the background rate of cancer was low in women compared with men. Age at time of exposure modified radiation-induced cancer risk in a site-specific manner: the risk was larger in those exposed in childhood for cancers of the thyroid, skin, breast, and brain, but tended to be lower for lung cancer.[28,29,30]

Investigation of the joint effect of smoking and radiation on lung cancer risk showed that radiation-associated ERR for moderate smokers was similar to that for heavy smokers, and patterns were similar among different histological types.[38,39] Results of studies of radiation effects on occurrence of multiple primary cancers showed that the dose–response relations for risks of both first and second primary solid cancers and leukaemias were similar; however, incidence rates were higher for second solid cancers and leukaemias than for first cancers.[40] This finding suggests that radiation effects on cancer pathogenesis are similar in people who developed multiple primary cancers and those who did not, although
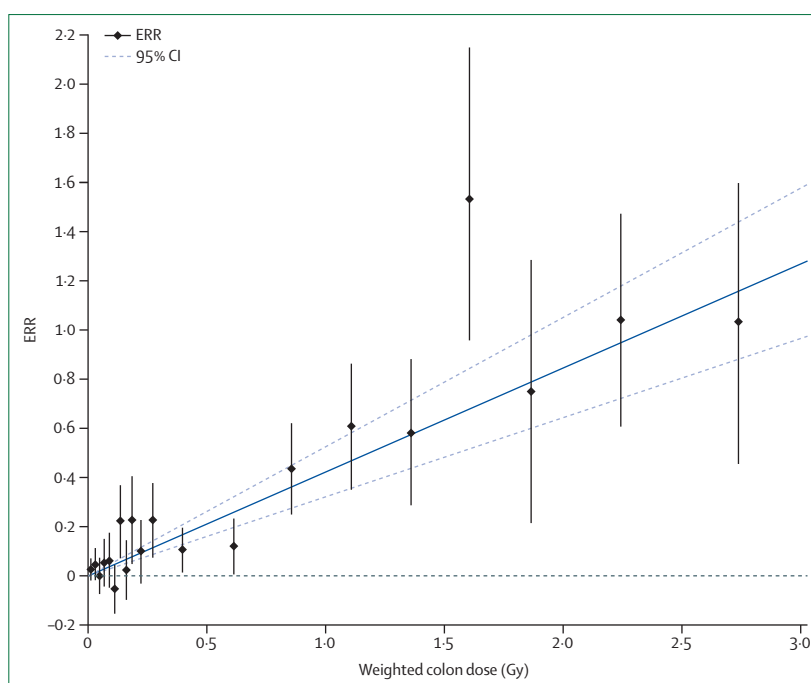


***Figure 1:*** **Dose–response relation of solid cancer mortality in the Life Span Study cohort, 1950–2003**
Fitted linear, sex-averaged excess relative risk (ERR) dose–response relation. Points are non-parametric estimates of the ERR in dose categories and bars are 95% CIs. Non-parametric estimates at low doses suggest uncertainty in risk estimates that is not shown in the linear fit and its 95% CI because the dose–response was mostly due to the association at dose of 1 Gy or more. Reproduced from Ozasa and colleagues,[28] by permission of Radiation Research Society.
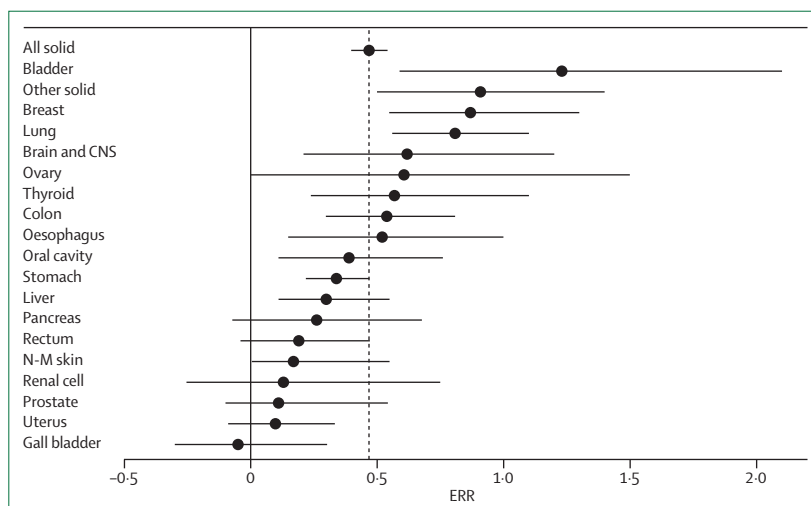


