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Radiation and Childhood Cancer:
the risks of low-level radiation with particular reference to cancer incidence and mortality among children

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https://www.childrenwithcancer.org.uk
Salus populi suprema lex esto - Cicero (109 BC- 46 BC)
The health/welfare of the people is the supreme law

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Executive Summary

This report was commissioned by the UK charity “Children with Cancer UK” to examine radiation and childhood cancer. It has two main aims. The first is to provide an independent scientific examination of the health effects of ionising radiation in general terms in response to recent reports suggesting that radiation may be less dangerous than thought in the past. The second aim is to discuss UK cancer incidence and mortality among children below 15 years of age in order to improve our understanding of the causes of childhood cancer.

Recent authoritative epidemiological studies and corroborative articles provide strong scientific evidence that radiation risks as presently presented do not overestimate radiation risks. Indeed the opposite is the case: much evidence indicates we need to increase our perceptions of radiation risks and tighten current radiation limits, especially for women of child-bearing age and for boys and girls – the subject of this report.

Contrary to popular perception, low doses of radiation are serious matters. For example, even very low levels of background radiation are estimated to cause about a fifth of all childhood leukemias. Official US reports state that radiation risks in children are ten times greater than in adults, but these increased risks are poorly addressed in ICRP risk models or limits; for example, no UK risks or limits are published for radiation exposures to boys and girls, or to women for that matter.

Childhood cancer is a worrisome issue in the UK: the annual cancer death toll of children is about six times greater than child deaths from road accidents. Just as worrying is the fact that the incidence of childhood cancer has been rising inexorably for more than the past two decades and we are little closer to determining the cause or causes than we were 20 years ago. Radiation is the only external environmental factor for which incontrovertible evidence exists of its potential to cause cancers, especially blood cancers, i.e. leukemias.

Radiation exposures to children from CT scans and radiation therapy remain matters of concern, as several powerful studies report ill effects - including increased leukemias - arising afterwards. Of course clinical benefits arise from CT scans, but it is still recommended that boys and girls should be not exposed to CT diagnostic scans unless two independent clinical assessments have been made and the consequent risks fully explained to their parents/guardians.

From cellular studies and epidemiological evidence, this report suggests that about half of infant and childhood leukemias arise from radiation exposures in utero. This means that radiation is a teratogen, like thalidomide. The main difference is that with thalidomide the effects – malformations – are apparent at birth whereas with radiation the effects – mutations in blood-forming tissues - only become apparent in later months and years. Therefore it is recommended that precautionary steps should be taken to protect pregnant women and to increase their rights not to be irradiated. For example, official advice should be issued that pregnant women should not to be subject to radiation exposures from any medical procedures and not to be scanned by airport security devices (unless consented to). Information should be made available about the increased risks of residing within 5 km of industrial facilities emitting large amounts of radioactivity.

Perhaps the most important recommendations are that the Precautionary Principle should be used when assessing radiation risks to children and women and that a national preventative programme against childhood cancer should be established by the NHS. Several technical recommendations are also made.
Acknowledgements

The author thanks Dr Ausrele Kesmeniene for information on IARC's EPI-CT study; Ian Goddard www.iangoddard.org for permission to use the graph on page 14 and for his help with the graph on page 52; and Peter Roche for his help in making the references accessible via the web.

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Any errors remain the sole responsibility of the author.

Introduction and Aims

1. This report has been commissioned by the UK Charity “Children with Cancer UK” to study the effects of low-level radiation on children. It has two main aims. The first is to provide an impartial scientific examination of the health effects of ionising radiation in general terms. This is in response to recent reports suggesting that radiation may be less dangerous than thought in the past. The second aim is to discuss cancer incidence and mortality among children below 15 years of age in order to improve our understanding of the causes of childhood cancer.

2. As radiation and its close precursor radioactivity are relatively rarely discussed in the popular media, it would be fair to say that a lack of knowledge exists about them and their risks among the general public. They are certainly not on the national syllabi of schools in England and Wales, and relatively few Universities or Colleges teach these matters - especially as regards their health effects.

