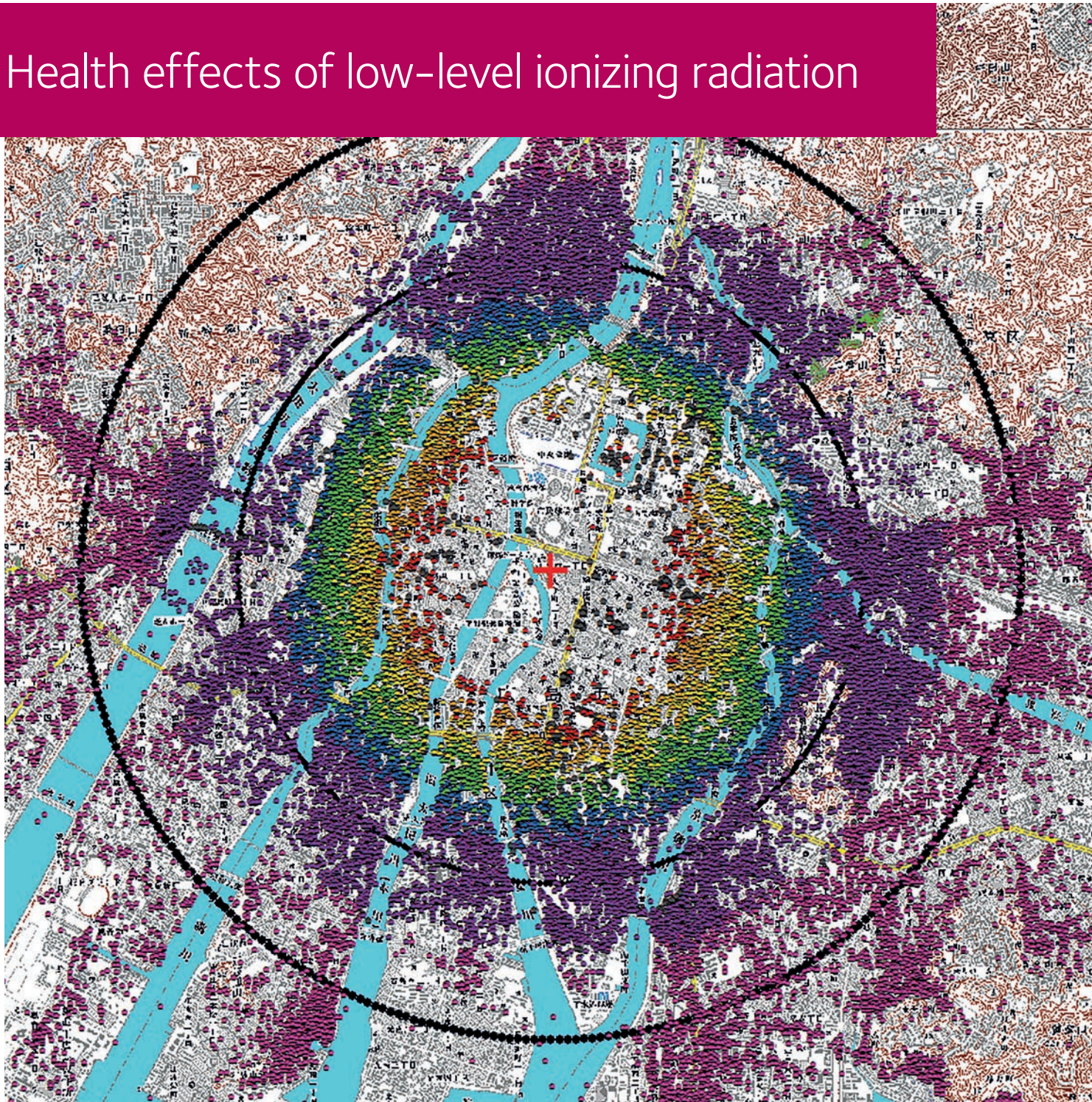OXFORD
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Health effects of low–level ionizing radiation

Oxford Martin Restatement 5:

A restatement of the natural science evidence base concerning the health effects of low-level ionizing radiation

Oxford Martin Restatements review the natural science evidence base underlying areas of current policy concern and controversy. Written in policy neutral terms and designed to be read by an informed but not technically specialist audience, restatements are produced by a writing team reflecting the breadth of opinion on the topic in the science community and involve wide consultation with interested stakeholders. The final version of the restatement is peer-reviewed prior to publication.

This paper was published in September 2017 in the Proceedings of the Royal Society B. It deals with the health effects associated with low-doses of ionizing radiation.

Exposure to ionizing radiation is ubiquitous, and it is well established that moderate and high doses cause ill-health and can be lethal. The health effects of low doses or low dose-rates of ionizing radiation are not so clear. This restatement sets out to summarize, as a restatement, the natural science evidence base concerning the human health effects of exposure to low-level ionizing radiation. A novel feature, compared to other reviews, is that a series of statements are listed and categorized according to the nature and strength of the evidence that underpins them. The restatement provides a concise entrée into this vibrant field, pointing the interested reader deeper into the literature when more detail is needed. It is not the purpose of the restatement to reach conclusions on whether the legal limits on radiation exposures are too high, too low or just right. The aim is to provide an introduction so that non-specialist individuals in this area (be they policy-makers, disputers of policy, health professionals or students) have a straightforward place to start.

This pdf contains:

Cover: Locations and dose estimates of survivors of the Hiroshima atomic bomb. Black circles denote 2 and 3 km distances from the hypocenter. Dark grey dots = unknown dose; pink < 5 mGy; purple 5-100 mGy; blue 100-200 mGy; green 200-500 mGy; yellow 500-1000 mGy; orange 1000-2000 mGy; red >2000 mGy. All doses are weighted adjusted colon doses. Map is from the Geographical Survey Institute of Japan, 2002. Figure is reproduced with permission from Cullings et al. (2017) Health Phys. 112(1): 56-97.

Authors for correspondence:
Angela R. McLean
e-mail: angela.mclean@zoo.ox.ac.uk
Ella K. Adlen
e-mail: ella.adlen@oxfordmartin.ox.ac.uk

†Deceased 14th April 2016. Prof. Sir David Mackay died during the writing of the restatement project. He remains an author as a reflection of his substantial and valued contribution.
‡Retired.

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A restatement of the natural science evidence base concerning the health effects of low-level ionizing radiation

Angela R. McLean[1,2], Ella K. Adlen[2], Elisabeth Cardis[3], Alex Elliott[4], Dudley T. Goodhead[5], Mats Harms-Ringdahl[6], Jolyon H. Hendry[7], Peter Hoskin[8], Penny A. Jeggo[9], David J. C. Mackay[10,†], Colin R. Muirhead[11,‡], John Shepherd[12], Roy E. Shore[13,‡], Geraldine A. Thomas[14], Richard Wakeford[15] and H. Charles J. Godfray[1,2]

[1]Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, UK
[2]Oxford Martin School, University of Oxford, 34 Broad Street, Oxford OX1 3BD, UK
[3]Barcelona Institute for Global Health (ISGlobal), Center for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
[4]College of Medical, Veterinary and Life Sciences, Wellcome Surgical Institute, University of Glasgow, Garscube Estate, Glasgow G61 1QH, UK
[5]Medical Research Council, Harwell, Didcot OX11 0RD, UK
[6]Center for Radiation Protection Research, Department of Molecular Biosciences, The Wenner-Gren Institute, Stockholm University, Stockholm, Sweden
[7]Christie Medical Physics and Engineering, Christie Hospital and University of Manchester, Manchester, UK
[8]Mount Vernon Cancer Centre, Northwood HA6 2RN, UK
[9]Genome Damage and Stability Centre, University of Sussex, Science Park Road, Falmer, Brighton BN1 9RQ, UK
[10]Department of Engineering, University of Cambridge, Trumpington Street, Cambridge CB2 1PZ, UK
[11]Institute of Health and Society, Newcastle University, Baddiley-Clark Building, Richardson Road, Newcastle upon Tyne NE2 4AX, UK
[12]Ocean and Earth Science, University of Southampton, Southampton SO14 3ZH, UK
[13]Radiation Effects Research Foundation, Hiroshima, Japan
[14]Department of Surgery and Cancer, Imperial College London, Room 11L04, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, UK
[15]Centre for Occupational and Environmental Health, Institute of Population Health, Faculty of Medical and Human Sciences, University of Manchester, Ellen Wilkinson Building, Oxford Road, Manchester M13 9PL, UK

ARM, 0000-0001-7857-9014; EKA, 0000-0003-0626-8246; HCJG, 0000-0001-8859-7232

Exposure to ionizing radiation is ubiquitous, and it is well established that moderate and high doses cause ill-health and can be lethal. The health effects of low doses or low dose-rates of ionizing radiation are not so clear. This paper describes a project which sets out to summarize, as a restatement, the natural science evidence base concerning the human health effects of exposure to low-level ionizing radiation. A novel feature, compared to other reviews, is that a series of statements are listed and categorized according to the nature and strength of the evidence that underpins them. The purpose of this restatement is to provide a concise entrée into this vibrant field, pointing the interested reader deeper into the literature when more detail is needed. It is not our purpose to reach conclusions on whether the legal limits on radiation exposures are too high, too low or just right. Our aim is to provide an introduction so that non-specialist individuals in this area (be they policy-makers, disputers of policy, health professionals or students) have a straightforward place to start. The summary restatement of the evidence and an extensively annotated bibliography are provided as appendices in the electronic supplementary material.

1. Introduction

Ionizing radiation is radiation that carries enough energy that it can ionize atoms or molecules (i.e. strip electrons from them) as it passes through matter. Life on the
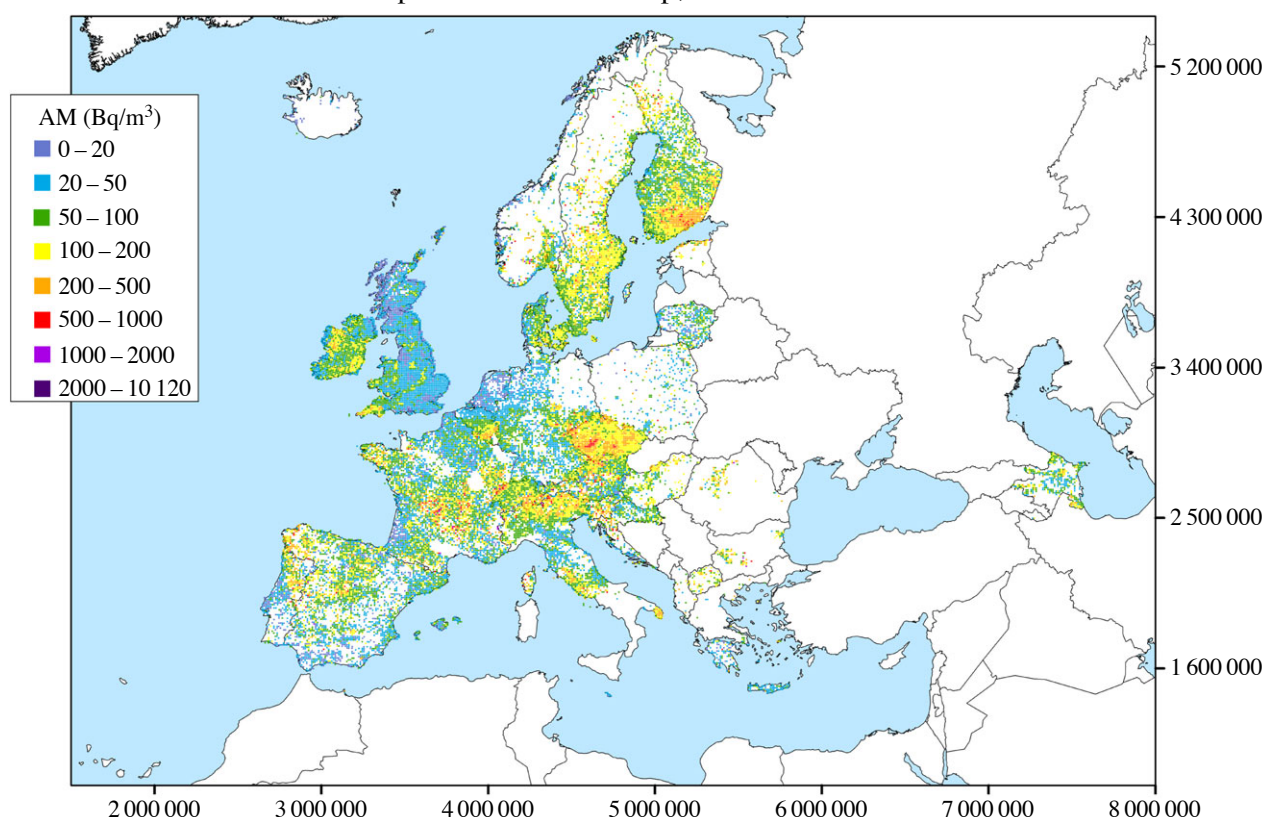
European indoor radon map, November 2015

Figure 1. European indoor radon map, November 2015. The map shows arithmetic means (AM) over 10×10 km cells of long-term radon concentration in ground floor rooms. The cell mean is neither an estimate of the population exposure, nor of the risk. The data are from the European Commission Joint Research Centre (JRC), Institute for Transuranium Elements (ITU), REM project. Reproduced with permission from Hoffman *et al.* [1]. (Online version in colour.)

Earth has always been exposed to ionizing radiation from natural sources, for example radon gas (figure 1). During the past 120 years the development of medical, military and industrial uses of radiation has created additional exposure from man-made sources. Large doses of radiation are known to be detrimental to the health of organisms including humans, but the health effects of low doses and doses delivered at low dose-rates are not completely clear. A 'low dose' of radiation has been defined by several organizations as 100 milligray (mGy) or less of sparsely ionizing radiation (e.g. electrons), and a 'low dose-rate' as less than 0.1 mGy min^{-1} of sparsely ionizing radiation when averaged over about 1 h. The sievert (Sv) is a non-physical derived unit used in the context of radiological protection, which weights the amount of energy deposited in tissue (the absorbed dose measured in gray (Gy), where $1 \text{ Gy} = 1 \text{ J kg}^{-1}$) by different types of radiation (giving equivalent dose, in Sv), and the relative sensitivity of tissues (giving effective dose, in Sv) to probabilistic (stochastic) effects such as cancer induction by low doses or low dose-rates. The weights used in calculating effective dose are based upon an expert consensus grounded in scientific evidence, but with elements of subjectivity [2,3]. Effective dose is a measure of detriment devised for the purposes of protection, so that doses from different sorts of radiation and dose distributions can be combined appropriately. In the UK, the average annual effective dose from natural background radiation is 2.3 mSv [4], so an accumulated dose of 100 mSv would commonly arise over 40–50 years of exposure at a low dose-rate. Any medical exposure (or other man-made exposure) would be additional to that.

There is an international system of radiological protection which considers situations of planned, existing and emergency exposures and, specifically for planned exposures, recommends annual limits on the amount of additional effective dose that should not be exceeded. Those annual limits are 1 mSv for the public and 20 mSv for radiation workers (these limits exclude natural background radiation and radiation doses received in medical procedures) [5]. Most countries use these recommendations in their legislation, but some do not. For example in the USA, the annual limit for workers is 50 mSv [6]. These limits, and the radiological protection system in general, are based upon the 'linear, no threshold' (LNT) dose–response model, which assumes that the excess risk from low-level exposure is directly proportional to dose and that there is no dose so small that it has no effect. On this basis, it is recommended that all relevant doses should be summed to ensure that individuals do not exceed the annual limits.

Both the LNT model and the dose limits are widely debated [7,8]. Some believe that they are too strict and impose unreasonable costs on the use of radiation. Others believe that they are not strict enough and allow too much risk from radiation exposure. A widely accepted illustration of the approximate magnitude of the risk from a low dose is that if 100 individuals were each exposed to 100 mSv then, over a lifetime, approximately one of them would be expected to develop a radiation-induced cancer, whereas around 42 of them would be expected to develop cancer from other causes [9]. Although the potential risks considered here may be small for any individual, very large populations may be exposed, so the magnitude of these health effects should not be dismissed as unimportant [10].

Within a year of Röentgen's 1895 discovery of X-rays [11], dermatitis caused by high-dose X-ray radiation had been described [12] and protective measures to reduce exposure were already advised [13]. In the ensuing 120 years, a large literature has established a detailed, quantitative description of
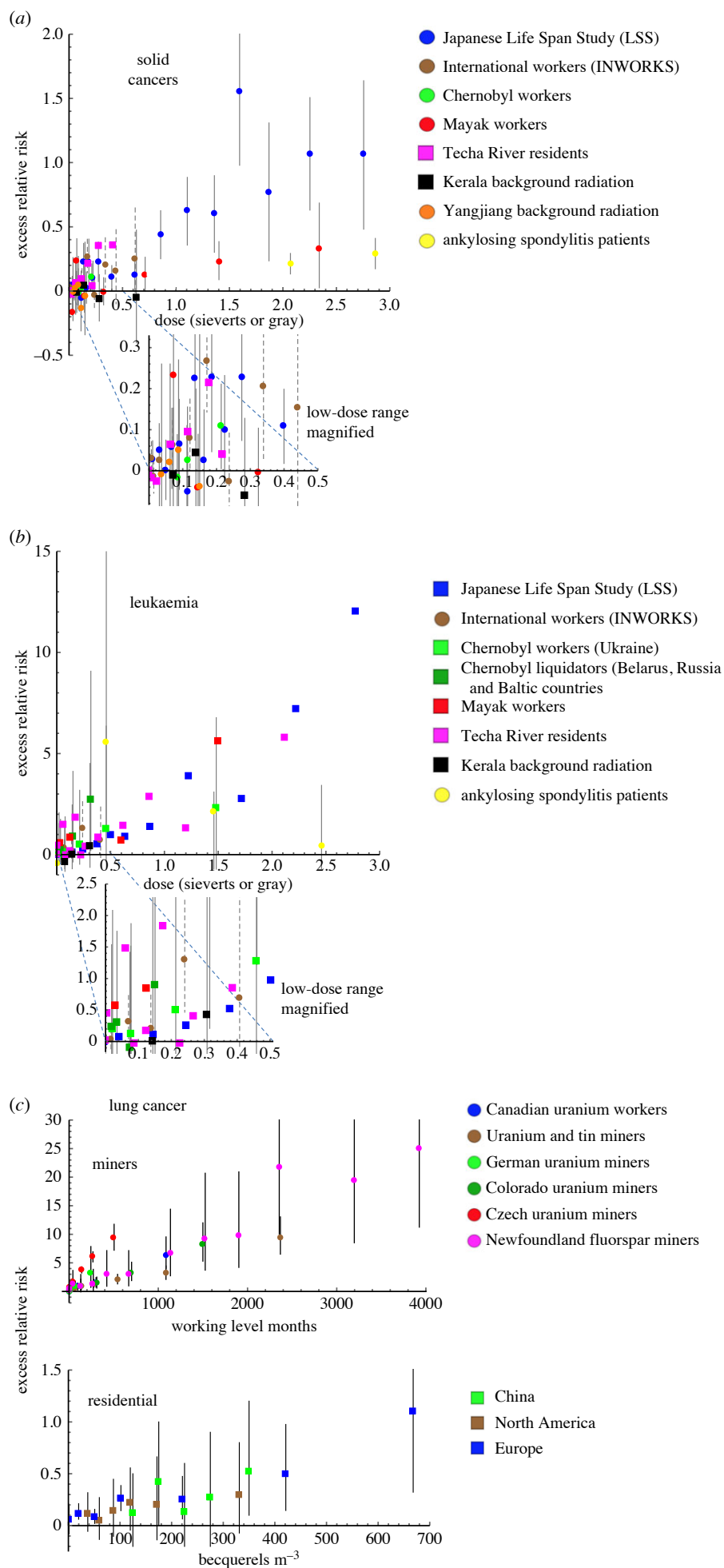
Figure 2. (*Caption overleaf.*)

Figure 2. (*Overleaf*). Estimates of excess relative risk of cancers from large epidemiological studies. The cohorts include a variety of exposure types including via nuclear weapons, occupational exposure in mines or nuclear facilities, environmental contamination from nuclear facilities, naturally high background radiation, medical therapy and radon. Outcomes are mortality (round data points) or incidence (square data points). Confidence intervals have been added where they are available. Dashed lines denote 90% CIs and solid lines denote 95% CIs. Some confidence intervals exceed the range of the *y*-axis. Table 8 in the electronic supplementary material, at paragraph 23 annotated bibliography (appendix B) contains further detail on these datasets, and see paragraph 37 for explanations of epidemiological association measures used. (*a*) Solid cancers. The Japanese Life Span Study (LSS) data are for solid cancer mortality in the cohort of survivors of the Japanese atomic bombings. The international workers data are for mortality from all cancers excluding leukaemia in a cohort of French, US and British nuclear workers (INWORKS). The Chernobyl workers data are for solid cancer mortality in a cohort of Russian Federation clean-up workers. The Mayak workers data are for mortality from solid cancers excluding bone, lung and liver cancer in workers at the Mayak weapons plant in Russia. The Techa River residents data are for solid cancer incidence in the cohort of individuals living downstream from the Mayak plant. The Kerala background radiation data are for cancer incidence excluding leukaemia in a cohort of residents of a high background radiation area in India. The Yangjiang background radiation data are for solid cancer mortality in a cohort of residents of a high background radiation area in China. The ankylosing spondylitis data are for solid cancer mortality among UK patients with ankylosing spondylitis treated with X-rays. (*b*) Leukaemia, excluding CLL. The Japanese Life Span Study (LSS) data are for leukaemia incidence in the cohort of survivors of the Japanese atomic bombings, excluding both CLL and ATL. The international workers data are for mortality from leukaemia excluding CLL in a cohort of French, USA and British nuclear workers (INWORKS). The Chernobyl workers data are for leukaemia incidence excluding CLL in a cohort of Ukrainian clean-up workers, and the Chernobyl liquidators data are for leukaemia incidence excluding CLL in a cohort of workers from Belarus, Russia and Baltic countries. The Mayak workers data are for incidence of leukaemia excluding CLL in workers at the Mayak weapons plant in Russia. The Techa River residents data are for leukaemia incidence excluding CLL in a cohort of individuals living downstream from the Mayak weapons plant in Russia. The Kerala background radiation data are for leukaemia incidence excluding CLL in a cohort of residents of a high background radiation area in India. The ankylosing spondylitis data are for leukaemia excluding CLL mortality among UK patients with ankylosing spondylitis treated with X-rays. (*c*) Lung cancer following radon exposure. Because of the difference in magnitude in exposures to radon between mining and residential contexts, studies have been split into two charts. The top chart denotes six studies of lung cancer mortality in miners of uranium, tin or fluorspar in relation to cumulative exposure (in 'working level months'). The uranium and tin miners study consists of 11 pooled international cohorts (including the Newfoundland and Czech cohort). The Newfoundland and Czech single cohort studies have been more recently updated for results and have therefore also been drawn separately. The bottom chart shows residential studies in relation to radon concentration (in Bq m^{-3}). The Chinese residential data are for lung cancer incidence across China; the North America residential data are for lung cancer incidence across North America; and the European residential data are for lung cancer incidence across Europe. (Online version in colour.)
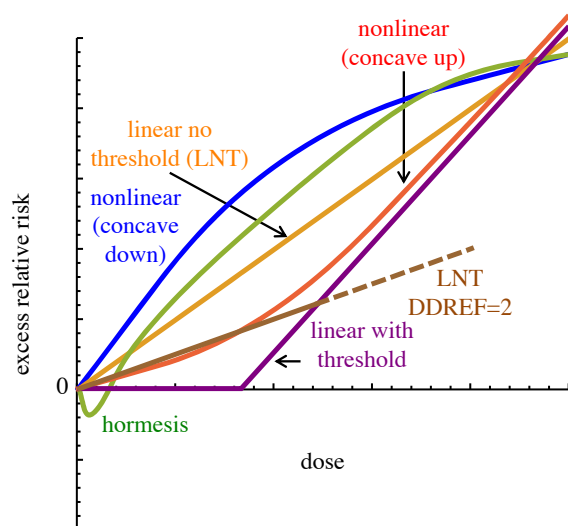

Figure 3. Potential risk models, relating risk of disease and dose of radiation at low dose and low dose-rate. The different models are described in the electronic supplementary material, appendices A and B, paragraph 24. At sufficiently low doses, all models are consistent with available datasets. Adapted from [15].

the health risks of radiation. Both sides of the debate about risks from low-level exposure cite this underlying natural science evidence base in support of their arguments. The aim of the project described here is to provide a 'restatement' of that evidence base in a succinct and accessible manner to a non-technical reader.