***Figure 2:*** **Excess relative risk (ERR) per Gy for site-specific solid cancers in the Life Span Study cohort**
Risk is standardised as exposure at age 30 years (sex-averaged) and diagnosed at age 70 years. Horizontal bars show 90% CIs. Data from Preston and colleagues.[29] CNS=central nervous system. N-M=non-melanoma.

predisposition to cancer development was generally higher in people who developed multiple primary cancers than those who did not.

Although radiation-specific pathways of carcinogenesis have not been identified, some molecular mechanisms were frequently seen in cancers that developed in survivors exposed to high doses of

radiation. For example, rearrangements of *RET/PTC* occurred in papillary thyroid cancer in atomic bomb survivors exposed to high radiation doses more often than in non-exposed people, although the comparison was not adjusted for age at exposure.[41] Some *IL10* gene haplotypes affect dose dependence of diffuse-type gastric cancer risk.[42]

### Non-cancer diseases in the LSS

Risk of non-cancer somatic diseases has been assessed based on mortality statistics, health examination programmes, and information from mailed question-naires.[43–48] Owing to recorded associations between high radiation exposure and development of non-cancer diseases, radiation is thought to be an independent risk factor for non-cancer diseases. Although the mortality risk of heart diseases was characterised by a modest linear increase with dose, risk varied between subtypes of heart disease and between periods of observation.[43] Risk of stroke slightly increased and was more pronounced at high doses, and the dose–response curve was concave when non-fatal cases were included.[44,45] At high doses, tissue damage to the circulatory system directly is likely to have a major role in causation of vascular disease (as after radiotherapy); however, radiation might cause chronic kidney disorders, which induce hypertension and thus might contribute to the increased risk of these cardiovascular diseases.[46,47] Whether a radiation-induced excess risk of circulatory disease persists at low doses is the subject of much debate and research. Mortality risk of non-cancer respiratory diseases slightly increased, with a linear dose–response relation in 1980–2005, but not before 1980.[48] Pathogenesis of non-cancer diseases due to low-level exposure to radiation has not been identified, although some findings suggest that immuno-senescence and enhanced inflammatory responses occur in atomic bomb survivors. These responses include attrition of T-cell functions, such as reduced mitogen-dependent proliferation and interleukin-2 production, decreased T-helper-cell populations, and increased blood inflammatory cytokine concentrations.[49] A radiation dose-dependent increase in percentages of CD25+CD127– regulatory T cells in the CD4 T-cell population,[50] and dose-dependent and age-dependent increased plasma concentrations of reactive oxygen species, interleukin 6, and C-reactive protein, and increased erythrocyte sedimentation rate have been reported in survivors.[51]

### Individuals exposed in utero

Some individuals exposed in the womb to atomic bomb radiation have disturbed brain development—so-called atomic bomb microcephaly[52]—characterised by mental retardation. Association with radiation exposure becomes clear at a radiation dose of 0·5 Gy or higher, and shows a dose–response with highest risk with exposure during weeks 8–15 of gestation. This effect is thought to be deterministic because fetal brain cells are especially susceptible to radiation damage during this period. Exposure in utero to high doses caused disturbed growth during childhood—ie, low stature.[52,53] Mortality and cancer incidence in this population have been followed up, and an increased ERR of solid cancer incidence was reported, similar to the risk of cancer in people exposed during childhood.[54]

### F1 cohort

The F1 cohort includes children of survivors conceived after the bombings. Hereditary effects of exposure to atomic bomb radiation have been of public concern since the atomic bombings, and various studies of children of survivors have been done. Among the outcomes studied were stillbirth, malformations, neonatal death, sex ratio of newborns, chromosome aberrations, protein electrophoresis, and DNA polymorphism, but no abnormalities were associated with parental exposure to radiation.[55–59] Epidemiological follow-up of survivors' children showed no increased risk of mortality or cancer associated with parental radiation dose, although follow-up will continue for many years owing to the young age of the cohort (appendix).[60,61] Based on a health examination programme for the offspring of survivors, prevalence of multifactorial diseases—hypertension, hyper-cholesterolaemia, diabetes, angina, myocardial infarction, or stroke—was not associated with paternal or maternal atomic bomb radiation dose, or the sum of their doses, in either male or female children.[62]