3. Partly as a result, it is common for people to feel apprehensive about radiation. Because we cannot hear, see, feel, or smell radiation, we tend to fear it. Meara (2002) gave additional reasons - radiation is often difficult to avoid, causes hidden or irreversible damage, is dangerous to future generations, and its risks are the subject of differing views among scientists. But above all, radiation is feared because its exposures can cause dreaded illnesses, and prime among these is cancer.

4. A related matter is that radiation, including its risks, doses, biology, statistics and epidemiology are complex matters - certainly when first approached. They are difficult to describe with the result that the mainstream media seem to carry fewer and fewer articles on them. This report shall make an effort to explain these matters as simply as possible without doing damage to the science. For example, it is written in plain English rather than in academic style. It avoids jargon or insider terms, and explains scientific acronyms and abbreviations. It is aimed at an audience of first-year college students, but is fully referenced so that everyone can check data sources and statements in the report, and can read further.
5. Although cancer is not the only effect of exposures to radiation in children, it is by far the most studied one. We shall discuss other effects including cardiovascular diseases (CVD) and stroke below. Examinations of children exposed to high levels of radiation from various studies, including from the Chernobyl nuclear disaster in 1986 (Fairlie, 2016) reveal a wide variety of other adverse effects to children from radiation. In addition, Fucic et al (2016) observed higher frequencies of dicentric and ring chromosomes, chromatid and chromosome breaks, acentric fragments, translocations, and micronuclei in the germ cells of children in areas contaminated by the fallout from Chernobyl.

6. This report reviews recent evidence of radiation risks up to January 2021 relying almost exclusively on scientific articles published in peer-reviewed journals. Inevitably, there remains an element of subjectivity in the choice of references, and there may well be studies which have escaped attention. Also, this report is a ‘snapshot’ of a moving scene as new findings will change our understanding of radiation’s effects, just as they have in the past. European, including UK, data are prioritised in this study but, in their absence, international (particularly US and Canadian) references and sources of data have been cited.

7. At the outset, it must be admitted that there is no such thing as completely bias-free reporting in science. The best that can be done is to adhere closely to the available evidence and to be transparent about one’s own bias or biases. With that in mind, this report is written from a public health point of view. In other words, to the extent that this report is biased, it is towards public health concerns.

**Part 1: Radiation and its Risks**

(a) What is radiation?

8. Radiation is the collective term given to electromagnetic waves\(^1\), most commonly in the form of gamma rays\(^2\) and X-rays\(^3\). However the term also applies to energetic particles such as beta particles\(^4\), alpha particles\(^5\) and neutrons\(^6\). Conventionally, most scientific studies are concerned with **ionising radiation**: that is, radiation with sufficient energy to knock electrons out of the orbital shells around atomic nuclei, ie to “ionise” these atoms. The reason

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\(^1\) The electromagnetic spectrum is generally divided into seven regions, in order of decreasing wavelength and increasing energy and frequency. These are: radio waves, microwaves, infrared (IR), visible light, ultraviolet (UV), X-rays and gamma rays. This report is mainly concerned with the latter two most energetic regions.

\(^2\) Gamma rays are a penetrating form of radiation arising from radioactive decay.

\(^3\) X-rays are another form of penetrating radiation produced by the sudden deceleration of electrons when they collide and interact with metal targets.

\(^4\) Beta particles are negatively charged electrons.

\(^5\) Alpha particles consist of two protons and two neutrons bound together into a particle identical to a helium nucleus.

\(^6\) Neutrons are neutrally charged constituents of the nuclei of atoms.
is that it is usually thought that radiation’s adverse health effects are mostly due to such ionisations particularly of DNA and RNA macromolecules.

9. Ionising radiation is different from the radiation used by mobile phones, 3G, 4G, 5G networks and radio and TV stations. These sources use non-ionising radiation, that is radio-frequency (RF) radiation, with lower energy levels. Some authorities (IARC, 2018; PHE, 2011) consider that the evidence for health effects from exposures to RF sources is not strong. The main report does not discuss this type of radiation due to length considerations, but see Appendix A.