2. Methods

A preliminary draft review of the literature on health risks of low-level radiation was constructed. At a 1-day workshop, most authors met to discuss the different evidence components. A second draft was then made and each piece of evidence was assigned a descriptor. Because of the very extensive nature of the underlying evidence base, we devised a set of categories that are broadly speaking a ranked score of the strength and consistency of the supporting evidence. In these descriptors, a 'well-powered study' means a study that has high

probability of detecting an effect of a given size when that relationship genuinely exists. Statements are considered to be supported by:

[C_{ons}] data support a consensus based upon a single well-powered study, or one or more pooled analyses with consistent results, or several lower powered studies with consistent results;

[E_{mco}] data support an emerging consensus based upon a single, well-powered study (which may be an individual study or a pooled analysis), but in a context where other studies report disparate results or repeat analyses have not yet been performed;

[N_{oco}] there is no consensus interpretation because the data are insufficient in quantity or too variable; and

[P_{rojn}] projections based on available evidence but with substantial uncertainties.

The second draft was sent to 16 scientists who are experts in low-level radiation including representatives from academia, government and non-governmental organizations.

The project was funded by the Oxford Martin School (part of the University of Oxford) and though many groups were consulted, the project was conducted completely independently of any stakeholder.

This is not a systematic review and the categorization of the evidence statements represents the opinion of the authors arrived at through debate, but not through other formal consensus procedures. Systematic reviews of the literature on the health effects of ionizing radiation exist elsewhere and are hundreds of pages long (e.g. [5,9,14]).

3. Results

The full summary of the natural science evidence base is given as a restatement of the evidence in appendix A with an annotated bibliography as appendix B, both in the electronic supplementary material. Each section of the restatement ends with a short paragraph summarizing the evidence. Those 'summaries of summaries' are presented here.

(a) Definitions and units

The absorbed dose of radiation is quantified in gray (Gy) and is the amount of energy deposited in joules per kilogram.

Equivalent dose and effective dose use weightings of absorbed dose and are described in sievert (Sv). For the purposes of radiological protection at low-level exposure, recommendations regarding stochastic effects are issued using effective dose in sievert. Ill-effects of radiation are divided into two broad types: 'harmful tissue reactions' at higher doses and 'stochastic effects' (such as cancer) across all doses including lower doses.

(b) Background exposure and uncertainties at low dose

Across the world, the average effective dose from natural background radiation is $2.4 \, \mathrm{mSv \, yr^{-1}}$. Large epidemiological studies can be used to estimate the health risk of higher doses and, through statistical calculation of confidence intervals, infer that risks are greater than zero. But at doses in the range of the natural background, even the largest epidemiological studies have substantial difficulties in reliably distinguishing between low risk and zero risk (figure 2). Radiobiological knowledge of relevant processes following low-level exposure is incomplete and therefore point estimates for low dose or low dose-rate risks above the background are inferred by extrapolation from the results of epidemiological studies at higher doses. Several different models can be used for such extrapolation and most are largely consistent with the low-level data available (figure 3).

(c) Acute high-dose exposures

High doses are described in units of gray. With a whole-body acute dose of greater than 15 Gy, death is certain within 5 days. With a whole-body acute dose of 2.5–5 Gy, without good medical care, death owing to bone marrow damage may follow within two months in around 50% of healthy adults exposed. With a whole-body acute dose of 1 Gy, without good medical care, death owing to bone marrow damage may follow in about 10% of those exposed. Doses above about 0.5 Gy will depress blood-forming processes over the coming week and cause a range of other morbidities including erythema, epilation and sterility. Cataracts and damage to the circulatory system that may become apparent many years later are also caused at doses above about 0.5 Gy; whether or not lower doses cause cataracts and circulatory disease is a topic of ongoing study and debate. Even at high doses no statistically significant excess of hereditary effects have been seen in the offspring of people who were exposed prior to conception, although animal experiments do show such effects and imply that they may occur at a very low frequency in humans.

(d) Low dose exposures

The primary ill-health caused by low to moderate doses of ionizing radiation is cancer, although the possibility of non-cancer effects (particularly cardiovascular disease) is of increasing concern. Very large studies would be required to detect the ill-effects of doses of around 1–10 mSv. Doses of this size are routinely encountered—for example, from natural background radiation and medical diagnostic exposures. Radiation epidemiology is primarily informed by studies that compare individuals with varying levels of radiation exposure.

(e) The Japanese Life Span Study

The study of survivors of the atomic bombings of Japan (the Japanese Life Span Study; LSS) is the largest and longest study of risks from ionizing radiation. It is treated as the 'gold standard' in the sense that the results of other studies

are compared with its results. Its headline results are that at 1 Gy (dose to the colon) the risk of mortality from solid cancer is raised by 50% and at 1 Gy (dose to the red bone marrow) the risk of mortality from leukaemia is quadrupled. Note that the excess relative risk quoted here is different from the nominal excess absolute lifetime risk coefficient for cancer of 5.5% per Sv derived by the ICRP and used in optimization calculations. Excess relative risk (the proportional increase in risk) is only meaningful in the context of the underlying risk in an unexposed population. So, for example, in the LSS to 2003 there were 50 620 deaths, of which 10 929 were from solid cancers, and 318 from leukaemia. Thus, even though the excess relative risk at 1 Gy is much higher for leukaemia than for solid cancer, around 525 of the solid cancer deaths and only around 105 of the leukaemia deaths are estimated to be radiation-associated. Large studies of individuals conceived to parents who were survivors of the atomic bombings find no statistically significant adverse effects.

(f) The Chernobyl nuclear power plant accident

A number of early emergency workers at the accident at the Chernobyl nuclear power plant received high doses which produced tissue reactions and 28 early deaths. The long-term health impacts are contested. There is consensus on two major health impacts: thyroid cancers caused by high levels of exposure of children to radioactive iodine, and ill-effects to mental health caused by widespread fear of potential risks and social disruption. There is emerging evidence on the risk of leukaemia among recovery workers and those risks are broadly in line with what is expected from the LSS. At present, there is little convincing evidence of other radiation-associated effects in recovery workers or the wider public.

(g) The Fukushima Dai-ichi nuclear power plant accident

The Fukushima Dai-ichi nuclear power plant accident has caused substantial ill-health through the effects of the evacuations, continued displacement and fear of radiation. It is unclear if there will be a detectable excess in thyroid cancer in the coming years. No other discernible increase in ill-health attributable to radiation exposure is expected in either emergency workers or members of the public.

(h) Studies of workers exposed to radiation

Workers in the nuclear industries often have both external and internal radiation exposure. Their risks from external doses for solid cancer and leukaemia are consistent with those observed in the LSS even though their doses are accumulated at low dose-rates over many years. In the International Nuclear Workers Study (INWORKS), even among those who have total accumulated doses below 100 mGy, the risk of mortality from solid cancer is consistent with the LSS estimate (although the confidence intervals are wide). Radiologists and radiation technicians who worked during the early years have increased risks of leukaemia, skin cancer and, for women, breast cancer. More recent cohorts (from an era of lower doses to workers) have not yet displayed excess risks, but are still young. Cataract risk may be increased in medical workers who use X-ray imaging to guide interventions. Underground hard rock miners have an elevated risk of lung cancer roughly in proportion to their exposure to radon gas and its radioactive progeny.

(i) Environmental exposure

Radon in the home increases the risk of lung cancer, particularly for smokers. Regions of the world with high natural background radiation do not consistently show an excess risk of solid cancers even in large studies. Fallout from nuclear weapons testing caused low-level internal exposures that were concentrated in time and, to a lesser extent, space, with risks of childhood leukaemia that are consistent with the risks estimated from the LSS. There have been clusters of childhood leukaemia close to and away from nuclear installations that remain unexplained.

(j) Medical exposure

After adjustment for dose fractionation and high-dose cell killing, the risks posed by radiation received as therapy are broadly in line with LSS data. Doses from diagnostic X-rays are much lower, but some studies describe raised risks of childhood leukaemia and other childhood cancers after *in utero* exposure. Recent studies of leukaemia and brain cancer after childhood computed tomography (CT) scans report raised risks, but the extent to which the pre-existing health status of the patients might confound this association needs further consideration. The principle of justification emphasizes that health benefits of radiation use in medicine must outweigh any radiation exposure risks.

(k) Experimental studies of mechanisms of damage

Studies *in vitro* have clearly established that radiation can damage DNA in ways that if mis-repaired could, *in vivo*, lead to cancer. Because of the stochastic nature of interactions of radiation with DNA and other molecules, it is reasonable to expect initial damage at low doses to have a linear dose–response, but subsequent cellular responses may not have a linear dose–response and may be different at low versus high doses. Despite much elucidation of the underlying cellular processes, it is still not clear precisely what steps are necessary and sufficient for a dose of radiation to eventually lead to cancer (sometimes decades later). Currently, there are no validated bio-markers of radiation-induced cancers. Understanding of the mechanisms whereby radiation causes cardiovascular disease and cataracts is still less advanced.

(l) Experimental studies that inform risk assessment

Studies *in vitro* demonstrate a linear dose–response for chromosome aberrations at doses between 20 and 100 mGy. Irradiation of animals has clearly established that moderate and high doses of radiation (usually 100 mGy to several Gy) can cause cancer and life-shortening (also largely owing to cancer). Dose–response relationships at low dose are mostly linear. Irradiation of male mice before mating has demonstrated that radiation-induced mutations can be passed to offspring in a manner that is proportional to parental dose. Analysis comparing dose–response slopes at low and high doses implies that radiation delivered at a low dose or a low dose-rate carries two-to fourfold less risk than acute doses of the same total dose. An equivalent analysis that combines human epidemiological data and animal experimental data estimated that the dose and dose-rate effectiveness factor may only be about 1.5-fold and this factor is under further investigation.

(m) Perspectives

Compared with other common health risks (obesity, tobacco smoking, exposure to ambient particulate air pollution), the number of years of life lost owing to radiation exposure is small.

4. Discussion

This restatement appears in the context of a global system designed to integrate and summarize the body of knowledge on the outcome of human exposure to ionizing radiation. That system starts with a disseminated, natural science endeavour that produces a primary literature [16]; continues with several national and international bodies that synthesize the literature on the biology and epidemiology of radiation risks [9,14]; produces recommendations based upon the science [5]; which are turned into safety standards [17]; and then enacted as international and national law [18]. The published syntheses are very much longer and more detailed than this restatement. It is our aim to provide a concise introduction that can point the interested reader deeper into the literature when more detail is needed.

There are several aspects of radiation risk that we do not attempt to address. For example, we do not cover the science of estimating the dispersal of radionuclides after a release; a review is provided by Yao [19]. Nor do we cover the regulation of radioactivity in food [20]. The project considers only the natural science evidence base (although we make some reference to the psycho-social science of the impact of accidents). There are other important social science issues involved in the making of policy around radiation risks. Among these are economic considerations of the valuation of any damage caused, and the costs associated with radiation protection [21] and clean-up operations [22,23]. Finally, in focusing on human health effects of radiation, we have not considered environmental impacts and do not discuss the effects of radiation contamination on wildlife [24].

The purpose of this restatement is not to reach conclusions on whether the legal limits on radiation exposures are too high, too low or just right, nor to declare whether it is defensible to use the LNT model to approximate the risks of stochastic effects (largely cancer but including hereditary effects). Our purpose is to provide an entrée to this large and vibrant literature so that non-specialist individuals with responsibility for making or disputing policy in this area have a straightforward place to start.

7

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Appendix A
A restatement of the natural science evidence base concerning the health effects of low-level ionizing radiation

Angela R. McLean, Ella K. Adlen, Elisabeth Cardis, Alex Elliott, Dudley T. Goodhead, Mats Harms-Ringdahl, Jolyon H. Hendry, Peter Hoskin, Penny A. Jeggo, David J.C. Mackay, Colin R. Muirhead, John Shepherd, Roy E. Shore, Geraldine A. Thomas, Richard Wakeford & H. Charles J. Godfray

Paragraph numbering corresponds to that in the main document; annotated references are in Appendix B.

INTRODUCTION AND AIMS

1. Radiation is the emission and transmission of energy as electromagnetic waves or subatomic particles. "Ionizing radiation" can damage living things because it carries enough energy to strip electrons from atoms or molecules, leaving them electrically charged, a process called "ionization".

2. A major mechanism whereby ionizing radiation harms living things is to damage DNA, including the creation of breaks in DNA strands. Although much has been learnt about the radiobiology of the processes that lead to adverse health effects consequent to radiation exposure, knowledge of mechanisms is insufficiently complete to permit the determination of risks from first principles. Thus, risk estimates must be obtained from (overwhelmingly observational) epidemiological studies of exposed groups, which usually pose interpretational challenges to some degree or another.

3. All people are exposed to ionizing radiation from both natural and man-made sources. Policy questions arise concerning how much exposure is acceptable and those questions become debatable and often contentious, particularly at low doses and low dose-rates, where the effects are small or uncertain because they are obscured by variability of the available data and by the high background incidence of cancer and other potentially radiation-induced diseases.

4. The aim here is to provide a succinct summary of the evidence-base relevant to policy-making in this area as of April 2017. This restatement also provides a consensus judgement by the authors on the level of confidence in the different evidence components; it presents a shared opinion based upon the studies listed in the annotated bibliography. For statements concerning evidence we use the following descriptors, indicated by abbreviated codes. In these descriptors a "well-powered study" means a study that has high probability of detecting an effect of a given size when that relationship genuinely exists. Statements are considered to be supported by:

   [C_{ons}] data support a **consensus** based upon a single well-powered study, or one or more pooled analyses with consistent results, or several lower powered studies with consistent results.

   [E_{mco}] data support an **emerging consensus** based upon a single, well-powered study (which may be an individual study or a pooled analysis), but in a context where other studies report disparate results or repeat analyses have not yet been performed.

   [N_{oco}] there is **no consensus** interpretation because the data are insufficient in quantity or too variable.

   [P_{rojn}] **projections** based on available evidence but with substantial uncertainties.

5. This review focuses on the natural science evidence relevant to radiation risks at low doses or low dose-rates although we do include some psycho-social impacts of accidents. The statements are based on evidence in the recognised peer-reviewed scientific literature and in the published summaries provided by authoritative bodies such as those of the United Nations and others.

THE SYSTEM OF RADIOLOGICAL PROTECTION

6. It is well established that moderate and high levels of exposure to radiation are harmful to human health and to other living things. For this reason there are systems of radiological protection designed to prevent or limit radiation-induced

damage, depending on the nature of this damage (see paragraph 18 below).

7. The pre-eminent body issuing such advice is the International Commission on Radiological Protection (ICRP); which is, in its own words, *"an independent, international organization with more than two hundred volunteer members from approximately thirty countries across six continents. These members represent the leading scientists and policy makers in the field of radiological protection."*

8. The ICRP's work is to "*contribute to an appropriate level of protection for people and the environment without unduly limiting the desirable human activities that may be associated with radiation exposure*."

   a. The ICRP does not have legislative power. Instead it issues recommendations which are widely used as the basis for national and international regulations and guidance. The ICRP publishes many reports, most of which are on specific aspects of radiation. Occasionally it publishes "fundamental recommendations" which describe the overall system of radiological protection. The most recent of these recommendations, in "ICRP Publication 103", were issued in 2007. On the basis of ICRP recommendations, international and regional bodies (the International Atomic Energy Agency (IAEA) and, for example, the European Commission's Euratom Programme) publish basic safety standards which are then used as the basis for national legislation.

   b. Other organizations play an important role in synthesizing the large scientific literature on radiobiology and the epidemiology of radiation risks. Chief amongst these are the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and the reports on the Biological Effects of Ionizing Radiation (BEIR) produced by the National Research Council of the US National Academies.

9. Current Recommendations.

   a. The ICRP's recommendations are based principally on a derived quantity called **effective dose,** which is a weighted measure of the energy per unit mass deposited by different types of radiation in different tissues of the body (see paragraph 15

below). The unit of effective dose is called the "sievert" (abbreviated Sv).

   b. The average natural background effective dose experienced by an individual in the UK is 2.3 mSv/yr[1]. There is wide variation around this average.

   c. ICRP's system of protection intends to avoid injury through the effects of high doses and reduce the risks imposed by low doses or low dose-rates to an extent as low as reasonably achievable (ALARA). It does this through the application of three fundamental principles:

   i. Justification – any decision that alters radiation exposure should do more good than harm.

   ii. Optimization – numbers, likelihoods and magnitudes of exposures should all be kept as low as reasonably achievable (ALARA) taking into account economic and societal factors.

   iii. Application of dose limits – in planned exposures (other than medical exposures) the total dose to any individual (over their background exposure) should not exceed recommended limits.

   d. Justification requires consideration of all the consequences of a change in an activity involving radiation exposure. These include the risks associated with radiation and other risks, costs and benefits. Deliberations of justification are therefore much broader than radiological protection.

   e. Optimization is an ongoing qualitative and quantitative process, adapted to address each given situation, for both worker and public protection. Cost-benefit analyses are the main decision-aiding techniques in optimization procedures.

   f. For planned exposures the ICRP's effective **dose limit** for an individual member of the public is 1 mSv/yr and for an occupationally-exposed worker 20 mSv/yr. In practice, doses in planned situations will rarely approach dose limits because control is exercised by optimization of protection. Optimization of protection makes use of **dose constraints** applied to single sources. These are never greater than the pertinent dose limits of 1 mSv/yr for a member of the public and 20 mSv/yr for a worker.

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[1] A millisievert or mSv is one thousandth of a sievert and a dose of a millisievert per year is written as 1 mSv/yr

g. For emergency and existing exposures the equivalent quantities are called **reference levels**. These are restrictions on doses below which optimization should be implemented. For naturally occurring radioactive materials and radioactive residues, the reference level is 1-20 mSv/yr according to the situation. For the specific case of the radioactive gaseous element radon, and its radioactive progeny, in the home or at work the reference level is of the order <10 mSv/yr.

h. For medical exposures the ICRP does not make numerical recommendations but instead emphasises the principle of justification: that the procedure should do more good than harm to the patient; that it should have a specified objective; and that these considerations should be specifically applied to each patient as an individual. The ICRP also emphasises the principle of optimization for medical exposures with the associated concept that doses should be as low as reasonably achievable (ALARA) consistent with achieving the clinical objective. Although there are no firm recommendations there are "diagnostic reference levels" which act as benchmark figures to help define good practice.

10. If these recommendations were under-precautionary, workers, members of the public and patients might be exposed to unacceptable health risks. Examples of situations where unacceptable risks might be incurred are:

a. Working conditions for workers in the nuclear industry.

b. Working conditions for medical and technologist staff in areas such as interventional radiography and cardiology, CT scanning, radiotherapy and positron emission tomography.

c. Working conditions in other industries with high exposures e.g. underground hard-rock miners, industrial radiographers.

d. Exposure to radon in the workplace or to the public in their homes.

e. Excessive exposure of the public from contaminated environments.

f. Excessive exposure of patients to diagnostic and therapeutic radiation.

g. Insufficient evacuation of the public after nuclear accidents.

h. Insufficient clean-up by nuclear workers after accidents or legacy operations.

11. These recommendations have profound effects upon costs for many industries and implications for medical practice. If the recommendations were over-precautionary these costs would be too high, or standards may even be unachievable. Examples of areas where unduly disadvantageous effects might be incurred are:

a. Working conditions for workers in nuclear and other industries (e.g. air-crew and miners).

b. Day-to-day functioning of existing nuclear industries (e.g. storage, zoning, transportation).

c. Commissioning of future nuclear facilities.

d. Patients may not undergo diagnostic procedures because of concerns about over-exposure.

e. Some medical practitioners (e.g. interventional cardiologists) may be limited in their specialist work.

f. Provision and staffing of clinical facilities using ionizing radiation.

g. Environmental clean-up of contaminated sites or installations (e.g. the legacy of operations at the Hanford and Sellafield nuclear sites).

h. Actions after accidents (e.g. Chernobyl and Fukushima).

i. There are known to be substantial psycho-social and other health costs linked to the evacuation of populations after nuclear accidents.

j. There is potential for substantial human cost in excess anxiety about exposure to ionizing radiation.

12. *Summary*. There is an international system of radiological protection which exists to protect people and the environment from the harmful effects of ionizing radiation. Natural science evidence is collected and summarised by various national and international bodies, recommendations are made at the international level and those recommendations are enacted as law and guidance by regional and national bodies.

DEFINITIONS AND UNITS

13. All ionizing radiation deposits energy as it passes through matter. The fundamental unit of dose from ionizing radiation is called the "**absorbed dose**", which is the amount of energy absorbed per unit of mass of material. It is measured in joules per kilogram using the SI unit the gray (1 Gy = 1 J/kg).

14. Ionizing radiation takes diverse forms which vary in their nature, their source, their distance of travel through materials and their biological effect for a

given absorbed dose (see Table 7 in the annotated bibliography). For the purposes of radiological protection some of the important dichotomies and variables are:

a.   High-LET versus low-LET. Radiation that deposits energy densely along its "track" as it passes through matter is called "high-linear-energy-transfer" radiation (high-LET). Points of microscopic molecular alteration produced by a high-LET track, such as DNA strand breaks, are more likely to be spatially clustered and thus more difficult to repair than spatially separated lesions. For this reason high-LET radiation is more biologically damaging for the same absorbed dose than low-LET (i.e. sparsely ionizing) radiation.

b.   Internal versus external exposure. The ionizing radiation from some common sources (e.g. alpha particles from naturally occurring radon) cannot penetrate the skin. However, a source of such radiation that is inhaled or ingested generates internal exposure and some tissues within the body are exposed. Assessing the risks from internal emitters is particularly difficult.

c.   Partial versus whole-body exposure. Different organs and tissues within the body have different sensitivity to radiation, so the damage done by the same absorbed dose varies according to which organs or tissues were exposed to the radiation. Since absorbed dose is measured in joules per kilogram, the effect of a particular absorbed dose can only be interpreted in the context of how much and which parts of the body are exposed.

d.   Rate of exposure. A dose can be acquired briefly in a single exposure (e.g. the brief exposure of the Japanese atomic bomb survivors), multiple exposures, or slowly accumulated from environmental or work-place exposure. The differences are described by "dose fractionation" (e.g. in radiotherapy when doses are separated in time) and "dose-rate". The unit of measurement for dose-rate is Gy/min.