## Nuclear power plant accidents

During the past 60 years, five major nuclear accidents have taken place, which are discussed in paper 2[63] in this Series. The worst accident in the history of the nuclear industry occurred in 1986 when massive explosions completely destroyed unit 4 of Chernobyl nuclear power plant.

### Chernobyl

The Chernobyl nuclear power plant accident released huge quantities (approximately 5 200 000 TBq) of radionuclides into the atmosphere. Of particular importance for its effects on human health was the release of radioisotopes of iodine (mainly $^{131}I$) and caesium (mainly $^{137}Cs$ and $^{134}Cs$), since heavily contaminated foods, especially milk, became a source of internal exposure of organs and tissues.[16] For people living in heavily contaminated areas, the average radiation dose to the thyroid gland due to $^{131}I$ was estimated to be 650 mGy in Ukraine and 560 mGy in Belarus. Doses were assessed based on individual radioactivity measurements taken within 2 months of the accident, on environmental transport models, and on interview data.[64,65]

Immediately after the accident, about 600 workers were involved in the emergency response. 134 developed acute radiation syndrome, resulting in 28 deaths.[63,66,67] In subsequent recovery work, about 600 000 civil and military personnel, known as liquidators, were employed for different periods of time and took part in building of the sarcophagus over the destroyed reactor and in decontamination work. Although many studies of late effects among recovery workers have been done, these studies have been inconclusive owing to low statistical power and uncertainties in dose reconstruction. Therefore, the association between radiation exposure and incidence of malignancies, such as leukaemia, thyroid cancer and other solid cancers, and benign disorders such as cardiovascular diseases, among recovery workers is unclear at present.[66,67]

Results of epidemiological studies of the population from heavily contaminated areas around Chernobyl showed a pronounced increase in incidence of thyroid cancer in people who had received high thyroid doses (>1 Gy) as children, starting a few years after the accident.[66–68] ERR of thyroid cancer per Gy was estimated at 1·91 in Ukraine and 2·15 in Belarus.[64,65] The increase in thyroid cancer was especially high in children aged 0–5 years at exposure, but no increase was reported in adults. Interestingly, incidence of thyroid cancer in children born after the accident was around background levels, which suggests that the increase in thyroid cancer near Chernobyl was mainly due to internal exposure to radioactive iodine, which has a short half-life of 8 days.[69]

So far, many studies have been done to clarify the molecular mechanisms of radiation-induced thyroid cancer. Early childhood thyroid cancer cases in Chernobyl showed a significantly higher prevalence of *RET* gene rearrangements, such as *RET/PTC3*, *RET/PTC1*, and, in rare cases (3%), *RET/PTC2* rearrangements.[70,71] However, accumulating in-vivo data suggest that the *RET/PTC* rearrangements in childhood thyroid cancer after the Chernobyl accident might not be the result of internal exposure to radiation from radioactive iodine, but rather radiation exposure might have a non-targeted role in creation of a tissue microenvironment that eventually selects thyroid follicular cells with spontaneous *RET/PTC* rearrangement.[70,71]

Doses to tissues other than the thyroid from external or internal exposures were low. According to retrospective reconstruction of external gamma radiation exposure doses, the average cumulative dose was estimated to be about 40 mSv in the most contaminated districts around Chernobyl.[72] Evidence for a radiation-related increase of other health effects, including leukaemia and congenital malformations, has been equivocal.[68]

However, adverse psychosocial effects of changes in living environment and the social and economic effects of the accident are readily apparent.[17,73] Prevalence of depression and PTSD is increased two decades after the accident in emergency and recovery workers, and general population studies report increased rates of poor self-rated health, clinical and subclinical depression, anxiety, and PTSD.[17,73] Continued research is needed to clarify mental health effects of nuclear disasters.