15.   ICRP has devised the principal protection quantity of effective dose for the control of stochastic effects of radiation (cancer and hereditary effects). Because radiation types differ in their effectiveness per Gy of absorbed dose in causing stochastic effects, these differences are taken into account using radiation weighting factors: components of absorbed dose to individual tissues or organs are multiplied by these weighting factors to calculate **equivalent dose** (in

Sv) to the tissues or organs. Equivalent doses to tissues or organs are then summed, multiplying them by tissue weighting factors that are simple representations of their fractional contribution to overall stochastic detriment, to obtain **effective dose** (in Sv). Effective dose provides a single metric for the summation of all doses, from external and internal sources that may irradiate the body uniformly or irradiate specific organs or tissues, for comparison with limits (or other control criteria) also set in effective dose. Effective dose is specifically formulated for use in the context of radiological protection for radiation exposures at low doses or low dose-rates, with defined weighting factors being recommended by the ICRP from its judgement based on scientific evidence available at the time. A unit effective dose is specified so that it is estimated to produce the same predicted risk to health as a unit absorbed dose of reference low-LET (e.g. gamma) radiation delivered uniformly to the whole body as a low dose or at a low dose-rate.

16.   At high doses and regarding tissue reactions (deterministic effects, see paragraph 18a), organ or tissue doses are usually quoted in terms of absorbed dose in gray (Gy), and if high-LET radiations are involved, an RBE-weighted dose, RBE.D (Gy), may be used, where RBE is the relative biological effectiveness of the high-LET radiation for the specific effect under consideration.

17.   Radioactivity is the transformation of an unstable atomic nucleus from one state to another during which radiation is emitted. Radioactive decay is measured in units of becquerel (Bq) where 1 Bq is the activity of one nuclear transformation per second. Dose delivered to the various organs or tissues of the body will depend on the location of the radionuclide, and the energy and tissue penetration of the emitted radiation. Thus, for example, external exposure from a radionuclide emitting gamma rays can lead to uniform whole-body irradiation (essentially delivering the same dose to all organs), while internal exposure from an inhaled radionuclide emitting alpha particles (for instance, radon) may irradiate principally one organ or tissue region within that organ (for instance, airways of the respiratory tract from deposited radon progeny). Some radionuclides form part of radioactive decay chains; that is, the elements formed by successive transformations are also radioactive and in turn decay emitting radiation.

For example, radon-222 decays through a series of solid elements, including polonium isotopes (radon progeny) that are alpha particle emitters and are responsible for 'radon-induced' lung cancer.

18. The nature of the damage done to organs and tissues by ionizing radiation is different at different doses. There are two broad categorizations.

   a. "Harmful tissue reactions" (previously called "deterministic effects"; the name changed because of the development of response modifying compounds which can reduce or delay the pre-determined effect or reaction after a given dose) occur mostly after high doses. Such damage will be experienced by all exposed individuals above a certain absorbed dose to the organ, tissue, or population of cells, and the severity of these effects then increases with increasing dose. The underlying mechanism is mainly cell killing; examples include gonadal sterility and suppression of haematopoiesis, as well as other functional tissue injury at later times. Massive cell killing, particularly of the most sensitive and critical stem cell populations, can be sufficient to cause death as a result of, for example, damage to the haematopoietic system or loss of integrity of the intestinal epithelium. There are threshold doses below which these kinds of tissue reaction do not occur. **[C_ons]**

   b. At all doses, ranging from high doses down to low doses, the term "stochastic effects" is used to describe damage that leads probabilistically to effects (largely cancer, but also hereditary effects) that will not occur in all exposed individuals. The underlying mechanism is non-lethal modification of structures within the cell (largely DNA damage), and the effects are cancer in the exposed individual and hereditary changes to the descendants of exposed individuals (these latter are seen in animal experiments, but not conclusively observed in humans). Here, the probability of experiencing ill-effects, but not the severity of the effect, is determined by the dose received by organs and tissues. **[C_ons]**

   c. Whether or not there is a threshold dose below which the probability of stochastic effects becomes zero is a matter of debate. **[N_oco]**

   d. The assumption that risk is proportional to dose (the LNT model) is central to the operation of the radiation protection system. It is a pragmatic approach to a practical problem and most

scientists working in the field (but not all) view it as prudent.

   e. Some radiogenic diseases (particularly cataracts and cardiovascular disease) do not fall neatly into the harmful tissue reactions versus stochastic effects dichotomy, and there is substantial debate as to whether such health effects are produced by low-level exposure. **[N_oco]**

19. Not all people are equally sensitive to damage from ionizing radiation. The factors that govern individual sensitivity to radiation are not fully understood.

   a. Children generally have higher sensitivity than adults. **[C_ons]**

   b. There are certain known rare genetic disorders that are known to increase the probability of adverse effects of radiation exposure. **[C_ons]**

   c. It is assumed that some variation in radiosensitivity exists in the general population, but the extent of this variation is not properly understood. **[N_oco]**

   d. Some behaviours increase the risk of damage from radiation (e.g. smoking greatly increases the absolute risk of lung cancer from radon exposure, see paragraph 88b below), but there is an incomplete understanding of the nature of the interactions between radiation and other risk factors. **[C_ons]**

20. *Summary*. The absorbed dose of radiation is quantified in gray (Gy) and is the amount of energy deposited in joules per kilogram. Equivalent dose and effective dose use weightings of absorbed dose and are described in sievert (Sv). For the purposes of radiological protection at low-level exposure, recommendations regarding stochastic effects are issued using effective dose in sievert. Ill-effects of radiation are divided into two broad types: "harmful tissue reactions" at higher doses and "stochastic effects" (such as cancer) across all doses including lower doses.

BACKGROUND EXPOSURE AND UNCERTAINTIES AT LOW DOSE

21. In the UK the average annual effective dose from natural background radiation is 2.3 mSv and about half of this is from radon (a naturally occurring radioactive gas) and its radioactive progeny. The global annual average from natural sources is 2.4 mSv. Medical procedures are a source of substantial and growing additional exposure – an additional 0.44 mSv/yr in the UK, and an additional

3 mSv/yr in the US. The ICRP's recommended annual effective dose limit for the public in planned situations is for additional exposures over and above these background and medical exposures. At 1 mSv in a year, it is about half the global average annual dose received from natural background radiation. **[C$_{ons}$]**

22. Background radiation varies greatly with location, largely driven by underlying geology, but also by other factors like altitude. At finer spatial scales even individual houses can have different radon gas concentrations because of geological features and the way they are built. Indoor radon levels across Europe have been mapped at a resolution of 10 km x 10 km (Figure 1), revealing that even within Europe this source of radiation varies by two orders of magnitude. **[C$_{ons}$]**

23. Because of intense interest in the risks posed by ionizing radiation, there are many epidemiological studies of the relationship between risk of disease and dose of radiation. Many of these are described in paragraphs 41-99. Figure 2 summarises the results of some of the bigger and statistically better-powered studies of solid cancer, leukaemia and lung cancer risk. The figure shows how the risks of various cancers are clear at high doses and reduce as dose decreases. As lower and lower doses are considered, larger and larger well-designed epidemiological studies are needed to distinguish reliably between low risk and no risk. **[C$_{ons}$]**

24. Knowledge of the radiobiological mechanisms that govern the disease risks posed by low-level exposure to radiation is incomplete, so risks from low doses or low dose-rates must be inferred by extrapolation from the risks obtained from epidemiological studies of higher doses delivered briefly but informed by what is known from experimental systems. For epidemiological data generated by studies at low doses the wide confidence intervals on the estimated risks are compatible with a wide range of different dose response models. Figure 3 presents six potential risk models. **[P$_{rojn}$]**

   a. Linear no-threshold (LNT) assumes that the risk is directly proportional to dose.

   b. LNT with a dose and dose-rate effectiveness factor (DDREF) >1 assumes that risk is proportional to dose, but that at low doses or low dose-rates the risk per unit dose (and hence the slope of the response) is smaller than that measured at acute

moderate-to-high doses. The DDREF encompasses a low dose effectiveness factor (LDEF) and a dose rate effectiveness factor (DREF), both currently assumed to be 2 although it is recognised that these are separate entities. This is the model currently used by the ICRP with DDREF = 2.

   c. LNT is not necessarily the most conservative assumption. Hypothetically, if a small subset of the exposed population were particularly sensitive to radiation risk, or if there were a "bystander" effect (whereby cells not directly traversed by radiation are affected by neighbouring cells that are hit) that became saturated at higher doses, the expected shape of the dose-response curve could be non-linear with an initial higher slope and then a reduced slope.

   d. Models of the interaction or competitive-repair of DNA damage as the drivers of risk can generate a non-linear curve with an initial lower slope and then an upward curve. Other biophysical mechanisms can also account for such shapes.

   e. Models with a threshold assume that there is a dose below which there is no excess risk.

   f. The concept of hormesis is that very low doses and very low dose-rates are beneficial to health and protective with regard to subsequent exposure.

25. *Summary*. Across the world the average effective dose from natural background radiation is 2.4 mSv/yr. Large epidemiological studies can be used to estimate the health risk of higher doses and, through statistical calculation of confidence intervals, infer that risks are greater than zero. But at doses in the range of the natural background, even the largest epidemiological studies have substantial difficulties in reliably distinguishing between low risk and zero risk. Radiobiological knowledge of relevant processes following low-level exposure is incomplete and therefore point estimates for low dose or low dose-rate risks above the background are inferred by extrapolation from the results of epidemiological studies at higher doses. Several different models can be used for such extrapolation and most are largely consistent with the low-level exposure data available.

ACUTE HIGH DOSE EXPOSURES

26. At high doses (1 Gy or above) the damage done to organs and tissues is relatively easy to recognise. For this type of exposure, dose is expressed as absorbed dose in gray.

27. Mortality and morbidity is caused by stochastic effects such as cancer and tissue reactions such as severe damage to the central nervous system (CNS), the gastrointestinal system, the heart, the lungs and the haematopoietic system, over different ranges of dose and latency times. **[Cons]**

28. Table 1 lists deterministic causes of mortality and morbidity after acute high dose irradiation. For both mortality and morbidity the table records the impact of a whole-body dose of low LET radiation delivered in a single brief exposure. For morbidity the dose recorded is the minimum threshold dose above which >1% of a healthy adult population would experience the ill effect. Above these estimated threshold doses incidence and severity rise. **[Cons]** At doses above about 0.5 Gy, cataracts and circulatory disease effects are deterministic but late acting. Whether or not doses below about 0.5 Gy cause cataracts **[Noco]** and circulatory disease **[Noco]** are topics of current study and debate.

29. Tissue reactions in the embryo or fetus depend upon the stage of gestation when exposure occurs as well as the dose. Prior to implantation (days 0-9) the main effect is lethality to the embryo. Malformations are mainly induced during the period of major organogenesis. Japanese A-bomb survivors who were exposed in utero showed a clear excess of mental retardation and a generalised decrease in IQ; however, these deficits were only observed in children who had been exposed during weeks 8 – 25 of gestation. The same population exhibited an excess of microcephaly amongst those exposed during the first and second trimesters and reduced stature after exposure in any trimester. They also exhibited stochastic effects described at paragraph 50. **[Cons]**

30. Even at moderate or high doses no statistically significant excess hereditary effects have been seen in the offspring of people who were exposed prior to conception. Nevertheless estimated hereditary risk <u>is</u> included in the ICRP recommendations, because of the clear evidence from large-scale mouse studies that radiation can cause hereditary effects in mammals. **[Cons]**

31. *Summary.* High doses are described in units of gray. With a whole-body acute dose of >15 Gy, death is certain within 5 days. With a whole-body acute dose of 2.5-5 Gy, without good medical care, death due to bone marrow damage may follow within 2 months in around 50% of healthy adults exposed. With a whole-body acute dose of 1 Gy, without good medical care, death due to bone marrow damage may follow in about 10% of those exposed. Doses above about 0.5 Gy will depress blood-forming processes over the coming week and cause a range of other morbidities including erythema, epilation and sterility. Cataracts and damage to the circulatory system that may become apparent many years later are also caused at doses above about 0.5 Gy; whether or not lower doses cause cataracts and circulatory disease is a topic of ongoing study and debate. Even at high doses no statistically significant excess of hereditary effects have been seen in the offspring of people who were exposed prior to conception, although animal experiments do show such effects and imply that they may occur at a very low frequency in humans.

Table 1. Mortality and morbidity after acute high dose irradiation (harmful tissue reactions or deterministic effects).

Dose in Gy	Consequence
Mortality: after acute low LET uniform whole body exposure	
>15	Death via nervous system damage, in 0-5 days
5-15	Death via gastrointestinal tract damage, in 7-20 days or via lung and kidney damage within 60-150 days
3-5	Without medical care, death of 50% of an exposed healthy adult population via haematopoietic syndrome, within 60 days
1-2	Without medical care, death of ~ 10% of patients via haematopoietic syndrome, in 30-60 days
Morbidity: early effects in specific tissues	
6-7	Acute pneumonitis, 1-3 months onset
6	Erythema reaction, 10 days onset
6	Permanent male sterility, 3 weeks onset
4	Temporary epilation, 3 weeks onset
3	Permanent female sterility, <1 week onset
2	Early transient erythema, 2-24 hr onset
1	Vomiting, 1-24 hr onset
1	Haematopoietic syndrome onset, 1 hour to 2 days onset
0.5	Depressed haematopoiesis, 3-7 days onset
0.1	Temporary male sterility, 3-9 weeks onset
Morbidity: later effects	
1-2	Cognitive defects, onset after several years
0.5	Cataracts or circulatory disease many years after acute or fractionated exposure
0.1-0.2	Cognitive defects in infants, onset after several years

LOW DOSE EXPOSURES

32. The primary health effect of low or moderate doses of ionizing radiation is an increased risk of cancer in the exposed individual. [**C~ons~**]

33. There is a view that the burden of non-cancer mortality (in particular cardiovascular disease) may be of a similar magnitude, although this remains under debate. [**N~oco~**] Whether cataracts can be induced by low-level exposure is a subject of current investigations. [**N~oco~**]

34. Cancers are common in human populations and (in almost all cases) it is not currently possible to distinguish whether an individual case of cancer is due to radiation or some other cause. For this reason it is necessary to study a large number of people in order to detect additional radiogenic cancer cases with confidence. This is particularly true if the dose is small. Theoretically, under a linear no-threshold model, a population of 1 billion would probably be required to detect a statistically significant overall cancer risk from an exposure of 1 mSv above background levels. Such a study would not be feasible even if uncertainties in dosimetry and confounding factors were not present. For some especially sensitive outcomes, such as leukaemia following exposure in early childhood, the number of individuals required will be smaller, but will still number in the tens of thousands. [**C~ons~**]

35. Most cancers tend to occur later in life and radiogenic cancers tend to occur long after exposure, although leukaemia and thyroid cancers can sometimes appear within a few years of exposure. Well-powered studies therefore have to be carried out over protracted periods as well as including many people. [**C~ons~**]

36. Many studies in radiation epidemiology have low power to detect radiogenic disease at low doses or low dose-rates. Such studies would be expected to generate very variable results in which only unusually large effects achieve statistical significance and many of those will be false positives due to chance or sampling variation. This is exactly the pattern observed at low doses. [**C~ons~**]

37. Epidemiological associations can be expressed in a number of ways. Common measures used in radiation epidemiology are:

    a. Excess relative risk (ERR) – the proportional increase in the rate of disease in the exposed population. This is calculated as the ratio of the excess rate of disease in the exposed population to the rate of disease in an equivalent but unexposed population.

    b. Excess absolute risk (EAR) – the difference between the rate of disease in the exposed population and the rate of disease in an equivalent but unexposed population.

    c. Odds ratio (OR) – the odds of disease occurrence in an individual in the exposed group divided by the odds of disease occurrence in an individual in an equivalent but unexposed group.

    d. Other measures are also used, including relative risk (RR=ERR+1), hazard ratio (HR), and standardised incidence/mortality ratio (SIR/SMR).

    e. Each of these metrics has advantages and disadvantages that depend on the circumstances. In this restatement, where the data are available, we generally express risks as the ERR with a 95% confidence interval (CI). We chose ERR because it is often the most appropriate measure when comparing results from diverse studies and is commonly available. ERR must always be interpreted in the light of the magnitude of the underlying risk. ERR per gray is a useful measure for our purpose of comparing different studies. Our use of it recognises the uncertainties associated with the application of an LNT dose-response relationship.

38. Table 2. Effective doses received from common sources of exposure. [**C~ons~**]

Source of exposure	Dose in mSv
Dental x-ray	0.005
Consuming 100g of Brazil nuts	0.010
Chest x-ray	0.014
Transatlantic flight	0.08
UK annual average radon dose	1.3
CT scan of the head	1.4
UK average annual radiation dose (excluding medical diagnostics)	2.3
UK average annual radiation dose (including medical diagnostics)	2.7
USA average annual radiation dose (excluding medical diagnostics)	3.2
USA average annual radiation dose (including medical diagnostics)	6.2
CT scan of the chest	6.6
Average annual radon dose to people residing in Cornwall	7.8
CT scan of the whole spine	10.0

39. Epidemiological studies have followed individuals exposed in the Japanese atomic bombings, the Chernobyl nuclear accident, the Fukushima Dai-ichi nuclear accident, at work, through their environment and through medical procedures.

40. *Summary*. The primary ill-health caused by low to moderate doses of ionizing radiation is cancer, although the possibility of non-cancer effects (particularly cardiovascular disease) is of increasing concern. Very large studies would be required to detect the ill-effects of doses of around 1 – 10 mSv. Doses of this size are routinely encountered – for example, from natural background radiation and medical diagnostic exposures. Radiation epidemiology is primarily informed by studies that compare individuals with varying levels of radiation exposure.

THE JAPANESE LIFE SPAN STUDY (LSS)

41. In August 1945, two atomic bombs were detonated above the Japanese cities of Hiroshima and Nagasaki. In 1950 a study was set up to follow the long-term after-effects of radiation on survivors, and this cohort study, known as the Life Span Study, or LSS, now forms the key reference population for the radiological protection community. This cohort study is of high quality for evaluating radiation risks because of its large size; broad range of ages at exposure; completeness, duration and fidelity of follow up; and high quality dose estimation over a wide range of doses. [Cons]

42. The study commenced in 1950, 5 years after the bombings and some (but far from all) commentators consider that this delay might have led to bias because relatively unhealthy exposed people might have died before then, due to the generally difficult living conditions after the war, causing a "healthy survivor" effect. [Noco]

43. The original cohort consisted of around 120,000 people: 55,000 who were within 2.5 km of the blasts; 38,500 city-, age- and sex-matched controls who were present in the cities but further from the blasts; and 26,500 who were not in the city at the times of the bombings. The mean dose in the group within 2.5 km of the explosions was estimated to be around 200 mGy. Mortality and cancer incidence are assessed in the survivors at regular intervals. [Cons]

44. Because dose could not be accurately estimated for 7,000 people and those not in the city were excluded from most analyses of the study, there were approximately 86,500 individuals in the LSS with a reliable dose estimate. As of 1 January 2004 (the end of follow-up for the most recently published major review of mortality data) 50,620 of those had died. Approximately 1,000 of those deaths are attributed as excess deaths due to radiation exposure during the bombings. [Cons]

45. The Adult Health Study (AHS) is a study of a sub-cohort of the LSS in which clinical examinations of about 10,000 survivors are conducted and blood samples collected every two years. The AHS investigates the risk of non-cancer diseases and physiological changes.

46. An excess of cases of leukaemia among highly exposed survivors started to become apparent from clinical observations in the late 1940s. Excesses of other cancers were reported from the LSS in later years, and now radiation-related excesses are apparent for most types of cancer, although not for all types – for example, there are no significant excesses of pancreatic or rectal cancers. [Cons]

47. Table 3. Current estimates for mortality ERR from the LSS. [Cons]

Disease	ERR/Gy	95% CI
All solid cancers (based on dose to colon)	0.47	0.38 to 0.56
Leukaemia (ERR at 1 Gy, not per Gy) (based on dose to bone marrow)	3.10	1.80 to 4.30

48. Cataract incidence has also been linked to radiation dose, and – because of recent studies at longer follow-up times showing a lower dose threshold – this is coming to be viewed as possibly a stochastic effect rather than a harmful tissue reaction which one might expect to see only at higher dose. [Noco]

49. A follow-up of survivors exposed *in utero* has detected an excess risk of the incidence of solid cancers, but no evidence of increased childhood leukaemia [Cons] This could be due to cell-killing by moderate and high doses to the haematopoietic system.

50. Studies of children exposed *in utero* found clear evidence for severe mental retardation amongst those exposed at weeks 8-25 post-conception, with the effect being greatest for those exposed at weeks 8-15 post-conception. There was also a generalised downward shift in IQ for those exposed in weeks 8-

25, but there was no evidence of a radiation effect on intelligence for those exposed before week 8 or after week 26 of gestation. **[C$_{ons}$]**

51. Studies of over 75,000 individuals have found no statistically significant radiation-associated adverse hereditary effects in the offspring of Japanese atomic bomb survivors who were conceived after their parents were exposed. For example, a study with a median of 54 years of follow up reported a hazard ratio (the hazard in the exposed group divided by the hazard in the unexposed group, which has a baseline value of 1) at 1 Gy of 0.89 (95% CI: 0.69 to 1.15) for maternal gonadal radiation exposure and risk of cancer mortality, and a hazard ratio of 0.82 (95% CI: 0.61 to 1.08) for paternal gonadal radiation exposure and risk of cancer mortality. **[C$_{ons}$]**

52. *Summary.* The study of survivors of the atomic bombings of Japan (the LSS) is the largest and longest study of risks from ionizing radiation. It is treated as the "gold standard" in the sense that the results of other studies are compared with its results. Its headline results are that at 1 Gy (dose to the colon) the risk of mortality from solid cancer is raised by 50% and at 1 Gy (dose to the red bone marrow) the risk of mortality from leukaemia is quadrupled. Note that the excess relative risk quoted here is different from the nominal excess absolute lifetime risk coefficient for cancer of 5.5% per Sv derived by the ICRP and used in optimization calculations. Excess relative risk (the proportional increase in risk) is only meaningful in the context of the underlying risk in an unexposed population. So, for example, in the LSS to 2003 there were 50,620 deaths, of which 10,929 were from solid cancers, and 318 from leukaemia. Thus, even though the ERR at 1 Gy is much higher for leukaemia than for solid cancer, around 525 of the solid cancer deaths and only around 105 of the leukaemia deaths are estimated to be radiation-associated. Large studies of individuals conceived to parents who were survivors of the atomic bombings find no statistically significant adverse effects.