## Conclusions

Knowledge of effects of radiation on human health has been accumulated by epidemiological studies of atomic bomb survivors, supplemented by studies of occupational, medical, and environmental exposures, and has formed the basis of the radiation protection system of the ICRP, which has been used by governments worldwide for various regulatory frameworks. However, the low statistical power of epidemiological studies has meant that the risk of cancer for doses of less than 100 mGy, or for moderate doses delivered at low dose rates, cannot be inferred definitively.[74] Additionally, various other issues relating to radiation carcinogenesis are unresolved and can be addressed only by an approach that combines radioepidemiology and radiobiology.

Progress has been made in understanding the sensitivity of the fetus to leukaemogenesis. Results of the Oxford Survey of Childhood Cancers[75] and other case-control studies[34] of antenatal radiography have shown that low-dose exposure of the fetus increases risk of childhood leukaemia, and that ERR per Gy is similar to that of children younger than 10 years in the LSS. By contrast, atomic bomb survivors exposed in utero did not develop childhood leukaemia, although the statistical power of the study was low.[76] Interestingly, lymphocytes from survivors exposed in utero did not show excess stable chromosomal translocations, except a small increase in chromosome aberrations at doses of less than 100 mSv.[77] Experimental exposure of mice to doses of 1 Gy and 2 Gy in utero did not result in lymphocytes with translocations.[78] These data suggest a mechanism to eliminate aberrant stem cells induced by exposure to moderate and high doses of radiation in utero, and in contrast to exposure of children, suggests low sensitivity to radiation leukaemogenesis at moderate and high does. Results of animal studies of irradiation in utero have not shown radiation-induced leukaemias;[79] however, these experiments used moderate and high doses and have not addressed low-dose risks.

Technological advances have made a new approach to epidemiology possible: molecular epidemiology relates genomic variations among individuals to their sensitivity to radiation carcinogenesis. Similar technological advances have enabled a high-throughput approach to radiation biology in which biomarkers (eg, DNA, RNA, protein, metabolites, or chromosomes) associated with detrimental outcomes of radiation, such as cancer, are identified.[80] This powerful approach has limitations. Most biomarkers are early indicators,

responding to radiation minutes to several days after irradiation, and are separated from the final outcome, such as cancer, by many years. After radiation exposure, many steps of carcinogenesis occur before a normal cell acquires the changes necessary for full malignancy. Thus, a carcinogenic outcome cannot be predicted by early biomarkers alone. However, high-throughput radiation biology is an emerging specialty that provides strong analytical power when combined with classical hypothesis-driven radiation biology. This advance, when combined with analytical epidemiology, is the only realistic approach to elucidate mechanisms and assess risks of radiation-induced cancer with improved accuracy.[81]

Study of radiation effects has previously focused on natural science, and has tended to ignore psychosocial aspects of radiation exposure. However, the Chernobyl nuclear power plant accident provided evidence of adverse psychological effects among people who experienced the trauma of the accident.[82] In the case of the Fukushima Daiichi nuclear power plant accident, the dose to the public was estimated to be low and health effects are thought to be indiscernible.[63,83] Nonetheless, psychosocial problems in Fukushima have a devastating effect on peoples' lives.[84,85] In addition to the natural science of radiation effects, psychosocial studies should be integrated into recovery planning after nuclear accidents such as that at Fukushima.[63,85]