THE CHERNOBYL NUCLEAR POWER PLANT ACCIDENT

53. In April 1986 an explosion, a fire and severe damage to fuel in a nuclear reactor at the Chernobyl power plant in Ukraine released large quantities of radioactive material into the atmosphere. **[C$_{ons}$]**

54. Exposure ranged from high whole-body doses leading to acute radiation sickness (134 people including 28 fatalities) in early emergency workers, high thyroid and moderate whole-body exposures in the local population (hundreds of thousands of people received whole-body doses of around ten to several hundred mGy), whilst hundreds of millions of people across Europe were exposed to additional doses of less than 1 mGy. **[C$_{ons}$]**

55. In the local population, tens of thousands of children received thyroid doses of greater than 1 Gy, mainly due to drinking milk heavily contaminated with radioactive isotopes of iodine. **[C$_{ons}$]**

56. By 2005 there were around 50 deaths that could be unequivocally attributed to the disaster: the 28 early fatalities above; some, but not all of 19 acute radiation sickness survivors who have since died; and 15 children who had died from thyroid cancer. **[C$_{ons}$]**

57. There is a well-documented excess incidence of thyroid cancer amongst people who were highly exposed as children with around 6,000 cases detected by 2005. One recent study reports an ERR/Gy of 1.91 (95% CI: 0.43 to 6.34) **[C$_{ons}$]**. There is no matching convincing evidence of any excess risk of thyroid cancer among those children less exposed to fallout. **[N$_{oco}$]**

58. Studies of leukaemia risk amongst workers have frequently been limited by low statistical power, dose reconstruction uncertainties and absence of case verifications. Studies of a large cohort of Ukrainian cleanup workers found an ERR/Gy for leukaemia incidence of 1.26 (95% CI: 0.03 to 3.58) – in line with what would be expected from the LSS. **[E$_{mco}$]** Some, but not all, studies of leukaemia incidence amongst Chernobyl workers have found significant results for chronic lymphocytic leukaemia (CLL) which is generally considered to have a low sensitivity to induction by radiation, suggesting study problems or a hitherto unacknowledged radiogenicity for CLL amongst these cohorts. **[N$_{oco}$]**

59. There is no consistent evidence of excess risk of leukaemia for those exposed *in utero* or as children, or for the general adult population. **[C$_{ons}$]**

60. For solid cancers the picture is less clear – partly because of the absence of suitable cohorts. A number of studies of highly exposed workers found no relationship between radiation dose and incidence of solid cancers. However, a recent study of 67,500 Russian recovery workers found a significantly elevated risk of solid cancer incidence with an ERR/Gy of 0.47 (95% CI: 0.03 to 0.96). Some

studies have reported an increased risk of thyroid cancer in workers. However, surveillance bias is possible in these studies of recovery workers. Studies of residents of highly contaminated areas have found no excess of solid cancers. **[Emco]**

61. A relatively small study of breast cancers in the most contaminated areas of Belarus and Ukraine found a significant increase in risk for the years 1997-2001, but this result was not replicated in a follow-on study. **[Noco]**

62. There is a plethora of small studies with low power, some of which describe excess risk of solid cancers attributable to the Chernobyl accident, but these studies are very difficult to interpret reliably. **[Noco]**

63. Thus far no other type of cancer has been shown unequivocally to be increased in people exposed to radiation in the environment from the accident. **[Noco]**

64. There is emerging evidence for an increase in benign thyroid adenomas as well as some other thyroid non-cancer disorders in adolescents and children exposed to Chernobyl fallout. **[Emco]**

65. There is evidence of excess risk of cataracts in recovery workers **[Emco]**, and some evidence for an elevated risk of the incidence of circulatory disease. **[Noco]**

66. Although there is, in general, little evidence for an excess risk of congenital malformations associated with Chernobyl exposure, a high rate of neural tube defects has been reported from northern Ukraine although the interpretation is unclear. **[Noco]**

67. Some risk projections for the expected numbers of additional cancers across Europe arising from the Chernobyl accident have been published. These additional cancers account for around 0.01% of total expected cancers, and would not be detectable in studies using national cancer statistics. **[Cons]**

68. The most significant public health consequences of the Chernobyl accident are likely to be social and mental health effects with large and sustained consequences, particularly with regards to depression. **[Cons]**

69. Studies of health effects resulting from the Chernobyl accident are complicated by the substantial background effects arising from the socioeconomic turmoil that followed the collapse of the USSR. There are considerable difficulties in distinguishing between the causes of health effects in the former USSR.

70. *Summary*. A number of early emergency workers at the accident at the Chernobyl nuclear power plant received high doses which produced tissue reactions and 28 early deaths. The long-term health impacts are contested. There is consensus on two major health impacts: thyroid cancers caused by high levels of exposure of children to radioactive iodine, and ill-effects to mental health caused by widespread fear of potential risks and social disruption. There is emerging evidence on the risk of leukaemia amongst recovery workers and those risks are broadly in line with what is expected from the LSS. At present, there is little convincing evidence of other radiation-associated effects in recovery workers or the wider public.

THE FUKUSHIMA DAI-ICHI NUCLEAR POWER PLANT ACCIDENT

71. In March 2011 a magnitude 9 earthquake off the east coast of Japan caused tsunamis that led to over 15,000 deaths and over 2,500 missing people. At the time of the earthquake, 3 of the 6 reactors at the Fukushima Dai-ichi nuclear power station were operating, and these shut down as planned. However, the tsunamis damaged equipment and flooded the emergency generators leaving the site without electrical power and the means to cool the recently operational reactors, the fuel of which was then seriously damaged, leading to a severe nuclear accident. A 20 km radius area around the station was evacuated. **[Cons]**

72. Several thousand emergency and recovery workers were exposed to radiation with most exposed to less than 10 mSv. Of those workers involved in the emergency in the first few days of the accident, 6 received effective doses in excess of 250 mSv, mainly due to high thyroid doses (>1 Gy) from inhaled radioiodine. **[Cons]**

73. There were no cases of acute radiation sickness after the accident. Although 5 workers died at the site, their deaths were caused by heart disease and accidents, not by radiation. One worker, who received 16 mSv while involved in recovery work during 2012-13, has developed leukaemia and is eligible for compensation as a consequence, but a causal link between this low dose and the disease is unlikely. **[Cons]**

74. Additional lifetime effective doses to members of the public (whether in the evacuated districts or in nearby districts that were not evacuated) are

estimated to be around 10 mSv for adults and about 2-fold higher for children and infants. These are expected to be overestimates because of assumptions that were made with inadequate data. **[C_{ons}]**

75. In the most affected district, doses to the thyroid for infants of up to 80 mGy were initially estimated. Actual measurements of thyroid doses in some evacuees gave a median value of 4.2 mGy in children; 98.8% of the measured children had doses of <15 mGy. **[C_{ons}]**

76. Owing to the low doses and small number of people exposed, no general radiation-related increase in ill-health is expected to be discernible. However, it is less clear whether an increased incidence of thyroid cancer among those exposed as children may become apparent, but because the doses were substantially lower than those after the Chernobyl accident, it is expected that there will no discernible increase in thyroid cancer. **[C_{ons}]**

77. A programme to screen the thyroids of all residents of Fukushima prefecture below 19 years old using ultrasound was initiated a few months after the accident. That study detected 113 confirmed or suspected thyroid cancers in its first few years – many-fold more than would be expected from Japanese cancer registry data. However, this excess is attributable to the large and sensitive screening effort and not to an effect of radiation exposure. **[C_{ons}]**

78. The major health impacts have been non-radiation health effects. For example excess deaths amongst evacuated hospitalized patients and senior citizens' homes, and widespread, ongoing psycho-social ill-health. **[C_{ons}]**

79. *Summary.* The Fukushima Dai-ichi nuclear power plant accident has caused substantial ill-health through the effects of the evacuations, continued displacement and fear of radiation. It is unclear if there will be a detectable excess in thyroid cancer in the coming years. No other discernible increase in ill-health attributable to radiation exposure is expected in either emergency and recovery workers or members of the public.

STUDIES OF WORKERS EXPOSED TO RADIATION

80. Studies of those exposed in the workplace give direct evidence of the impact of protracted exposures to low-level external radiation. Some workers, such as underground hard-rock miners

exposed to radon and its radioactive progeny, also receive doses from internal emitters.

81. Those who work in the nuclear industries have been the subject of a number of studies.

   a. Because nuclear workers' exposure to radiation is monitored, measuring doses for external exposure is comparatively straightforward. Table 4 summarises results from 5 discrete and relatively large studies of nuclear workers for solid cancer and leukaemia. Equivalent results for the LSS are given for comparison. In the International Nuclear Workers' Study (INWORKS), when analysis is restricted to those whose total accumulated dose is 100 mGy or less, the ERR/Gy for solid cancer mortality is marginally significant at the 90% level. Despite disparity between dose-rates, results from the worker studies and the LSS are in broad agreement. **[C_{ons}]**

   b. There are fewer published analyses of the risk from internal doses (apart from the large literature on radon). Studies of the workers of the Mayak weapons plant (in the Russian Federation) describe increased risks from inhalation of high levels of plutonium. For example, for lung cancer in males the estimated ERR/Gy is 7.4 (95% CI: 5 to 11) based on 446 deaths. The Mayak workers' risks from external radiation are included in Table 4 for comparison. **[C_{ons}]**

   c. Studies of non-cancer disease risk such as circulatory disease in nuclear workers have produced mixed results. Because such disease is common compared with cancer, even a small ERR would lead to a large number of extra deaths. It is not yet possible to draw a confident conclusion on low-level radiation exposure and circulatory disease risk. **[N_{oco}]**

82. Table 4 lists ERR/Gy for solid cancers and leukaemia following external radiation exposure, estimated from some of the larger studies of workers in nuclear industries.

Table 4. ERR/Gy for solid cancers and leukaemia following external radiation exposure, estimated from some of the larger studies of workers in nuclear industries.

Study	N Total	Mean dose (mGy)	Mean dose per year (mGy/yr)	ERR/Gy (confidence interval)	# deaths
Solid cancer mortality					
LSS male survivors exposed ages 20-60 years				0.32 (95%, 0.01 to 0.50)	3,246
INWORKS international nuclear workers*	308,297	20.9**	1.7	0.47 (**90%**, 0.18 to 0.79)	19,064
*INWORKS (<100 mGy)**				*0.81 (**90%**, 0.01 to 1.64)*	*17,814*
Japan nuclear workers *	200,583	12.2		0.20 (95%, -1.42 to 2.09)[#]	2,636
Chernobyl clean-up workers	67,568	132.0	132	0.58 (95%, 0.00 to 1.25)	2,442
US nuclear power plant workers	53,698	25.7		0.51 (95%, -2.01 to 4.64)	368
Mayak nuclear workers	25,757	354.0		0.12 (95%, 0.03 to 0.21)[##]	1,825
Leukaemia excluding CLL mortality					
LSS male survivors exposed ages 20-60 years				1.40 (90%, 0.10 to 3.40) [++]	83
INWORKS international nuclear workers	308,297	15.9[+]	1.1	2.96 (**90%**, 1.17 to 5.21)	531
Japan nuclear workers	200,583	12.2		-1.93 (95%, -6.12 to 8.57)	80
US nuclear power plant workers	53,698	25.7		5.67 (95%, -2.56 to 30.4)	26
Mayak nuclear workers	22,373	390.0		3.57 (90%, 1.55 to 8.22)	56

*result is for all cancers excluding leukaemia, rather than for solid cancers

** mean colon dose

[#]excluding alcohol-related cancers

[##] adjusted for plutonium exposure and excluding lung, liver and bone cancers

[+] mean red bone marrow dose

[++] based on the linear term of the linear-quadratic model

83. Excess skin cancer and leukaemia amongst radiologists was the first evidence of elevated cancer risks following radiation exposure. **[C$_{ons}$]**

    a. Analysis of cancer risks amongst medical workers has to allow for great reductions in their exposure over the years. The earliest cohorts worked in a time (the 1920s) when the radiological protection standard for occupational exposure was to restrict exposure to less than the equivalent of 700 mSv/yr. A review of 8 large studies (totalling 278,000 workers) of radiologists and radiological technicians found excess risks of leukaemia, cancers of the skin and, in women, breast cancer amongst early cohorts and no excess cancer risk in more recent workers. That study cautions that recent workers are still young and will need to be followed as they age and enter those age groups in which background cancer risks are higher. **[C$_{ons}$]**

    b. There is evidence of excess risk of circulatory disease mortality in early cohorts of US radiological technicians, when compared with cohorts who started work after 1960. Studies of circulatory disease risk in other cohorts have given mixed results. **[N$_{oco}$]**

    c. For cataract risk there is mounting evidence of risks of lens opacities for medical specialists who conduct interventional procedures whilst using X-ray imaging without protective eyewear. **[E$_{mco}$]**

84. During the first half of the 20th Century workers (mostly female) employed to apply radium-based luminous paint to instrument dials inadvertently ingested large quantities of the radium radioisotopes ^{226}Ra and ^{228}Ra. Radiation dose estimates can only be crude but for the US workers are in the region of 10 Gy to the skeleton, where radium deposits. Clear excesses of bone cancers were observed in US and (less so) in UK cohorts, and the US workers had an excess of head cancers thought to be due to radon from the decay of ^{226}Ra **[C$_{ons}$]**. The cohorts also experienced excess breast cancer (possibly due to external radiation from the paint pots) **[N$_{oco}$]**, but not of leukaemia. **[C$_{ons}$]**

85. Aircrew are exposed to a few mSv/yr of additional cosmic radiation. Studies of their cancer risks have revealed excess risk of malignant melanoma when compared with the general population, which is likely to be due to behavioural factors other than their additional exposure to ionizing radiation. **[E$_{mco}$]**

86. Underground hard-rock miners are exposed to radon and its radioactive progeny – a source of internal alpha-emitters when inhaled – delivering radiation doses mainly to the upper lung. Occupational exposure to radon is measured in terms of the length of time an individual is exposed to a certain air concentration of radon progeny, the so-called "working-level-month" or "WLM".

    a. It had long been known that such miners had increased risk of lung cancer and extensive cohort studies have quantified this risk. A reasonable summary estimate is an ERR per 100 WLM of 0.5. **[C$_{ons}$]**

    b. Studies of other cancers (including leukaemia) in underground miners mostly find no evidence of a relationship between exposure to radon and cancers other than lung cancer. A large study of uranium miners found a positive non-significant association (ERR of 2.18, 95% CI: -0.41 to 6.37) between leukaemia mortality excluding chronic lymphocytic leukaemia with cumulative radon exposure. **[N$_{oco}$]**

    c. The risk of cardiovascular disease does not currently appear to be related to exposure to radon. **[C$_{ons}$]**

87. *Summary.* Workers in the nuclear industries often have both external and internal radiation exposure. Their risks from external doses for solid cancer and leukaemia are consistent with those observed in the LSS even though their doses are accumulated at low dose-rates over many years. In the International Nuclear Workers Study (INWORKS), even amongst those who have total accumulated doses below 100 mGy, the risk of mortality from solid cancer is consistent with the LSS estimate (although the confidence intervals are wide). Radiologists and radiation technicians who worked during the early years have increased risks of leukaemia, skin cancer and, for women, breast cancer. More recent cohorts (from an era of lower doses to workers) have not yet displayed excess risks, but are still young. Cataract risk may be increased in medical workers who use X-ray imaging to guide interventions. Underground hard rock miners have an elevated risk of lung cancer roughly in proportion to their exposure to radon gas and its radioactive progeny.

ENVIRONMENTAL EXPOSURE

88. On average, about one half of the effective dose from natural sources is from the inhalation of radon whilst indoors.

    a. Three analyses of pooled data from different geographic regions indicate a significant association between exposure to residential radon and the risk of lung cancer. Residential radon concentration is described using Bq/m^3. Those studies are based in: Europe, ERR per 100 Bq/m^3 = 0.08 (95% CI: 0.03 to 0.16); North America ERR per 100 Bq/m^3 = 0.10 (95% CI: -0.01 to 0.26); and China ERR per 100 Bq/m^3 = 0.13 (95% CI: 0.01 to 0.36). [Cons]

    b. For people who have never smoked the data are less clear. The largest of the pooled studies finds approximately the same excess relative risk for lung cancer in never-smokers as in smokers. Since the underlying risk of lung cancer is around 25-fold higher for smokers than for lifelong non-smokers, the increase in absolute risk from radon is much greater for smokers. Other smaller studies tend to find a positive association between exposure to residential radon and the risk of lung cancer for never smokers, but this association is frequently not statistically significant. [Emco]

    c. A study of domestic radon and childhood cancer in Denmark found an association between acute lymphoblastic leukaemia (ALL) and radon exposure with an ERR per 1000 Bq/m^3 years = 1.44 (95% CI: 0.24 to 3.81). The study had 860 cases of ALL and found no associations with other types of childhood cancer. A 10-fold larger UK study (see paragraph 90 in the annotated bibliography) did not replicate this finding, with an equivalent ERR of 0.03 (95% CI: -4 to 11). [Noco]

89. Some parts of the world have high levels of natural background gamma radiation: for example Guarapari in Brazil, Ramsar in Iran, Yangjiang in China and Kerala in India. Average external doses of 5-6 mGy/yr are common in these regions, with higher levels in a few areas. Two large cohort studies have assessed the risks posed by this high background radiation. The Kerala cohort of 70,000 individuals yields an ERR/Gy = -0.13 (95% CI: -0.58 to 0.46) for incidence of cancers excluding leukaemia. The Yangjiang cohort of 81,000 individuals yields an ERR/Gy = 0.19 (95% CI: -0.65 to 3.04) for solid cancer mortality. [Cons]

90. Four recent European studies have compared risks of childhood cancer with natural variation in normal background radiation. Statistically significant positive associations were reported in the UK and Switzerland but not in studies in Finland and France. [Noco]

91. Residents close to the Techa River, downstream from the Mayak weapons plant which released large quantities of radionuclides into the river in the early years of operations, have had documented raised risks of both solid cancer incidence (ERR/Gy = 0.77 (95% CI: 0.13 to 1.5)) and leukaemia (except CLL) incidence (ERR/Gy = 2.2 (95% CI: 0.8 to 5.4)). For circulatory disease and ischaemic heart disease mortality in the same cohort, whether or not risk was significantly raised depended on the time-lag used in the analysis. [Cons]

92. From 1945 to 1980 there were more than 500 atmospheric tests of nuclear weapons. Those tests released radioactive material into the atmosphere, which, as it fell and settled on the ground, created both temporal and spatial patterns of increased exposure to ionizing radiation received both externally and internally. The global average individual effective dose arising from this fallout peaked in the early 1960s at an annual effective dose of around 0.11 mSv. A large-scale study of 11 cancer registries found no evidence of excess cases of childhood leukaemia corresponding to the timing of those atmospheric tests. A study that focussed on Nordic countries (where high rainfall would have led to doses of around 1.3 mSv to the red bone marrow over the four years of highest exposure) did find a slight increase in the incidence of childhood leukaemia in the years just after fallout was at its highest, when compared with children born a few years earlier or later. These two temporal observations are particularly important because the levels of internal emitters from atmospheric tests of weapons are similar to those discharged from nuclear installations. [Cons]

93. Residential areas around nuclear facilities.

    a. There have been notable clusters of childhood leukaemia close to nuclear installations at Sellafield in England, Dounreay in Scotland and Kruemmel in Germany. [Cons]

    b. In addition, a case-control study in Germany found an excess of leukaemia in children under 5 years of age living within 5 km from a nuclear power plant.

When matching studies were conducted in the UK and France no such association was found. **[Noco]**

c. Doses from radioactive discharges from the facilities are too low by a factor of 100 to > 1000 to explain the excess cases on the basis of standard risk models (but see paragraph 93g below). Although over a hundred studies in ten countries have failed to find such clusters close to other nuclear facilities, the three clusters and the German case-control study require explanation and various hypotheses have been put forward. **[Noco]**

d. It has long been thought that childhood leukaemia cases tend to occur in clusters – although not every study confirms such clustering. Such clusters can be observed at sites far from nuclear installations. An especially marked cluster has occurred in the rural community of Fallon, Nevada, away from any nuclear installation. **[Cons]**

e. The population mixing hypothesis proposes that childhood leukaemia is a rare complication of a common, but presently unidentified, infection which is augmented when there are marked influxes of urban populations into remote rural areas. **[Noco]**

f. Occupational exposure of fathers prior to conception was also considered as an explanation for excesses of childhood leukaemia, but was not compatible with the data and is now abandoned as a reasonable explanation. **[Cons]**

g. It has recently been re-proposed that radioactive discharges are responsible and that the discrepancy between the calculated risk and the observed numbers of cases can be explained by a combination of temporal spikes in radionuclide emissions, uncertainties in dosimetry calculations for internal emitters and very high radio-sensitivity of embryos and fetuses. However, this explanation is incompatible with the observed incidence of childhood leukaemia after exposure to internal emitters from the fallout from nuclear weapons tests, as well as the numerous studies that have failed to establish the general occurrence of clusters close to nuclear facilities. **[Noco]**

94. Workers in many other industries (particularly those handling oil, gas and phosphates) are exposed to naturally occurring radioactive materials (NORM). Enhanced exposures can occur in these industries but they have not been as closely studied as the workers described above.

95. *Summary.* Radon in the home increases the risk of lung cancer, particularly for smokers. Regions of the world with high natural background radiation do not consistently show an excess risk of solid cancers even in large studies. Fallout from nuclear weapons testing caused low-level internal exposures that were concentrated in time and, to a lesser extent, space, with risks of childhood leukaemia that are consistent with the risks estimated from the LSS. There have been clusters of childhood leukaemia close to and away from nuclear installations that remain unexplained.

MEDICAL EXPOSURE

96. Treatment with radiotherapy for a range of illnesses is effective and common and relies on the ability of radiation to kill cells. After appropriate correction for dose fractionation and cell sterilization effects, radiotherapy data are consistent with risks from the LSS. **[Cons]**

97. Some groups of patients have received doses from internal emitters. Injections of the short-lived alpha-emitter Ra-224 were administered in Germany for the treatment of a number of diseases. A large excess of bone cancers occurred in these patients. Other patients were injected with the radioactive thorium-based diagnostic contrast medium Thorotrast, resulting in a pronounced excess of liver cancer and also of leukaemia. **[Cons]**

98. Medical imaging has undoubted benefits for patients. Currently the effective dose from a single modern digital chest X-ray at 0.014 mSv is very low – equivalent to a few days' natural background exposure – but it would have been greater in the past due to the use of less advanced equipment. However, the newer technology of computed tomography (CT) scanning delivers much higher doses. A single CT scan of the spine can deliver an effective dose of 10 mSv, equivalent to 4 years' background exposure in the UK and the highest diagnostic radiation doses in current practice come from PET/CT scans, where the effective dose from a combined diagnostic whole-body PET and CT investigation is around 20 mSv, equivalent to 8 years' background equivalent. As for radiotherapy, data from diagnostic radiation have to be treated with caution as most individuals are scanned or X-rayed because they have a suspected or previous pathology.

a. As early as 1956, diagnostic X-rays *in utero* were linked to excess paediatric cancer mortality. A single large UK case-control study (the Oxford Survey of Childhood Cancers, OSCC) found a relative risk (RR) of 1.49 (95% CI: 1.33 to 1.67) for leukaemia in childhood and an RR of 1.45 (95% CI: 1.30 to 1.62) for all other childhood cancers after antenatal diagnostic exposure of the maternal abdomen (mainly in the last month of pregnancy). A pooled analysis of 32 other studies reported an RR of 1.32 (95% CI: 1.19 to 1.46) for childhood leukaemia. These results compare children irradiated *in utero* with those who were not, but do not make any further distinction about the level of dose received. The estimated average X-ray dose received by a fetus in 1958 in the UK was just 10 mGy, leading some to question an interpretation of causality underlying the observed risks. Nonetheless, the approximate ERR/Gy estimate for childhood leukaemia that can be obtained from the OSCC is compatible with that from the LSS for those exposed in early childhood **[N_oco]**

b. Studies of the risks from diagnostic X-rays for children and adults generally show mixed results. A recent summary of results from larger studies (>30 cases) of diagnostic X-rays and leukaemia found a statistically significant excess in 4 out of 13 studies. A series of studies of patients who received multiple fluoroscopic examinations of the chest whilst being treated for tuberculosis found a radiation-related risk of breast cancer which is very similar to the absolute risk of breast cancer in the LSS: an excess absolute risk (EAR) per 10,000 person years/Sv = 5.48 (95% CI: 0.90 to 10.43) for fluoroscopy patients versus EAR per 10,000 person years/Sv = 4.95 (95% CI: 3.37 to 6.71) in the LSS. This is despite the fact that the fluoroscopy patients' doses were highly fractionated into doses of ~10 mSv given at intervals of 2-3 weeks. A similar finding for breast cancer was reported for female patients who had been exposed to fractionated diagnostic radiation while being monitored for scoliosis. Other studies have reported null dose-response results for lung cancer risk after multiple fluoroscopic examinations. **[E_mco]**

c. Several studies have reported dose-related risks of cancer following childhood CT scans. These studies stimulated extensive discussion and suggestions that "reverse causation" might be at play, with early symptoms of cancer or some underlying pre-disposition to cancer causing the need for CT scans, not vice versa. As the use of CT scans globally increases, this is increasingly an important question. **[N_oco]**

99. *Summary.* After adjustment for dose fractionation and high-dose cell killing, the risks posed by radiation received as therapy are broadly in line with LSS data. Doses from diagnostic X-rays are much lower, but some studies describe raised risks of childhood leukaemia and other childhood cancers after *in utero* exposure. Recent studies of leukaemia and brain cancer after childhood CT scans report raised risks, but the extent to which the pre-existing health status of the patients might confound this association needs further consideration. The principle of justification emphasises that health benefits of radiation use in medicine must outweigh any radiation exposure risks.

EXPERIMENTAL STUDIES OF MECHANISMS OF DAMAGE

100. A large body of cellular and molecular data supports the idea that ionizing radiation increases the risk of cancer through damage to DNA. This damage is mediated both directly by ionization of the DNA and indirectly via water molecules that become ionized and create products (such as hydroxyl radicals) which may damage DNA and other cellular components. The most important types of DNA damage are double-strand breaks (DSBs), which arise from clustering of ionizations within radiation tracks and are produced linearly with dose. Complex DSBs, which include additional DNA strand breaks or altered DNA bases within very close proximity, are difficult for the cell to repair and very different from the kind of damage that routinely arises during normal metabolism. Such damage can be produced by the lowest possible dose of a single particle track passing through a cell, even by an electron from X-ray exposure but more efficiently by a high-LET particle. **[C_ons]**

101. There are several cellular mechanisms that promote DNA repair, but they are not completely efficient and, if mis-repaired, DSBs can produce mutations and chromosome aberrations composed of various types of rearrangements. Counts of chromosome exchange aberrations have an upwardly curving, linear-quadratic dose response, but at doses below 100 mGy the curve is dominated by the linear

component. There is also a clear relationship with dose-rate, in which the same dose delivered at a lower rate yields a smaller number of aberrations. **[C$_{ons}$]**

102. There are other damage-response mechanisms apart from repair of which checkpoint-arrest is the most important in the context of carcinogenesis. Checkpoint arrest pauses the cell-cycle before mitosis or replication, enhancing the chances for accurate repair. One of these mechanisms of checkpoint arrest is only activated when there are more than 20 DSBs in a cell, so does not operate efficiently at doses below about 200 mGy. Failure of checkpoint arrest at low doses may cause hypersensitivity to killing (a phenomenon called low dose hypersensitivity). Whether it confers hypersensitivity to carcinogenesis is unknown. **[E$_{mco}$]**

103. Although chromosome aberrations and rearrangements are often present in malignant cells, it remains unclear precisely what role they play in initiating carcinogenesis. Modern methods of characterising them have revealed a great diversity of types of aberration and it is becoming clear that some types are much more likely to lead to cancer than others. Neither counts of chromosome aberrations nor any other biomarker of radiation dose has yet yielded a validated predictor of cancer risk. **[C$_{ons}$]**

104. It has long been thought that cancers (including radiation-induced cancers) are caused by a multistep process in which a series of particular mutations (so-called 'oncogenic' mutations) accumulate in a cell and its progeny, driving their proliferation, creating cells with clonal advantage and eventually leading to the formation of tumours. Radiation can contribute both to the initial mutations and to the accumulation of later mutations. **[C$_{ons}$]**

105. Such a multistep process takes time, and it is increasingly accepted that only stem cells (or, in some tissues, their daughter progenitor cells) are resident for long enough in the body to accumulate the mutations, and possibly other changes, necessary to become malignant. This has led to an increasing focus on stem cells as the target cells for carcinogenesis. Understanding which cells in the body are the target cells responsible for carcinogenesis is fundamental to understanding its biological basis. **[E$_{mco}$]**

106. The cellular response to a dose of radiation can depend upon that cell's prior exposures. In adaptive responses a priming dose reduces the damage done by subsequent doses, with the frequency of chromosomal aberrations after the second (challenge) dose reduced. The priming dose is usually in the range of 1 – 100 mGy and the challenge dose is larger. The mechanism of action is via the induction of additional repair processes. **[C$_{ons}$]**

107. Radiation can have an impact upon cells which are not themselves irradiated. Such "non-targeted effects" can be seen in cells in close proximity to irradiated cells, and at distant sites and in the progeny of irradiated cells. Non-targeted effects fall into two broad categories: genomic instability, and bystander effects.

    a. Genomic instability describes the observation that the progeny of irradiated cells have an enhanced rate of generating genetic change. Genomic instability can be induced by doses as low as 10 mGy.

    b. In bystander effects irradiated cells transmit signals of their damage to non-irradiated cells. Various responses are observed in cells that receive these signals – including cell death, adaptive responses and chromosomal damage. These could be either beneficial (e.g. increasing the likelihood that damaged cells will die so reducing eventual cancer risk) or detrimental (e.g. increasing the number of damaged cells). Bystander effects appear to be a low-dose effect and are not seen in all experimental systems. The existence of bystander effects demonstrates that radiation damage occurs at the level of populations of cells organised in tissues and organs, and not just a process that concerns individual, isolated cells.

    These processes (adaptive response and non-targeted effects) could act to either increase or decrease risks at very low dose and it is not yet clear how important they are in relation to radiogenic disease *in vivo*. Whether they are beneficial or detrimental in terms of health effects, when they occur, their impact will be included in the risks observed in epidemiological studies. Their importance is therefore in consideration of the expected shape of the dose-response curve at low doses and low dose-rates. **[N$_{oco}$]**

108. Recent advances in biotechnology allow measurement of the expression of genes and proteins in cells. These techniques are called "transcriptomics" and "proteomics" when they study the expression of genes and proteins respectively. There is now substantial evidence showing that such cellular responses after low dose exposure show differences from those after higher doses, with activation of stress responses being the most significant changes. [C_{ons}]

109. If there were a mechanistic understanding of the pathways linking an initial radiation event to a consequent tumour, along with proper quantification of each step, it would be possible to derive the dose-response relationship. That understanding would need to comprise the initial damage and all the defence mechanisms – at the cell, tissue and organismal level. For cancer, the dose response for initial damage is expected to be linear and most subsequent processes to be non-linear. This might eventually provide support for one or other of the theoretical shapes of the dose response relations for cancer or non-cancer diseases in the low-dose and low dose-rate region where reliable epidemiological results are difficult to obtain. [E_{mco}]

110. There is no *a priori* reason to assume that the dose-response relationship will be the same for all types of cancers. There are likely to be different dose response relations for non-cancer diseases such as cardiovascular disease, where the aetiology of the diseases may be different from the cancer aetiology. [E_{mco}]

111. In vitro studies suggest that chronic low dose-rate exposures can induce premature senescence in endothelial cells. Premature senescence in different organs could contribute to low-level radiation risk with implications for the immune defence and neurological disease. [E_{mco}]

112. Mechanistic studies *in vitro* and in animal models at low dose and low dose-rate which aim to understand the cellular processes that are induced from functional aspects may eventually also provide new biomarkers for exposure, disease and tissue sensitivity.

113. It is widely believed that individuals differ in their inherent susceptibility to radiation induced carcinogenesis. It would be very useful to be able to identify individuals with higher than average susceptibility (e.g. risk-benefit calculations concerning therapeutic and diagnostic radiation are different for people with higher than average sensitivity to radiation.) Apart from a few rare genetic disorders (see paragraph 19b), variation in radio-sensitivity is not yet properly understood. A better understanding of the mechanisms of disease induction should, eventually, allow a deeper understanding of such variation in individual sensitivity to radiation.

114. The biological mechanisms that underlie cardiovascular disease caused by medium and high doses of radiation are microvascular changes and atherosclerosis (the thickening of artery walls because of the accumulation of white blood cells) through pro-inflammatory effects. It is likely that the mechanisms at low doses or low dose-rates will have differences from those at medium and high doses and long-term changes in immunity are postulated to be involved. [E_{mco}]

115. The mechanism whereby ionizing radiation induces cataracts is not well understood. Cataracts are defined as progressive opaqueness of the lens of the eye, leading to loss of vision. Genomic damage of lens epithelial cells is considered one of the key mechanisms and such damage has been observed in mice experimentally exposed to whole body doses as low as 20 mGy. Oxidative damage, changes in morphology and altered cell signalling also play a role. [E_{mco}]

116. *Summary* Studies *in vitro* have clearly established that radiation can damage DNA in ways that if mis-repaired could, *in vivo,* lead to cancer. Because of the stochastic nature of interactions of radiation with DNA and other molecules, it is reasonable to expect initial damage at low doses to have a linear dose-response, but subsequent cellular responses may not have a linear dose response and may be different at low versus high doses. Despite much elucidation of the underlying cellular processes it is still not clear precisely what steps are necessary and sufficient for a dose of radiation to eventually lead to cancer (sometimes decades later). Currently there are no validated bio-markers of radiation-induced cancers. Understanding of the mechanisms whereby radiation causes cardiovascular disease and cataracts is still less advanced.

EXPERIMENTAL STUDIES THAT INFORM RISK ASSESSMENT

117. *In vitro* studies of radiation-induced DNA damage and subsequent mutations and chromosome aberrations have yielded substantial information on the shape of the dose-response relationship, and on the modulating effects of dose rate. Chromosome aberration counts from a number of studies follow a linear dose-response at doses in the range of 20 – 100 mGy, but below 20 mGy the data cannot distinguish between a linear model and a model with a threshold. Values for DDREF in such studies are generally in the range 2 – 4 implying that, compared to the risks from acute high doses, risks from low doses or doses delivered at low doses rate are halved or quartered. **[C$_{ons}$]**

118. Animal experiments with cancer endpoints illustrate the diversity of dose response curves seen for different types of cancer. Some experimental systems generate data compatible with a linear-quadratic model: for example the induction of leukaemia in mice at doses of 250 mGy to 3 Gy or mammary cancer in female mice at doses of 100 mGy to 2 Gy. But other kinds of cancer show a linear dose response: for example mammary tumours in Sprague-Dawley rats at doses of 100 mGy to 2 Gy. A threshold effect is observed for skin cancer in both mice and rats with no tumours generated at doses below about 10 Gy. Most of these studies do not explore doses in the range below 100 mGy, with the smallest dose usually at 100 mGy. Values for DDREF from appropriate animal carcinogenesis studies are in the range 4-5. **[C$_{ons}$]**

119. Mice and dogs have been used in a large number of experiments that study the life-shortening effects of radiation. When doses and dose-rates are low most early deaths in these experiments are from radiation-induced cancers. There is a common pattern across many of these studies in which the reciprocal of mean age at death rises linearly with total dose. When the total dose is delivered at a lower dose-rate the slope of the linear relationship is smaller. **[C$_{ons}$]**

120. Studies of radiation-induced heritable effects in mice form the main basis for quantitative estimates of the risk of heritable disease in humans by UNSCEAR and ICRP. Such studies count the number of radiation-induced mutations in the offspring of irradiated male mice. The conclusion from studying tens of thousands of such offspring is that at ~ 1 Gy of chronic low-LET radiation the number of radiation-induced mutations in one generation is as large as the number that arise from other causes. **[C$_{ons}$]**

121. Probably the largest contribution to radiation protection from experimental data has been for decisions on radiation weighting factors. ICRP (and others) have relied heavily on both *in vitro* and animal experiments because of the paucity of appropriate human data. **[C$_{ons}$]**

122. The BEIR VII report combined radiobiological evidence from animal experiments with the LSS data in a Bayesian statistical analysis in order to estimate a DDREF (defined at paragraph 24b) from both kinds of data. The radiobiological evidence came from mouse experiments comparing acute, fractionated and chronic doses on both cancer risk and on life-shortening. The resulting estimate was DDREF = 1.5 (95% CI: 1.1 to 2.3). Despite the sophistication of the approach, the committee drew attention to how difficult it is to measure DDREF with the comment that it "recognizes the limitation of the data and the uncertainties in estimating the DDREF". The DDREF is under further investigation. **[E$_{mco}$]**

123. *Summary.* Studies *in vitro* demonstrate a linear dose-response for chromosome aberrations at doses between 20 mGy and 100 mGy. Irradiation of animals has clearly established that moderate and high doses of radiation (usually 100 mGy to several Gy) can cause cancer and life-shortening (also largely due to cancer). Dose response relationships at low dose are mostly linear. Irradiation of male mice before mating has demonstrated that radiation-induced mutations can be passed to offspring in a manner that is proportional to parental dose. Analysis comparing dose-response slopes at low and high doses implies that radiation delivered at a low dose or a low dose rate carries 2 – 4 fold less risk than acute doses of the same total dose. An equivalent analysis that combines human epidemiological data and animal experimental data estimated that the DDREF may be only about 1.5-fold, and this factor is under further investigation.

PERSPECTIVES

124. The risks from ionizing radiation have been, and continue to be, exceptionally well studied and can be compared with the risks posed by other factors.

   a. Whilst the risks at very low levels of a few millisievert can be inferred only by extrapolation, risks at higher levels can be directly measured. Comparing those risks with the impact of other

insults to health is illuminating. An individual in the very heavily exposed group of survivors of the Japanese atomic bombings (those who received > 1 Gy) can on average expect to lose fewer years of life than a lifelong smoker or someone who is severely obese (Table 5). [C_{ons}]

b. Across the world, radiation arising from residential radon poses health risks to very large populations. Nevertheless, a comprehensive analysis of the global modelled burden of disease attributable to a wide range of risk factors compared estimated deaths from residential radon and found them to be around 30-60 times lower in number than deaths that could be attributed either to ambient particulate matter pollution, or to tobacco smoking (Table 5). [C_{ons}]

125. Table 5. Comparisons of average years of life lost and numbers of attributable deaths for radiation versus other risks.

Average years of life lost		
Japanese atomic bomb survivor in the very heavily exposed group (>1 Gy)	35 year old white, severely obese male	Lifetime smoking male doctor
2.6 years	4 - 10 years	10 years
Annual number of attributable deaths, worldwide, 2010		
Residential Radon	Air pollution, ambient particulate $PM_{2.5}$	Tobacco Smoking
99,000	3,200,000	6,300,000

126. *Summary.* Compared with other common health risks (obesity, tobacco smoking, exposure to ambient particulate air pollution), the number of years of life lost due to radiation exposure is small.

Appendix B
A restatement of the natural science evidence base concerning the health effects of low-level ionizing radiation

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Angela R. McLean, Ella K. Adlen, Elisabeth Cardis, Alex Elliott, Dudley T. Goodhead, Mats Harms-Ringdahl, Jolyon H. Hendry, Peter Hoskin, Penny A. Jeggo, David J.C. Mackay, Colin R. Muirhead, John Shepherd, Roy E. Shore, Geraldine A. Thomas, Richard Wakeford & H. Charles J. Godfray

Paragraph numbering corresponds to that in the main document. Website URLs were accessed 29/11/2016.

INTRODUCTION AND AIMS

1. The UK National Physical Laboratory has an educational poster on the subject of ionizing radiation http://www.npl.co.uk/educate-explore/factsheets/ionising-radiation/. Three major publications summarise the natural science evidence base: that from the United Nations UNSCEAR (2006a), that from the US National Academies BEIR VII (2006) and the latest recommendations of the International Commission on Radiological Protection ICRP 103 (2007).

2. See UNSCEAR (2006a) (Annex A, Section I), and the epidemiology guidelines published by Bradford-Hill in 1965 and reproduced in 2015 Hill (2015) with the accompanying editorial Wakeford (2015). Doll (2002) gives a further review.

3. UNSCEAR (2008) gives global figures on natural and artificial background radiation. Abbot (2015) gives comparative figures for different countries and different years. In this paper we define, for sparsely ionizing radiation, a low dose as being <100 mGy and a low dose-rate as being <0.1 mGy/min averaged over one hour, following UNSCEAR (2012b).

4. The use of the descriptors [Cons], [Emco], [Noco] and [Projn] follows practice in previous restatements Godfray et al. (2013), Godfray et al. (2014), Godfray et al. (2015), Dadson et al. (2017).

5. Since its inception UNSCEAR has published 25 major reports available here: http://www.unscear.org/unscear/en/publications.html. The National Academies series of BEIR reports are available here: http://www.nap.edu/search/?term=BEIR . ICRP publications are here: http://www.icrp.org/publications.asp.

THE SYSTEM OF RADIOLOGICAL PROTECTION

6. Chapter 5 of ICRP 103 (2007) describes the system of radiological protection of humans. Wrixon (2008) provides a summary and contextualises the changes in recommendations.

7. ICRP website at: http://www.icrp.org/index.asp

8. See Cooper (2012) for a summary of current radiation protection principles. Chapter 8 of ICRP 103 describes protection of the environment.
   a. ICRP 103 (2007), IAEA (2014). Countries within the European Union are currently working to enact the Basic Safety Standards in BSS 2013/59/Euratom Euratom (2013), work which they are obliged to complete by February 2018. The most recent and only change to the 2007 ICRP recommendations is the Statement on Tissue Reactions, specifically the reduced dose limits to the eye lens Stewart et al. (2012).
   b. UNSCEAR (2008), BEIR VII (2006). Figure 3.1 in Clarke and Valentin (2009) represents the basis for and use of ICRP recommendations in a flow chart. Some of the proponents of alternative theories about the dangers (or otherwise) of radiation do not view reports by these international bodies as authoritative and instead view them as representing an establishment position that attempts to argue 'from authority'. However, these reports are widely recognised as representing the views of the majority working in the field.

9.
   a. UNSCEAR (2008). Table 8, pages 116-117 of ICRP 103 (2007) summarises the current recommendations for radiological protection in planned, emergency and existing situations.
   b. See Oatway et al. (2016) for UK radiation exposures.
   c. ICRP 103 (2007) Paragraph 2.2, page 42 and Paragraph 5.6, page 88.
   d. ICRP 103 (2007) Paragraph 5.7, page 89.
   e. ICRP 103 (2007) Paragraph 5.8, page 91, Mobbs et al. (2011). For an example of an optimization procedure in the context of management of occupational exposure, see Figure 1 in IAEA (2002).
   f. For example, the average annual dose to occupationally exposed workers in the UK is 0.0004 mSv Oatway et al. (2016). For sources that arise from the disposal of radioactive waste the recommended effective dose constraint for public exposure is 0.3 mSv/yr and for prolonged exposure from long-lived radionuclides, if dose assessment is problematic, the recommended dose constraint is <0.1 mSv/yr. A radionuclide is a particular version of an atomic nucleus characterised by its number of protons and neutrons and their arrangement within the nucleus. For example iodine-131 (^{131}I) is the radionuclide of iodine with 53 protons and 78 neutrons, whereas the nucleus of technetium-99m has 43 protons and 56 neutrons in a metastable state.
   g. Lecomte et al. (2014) refers to an upper reference level of 300 Bq/m^3 for radon-222 corresponding to about 4.5 mSv/y in workplaces and 15.8 mSv/y in homes. Radon-related risk in the home is determined by a person's smoking status as well as indoor radon concentration Gray et al. (2009). The phrase "according to the situation" is a quote from Table 8 ICRP 103 which refers to the judgement required when levels of radiation are abnormally high.
   h. Chapter 7 of ICRP 103 (2007) describes the system of recommendations for medical exposures. See also Wrixon (2008).

10. Brenner (2010), Muller (2015), Auvinen et al. (2015).

11. Morgan and Bair (2013), Niles (2014), Pearce (2015). Annex IV of UNSCEAR (2008) and the WHO (2006) Chernobyl Forum report both document the large health impact of the Chernobyl accident because of fears about radiation.

12. Authors' summary.

DEFINITIONS AND UNITS

Table 6. List of abbreviations.

Organizations	
Organizations	
BEIR	Biological Effects of Ionizing Radiation
CERRIE	Committee Examining Radiation Risks of Internal Emitters
COMARE	Committee on Medical Aspects of Radiation in the Environment
IAEA	International Atomic Energy Agency
ICRP	International Commission on Radiological Protection
ICRU	International Commission on Radiation Units and Measurements
RERF	Radiation Effects Research Foundation
UN	United Nations
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation
WHO	World Health Organization
Units	
Bq	becquerel
Gy	gray
PM	Particulate Matter
Sv	sievert
WLM	Working Level Month
Cohorts/Studies	
ECLIS	European Childhood Leukaemia-Lymphoma Study
KiKK	Kinderkrebs in der Umgebung von Kernkraftwerken
LSS	Life Span Study
OSCC	Oxford Survey of Childhood Cancers
Other Acronyms	
ALL	Acute lymphocytic leukaemia
CI	Confidence interval
CLL	Chronic lymphocytic leukaemia
CT	Computed tomography
DDREF	Dose and dose-rate effectiveness factor
DNA	Deoxyribonucleic acid
DSB	Double strand break
EAR	Excess absolute risk
ERR	Excess relative risk
HR	Hazard ratio
LD	Lethal dose
LET	Linear energy transfer
LNT	Linear no threshold
NIC	Not in city
NPP	Nuclear power plant
OR	Odds ratio
RBE	Relative biological effectiveness
RR	Relative risk
SI	System Internationale d'Unites or international system of units
SIR	Standardized incidence ratio
SMR	Standardized mortality ratio
SRR	Standardized rate ratio (or standardized registration ratio)
UV	Ultra violet

13. Chapter 4 in ICRP 103 (2007) is devoted to explanations and definitions of doses, exposures and the associated uncertainties. The International Commission on Radiation Units and Measurements (ICRU) issues periodic reports, in particular see ICRU (2011).

14. Chapter 1 in Mettler and Upton (2008) covers basic radiation physics, chemistry and biology and Chapter 2 covers sources of exposure. CERRIE (2004) reviewed data on radiation risks of internal emitters as does COMARE (2004). Tables 2 and 3 in ICRP 103 (2007) document radiation weighting factors and tissue weighting factors. There are no universally agreed definitions of low dose or low dose-rate. Tables 6 and 7 in UNSCEAR (2006a) summarize definitions that have been used for low dose and low dose-rate respectively. Ruhm *et al.* (2016) summarise recent evidence and debate on the impact of dose-rate upon the health effects of radiation.

15. BIPM (Bureau International des Poids et Mesures) pages defining SI units for ionizing radiation are at: http://www.bipm.org/en/measurement-units/history-si/radioactivity/. Tables 2 and 3 in ICRP 103 (2007) document radiation weighting factors and tissue weighting factors.

16. Streffer *et al.* (2003). The recommended ICRP limits to prevent deterministic effects are set in equivalent dose, although strictly these should be set in absorbed dose.

17. The relationship between activity (Bq) and the resulting dose (Sv) depends on multiple factors including the nature and energy of the decay, and the location of the radioactive material with regards to the receptor. See Marsh *et al.* (2010), Tirmarche *et al.* (2010), Harrison and Marsh (2012), Muller *et al.* (2016).

18.
   a. Tissue reactions are discussed more fully under the section "Acute high dose exposures", paragraphs 26-31.
   b. Stochastic effects are discussed more fully under the section "Lower dose exposures", paragraphs 32-40.
   c. Brenner *et al.* (2003), Doss (2013).
   d. The matched pair of review articles by Little *et al.* (2009) and Tubiana *et al.* (2009) presents the arguments for and against LNT. Also see paragraph 24.
   e. Stewart *et al.* (2012) is the ICRP document reviewing both circulatory disease and diseases of the eye after radiation exposure. Little *et al.* (2008b), Little *et al.* (2012), Little (2013) review the literature on the risks of non-cancer disease and radiation. Kitahara *et al.* (2015) summarise data on low dose radiation and circulatory disease or cataracts published after 2006. Darby *et al.* (2013) found a linear dose-response relationship between radiation-related risks and major coronary events, suggesting that the LNT concept may be relevant to some forms of circulatory disease, although this was a study of high doses received during radiotherapy.