### References
1. Codman E. A study of the cases of accidental X-ray burns hitherto recorded. *Phila Med J* 1902; **9:** 438–42.
2. Daniel J. The X-rays. *Science* 1896; **3:** 562–63.
3. ICRP. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP publication 103. *Ann ICRP* 2007; **37:** 1–332.
4. Muller HJ. The measurement of gene mutation rate in Drosophila, its high variability, and its dependence upon temperature. *Genetics* 1928; **13:** 279–357.
5. Weinberg R. The biology of cancer. NY, USA: Garland Science, 2013.
6. Atomic Bomb Survivors Support Division Hiroshima Prefectural Government. Atomic Bomb Survivors Support Program Overview, Hiroshima city. Hiroshima: Hiroshima Prefectural Government, 2014: 1 (in Japanese).
7. Atomic Bomb Survivors Support Division Nagasaki Prefectural Government. Atomic Bomb Survivors Support Program Overview, Nagasaki city. Nagasaki: Nagasaki Prefectural Government, 2014: 8 (in Japanese).
8. Francis T, Jablon S, Moore FE. Report of ad hoc committee for appraisal of ABCC program. Hiroshima and Nagasaki: Atomic Bomb Casualty Commission, 1955: Technical report 33–59.
9. Ishida M, Beebe GW. Research plan for joint NIH-ABCC study of life-span of A-bomb survivors. Hiroshima and Nagasaki: Atomic Bomb Casualty Commission, 1959: technical report 4–59.
10. Yamada M, Kodama K, Wong F. The long-term psychological sequelae of atomic bomb survivors in Hiroshima and Nagasaki. In: Ricks R, Berger ME, O'Hara RM, eds. The medical basis for radiation preparedness III: the psychological perspective. New York: Elsevier, 1991: 155–63.
11. Yamada M, Izumi S. Psychiatric sequelae in atomic bomb survivors in Hiroshima and Nagasaki two decades after the explosions. *Soc Psychiatry Psychiatr Epidemiol* 2002; **37:** 409–15.
12. Honda S, Shibata Y, Mine M, et al. Mental health conditions among atomic bomb survivors in Nagasaki. *Psychiatry Clin Neurosci* 2002; **56:** 575–83.
13. The Committee for the Compilation of Materials on the Damage by the Atomic Bombs in Hiroshima and Nagasaki, ed. The damage by the atomic bombings in Hiroshima and Nagasaki and their after-effects. Tokyo: Iwanami Shoten, 1979: 241–368 (in Japanese).
14. Ministry of Health, Labor and Welfare. Atomic Bomb Survivors Comprehensive medical care and welfare (in Japanese). http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/kenkou/genbaku/index.html (accessed June 18, 2015).
15. Yasumura S, Hosoya M, Yamashita S, et al, and the Fukushima Health Management Survey Group. Study protocol for the Fukushima health management survey. *J Epidemiol* 2012; **22:** 375–83.
16. Drozdovitch V, Minenko V, Khrouch V, et al. Thyroid dose estimates for a cohort of Belarusian children exposed to radiation from the Chernobyl accident. *Radiat Res* 2013; **179:** 597–609.
17. Bromet EJ, Havenaar JM, Guey LT. A 25 year retrospective review of the psychological consequences of the Chernobyl accident. *Clin Oncol (R Coll Radiol)* 2011; **23:** 297–305.
18. Cullings HM, Fujita S, Funamoto S, Grant EJ, Kerr GD, Preston DL. Dose estimation for atomic bomb survivor studies: its evolution and present status. *Radiat Res* 2006; **166:** 219–54.
19. RERF. A brief description. Hiroshima: Radiation Effects Research Foundation, 2008. http://www.rerf.jp/shared/briefdescript/briefdescript_e.pdf (accessed July 14, 2015).
20. Stewart AM, Kneale GW. A-bomb survivors: factors that may lead to a re-assessment of the radiation hazard. *Int J Epidemiol* 2000; **29:** 708–14.
21. Little MP. Absence of evidence for differences in the dose-response for cancer and non-cancer endpoints by acute injury status in the Japanese atomic-bomb survivors. *Int J Radiat Biol* 2002; **78:** 1001–10.
22. UNSCEAR. Scientific annex A: epidemiological studies of radiation and cancer. Volume I: effects of ionizing radiation. UNSCEAR Report 2006. New York: United Nations Scientific Committee on the Effects of Atomic Radiation, 2008.
23. UNSCEAR. Scientific annex B: epidemiological evaluation of cardiovascular disease and other non-cancer disease following radiation exposure. Volume I: effects of ionizing radiation. UNSCEAR Report 2006. New York: United Nations Scientific Committee on the Effects of Atomic Radiation, 2008.
24. Folley JH, Borges W, Yamawaki T. Incidence of leukemia in survivors of the atomic bomb in Hiroshima and Nagasaki, Japan. *Am J Med* 1952; **13:** 311–21.
25. Richardson D, Sugiyama H, Nishi N, et al. Ionizing radiation and leukemia mortality among Japanese atomic bomb survivors, 1950–2000. *Radiat Res* 2009; **172:** 368–82.
26. Hsu W-L, Preston DL, Soda M, et al. The incidence of leukemia, lymphoma and multiple myeloma among atomic bomb survivors: 1950–2001. *Radiat Res* 2013; **179:** 361–82.
27. Iwanaga M, Hsu W-L, Soda M, et al. Risk of myelodysplastic syndromes in people exposed to ionizing radiation: a retrospective cohort study of Nagasaki atomic bomb survivors. *J Clin Oncol* 2011; **29:** 428–34.