Table 7. Major types of ionizing radiation and their properties.

Radiation type	Wave or particle type	Radiation weighting factor, w_R	Effective Shielding	High/Low Linear Energy Transfer	Common source
X rays	Electromagnetic wave	1	Lead plate	Low	Diagnostic x rays
Gamma rays	Electromagnetic wave	1	Lead plate	Low	Terrestrial radionuclides and building materials
Beta particles	Emitted electron or positron	1	Aluminium plate	Low	Strontium-90 in radiotherapy
Neutrons	Emitted neutron	5-20	Metres of water or concrete	High	Neutron component of cosmic radiation
Alpha particles	2 protons + 2 neutrons	20	Sheet of paper	High	Radon

19. See UNSCEAR (2006a) pages 32-33 on human genetic susceptibility. Susceptibility and the development of biomarkers to identify radio-sensitive cancer patients is discussed in Manning and Rothkamm (2013).

   a. Whilst the excess relative risk of cancer is higher for exposures in childhood than for those in adulthood, the difference in excess absolute risk is not as marked (see paragraph 37b). Ozasa *et al.* (2012) document the impact of age at exposure on solid cancer mortality risk in Japanese atomic bomb survivors; Hsu *et al.* (2013) do the same for leukaemia.

   b. BEIR VII (2006) reviews data on genetic susceptibility to radiation-induced cancer noting unambiguous evidence of radio-sensitivity for two human genetic disorders: ataxia-telangiectasia Easton (1994) and Nijmegen breakage syndrome Zhao *et al.* (2000).

   c. See Sigurdson and Stram (2012) on potential implications for risk assessment.

   d. Darby *et al.* (2005), Pierce *et al.* (2003), Furukawa *et al.* (2010).

20. Authors' summary.

BACKGROUND EXPOSURE AND UNCERTAINTIES AT LOW DOSE

21. Oatway *et al.* (2016) review radiation exposure of the UK population based on data for 2010. Their Table 1 breaks exposure down for UK doses by source. UNSCEAR (2008) gives global averages. See NCRP (2009) for US exposures. Reference levels for exposures in emergencies would be much greater than background levels. The limits for planned situations are predicated on what might be acceptable or tolerable levels of risk for on-going continuous exposures from operations involving the use of radiation – for instance in the nuclear power industry or in hospitals.

22. For radon measurements at fine scales see Chen and Ford (2016). Hughes *et al.* (2005) report that some homes in the UK give rise to individual annual effective doses exceeding 100 mSv from radon, and a house with a very high radon level giving an annual effective dose to the occupants of 1.2 Sv has been reported from Ireland Organo *et al.* (2004). Construction differences such as sealed double glazing and closed cycle heating have an impact on radon levels via pressure differences UNSCEAR (2006b). Bossew *et al.* (2015) report on the European atlas of natural radiation. The map of indoor radon concentration, which covers 25 countries, is the most advanced component of that project Tollefsen *et al.* (2014), Hoffmann *et al.* (2016). Maps of geogenic radon potential, secondary cosmic radiation, terrestrial gamma radiation and concentration of the elements U, Th and K are also under construction.

23. Figure 2 refers to data from large studies of excess relative risk at different radiation doses. In this figure, relative risk (RR), odds ratios (OR) and standardised rate ratios (SRR) have been approximated to excess relative risk (ERR), under the assumption that the populations are homogenous and that the probabilities of the underlying diseases are small. Figure 2a describes excess relative risks of solid cancers. The **Japanese Life Span Study (LSS)** cohort are Japanese atomic bomb survivors Ozasa *et al.* (2012). The **international workers** cohort is a very large pooled study of radiation workers (INWORKS), most of whom are employed in the nuclear industry, from the UK, US, and France Richardson *et al.* (2015). Kashcheev *et al.* (2015) describe risks in **Chernobyl workers** who cleaned up after the accident. **Mayak workers** at the eponymous nuclear plant were subject to prolonged low

dose-rate external gamma radiation and plutonium exposure Sokolnikov *et al.* (2015), as were nearby **Techa River residents** due to discharges of radioactive waste Davis *et al.* (2015). **Yangjiang** is an area of high natural background radiation in China Tao *et al.* (2012) and **Kerala** is an area of high natural background radiation in India Nair *et al.* (2009). **Ankylosing spondylitis** patients in the UK were historically treated with X-rays in the mid-20th century Weiss *et al.* (1994).

Figure 2b describes excess relative risks of leukaemia for the **Japanese Life Span Study (LSS)** Hsu *et al.* (2013), **international workers** in the INWORKS nuclear worker cohort Leuraud *et al.* (2015), **Chernobyl clean-up workers** Zablotska *et al.* (2013) as well as a different cohort of **Chernobyl liquidators** Kesminiene *et al.* (2008), **Mayak workers** Kuznetsova *et al.* (2016), **Techa River residents** Krestinina *et al.* (2013b), residents receiving exposure from **Kerala** background radiation in India Nair *et al.* (2009) and patients with **ankylosing spondylitis** in the UK Weiss *et al.* (1995). For the purposes of representation and as the studies pertain almost entirely to low-LET radiation, Sv and Gy are assumed to be equivalent in Figures 2a and 2b. For the purposes of representation, ERRs for cancer incidence and mortality are also plotted on the same axis. In reality, the relationship between cancer incidence and mortality will depend on the ability and availability of diagnostics and therapies to improve survivorship. See Coleman *et al.* (1993).

Figure 2c describes excess relative risks of lung cancer for underground miners Lubin *et al.* (1995), Villeneuve *et al.* (2007), Schubauer-Berigan *et al.* (2009), Lane *et al.* (2010), Tomasek (2012), Kreuzer *et al.* (2015a) or after exposure to residential radon in Europe Darby *et al.* (2005), China Lubin *et al.* (2004) and North America Krewski *et al.* (2006).

For underground miners, risks are expressed relative to cumulative radon exposures given in WLM, and for domestic exposures to radon, risks are expressed relative to concentrations in Bq/m³.

These diverse studies include individuals who have been exposed at greatly varying dose-rates – some briefly, others very slowly. Ruhm *et al.* (2016) summarise recent evidence and debate on the impact of dose-rate upon the health effects of radiation, although a distinction needs to be made between low-LET and high-LET radiation.

Table 8 contains further detail about the data in this figure.

Table 8. Components of Figure 2.

	Cohort	Reference	Reference	Endpoint	Confidence Intervals	Y-Axis	X-Axis
Figure 2a	Japanese life span study (LSS)	Ozasa *et al.* (2012)	Figure 4	solid cancer mortality	95%	ERR	weighted colon dose, Gy
	International workers (INWORKS)	Richardson *et al.* (2015)	Figure 1	all cancer mortality other than leukaemia	90%	RR*	cumulative colon dose, Gy
	Chernobyl workers	Kashcheev *et al.* (2015)	Figure 6	solid cancer mortality	95%	RR*	dose, Gy
	Mayak workers	Sokolnikov *et al.* (2015)	Figure 2	solid cancer mortality ex bone, lung and liver	95%	ERR	colon dose, Gy
	Techa River residents	Davis *et al.* (2015)	Figure 1	solid cancer incidence	none	ERR	cumulative dose, Gy
	Kerala background radiation	Nair *et al.* (2009)	Table 4	all cancer incidence other than leukaemia	95%	RR*	cumulative radiation dose, Gy
	Yangjiang background radiation	Tao *et al.* (2012)	Table 2	all cancer mortality excluding leukaemia	95%	RR*	cumulative individual dose (range midpoint), mGy
	Ankylosing spondylitis patients	Weiss *et al.* (1994)	Figure 2	all neoplasms mortality except leukaemia	95%	RR*	total body dose, Gy
Figure 2b	Japanese life span study (LSS)	Hsu *et al.* (2013)	Figure 1b	leukaemia incidence ex CLL & ALL	none	ERR	weighted red bone marrow dose, Gy
	International workers (INWORKS)	Leuraud *et al.* (2015)	Table A2	leukaemia mortality excluding CLL	90%	RR*	dose, Gy
	Chernobyl workers (Ukraine)	Zablotska *et al.* (2013)	Figure 1	leukaemia incidence excluding CLL	95%	RR*	bone marrow dose, Gy
	Chernobyl liquidators (Belarus, Russia & Baltic countries)	Kesminiene *et al.* (2008)	Figure 1	leukaemia incidence excluding CLL	95%	OR	total red bone marrow dose, Gy
	Mayak workers	Kuznetsova *et al.* (2016)	Table 3	leukaemia incidence excluding CLL	None	RR	external dose to bone marrow, Gy (range midpoint)
	Techa River residents	Krestinina *et al.* (2013b)	Figure 1	leukaemia incidence excluding CLL	none	ERR	red bone marrow dose, Gy
	Kerala background radiation	Nair *et al.* (2009)	Table 6	leukaemia incidence	95%	RR*	cumulative radiation dose, Gy
	Ankylosing spondylitis patients	Weiss *et al.* (1995)	Table IV Figure 1	leukaemia mortality excluding CLL	95%	RR*	total marrow dose, Gy
Figure 2c	Canadian uranium workers	Lane *et al.* (2010)	Figure 1	lung cancer mortality	95%	RR*	WLM
	Uranium & tin miners	Lubin *et al.* (1995)	Figure 1a	lung cancer mortality	95%	RR*	cumulative WLM
	German uranium miners	Kreuzer *et al.* (2015a)	Figure 1a	lung cancer mortality	95%	RR*	cumulative WLM
	Colorado uranium miners	Schubauer-Berigan *et al.* (2009)	Table 4	lung cancer mortality	95%	SRR*	cumulative WLM (range midpoint)
	Czech uranium miners	Tomasek (2012)	Figure 1	lung cancer mortality	90%	O/E*	cumulative WLM
	Newfoundland fluorspar miners	Villeneuve *et al.* (2007)	Table 4	lung cancer mortality	95%	RR*	cumulative WLM
Figure 2c	China residential	Lubin *et al.* (2004)	Table 3	lung cancer incidence	95%	OR*	Radon concentration (range midpoint) Bq/m3
	North America residential	Krewski *et al.* (2006)	Figure 1A	lung cancer incidence	95%	OR*	Radon concentration Bq/m3
	Europe residential	Darby *et al.* (2006)	Figure 7	lung cancer incidence	95%	RR*	radon concentration Bq/m3 (corrected for random variation)

*converted to ERR by the approximations RR=SRR=OR=ERR+1

24. Figure 3 is adapted from Brenner *et al.* (2003) who review the biophysical processes that could generate the different curves. Valentin (2005) is a comprehensive review of radiation-related cancer risk extrapolation at low dose. The matched pair of review articles by Little *et al.* (2009) and Tubiana *et al.* (2009) present the arguments for and against LNT. There are many different experimental systems and different endpoints for modelling radiation carcinogenesis. Within one system, experiments are often replicable but they do not give a common answer to describe the shape of the dose response curve at very low dose.

a. Little *et al.* (2009) argue that LNT is "...(almost) the best we can do". Shah *et al.* (2012) argue that LNT is "prudent" as the basis for radiation protection policy. Calabrese and O'Connor (2014) give a critical history of the development and adoption of the LNT model.

b. The BEIR VII (2006) report used a Bayesian analysis that combined epidemiological and experimental data and settled on an estimate of DDREF = 1.5. Page 53 of ICRP 103 (2007) uses DDREF = 2. DDREF combines considerations of total dose and rate of delivery. Sometimes those are given separate consideration as: LDEF (low-dose effectiveness factor); and DREF (dose-rate effectiveness factor) Ruhm *et al.* (2016). Ruhm *et al.* (2015) summarises the development of the DDREF concept and the current findings of the active ICRP Task Group 91 in assessing its applicability. See our paragraph 122.

c. Figure 5 in Brenner *et al.* (2003) illustrates how a very small, highly radiosensitive population could generate a downwardly curving dose-effect relationship. To date, most studies do not support a dose response curve of this shape. Other hypothetical mechanisms could also lead to such an expectation, for example bystander effects or low-level radiation-induced instability discussed at paragraph 107.

d. Cornforth *et al.* (2002a) and Sachs *et al.* (1997) model the formation of chromosome aberrations. In their models it is interaction between points of damage from separate radiation tracks that brings in the upward curvature of the dose response. In Cucinotta *et al.* (2000) it is competition between repair pathways that brings in the curvature. Other biophysical mechanism/models are reviewed in Bodgi *et al.* (2016).

e. Tubiana (2005) summarises the conclusions of a joint report by the French Academie des Sciences and the Academie Nationale de Medecine which argues for the existence of threshold doses below which risk is negligible or zero. See Fritz (2002) for a study on dogs examining chronic whole-of-life effects which has similar conclusions.

f. Vaiserman (2010) gives a historical review of arguments in favour of radiation hormesis. Feinendegen (2005) presents a mechanistic argument for radiation hormesis, in particular his Figure 3 presents the argument that whilst the induction of DNA damage is expected to be linear in dose, protective responses against such damage are so strongly stimulated at low dose that there is a net hormetic effect. Luckey (2011) hypothesises that the optimal dose is 100 mGy/yr with a threshold at 10 Gy/yr separating beneficial from harmful effects. Sacks *et al.* (2016) argue that epidemiological studies based on linear assumptions are invalid because of hormesis, although it is usual in such studies to test for the appropriateness of a linear fit to the data.

25. Authors' summary.

ACUTE HIGH DOSE EXPOSURES

26. The Office of Science of the US Department of Energy has produced a chart summarizing the health effects of radiation at doses at different orders of magnitude. https://www.nrc.gov/docs/ML1209/ML120970113.pdf

27. ICRP 103 (2007) (Table A.3.3 page 167) lists cause of mortality at different dose thresholds. See also Edwards and Lloyd (1998) Table 1 which gives threshold doses for different tissue syndromes leading to mortality. Mettler and Upton (2008) Chapter 6 reviews tissue reactions across a range of tissues and doses. See Donnelly *et al.* (2010) on medical aspects of acute radiation syndrome.

28. ICRP 103 (2007) (Tables A.3.4. and A.3.3 pages 167-8) and Stewart *et al.* (2012) (Table 2.4, page 298) list thresholds for 1% incidence of morbidity and mortality involving various tissues. Edwards and Lloyd (1998) and Mettler and Upton (2008) as above. Several of the morbidity early effects in Table 1 are primarily of concern in partial body irradiation, for instance erythema (skin) and permanent sterility (gonads). Radiation effects upon cataracts and circulatory disease do not fall neatly into either tissue reaction or stochastic effects.

29. Streffer *et al.* (2003). Chapter 8 in Mettler and Upton (2008) gives a detailed review of tissue reactions of *in utero* exposure to radiation. Otake and Schull (1998) review radiation-related brain damage and growth retardation amongst prenatally exposed survivors.

30. Otake *et al.* (1990) describe studies of untoward pregnancy outcome (defined as stillbirth, major malformation or death within 14 days) amongst >65,000 offspring of atomic bomb survivors finding a positive association with joint parental dose, but the regression slope was not statistically significant. Fujiwara *et al.* (2008) found no evidence of an increased prevalence of adult-onset multi-factorial disease amongst 11,951 adult offspring (median age 50 years) of atomic bomb survivors. Odds ratios at a paternal or maternal dose of 1 Gy were 0.91 (0.81 – 1.01) and 0.98 (0.86 – 1.10) respectively. Neel and Schull (1991) is a book-length collection of essays on the children of atomic bomb survivors. Nakamura (2006) reviews more recent studies of the same children. Neel *et al.* (1990) summarise 40 years' effort to quantify the genetic effects of the atomic bombs with the words "no statistically significant findings have emerged". The most recent report of mortality amongst 75,000 offspring, after 62 years of follow-up, showed no excess of either cancer or noncancer mortality in relation to either paternal or maternal radiation dose Grant *et al.* (2015). See Searle (1974) and Nakamura *et al.* (2013) for animal studies.

31. Authors' summary.

LOWER DOSE EXPOSURES

32. Preston *et al.* (2003), Ozasa *et al.* (2012) Grant *et al.* (2017).

33. Preston *et al.* (2003), Shimizu *et al.* (2010), Little *et al.* (2012), Ozasa *et al.* (2012), Ozasa *et al.* (2016), Baselet *et al.* (2016), Little (2016), Ozasa *et al.* (2017), Shore (2016a).

34. Brenner *et al.* (2003), National Research Council (1995). New approaches in genomics and epigenetics offer promising advances in the ability to distinguish radiation induced cancers Behjati *et al.* (2016).

35. Shore (2009).

36. Land (1980). UNSCEAR 2006 Annex A Paragraph 16 discusses the problems of inadequately powered studies generating results which can overstate true risk despite being statistically significant. Pooled analyses and meta-analyses can sometimes

combine data from several smaller studies to create one well-powered study. Studies of radon in the home Lubin *et al.* (2004), Darby *et al.* (2006), Krewski *et al.* (2006) and of nuclear fuel cycle workers Leuraud *et al.* (2015), Richardson *et al.* (2015) have exploited this strategy.

37. The glossary in ICRP 103 (2007) defines ERR and EAR. Sistrom and Garvan (2004) explains relative risk (RR) and odds ratios (OR). Hernán (2010) discusses hazard ratios (HR). The standardized incidence ratio (SIR) is explained in Breslow (1987) and the standardized mortality ratio (SMR) in Everitt and Skrondal (2010). Schubauer-Berigan *et al.* (2009) describes the calculation of the standardized rate ratio (SRR).

38. Public Health England – guidance publication https://www.gov.uk/government/publications/ionising-radiation-dose-comparisons/ionising-radiation-dose-comparisons

39. Brenner *et al.* (2003), Little (2003), Wakeford (2004), Mullenders *et al.* (2009), Mobbs *et al.* (2011), Preston *et al.* (2013), Shore (2014), Kitahara *et al.* (2015), Mattsson and Nilsson (2015).

40. Authors' summary.

THE JAPANESE LIFESPAN STUDY (LSS)

Table 9. RERF reports on cancer mortality in LSS subjects

RERF report	12	13	14
Author	Pierce *et al.* (1996)	Preston *et al.* (2003)	Ozasa *et al.* (2012)
Time period	1950-1990	1950-1997	1950-2003
Solid cancer deaths	7,578	9,335	10,929
ERR/Gy solid cancer	0.29	0.37	0.47
95% confidence intervals	0.23 to 0.35	0.26 to 0.49	0.38 to 0.56

41. The Radiation Effects Research Foundation website www.rerf.jp describes the LSS and lists publications based upon the cohort. Key papers describing solid cancer mortality in the LSS are in Table 9. After the bombs were detonated 60-80,000 people were killed instantly in Hiroshima and another 90-166,000 died in the ensuing 4 months. In Nagasaki there were 22-75,000 instant fatalities and another 60-80,000 deaths in the ensuing months. The LD_{50} dose (at which 50% of the exposed population died) occurred at a radius of 1-1.3km of each blast and later dose reconstruction yielded a bone marrow dose estimate for the LD_{50} of 2.9-3.3 Gy Pierce *et al.* (1996), Preston *et al.* (2003), Wakeford (2004). The key message from the LSS papers is that risk of cancer mortality for people exposed on the day remains elevated 60 years on. The ERR is approximately linear with dose, persistently higher for those who were younger at exposure and approximately doubled for women Ozasa *et al.* (2012). The Osaza report indicated that by 2003 about 525 radiation-associated excess solid cancer deaths had occurred in the LSS cohort. A detailed presentation of cancer incidence by tumour site is provided in Preston *et al.* (2007), and an up to date report of solid cancer incidence including sex-specific analyses and the joint effects of smoking is Grant *et al.* (2017).

42. Stewart and Kneale (2000), Little and Charles (1990), Little (2002b), Tubiana *et al.* (2009). If there were a healthy survivor effect, LSS ERRs would be underestimates of the true values.

43. www.rerf.jp gives further details on cohort structure. The 55,000 individuals situated within 2.5 km of the blast were exposed to levels of radiation of 5 mGy or higher with a mean dose of 200 mGy. The 38,500 people 2.5-10 km from the blast received doses below 5 mGy. The 26,500 people not in the city were unexposed residents of Hiroshima or Nagasaki who were not in either city

('NIC') at the time of the bombings. 85% of the cohort experienced irradiation below the mean level of 200 mGy. Dose distribution of the cohort is given in Table 1 of Ozasa *et al.* (2012).

Table 10. Dose distribution amongst the LSS.

Weighted Colon Dose (Gy)	# Subjects	%
Not in City	26,500	22%
<0.005	38,500	32%
0.005-0.1	30,000	25%
0.1-0.2	6,000	5%
0.2-0.5	6,400	5%
0.5-1	3,400	3%
1-2	1,700	1.5%
>2	600	0.5%
Unknown dose	7,000	6%
TOTAL	120,000	

Concerns have been raised that internal or short-range external exposure from contaminated rainfall over the cities and surrounding areas following the atomic bombings distorts the dose distribution measurements in the LSS Takada *et al.* (1983), Sawada (2007). While data are limited, systematic analyses have failed to find deleterious health effects from rain exposure Sakata *et al.* (2014).

44. Up to date cause of death data is in Ozasa *et al.* (2012). The breakdown of excess deaths attributable to radiation is: ~500 from solid cancer, ~ 100 from leukaemia, and ~400 from non-cancer disease. See Ozasa's Table 9. Detailed analysis of leukaemia mortality is in Richardson *et al.* (2009) and incidence in Hsu *et al.* (2013). The not in city group has been included in some analyses, for instance Sugiyama *et al.* (2014).

45. For a list of Adult Health Study report titles, see http://www.rerf.jp/library/archives_e/ahstitle.html. On cardiovascular disease see Ozasa *et al.* (2017). Also see Shimizu *et al.* (2010) on circulatory disease and Yamada *et al.* (2004) on non-cancer disease.

46. Figure 1 in Ozasa *et al.* (2012) contains ERR per gray estimates for all specific causes of death in the latest LSS analysis. Also see Tables 2a and 2b in Furukawa *et al.* (2010). Hsu *et al.* (2013) report recent data on leukaemia incidence.

47. Ozasa *et al.* (2012).

48. Minamoto *et al.* (2004), Neriishi *et al.* (2007), Shore *et al.* (2010), Little (2013), Nakashima *et al.* (2006) .

49. The ERR/Sv for solid cancer incidence is 1.0 (95% CI: 0.2 to 2.3) for *in utero* exposure. The EAR did not increase with time/age as it did for an equivalent cohort exposed in early childhood, suggesting that lifetime risks following *in utero* exposure may be lower than for early childhood exposure Ohtaki *et al.* (2004), Preston *et al.* (2008). During the first 15 years of life for the *in utero* cohort 1 death and 2 cases of solid cancers were recorded, but no leukaemias Delongchamp *et al.* (1997) Jablon and Kato (1970). A surprising absence of stable chromosome aberrations among intrauterine exposed survivors who had received moderate and high doses (>100 mGy) contrasted with findings for mothers, and suggests high sensitivity of the haematopoietic system *in utero* to cell killing. This may be a reason for the absence of childhood leukaemia in this group. See Ohtaki *et al.* (2004).

50. Schull and Otake (1999), Otake and Schull (1998).

51. Jablon and Kato (1970), Delongchamp *et al.* (1997). The study of children of survivors is known as the F1 cohort. Little *et al.* (1994), Neel and Schull (1991), Nakamura (2006), Otake *et al.* (1990), Tatsukawa *et al.* (2013), Fujiwara *et al.* (2008), Neel *et al.* (1990), Kodaira *et al.* (2004), Kodaira *et al.* (2010), Izumi *et al.* (2003), Satoh *et al.* (1996), Grant *et al.* (2015). For a recent review see Little *et al.* (2013). For further discussion of genetic effects, see UNSCEAR (2010) Section B, ICRP 103 (2007) Annex A and BEIR VII (2006).