28 Ozasa K, Shimizu Y, Suyama A, et al. Studies of the mortality of atomic bomb survivors, Report 14, 1950–2003: an overview of cancer and noncancer diseases. *Radiat Res* 2012; **177:** 229–43.

29 Preston DL, Ron E, Tokuoka S, et al. Solid cancer incidence in atomic bomb survivors: 1958–1998. *Radiat Res* 2007; **168:** 1–64.

30 UNSCEAR. Scientific annex B: effects of ionizing radiation on children. Volume II: sources, effects and risks of ionizing radiation. Vienna: United Nations Scientific Committee on the Effects of Atomic Radiation, 2013.

31 Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. *Lancet* 2012; **380:** 499–505.

32 Mathews JD, Forsythe AV, Brady Z, et al. Cancer risk in 680 000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. *BMJ* 2013; **346:** f2360.

33 Walsh L, Shore R, Auvinen A, Jung T, Wakeford R. Risks from CT scans—what do recent studies tell us? *J Radiol Prot* 2014; **34:** E1–5.

34 Doll R, Wakeford R. Risk of childhood cancer from fetal irradiation. *Br J Radiol* 1997; **70:** 130–39.

35 Wakeford R, Little MP. Risk coefficients for childhood cancer after intrauterine irradiation: a review. *Int J Radiat Biol* 2003; **79:** 293–309.

36 Wakeford R. Childhood leukaemia following medical diagnostic exposure to ionizing radiation in utero or after birth. *Radiat Prot Dosimetry* 2008; **132:** 166–74.

37 Kendall GM, Little MP, Wakeford R, et al. A record-based case-control study of natural background radiation and the incidence of childhood leukaemia and other cancers in Great Britain during 1980–2006. *Leukemia* 2013; **27:** 3–9.

38 Furukawa K, Preston DL, Lönn S, et al. Radiation and smoking effects on lung cancer incidence among atomic bomb survivors. *Radiat Res* 2010; **174:** 72–82.

39 Egawa H, Furukawa K, Preston D, et al. Radiation and smoking effects on lung cancer incidence by histological types among atomic bomb survivors. *Radiat Res* 2012; **178:** 191–201.

40 Li CI, Nishi N, McDougall JA, et al. Relationship between radiation exposure and risk of second primary cancers among atomic bomb survivors. *Cancer Res* 2010; **70:** 7187–98.

41 Hamatani K, Eguchi H, Ito R, et al. RET/PTC rearrangements preferentially occurred in papillary thyroid cancer among atomic bomb survivors exposed to high radiation dose. *Cancer Res* 2008; **68:** 7176–82.

42 Hayashi T, Ito R, Cologne J, et al. Effects of IL-10 haplotype and atomic bomb radiation exposure on gastric cancer risk. *Radiat Res* 2013; **180:** 60–69.

43 Yamada M, Wong FL, Fujiwara S, Akahoshi M, Suzuki G. Noncancer disease incidence in atomic bomb survivors, 1958–1998. *Radiat Res* 2004; **161:** 622–32.

44 Shimizu Y, Kodama K, Nishi N, et al. Radiation exposure and circulatory disease risk: Hiroshima and Nagasaki atomic bomb survivor data, 1950–2003. *BMJ* 2010; **340:** b5349.

45 Takahashi I, Abbott RD, Ohshita T, et al. A prospective follow-up study of the association of radiation exposure with fatal and non-fatal stroke among atomic bomb survivors in Hiroshima and Nagasaki (1980–2003). *BMJ Open* 2012; **2:** e000654.

46 Adams MJ, Grant EJ, Kodama K, et al. Radiation dose associated with renal failure mortality: a potential pathway to partially explain increased cardiovascular disease mortality observed after whole-body irradiation. *Radiat Res* 2012; **177:** 220–28.

47 Sera N, Hida A, Imaizumi M, Nakashima E, Akahoshi M. The association between chronic kidney disease and cardiovascular disease risk factors in atomic bomb survivors. *Radiat Res* 2013; **179:** 46–52.

48 Pham T-M, Sakata R, Grant EJ, et al. Radiation exposure and the risk of mortality from noncancer respiratory diseases in the life span study, 1950–2005. *Radiat Res* 2013; **180:** 539–45.

49 Kusunoki Y, Hayashi T. Long-lasting alterations of the immune system by ionizing radiation exposure: implications for disease development among atomic bomb survivors. *Int J Radiat Biol* 2008; **84:** 1–14.

50 Kusunoki Y, Yamaoka M, Kubo Y, et al. T-cell immunosenescence and inflammatory response in atomic bomb survivors. *Radiat Res* 2010; **174:** 870–76.

51 Hayashi T, Morishita Y, Khattree R, et al. Evaluation of systemic markers of inflammation in atomic-bomb survivors with special reference to radiation and age effects. *FASEB J* 2012; **26:** 4765–73.

52 Otake M, Schull WJ. Radiation-related brain damage and growth retardation among the prenatally exposed atomic bomb survivors. *Int J Radiat Biol* 1998; **74:** 159–71.

53 Nakashima E. Relationship of five anthropometric measurements at age 18 to radiation dose among atomic bomb survivors exposed in utero. *Radiat Res* 1994; **138:** 121–26.

54 Preston DL, Cullings H, Suyama A, et al. Solid cancer incidence in atomic bomb survivors exposed in utero or as young children. *J Natl Cancer Inst* 2008; **100:** 428–36.

55 Otake M, Schull WJ, Neel JV. Congenital malformations, stillbirths, and early mortality among the children of atomic bomb survivors: a reanalysis. *Radiat Res* 1990; **122:** 1–11.

56 Schull WJ, Neel JV, Hashizume A. Some further observations on the sex ratio among infants born to survivors of the atomic bombings of Hiroshima and Nagasaki. *Am J Hum Genet* 1966; **18:** 328–38.

57 Neel JV, Satoh C, Goriki K, et al. Search for mutations altering protein charge and/or function in children of atomic bomb survivors: final report. *Am J Hum Genet* 1988; **42:** 663–76.

58 Neel JV, Schull WJ, Awa AA, et al. The children of parents exposed to atomic bombs: estimates of the genetic doubling dose of radiation for humans. *Am J Hum Genet* 1990; **46:** 1053–72.

59 Kodaira M, Ryo H, Kamada N, et al. No evidence of increased mutation rates at microsatellite loci in offspring of A-bomb survivors. *Radiat Res* 2010; **173:** 205–13.

60 Izumi S, Suyama A, Koyama K. Radiation-related mortality among offspring of atomic bomb survivors: a half-century of follow-up. *Int J Cancer* 2003; **107:** 292–97.

61 Izumi S, Koyama K, Soda M, Suyama A. Cancer incidence in children and young adults did not increase relative to parental exposure to atomic bombs. *Br J Cancer* 2003; **89:** 1709–13.

62 Tatsukawa Y, Cologne JB, Hsu W-L, et al. Radiation risk of individual multifactorial diseases in offspring of the atomic-bomb survivors: a clinical health study. *J Radiol Prot* 2013; **33:** 281–93.

63 Hasegawa A, Tanigawa K, Ohtsuru A, et al. Health effects of radiation and other health problems in the aftermath of nuclear accidents, with an emphasis on Fukushima. *Lancet* 2015; **386:** 479–88.

64 Brenner AV, Tronko MD, Hatch M, et al. I-131 dose response for incident thyroid cancers in Ukraine related to the Chornobyl accident. *Environ Health Perspect* 2011; **119:** 933–39.

65 Zablotska LB, Ron E, Rozhko AV, et al. Thyroid cancer risk in Belarus among children and adolescents exposed to radioiodine after the Chernobyl accident. *Br J Cancer* 2011; **104:** 181–87.