52. Authors' summary. The excess relative risk quoted here is different from the nominal cancer risk coefficient of 5.5% per Sv derived by the ICRP and used in optimization calculations. The ERR of 0.47 per gray for solid cancer is an estimate of the amount by which the underlying risk of solid cancer is increased proportionally for each gray of exposure. The ICRP's "nominal risk coefficient" of 5.5% per Sv is an estimate of the health detriment due to cancer experienced in a population exposed to low level radiation; it includes attributable fatal and non-fatal cancer, years of life lost and pain and suffering.

THE CHERNOBYL NUCLEAR POWER PLANT ACCIDENT

53. UNSCEAR (2008)'s Table 1 page 49 describes the accident and documents the principal radionuclides released. The radioactive release from Chernobyl lasted around 10 days, and two radionuclides, the short-lived iodine-131 and the long-lived caesium-137, were particularly significant. The radioactive plume spread over much of the western USSR and Europe. Maps are in Figures I and II in UNSCEAR (2008) and at http://www.unscear.org/unscear/en/chernobylmaps.html.

54. Data from Table 11 is from UNSCEAR (2008) Table 2, page 54. Extensive further details of radiation doses are presented in their Appendix B.

55. Local populations continued to drink milk that had been contaminated with radioactive iodine when cows grazed on contaminated pastures WHO (2006).

56. As of 2016 the most recently published summary figures are in UNSCEAR (2008). A recent update is at http://www.who.int/ionizing_radiation/chernobyl/Chernobyl-update.pdf?ua=1. Table D7 page 189 in UNSCEAR (2008) lists the causes of death of the 19 Chernobyl ARS survivors who died between 1993 and 2004. Of these 19 deaths only the 5 from malignancy are likely to be related to radiation. Literature on childhood thyroid cancer post-Chernobyl is discussed below.

57. The figure of 6,000 cases is given in Volume II, Annex D of UNSCEAR (2008) where Paragraphs 66-73 summarise childhood thyroid cancer as a confirmed effect of Chernobyl radiation exposure. Cardis and Hatch (2011) is a more recent review of published work. See also Cardis *et al.* (2006a), Boice (2005), Zablotska *et al.* (2011), Tronko *et al.* (2006) and Brenner *et al.* (2011). Ivanov *et al.* (2012) report that ERR/Gy is decreasing with time since exposure in a Russian cohort exposed as children.

Suzuki and Yamashita (2012) summarises the debate about low dose risk of thyroid cancer, concluding that a statistically significant increase has hardly been described with radiation doses below 100 mSv. A recent pooled analysis of 12 studies of thyroid cancer after childhood exposure to external radiation found a significant increase in RR for doses <0.10 Gy with no significant departure from linearity Veiga *et al.* (2016).

58. Zablotska *et al.* (2013) give the ERR of 1.26. See also Kesminiene *et al.* (2008) and Romanenko *et al.* (2008). Paragraphs D173-D179 in UNSCEAR (2008) summarise a large number of studies of leukaemia in emergency and recovery workers at Chernobyl. Reports of chronic lymphocytic leukaemia in Chernobyl liquidators Zablotska *et al.* (2013) and Kesminiene *et al.* (2008) showed positive non-significant increases in risk. A significant dose response was seen in the LSS cohort based on a simple trend test on 12 eligible cases of CLL, 4 of which occurred among survivors with doses in excess of 0.2 Gy Hsu *et al.* (2013). A significantly increased risk of the incidence of CLL was observed in uranium miners Rericha *et al.* (2006). However, no evidence for an increase in CLL risk has been seen in several other major studies Krestinina *et al.* (2013b), Leuraud *et al.* (2015), Kuznetsova *et al.* (2016). For a review of the open questions surrounding the radiogenicity of chronic lymphocytic leukaemia see Hamblin (2008) and Richardson *et al.* (2005).

59. Parkin *et al.* (1996) describe the largest and most comprehensive study to date, the European Childhood Leukaemia-Lymphoma Study (ECLIS), in particular their Figure 3, page 92, shows the lack of a dose-response relationship between leukaemia incidence and radiation dose. Davis *et al.* (2006) and Noshchenko *et al.* (2002) describe studies showing mixed results regarding leukaemia incidence amongst exposed children in the Ukraine which are criticised regarding selection bias in WHO (2006). Noshchenko *et al.* (2010) found an increase in leukaemia among Ukrainian children exposed at ages 0-5 to more than 10 mSv, but less than that reported by Noshchenko *et al.* (2002), and there are questions about possible biases in control selection UNSCEAR (2013b). Paragraphs D169-D172 in UNSCEAR (2008) review other peer-reviewed publications. Petridou *et al.* (1996) describe a low-powered study that suggested *in utero* radiation exposure from Chernobyl increased risk of infant leukaemia in Greece. Similar studies in Germany were unable to replicate the Greek results Steiner *et al.* (1998). The UK Committees COMARE and CERRIE concluded that there is insufficient evidence to support hypotheses of increased childhood leukaemia in European countries linked to Chernobyl CERRIE (2004) pages 67-68, COMARE (2004). Two members of the CERRIE committee criticized this conclusion of the majority and recorded in the report their belief that the current risk estimates are appreciably in error. Peer-reviewed scientific analyses of this argument have not lent support to this critique. For a review of the debate around risks of internal emitters subsequent to the publication of the ICRP 2007 recommendations, see Harrison and Day (2008).

Table 11. Dose distribution from the Chernobyl accident.

Population	Number	Average effective dose (mSv) from external and internal radiation* 1986 - 2005	Average thyroid dose (mGy) 1986
Recovery operation workers	530,000	117.0	-¥
Evacuees	115,000	31.0	490.0
Residents of contaminated areas (>37kBq m⁻²)	6,400,000	9.0	102.0
Residents of Belarus, Russian Fed and Ukraine	98,000,000	1.3	16.0
Other European Residents	500,000,000	0.3	1.3

*Excluding thyroid dose

¥ Data unavailable

60. Reviewed in Cardis and Hatch (2011) and UNSCEAR (2000a) Paragraphs D182 – D199. Ivanov *et al.* (2004), Rahu *et al.* (2006b), Ivanov *et al.* (2008), Rahu *et al.* (2013a), Rahu *et al.* (2013b) all study recovery workers and find non-significant dose-responses. Kashcheev *et al.* (2015) report the ERR/Gy of 0.47 for incidence, but find the studied cohort has lower solid cancer mortality than controls – attributed either to monitoring or a healthy worker effect. It is notable that Kashcheev et al have a longer follow-up than the other studies of solid cancers in highly exposed workers. Ivanov *et al.* (2004), Prysyazhnyuk *et al.* (2007) and Table D19 in UNSCEAR (2008) describe solid cancer risks for exposed (non-worker) population groups.

61. Pukkala *et al.* (2006), Bogdanova *et al.* (2010), Dardynskaia *et al.* (2006).

62. Cotterill et al. (2001) and Tondel et al. (2004) are studies of cancer trends in Western and Northern Europe finding increases of cancer that are attributed to Chernobyl. Cardis et al. (2006b) refute these (in particular their Figure 5, page 1232) with temporal trends in cancer incidence grouped by average dose and age at diagnosis across Europe that found no measurable association between solid cancer trends and the Chernobyl accident. Alinaghizadeh et al. (2014) (with authorship including Tondel) similarly found no measurable effect from Swedish data. Yablokov and Nesterenko (2009) is a book of papers published in Russian and then republished (but not peer-reviewed) in the Annals of the New York Academy of Sciences which contains a number of low-quality analyses and uncorroborated statements that have been misleading for those attempting to gauge the evidence surrounding Chernobyl and radiation impacts. http://www.nyas.org/Publications/Annals/Detail.aspx?cid=f3f3bd 16-51ba-4d7b-a086-753f44b3bfc1 gives access to the explicit statement from the journal that the publication is not peer reviewed and links to negative reviews (Charles (2010), Balonov (2012) and Jargin (2010)).

63. Hatch *et al.* (2015), Ostroumova *et al.* (2016).

64. Zablotska *et al.* (2008), Ostroumova *et al.* (2009), Ostroumova *et al.* (2013), Zablotska *et al.* (2015).

65. Worgul *et al.* (2007) is the key cataract risk study which calculated an ERR/Gy of 0.4 (95% CI 0.01 to 2.00). Ivanov *et al.* (2006) and Kashcheev *et al.* (2016) report on cerebrovascular disease in Chernobyl emergency workers. Kashcheev *et al.* (2016) report an increased incidence risk for cerebrovascular diseases (ERR/Gy = 0.45, 95% CI: 0.28 to 0.62). While the Kashcheev study was large, observing over 61,000 workers between 1986 to 2012, it was not able to adjust for known risk factors like weight, smoking and alcohol consumption, and the proportion of workers reported to have been diagnosed with a cerebrovascular disease is surprisingly high (43%).

66. For an assessment concluding that there is no convincing evidence of increased risk of birth defects from exposure to radiation in contaminated areas see UNSCEAR (2001) part VI-A, section 3-4, page 57. See WHO (2006) for data showing that increases in birth defects between 1986 and 1999 in Belarus were not different between contaminated and uncontaminated areas. This WHO study was criticised by some groups for underestimating the impact of low-level radiation on health in general. Holt (2010) gives some perspective. Wertelecki (2010) describes a study showing above average rates of birth defects in the Ukraine including neural tube defects (odds ratio 1.46 (95% CI: 1.13-1.93)) and microcephaly (odds ratio 2.8 (95% CI: 1.15-6.79)). This study lacked data about confounding risk factors such as maternal alcohol intake and diet. Weinberg *et al.* (2001) and Aghajanyan and Suskov (2009) describe genomic

abnormalities in children born to exposed individuals. Bridges *et al.* (2013) discuss potential design flaws in these studies. A series of studies describe germline excess minisatellite mutations in a Belarusian population exposed to Chernobyl radiation Dubrova *et al.* (1996), Dubrova *et al.* (1997), Dubrova *et al.* (2002). This phenomenon has not been observed in offspring of Japanese bomb survivors Satoh *et al.* (1996), Asakawa *et al.* (2004), Kodaira *et al.* (2004), Kodaira *et al.* (2010), nor in other Chernobyl-exposed groups Livshits *et al.* (2001), Kiuru *et al.* (2003), Slebos *et al.* (2004), Furitsu *et al.* (2005), nor in Sellafield workers Tawn *et al.* (2015). Little (2015) discusses possible reasons for differences. Mughal *et al.* (2012) suggests that genomic instability in offspring may be triggered only by a dose in excess of a threshold, higher for chronic exposure than acute. The implication for expressed phenotype of increased frequencies of minisatellite mutations is not known Bouffler *et al.* (2006).

67. Cardis *et al.* (1996) give a calculation suggesting that the predicted lifetime excess of cancer and leukaemia deaths due to Chernobyl radiation is 4000 for liquidators, evacuees and residents of the strict control zones, and a further 5000 deaths for the most exposed persons in Belarus, Russia and Ukraine (about 1% of the total numbers of cancers expected in these populations). Cardis *et al.* (2006b) give further extrapolation to European countries and conclude that Chernobyl radiation may eventually be responsible for 16,000 cases of thyroid cancer (95% CI: 3,400 to 72,000) and 25,000 cases of other cancer (95% CI: 11,000 to 59,000). This accounts for around 0.01% of total cancers expected over the time period to 2025. Concerns have been expressed about the calculation of numbers of potential deaths from theoretical risk models (for instance Gonzalez *et al.* (2013)).

68. For reviews finding elevated levels of depression and post-traumatic stress disorder in first responders and clean-up workers, as well as poor quality of life measures amongst the general population, see Kinley (2006),WHO (2006), Bromet *et al.* (2011), Bromet (2012). Rahu *et al.* (2006a) finds an increased risk of suicide amongst 5000 Estonian clean-up workers. Havenaar *et al.* (1996), Havenaar *et al.* (1997) describe a study showing that exposed Belarusian residents had poorer mental health scores than controls. Adams *et al.* (2002)), Adams *et al.* (2011) demonstrate the lasting nature of psychological impacts on evacuees in Kiev. There is no evidence of a dose response effect for psychological effects amongst evacuees or the general population. In one major study the key risk factors were the belief that one's health was affected by Chernobyl, and being diagnosed with a Chernobyl-related health problem Bromet and Havenaar (2007). A study on mental health of Ukrainian clean up workers found that high exposure level (roof workers) was associated with current somatic and post-traumatic stress disorder symptom severity Loganovsky *et al.* (2008).

69. Men *et al.* (2003).

70. Authors' summary.

THE FUKUSHIMA DAI-ICHI NUCLEAR ACCIDENT

71.   A brief description of the accident is given in Hasegawa *et al.* (2015) and a longer one in part II (page 28) of UNSCEAR (2013a).

72.   Table 2 of Hasegawa *et al.* (2015), summarised in Table 12 below.

Table 12. The distribution of effective radiation doses to workers in the emergency and recovery operations at the Fukushima Dai-ichi nuclear power plant.

Dose (mSv)	Number of Workers
<10	19,198
10-50	8,614
50-100	1,347
100-150	138
>150	35

73.   Tanigawa and Chhem (2013).

74.   Table 5 page 53 in UNSCEAR (2013a) and Table 3 in Nagataki and Takamura (2016) show estimated effective doses for the first year following the accident for members of the public. Tables 4.4-1 to 4.4-3 in IAEA (2015) present calculated additional lifetime risks for emergency workers. Section 4.4 to 5.3 in the same document describes modelled lifetime risks for members of the public.

75.   Measured doses are summarised in Nagataki and Takamura (2016) and Tokonami *et al.* (2012). Table 6 page 57 in UNSCEAR (2013a) shows estimated effective doses to evacuees.

76.   UNSCEAR (2013a).

77.   Between October 2011 and March 2014 300,476 residents of Fukushima Prefecture aged 18 or under at the time of the accident were screened Suzuki (2016a). The sensitive ultrasound technique revealed 113 cancers or suspected cancers. This number was around 30-fold higher than would have been expected from cancer registry data. Tsuda *et al.* (2016b) attributed the findings to radiation exposure, but this conclusion was vigorously contested Jorgensen (2016), Korblein (2016), Sallmen *et al.* (2016), Shibata (2016), Suzuki (2016b), Takahashi *et al.* (2016), Takamura (2016), Tsuda *et al.* (2016a), Wakeford *et al.* (2016) on multiple grounds. Wakeford (2016) and Suzuki (2016a) enumerate the reasons why this is an incorrect interpretation. There is a well-documented precedent for this pattern in South Korea where the introduction of sensitive ultrasound thyroid screening caused over-diagnosis of thyroid cancer Ahn *et al.* (2014), Ahn and Welch (2015), Williams (2015). A smaller but more directly applicable study of three unexposed Japanese prefectures, which found similar results to those observed iCardis *et al.* (2007)n Fukushima prefecture, is Hayashida *et al.* (2013). See Normile (2016) for an overview.

78.   Tanigawa *et al.* (2012). See also an editorial Thomas and Symonds (2016) and reviews of Hasegawa *et al.* (2015) and Hasegawa *et al.* (2016). During evacuation there were over 50 deaths amongst vulnerable populations and in the 3 months after the accident mortality among elderly people at nursing facilities increased three-fold.

79.   Authors' summary.

STUDIES OF WORKERS EXPOSED TO RADIATION.

80.   Wakeford (2009) gives an overview focussing on occupational exposure.

81.

a.   See Wernli (2016) for a history of individual monitoring and Ainsbury *et al.* (2011) for a review of retrospective dosimetry techniques. The studies' results are presented as ERR/Gy, although some studies include neutron doses in sieverts.

The large pooled study, INWORKS, includes studies of worker cohorts in the UK, France and the US. The results for the nuclear worker studies and the LSS are in broad agreement even though the workers usually accumulated their doses over many years, whilst the LSS subjects received theirs in a few seconds – supporting the assumption of additivity and dose-rate independence of radiation doses.   There are other key differences between the LSS and worker studies, including exposure to different types of radiation (e.g. gamma rays of different energies), and differences in the demographics, genetics and lifestyle features of the subject population Stewart and Kneale (2000), Little (2002a). The LSS figures for working-age males in Table 4 are as calculated by Cardis *et al.* (2005) and Muirhead *et al.* (2009). INWORKS is described by Richardson *et al.* (2015) for solid cancer risk and Leuraud *et al.* (2015) for leukaemia risk. See Nagataki and Kasagi (2015) and also Doss (2015) for comments and concerns regarding the INWORKS study design. The INWORKS study is a refinement of previously published pooled cohort studies known as the 14- and 15-country studies (the former being the 15-country study minus Canada); results from the 15-country study were found to be affected by historic dose estimate issues in one contributing cohort (i.e. Canada) Cardis *et al.* (2005), Cardis *et al.* (2007), Thierry-Chef *et al.* (2007), Ashmore *et al.* (2010), Wakeford (2014b), Zablotska *et al.* (2014). Japanese nuclear worker data originates from Akiba and Mizuno (2012), where they also discuss the risk of alcohol consumption confounding this result. The ERR/Sv estimate of all cancers excluding leukaemia and alcohol-related cancers in the Japanese study was 0.2 (95% CI -1.42 to 2.09). The Chernobyl Russian clean up worker cohort was analysed by Kashcheev *et al.* (2015). Mayak nuclear worker risks for solid cancers other than lung, liver and bone are from Sokolnikov *et al.* (2015) and for leukaemia from Kuznetsova *et al.* (2016). Rocketdyne data is from Boice *et al.* (2011) and US nuclear power plant workers from Howe *et al.* (2004).

b.   See Stabin and Xu (2014) for an explanation of basic principles in internal radiation dosimetry, focussing on the concept of phantoms. See Gilbert *et al.* (2013) for a Mayak study on lung cancer and Sokolnikov *et al.* (2015) for solid cancer other than lung, liver and bone. Vasilenko *et al.* (2007) details internal dosimetry methods at Mayak. A question of other factors influencing risks in groups of nuclear workers is raised by Gillies and Haylock (2014) and commented on in Boice (2014). A further (environmental) study examining the effects of intake of I-131 from emissions at the Hanford Nuclear Site in the USA is Davis *et al.* (2004).

c.   UNSCEAR (2006a) lists 18 studies of non-cancer disease risks in nuclear workers. Kitahara *et al.* (2015) update this list with a further 3 studies. Little *et al.* (2012) is a systematic review and meta-analysis of circulatory disease risk in 9 studies including 7 nuclear worker studies. Little (2013) is a further review. A series of studies of the Mayak cohort have appeared since the Kitahara update: Moseeva *et al.* (2014), Azizova *et al.* (2015). Azizova *et al.* (2016) report on cataract incidence in the Mayak cohort.

82.   See paragraph 81a for references in Table 4.

83.   Radiologists.

a.   Wakeford (2004), Mutscheller (1925). A review of the history of dose limits is given by Inkret (1995). Yoshinaga *et al.* (2004) review 8 studies of medical radiation workers. Those studies are of: 6,500 US radiologists (Matanoski *et al.*

(1987); 2,700 UK radiologists Berrington *et al.* (2001); 146,000 US radiological technologists Mohan *et al.* (2003); 6,600 US Army radiological technologists Jablon and Miller (1978); 27,000 Chinese X-ray workers Wang *et al.* (2002); 4,200 Danish radiation therapy workers Andersson *et al.* (1991); 12,200 Japanese radiation technologists Yoshinaga *et al.* (1999) and 73,100 Canadian radiation workers Ashmore *et al.* (1998).

b. Hauptmann *et al.* (2003) describe the circulatory risk for US radiological technicians. Shore (2014) summarises studies from this and three other studies of circulatory disease in medical radiation workers.

c. See Table 3 in Shore (2016b) for a summary that suggests that there is occupational radiation cataract risk amongst medical specialists who receive large cumulative doses (with estimated mean doses from various studies ranging from 0.028 Gy to 6 Gy).

84. 10 Gy is the average alpha dose to the skeleton as a whole: to endosteal surfaces, the putative originating cells for osteosarcoma, the average alpha dose would be about half this. In a US cohort of 820 people there were 46 deaths from bone cancer where less than 1 would have been expected, and a clear excess of cancers of the paranasal sinuses and mastoid air cells was also apparent due to radon formed on the decay of ^{226}Ra in the bones of the head. The equivalent UK workers ingested less radium and experienced 1 bone cancer death against 0.17 expected in a cohort of 1110 individuals. For studies on the US radium dial workers, see Rowland *et al.* (1978), Thomas (1994), Fry (1998) (US overviews), Spiers *et al.* (1983) (US leukaemia), Adams and Brues (1980) (US breast cancer). For studies on the UK radium dial workers, see Baverstock and Papworth (1989) (UK leukaemia) and Baverstock and Vennart (1983) (UK breast cancer). A careful analysis of the data on breast cancer in US radium dial painters suggested that the reported association may have been due to other factors and may not have been causal Stebbings *et al.* (1984).

85. Sigurdson and Ron (2004), Yong *et al.* (2014), dos Santos Silva *et al.* (2013), Hammer *et al.* (2014), Sanlorenzo *et al.* (2015), Shantha *et al.* (2015).

86. A working level (WL) is defined as any combination of the short lived progeny of radon in one litre of air that will result in the emission of 1.3 x 10^5 MeV of potential alpha energy, and a working level month (WLM) is defined as the cumulative exposure from breathing in an atmosphere at a concentration of 1 WL for a working month of 170 hours Tirmarche *et al.* (2010).

a. The 2006 UNSCEAR report combined data from 9 studies comprising over 3,000 lung cancer cases in miners and found an ERR per 100 WLM of 0.59 (95% CI: 0.35 to 1.0), in close agreement with an estimate of 0.49 (95% CI: 0.2 to 1.0) per 100 WLM made 10 years earlier, and a recent assessment concluded that a reasonable summary ERR estimate is 0.5 per 100 WLM. Reviewed in Tirmarche *et al.* (2010) and UNSCEAR (2006b), Annex E. For results from individual studies see Table 21 in UNSCEAR (2006b). For comparisons of meta-analyses see Tirmarche *et al.* (2010) Annex A page 51, UNSCEAR (2006b) Paragraph 427, Lubin (1994), BEIR VI (1999) and Tirmarche *et al.* (2012). A single large study of German Wismut uranium miners (3,016 lung cancer deaths in just under 2 million person-years of follow-up), not included in the earlier pooled analyses, found a smaller risk of 0.19 per 100 WLM (95% CI: 0.16 to 0.22), but when the study was limited to miners with comparatively low cumulative exposures the ERR became 1.3 per 100 WLM

(95% CI: 0.7 to 2.1) Walsh *et al.* (2015). Studies of hard rock miners show a *decrease* in ERR per unit of exposure as the rate of exposure *increases*, which may explain differences in results for different studies.

b. Reviewed in Darby *et al.* (1995), UNSCEAR (2006b) Annex E Paragraphs 485 – 491, Tirmarche *et al.* (2010) and (for the German uranium miners) Walsh *et al.* (2015). Also see Kreuzer *et al.* (2015b) and Mohner *et al.* (2010). The ERR of 2.18 is from Kreuzer *et al.* (2016).

c. UNSCEAR (2006a) Annex B, Table 11 summarises results on circulatory disease for 5 studies of miners. Walsh *et al.* (2015) summarise current results for the German uranium miners.