66 Kesminiene A, Evrard A-S, Ivanov VK, et al. Risk of thyroid cancer among chernobyl liquidators. *Radiat Res* 2012; **178:** 425–36.

67 Zablotska LB, Bazyka D, Lubin JH, et al. Radiation and the risk of chronic lymphocytic and other leukemias among chornobyl cleanup workers. *Environ Health Perspect* 2013; **121:** 59–65.

68 Cardis E, Hatch M. The Chernobyl accident—an epidemiological perspective. *Clin Oncol (R Coll Radiol)* 2011; **23:** 251–60.

69 Shibata Y, Yamashita S, Masyakin VB, Panasyuk GD, Nagataki S. 15 years after Chernobyl: new evidence of thyroid cancer. *Lancet* 2001; **358:** 1965–66.

70 Leeman-Neill RJ, Brenner AV, Little MP, et al. RET/PTC and PAX8/PPARγ chromosomal rearrangements in post-Chernobyl thyroid cancer and their association with iodine-131 radiation dose and other characteristics. *Cancer* 2013; **119:** 1792–99.

71 Leeman-Neill RJ, Kelly LM, Liu P, et al. ETV6-NTRK3 is a common chromosomal rearrangement in radiation-associated thyroid cancer. *Cancer* 2014; **120:** 799–807.

72 Pukkala E, Kesminiene A, Poliakov S, et al. Breast cancer in Belarus and Ukraine after the Chernobyl accident. *Int J Cancer* 2006; **119:** 651–58.

73 Bromet EJ. Emotional consequences of nuclear power plant disasters. *Health Phys* 2014; **106:** 206–10.

74 US National Academy of Sciences, National Research Council 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: 13.

75    Bithell JF, Stewart AM. Pre-natal irradiation and childhood malignancy: a review of British data from the Oxford Survey. *Br J Cancer* 1975; **31:** 271–87.

76    Delongchamp RR, Mabuchi K, Yoshimoto Y, Preston DL. Cancer mortality among atomic bomb survivors exposed in utero or as young children, October 1950–May 1992. *Radiat Res* 1997; **147:** 385–95.

77    Ohtaki K, Kodama Y, Nakano M, et al. Human fetuses do not register chromosome damage inflicted by radiation exposure in lymphoid precursor cells except for a small but significant effect at low doses. *Radiat Res* 2004; **161:** 373–79.

78    Nakano M, Kodama Y, Ohtaki K, et al. Chromosome aberrations do not persist in the lymphocytes or bone marrow cells of mice irradiated in utero or soon after birth. *Radiat Res* 2007; **167:** 693–702.

79    ICRP. Biological effects after prenatal irradiation (embryo and fetus). ICRP Publication 90. *Ann ICRP* 2003; **33:** 126.

80    Pernot E, Hall J, Baatout S, et al. Ionizing radiation biomarkers for potential use in epidemiological studies. *Mutat Res* 2012; **751:** 258–86.

81    Preston RJ. Integrating basic radiobiological science and epidemiological studies: why and how. *Health Phys* 2015; **108:** 125–30.

82    UNSCEAR. Scientific annex D: health effects due to radiation from the Chernobyl accident. Volume II: sources, effects and risks of ionizing radiation. New York: United Nations Scientific Committee on the Effects of Atomic Radiation, 2008.

83    UNSCEAR. Scientific annex A: levels and effects of radiation exposures due to the nuclear accident after the 2011 great east Japan earthquake and tsunami. Volume I: sources, effects and risks of ionizing radiation. New York: United Nations Scientific Committee on the Effects of Atomic Radiation, 2013.

84    Yabe H, Suzuki Y, Mashiko H, et al, and the Mental Health Group of the Fukushima Health Management Survey. Psychological distress after the Great East Japan Earthquake and Fukushima Daiichi Nuclear Power Plant accident: results of a mental health and lifestyle survey through the Fukushima Health Management Survey in FY2011 and FY2012. *Fukushima J Med Sci* 2014; **60:** 57–67.

85    Ohtsuru A, Tanigawa K, Kumagai A, et al. Nuclear disasters and health: lessons learned, challenges, and proposals. *Lancet* 2015; **386:** 489–97.