87. Authors' summary.

ENVIRONMENTAL EXPOSURE

88. UNSCEAR (2008), Table 1 in Hughes *et al.* (2005). Bossew *et al.* (2015) map indoor radon across Europe. Because radon is localised in some areas only, exposure prevention is required in such areas known to be affected.

a. Becquerels per metre cubed is strictly an improper (summary) measure: it is practical to use it because it is the ambient concentration that corresponds to a certain dose-rate. Pooled analyses from Europe Darby *et al.* (2006), North America Krewski *et al.* (2006) and China Lubin *et al.* (2004) are summarised in Table 2.2, page 30 of Tirmarche *et al.* (2010). When uncertainties associated with variations in exposure were accounted for, the estimated relative risk in the European pooled analysis increases from 0.08 to 0.16 per 100 Bq/m^3 Darby *et al.* (2006).

b. Figures 2 and 3 in Darby *et al.* (2005) compare risks for smokers and non-smokers. See also the large paper Darby *et al.* (2006). The small study of Torres-Duran *et al.* (2014) reviews studies of residential radon and lung cancer risk in never smokers.

c. See Raaschou-Nielsen *et al.* (2008) for the study of acute lymphoblastic leukaemia in Denmark and Kendall *et al.* (2013) for the study in the UK.

89. Radiation risks in areas with high natural background radiation are reviewed by Hendry *et al.* (2009) Boice (2010) and Aliyu and Ramli (2015). For Kerala results see Nair *et al.* (2009) and for Yangjiang results see Tao *et al.* (2012), the confidence intervals for Tao et al are calculated in Shore (2014). The results of these studies are not statistically significant, although they are of comparable size and dose to some of the worker studies that have identified positive, statistically significant estimates of ERR/Gy. Nevertheless, there is no statistical inconsistency between these estimates, although the Kerala risk estimate is close to statistical incompatibility with the LSS risk estimate.

90. A case-control study in Great Britain based on >27,000 cases from the National Registry of Childhood Tumours compared risks of childhood leukaemia and other cancers with cumulative dose through exposure to indoor gamma radiation and radon based on the mother's address at the time of the child's birth Kendall *et al.* (2013). It found a statistically significant relationship between dose from naturally occurring gamma radiation and the risk of childhood leukaemia, with an ERR/Sv = 120 (95% CI: 30 to 220). Radon exposure did not predict childhood leukaemia, and other childhood cancers were not related to either radon or gamma radiation exposure. UNSCEAR (2013b) cautions that there are large

uncertainties associated with this study with respect to its use of an ecological measure of dose. A census-based cohort study of childhood cancer in Switzerland (with 1,800 incident cases) reported positive relationships between cumulative dose of external radiation and both childhood leukaemia (ERR/Sv = 50 (95% CI: 0 to 100)) and central nervous system cancers (ERR/Sv = 50 (95% CI: 0 to 110)) Spycher et al. (2011). A Finnish case-control study (1093 cases) with full residential history found a non-significant odds ratio increase for childhood leukaemia with increasing dose-rate of background radiation, with a significantly elevated odds ratio in the age group 2-7 years Nikkila et al. (2016). These relationships between exposure to background gamma radiation and childhood leukaemia incidence are broadly comparable to those from the LSS, lending some support to the application of risk estimates derived from the LSS to the very low dose-rates received from naturally occurring background gamma radiation. However, a French census-based analysis with 9,056 incident cases over 20 years found no evidence of an association of childhood leukaemia risk with either radon (SIR by 100 Bq/m³ 1.01, 95% CI 0.91 to 1.12) or gamma radiation (SIR by 10 nSv/h 1.01, 95% CI 1.00 to 1.02) Demoury et al. (2016).

91. For Techa River residents see Schonfeld et al. (2013) and Davis et al. (2015) for solid cancer, Krestinina et al. (2013b) for leukaemia and Krestinina et al. (2013a) for cardiovascular disease.

92. Cancer risks due to fallout are reviewed in, for example, Simon et al. (2006), Simon and Bouville (2015). The analysis of 11 cancer registries is reported in Wakeford et al. (2010) and the study focussing on the Nordic countries is reported in Darby et al. (1992). The relative risk of leukaemia for ages 0-14 in the high exposure period versus the medium exposure period was 1.07 (95% CI: 1.00 to 1.14). Other populations exposed during fallout include the Marshall Islanders Land et al. (2010), Simon et al. (2010), inhabitants of Utah near to the Nevada Test Site Stevens et al. (1990) and inhabitants of Semipalatinsk in Kazakhstan Abylkassimova et al. (2000), Akleyev (2007). See Wakeford (2014a) for a discussion of fallout in the context of discharges from nuclear installations.

93. Residential areas around nuclear facilities.

a. The epidemiology of childhood leukaemia near nuclear installations has been reviewed in Laurier et al. (2008). See also Laurier et al. (2014), Kinlen (2011), Janiak (2014) and COMARE (2011). Wakeford (2014a) briefly summarises the history of investigations of childhood leukaemia near Sellafield and Dounreay. Bunch et al. (2014) report recent follow-up data from the same populations which have not exhibited excess cases of leukaemia since the early 1990s. The cluster near Krummel was first reported by Schmitz-Feuerhake et al. (1993). COMARE (2011) comprehensively reviews studies of the risk of leukaemia in young people living in the vicinity of nuclear power plants in Great Britain and other countries in Chapter 3 and in Germany in Chapter 4. COMARE (2016) reviews the incidence of childhood cancer around the Sellafield and Dounreay nuclear installations with data up to 2006 concluding that in the time period 1991-2006 the incidence rates of leukaemia and non-Hodgkins lymphoma had reduced to unexceptional levels in both locations.

b. The KiKK study was a German case control study of cancer diagnosed in children below the age of 5. Its main finding was a statistically significant positive association between the risk of leukaemia before 5 years of age and living less than 5km from a nuclear power plant Kaatsch et al. (2008a). A commentary by Little et al. (2008a) gives context. Chapter 4 of COMARE (2011) summarises further descriptions and analyses of the KiKK study. Additional analysis of the KiKK data compared observed and expected numbers of cases in the same group of children (leukaemia below 5 years of age and living within 5km of a nuclear power plant in Germany) and reported a standardised incidence ratio (SIR) not significantly different from 1 Kaatsch et al. (2008b). The KiKK case-control study design was repeated in France and Britain (set in context in Muirhead (2013)). The geographical approach was also repeated for the same risk group in France, Britain and Switzerland. Neither case-control study recapitulated the odds ratio (OR) significantly different from 1 and just one time interval from the French geographical study generated an SIR marginally significantly different from 1. When the French study broadened the age group under consideration to include children under 15, a marginally significant result was observed (see Table 2, Sermage-Faure et al. (2012)). Table 13 summarises numerical values of ORs and SIRs from these studies and gives references.

Other recent studies in Finland (2 NPPs (nuclear power plants)), Canada (3 NPPs) and Belgium (5 NPPs) report non-significant SIRs for children below 15 years with various definitions of residing close to NPPs Heinavaara et al. (2010), Bollaerts (2012), Lane (2013). Table 5.1, page 59 in COMARE (2011) calculates an SIR from a meta-analysis of older (pre-2009) data for children under 5 years "in the vicinity" of 80 nuclear power plants in 5 countries. The resulting SIR is 1.07 (0.92 to 1.26).

Table 13. Childhood leukaemia in children < 5 years old living < 5 km from a nuclear power plant published as the KiKK study and since. N is the number of cases of leukaemia in children below 5 years of age resident < 5km from a nuclear power plant (NPP).

Country	OR from case control studies	SIR from ecological and cohort studies
Germany	2.19 lower 95% CL = 1.51 1980-2003 N=37 Kaatsch et al. (2008a)	1.41 (0.98 to 1.97) 1980 - 2003 N = 34 Kaatsch et al. (2008b)
France	1.6 (0.7 to 4.1) 2002 - 2007 N=6 Sermage-Faure et al. (2012)	2.2 (1.0 to 4.4) 2002 – 2007 N=8 1.4 (0.8 to 2.3) 1990 – 2007 N=14 Sermage-Faure et al. (2012)
Britain	0.86 (0.49 to 1.52) 1962 - 2007 N = 10 Bithell et al. (2013)	1.22 (0.75 to 1.89) 1969 - 2004 N=20 COMARE (2011)
Switzerland		Incidence Rate Ratio 1.2 (0.6 to 2.41) 1985 - 2009 N = 8 Spycher et al. (2011)

c.   See Black (1984) for Sellafield, COMARE (1999) for Dounreay, SSK (2008) for KiKK.

d.   COMARE (2006) found that childhood leukaemia in Britain tends to cluster, but this is not a consistent result across all such studies. For example Alexander (1998) finds evidence of clustering in a dataset of 13,351 cases of childhood leukaemia from 17 countries, whilst Schmiedel et al. (2010) found no evidence of a tendency to clustering amongst 11,946 cases of childhood leukaemia in Germany. The town of Fallon in Nevada USA had an unusually high incidence of childhood leukaemia (14 cases) during the years 1997–2003 Francis et al. (2012). The town is not near a nuclear installation and the cause of the cluster remains unknown.

e.   Kinlen (1988) first proposed the population mixing hypothesis. Kinlen (2012) presents a review and meta-analysis of 20 years' data on childhood leukaemia and population mixing. Lupatsch et al. (2015) describe a Swiss cohort study in which population mixing did not predict the risk of childhood leukaemia, but see Kinlen's letter of response Kinlen (2015) and also Lupatsch et al. (2016) which found an association between Swiss population growth and childhood leukaemia.

f.   Gardner et al. (1990) proposed paternal pre-conceptional radiation as the cause of the cluster near Sellafield. Doll et al. (1994), COMARE (2002) and COMARE (1999) summarise the evidence against the hypothesis. Recent reviews are Wakeford (2013), Wakeford (2014a).

g.   Fairlie (2014), CERRIE (2004), Wakeford (2014a).

94.   Industrial processes such as the burning of coal, the production of phosphate fertilizers and the extraction of oil and gas have the potential to increase exposure to naturally occurring radioactive materials (NORMs) and hence to elevated exposure in workers and in the environment. Individuals in such industries have received less scrutiny than other exposed individuals described here. Doyi et al. (2016) IAEA (2003) and http://www.world-nuclear.org/information-library/safety-and-security/radiation-and-health/naturally-occurring-radioactive-materials-norm.aspx

95.   Authors' summary.

MEDICAL EXPOSURE

96.   Dose fractionation (in which the total dose is delivered as a number of doses separated in time) allows the optimization of the lethal effect on diseased cells while sparing healthy tissues. There are known risks from such therapy which have to be balanced against the benefits of treating the underlying disease. There is a large body of data on those risks which is growing as radiotherapy becomes more successful and people survive ever longer after their radiotherapy. These data have to be treated with caution as individuals treated with radiotherapy are already patients, so they are not a representative sample of the general population, and this could affect estimates of radiation risks. Further, radiotherapy is usually focused on localised diseased tissues, leading to a highly heterogeneous distribution of doses within the body. There is an overall pattern that the ERR/Gy from radiotherapy tends to be lower than the corresponding values in the LSS. This pattern is more marked at higher average radiotherapy dose and is therefore thought to be explained by spatially-focussed radiation used in therapy killing a large proportion of cells that might otherwise have become cancerous due to irradiation – the so called sterilization effect.

However these two patterns are not ubiquitous: some individual radiotherapy studies have a higher ERR/Gy than the corresponding values in the LSS. Little (2001) reviews 116 radiotherapy studies and compares ERRs for incidence and mortality with comparable risks in the LSS. Travis et al. (2003a) found that radiation related risk remained high even at the highest doses in women < 30 years of age treated for Hodgkin disease with radiotherapy (i.e., there was no evidence of a sterilization effect). Wakeford (2004) reviews cancer epidemiology amongst medically irradiated groups. Two of the largest studies are of 14,000 ankylosing spondylitis patients Weiss et al. (1994), Weiss et al. (1995)and 80,000 women treated for cervical cancer Boice et al. (1985), Boice et al. (1987), Boice et al. (1988). Little (2016) reviews risks from therapeutic and diagnostic doses, and Tran et al. (2017) updates analyses for two diagnostically treated groups.

97.   For studies on Ra-224 see Wick et al. (1999), Nekolla et al. (2000). For Thorotrast studies see Travis et al. (1992), Travis et al. (2001), Travis et al. (2003b).

98.   Linet et al. (2012) review risks from diagnostic imaging and their Table 4 gives estimates for dose from various different examinations.

a.   Bithell and Stewart (1975) describe the OSCC, Wakeford (2008) reports pooled results from 32 smaller studies of X-rays in utero. See Doll and Wakeford (1997) for dose estimates and comparisons with risks from post-natal radiation, and also Preston et al. (2008) for a study on the LSS.

b.   Linet et al. (2012) discuss the wide range of results of studies of X-rays in children and adults, and why they might be so variable. Table 2 in Shore (2014) summarises leukaemia risks from larger studies of medical exposures. Little and Boice (1999) compare breast cancer risks in fluoroscopy patients and the LSS. Ronckers et al. (2010) examines breast cancer and scoliosis. Howe (1995) reports strictly null dose-response results for lung cancer risk after multiple fluoroscopic examinations.

c.   A UK study calculated absorbed dose from CT scans to the red bone marrow and the brain and found an ERR/Gy = 37 (95% CI: 6 to 121) for leukaemia and ERR/Gy = 24 (95% CI: 11 to 47) for brain tumours Pearce et al. (2012). The equivalent values from the LSS based on age at exposure and follow up time were an ERR/Sv of 45 (95% CI: 16 to 188) for leukaemia and an ERR/SV of 6.1 (95% CI: 0.1 to 64) for brain tumours. An Australian study reported: an ERR/Gy = 39 (95% CI: 14 to 70) for leukaemia, using bone marrow dose; an ERR/Gy = 21 (95% CI: 14 to 29) for brain cancer after brain CT using dose to the brain; and an ERR/Sv = 27 (95% CI: 17 to 37) for solid cancer (excluding brain cancer after brain CT) using effective dose Mathews et al. (2013). See, for example Brenner (2014), Walsh et al. (2014), Journy et al. (2015) for discussion of these results. A French study Journy et al. (2015) that attempted to take into account predisposing factors was shown to suffer from some methodological limitations Cardis and Bosch de Basea (2015), Muirhead (2015). A further overview is Boice (2015).

99.   Authors' summary.

EXPERIMENTAL STUDIES OF MECHANISMS OF DAMAGE

100. Valentin (2005), page 11 and pages 313-315 of BEIR VII (2006), Annex A2 of ICRP 103 (2007), UNSCEAR (2012a) and NCRP (2015) all offer reviews of radiobiology. Complex DSB are a

combination of strand breaks and base damages all within a few nanometres along the DNA, containing at least one break on each strand of the DNA (hence "DSB") and at least one more break and/or base damage (hence "complex"). These are illustrated in Figure 5 of Goodhead (2009). Goodhead (1994) and Lomax *et al.* (2013) give general introductory explanations of the generation and relevance of clustered damage. Choi *et al.* (2015) give an explanation of indirect damage.

101. Molecular mechanisms of DNA repair are reviewed in pages 32-39 of BEIR VII (2006) and in Shibata and Jeggo (2014). Molecular mechanisms of DNA repair including a consideration of damage complexity are reviewed in Moore *et al.* (2014). At high doses the linear quadratic dose response saturates for counts of chromosome aberrations (e.g. for human lymphocytes saturation occurs at 4-5 Gy).

102. On checkpoints see ICRP 99. Lobrich and Jeggo (2007), Deckbar *et al.* (2007) and Fernet *et al.* (2010) discuss the threshold below which the G2/M checkpoint does not operate. Martin *et al.* (2013) review low dose hypersensitivity.

103. Hlatky *et al.* (2002) and Goodhead (2009) describe diversity in chromosome aberrations. Annex A, Paragraph A45 of ICRP 103 (2007) on radiation-associated tumours states "evidence for the presence of specific mutational signatures of radiation is currently lacking". The European research initiative DoReMi has this research area as one of its main priorities Salomaa *et al.* (2015). Pernot *et al.* (2012) provides a comprehensive review of attempts to identify biomarkers that would be of use in the epidemiology of radiation risk. There is current research into biomarkers for thyroid cancer Dom *et al.* (2012), Suzuki *et al.* (2015) and in experimental systems Sherborne *et al.* (2015).

104. The multistep model of carcinogenesis was proposed by Armitage and Doll (1954) and is supported by molecular data from human colon cancers Vogelstein *et al.* (1988). For a comprehensive review of cancer biology see Chapter 18 (p273) in Hall and Giaccia (2011). For a recent review see Mullenders *et al.* (2009).

105. Stem cell biology and its implications for radiological protection are discussed by Hendry *et al.* (2016). The important role of stem cells in carcinogenesis generally is supported by the recent observations of a strong correlation between cancer incidence and the number of lifetime stem cell divisions Tomasetti *et al.* (2017).

106. Adaptive responses appear to involve transcriptional modulation of specific gene sets Tapio and Jacob (2007). See Mullenders *et al.* (2009) for in vivo studies showing evidence of adaptive response, and Wolff (1996) on adaptive responses to very low radiation doses.

107. So-called "non-targeted effects" are reviewed by Morgan (2003a), Morgan (2003b). UNSCEAR (2012a) reviews more recent evidence. Little (2010) considers the shape of the dose response in light of non-targeted effects. Not all authors would categorise the adaptive response and genomic instability as non-targeted effects, but they are included in Little's 2010 review. A contrasting review of non-targeted effects is Hei *et al.* (2011).

108. Ding *et al.* (2005), Hauptmann *et al.* (2016) and Wahba *et al.* (2017) describe qualitative differences in cellular responses to low dose radiation. The proteomics of low dose radiation is reviewed in Leszczynski (2014). Brooks *et al.* (2016) reviews

molecular and cellular events after exposure to ionizing radiation at low dose-rate.

109. Preston (2017) and Ruhm *et al.* (2017) explain how the combination of biological and epidemiological data should, in time, allow development of a data-driven model of the dose-response curve at low dose and low dose-rate. The Euratom project DoReMi has produced a substantial body of literature towards a better understanding of the biological effects of ionizing radiation at low dose and low dose-rates. The project is described in Belli *et al.* (2011), Aerts *et al.* (2014), Belli *et al.* (2015) and the project's publications with their abstracts are listed at www.melodi-online.eu/DoReMi/Publications.html.

110. Animal studies of carcinogenesis directly illustrate the diversity of dose response curves for different cancers. See paragraph 118.

111. Premature cellular senescence after low dose-rate radiation is described in Yentrapalli *et al.* (2013b), Yentrapalli *et al.* (2013a), Rombouts *et al.* (2014).

112. A comprehensive review of radiation specific biomarkers from 2012 Pernot *et al.* (2012) has recently been updated Hall *et al.* (2017) emphasising the potential of a systems biology approach to integrate the rapidly growing "omics" into a mechanistic understanding.

113. Bouffler (2016) reviews variation in individual radio-sensitivity. Individual sensitivity was one of the foci of the Euratom DoReMi research programme Belli *et al.* (2011), Aerts *et al.* (2014), Belli *et al.* (2015), with resulting advances in understanding of susceptibility due to genetic and epigenetic mechanisms Sagne *et al.* (2013), Flockerzi *et al.* (2014), Gurtler *et al.* (2014), Pernot *et al.* (2014), Sagne *et al.* (2014), Schanz *et al.* (2014). An ATM mutation is emerging as a relative contraindication for radiotherapy. For example, ATM mutations in female breast cancer patients predict for an increase in radiation-induced late effects Iannuzzi *et al.* (2002). A-T heterozygotes may comprise 1% of the population, 4% of the cancer population and up to 14% of the breast cancer population Swift *et al.* (1991). The emerging field of radiogenomics aims to understand genetic risk factors for adverse reactions to radiotherapy (for a review see Roberson *et al.* (2016)) .

114. Biological mechanisms whereby ionizing radiation causes cardiovascular disease have been reviewed recently in Stewart (2012), Baselet *et al.* (2016) and Boerma *et al.* (2016). Atherosclerosis is described in Hansson and Hermansson (2011). Animal models have contributed to our understanding of the role of inflammation Monceau *et al.* (2013), Mathias *et al.* (2015) and also of the disruption of cellular organization Barjaktarovic *et al.* (2013) in low dose radiation damage to the heart.

115. Ainsbury *et al.* (2016) offer a recent review on mechanisms of cataract induction by ionizing radiation. Genomic damage is specifically discussed in Worgul *et al.* (1989), oxidative stress in Hamada (2016) and downstream effects including cell division in Jacob *et al.* (2012).

116. Authors' summary.

EXPERIMENTAL STUDIES THAT INFORM RISK ASSESSMENT

117. See, for example, Peacock *et al.* (2000) and Brooks *et al.* (2009) with reviews in Dauer *et al.* (2010) and Morgan and Bair (2013). Figure 2.4 in BEIR VII (2006) (p59) illustrates abnormal chromosome count data as a function of dose from studies of thousands of cells exposed up to 50 mGy. The

original data sources are Pohl-Ruling *et al.* (1983) and Lloyd *et al.* (1992).   For studies examining values of DDREF see Lloyd *et al.* (1992), Thacker (1992), UNSCEAR (2000b), Cornforth *et al.* (2002b).

118. Figure 3b in Haley *et al.* (2015) reviews dose response curves from 11 animal carcinogenesis experiments. These experiments and others are described on p73-4 of BEIR VII. The original data for leukaemia in mice is in Bouffler *et al.* (1996b), Bouffler *et al.* (1996a), Bouffler *et al.* (1997); for mammary cancer in mice in Ullrich *et al.* (1987); and for mammary cancer in rats in Shellabarger *et al.* (1980). Radiation induced skin cancer in mice and rats is reviewed in Coggle and Williams (1990).

119. Figures 5 in Haley *et al.* (2015) reviews life shortening data from 16 mouse studies. Life shortening studies in dogs are reviewed in Thompson *et al.* (1989) and Muggenburg *et al.* (2008).

120. Section A16, page 217 in ICRP 103 (2007) describes how the risk estimates for human heritable disease were calculated. Searle (1974) and Sankaranarayanan and Chakraborty (2000) review the large body of data on mutagenesis studies in mice whilst Nakamura *et al.* (2013) compare human and animal data.

121. ICRP (2003), ICRP 103 (2007).

122. Pages 246-250 of BEIR VII (2006) describe the methodology and results for calculating DDREF from animal experiments and human epidemiological data combined. Haley *et al.* (2015) performed an equivalent analysis with a larger database of animal experiments and a different methodology and challenged the BEIR estimate. Different radiation protection organisations use different measures of DDREF. ICRP used a different method and considered that a value of 2.0 was most appropriate for radiation protection purposes ICRP 99 (2005). There is a growing indication that the LDEF and DREF components of DDREF may differ Niwa (2010) with higher values suggested for DREF, e.g. Paunesku *et al.* (2017). Shore *et al.* (2017) conducted a meta-analysis of low dose-rate epidemiologic studies that provide dose-response estimates of total solid cancer risk in adulthood in comparison to corresponding acutely-exposed atomic bomb survivor risk, in order to estimate a dose rate effectiveness factor (DREF) of between 1 and 2. Ruhm *et al.* (2015) describe the historical development of the DDREF concept in light of emerging scientific evidence on dose and dose-rate effects, summarises the conclusions recently drawn by a number of international organisations, mentions current scientific efforts to obtain more data on low dose and low dose-rate effect effects at molecular, cellular, animal and human levels, and discusses future options to improve and optimize the DDREF concept for the purpose of radiological protection.

123. Authors' summary.

PERSPECTIVES

124.
   a.   Smith (2007), Cologne and Preston (2000).
   b.   Lim *et al.* (2013). For individuals in situations where radiation levels are high, radon dose represents a large risk and exposure prevention measures are well justified.

125. Smith (2007), Cologne and Preston (2000) Lim *et al.* (2013).

126. Authors' summary. Small health risks of radiation are due in part to the active prevention policies which have been implemented

and improved for decades in both industry and medicine. Clarke and Valentin (2009), Figure 1 in Inkret (1995).

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