10. The International Agency for Research on Cancer (IARC), an agency of the United Nations’ World Health Organisation (WHO), has stated that radiation, including X-rays gamma radiation and neutrons, are carcinogenic to humans (IARC, 2018). In addition, in utero radiation exposures can be mutagenic to the fetus and embryo, that is, both carcinogenic and teratogenic. These effects depend on the size of the exposure and the stage of fetal development.

11. Table 1 shows average doses from various exposures to radiation and as found in some large epidemiology studies.

<table>
<thead>
<tr>
<th>Source of exposure</th>
<th>average dose* - mSv</th>
<th>average dose rate - mSv/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation therapy for cancer treatment</td>
<td>~1,000 to ~16,000 mSv</td>
<td></td>
</tr>
<tr>
<td>International space station</td>
<td></td>
<td>170 /year</td>
</tr>
<tr>
<td>Radiation worker annual limit (1)</td>
<td></td>
<td>20/year</td>
</tr>
<tr>
<td>Pediatric abdominal CT scan</td>
<td></td>
<td>~25</td>
</tr>
<tr>
<td>UK background radiation</td>
<td></td>
<td>2.7/year</td>
</tr>
<tr>
<td>Public limit **</td>
<td></td>
<td>1/year</td>
</tr>
<tr>
<td>Round-trip flight, London to New York</td>
<td></td>
<td>~0.1</td>
</tr>
</tbody>
</table>

** Average doses in epidemiological studies **

<table>
<thead>
<tr>
<th>Source of exposure</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-bomb survivors in LSS cohort (2)</td>
<td>200</td>
</tr>
<tr>
<td>Medical X-rays - breast dose (4)</td>
<td>100</td>
</tr>
<tr>
<td>US Nuclear workers (5)</td>
<td>25</td>
</tr>
<tr>
<td>(former) diagnostic exposures in utero (3)</td>
<td>~10</td>
</tr>
</tbody>
</table>

* effective whole-body doses, except in medical exposures where doses are to specific organs

**UK public dose limit is defined in Schedule 3 of the Ionising Radiations Regulations 2017

1. International Commission on Radiological Protection (1991)

7 However many of the adverse effects seen from radiation exposures are also seen from exposures to chemical and biological agents which do not ionise cellular matter.

8 Resulting in malformations in the resulting babies

9 Dose is the amount of radiation absorbed by the body. The unit for dose is the sievert (Sv) or gray (Gy) which means one joule of energy deposited in one kilogram of tissue.

10 For the purposes of this report, the unit Sv is used for exposures expressed in reports in grays (Gy) and sieverts (Sv).

(b) External and Internal Radiation

12. Many people think about X-rays when they hear the word ‘radiation’ but they are only one example of two main types of radiation. The other type is internal radiation, for example when we breathe in radioactive radon in the air. This type of radiation is the more serious and the less understood of the two kinds of radiation. The best description of these risks for lay persons remains the report of the UK Government’s Committee on the Radiation Risks of Ionising Radiation (CERRIE, 2004).

13. When we assess internal radiation we need to discuss radioactivity. Many people are unsure of the difference between radiation and radioactivity: here is the distinction. When the nucleus of an atom is unstable\(^{11}\), ie it has too much energy, it will lose energy at characteristic intervals to become more stable. When this happens, it emits particles and/or energy. This process is called radioactive decay or radioactivity and the particles and energy given off are called radiation.

14. Unstable nuclei are called radionuclides\(^ {12}\) (often shortened to “nuclides”) and when they disintegrate they commonly emit alpha particles, beta particles, and gamma rays. Less commonly, they emit protons, positrons, X-rays and neutrons. These all come from the heart of the atom – its nucleus. Commonly mentioned radionuclides are caesium-137, strontium-90, radon-222, radium-226, hydrogen-3 (usually called tritium) and carbon-14.

15. No comprehensive hazard index exists for radioactive nuclides for scientists or members of the public (RWMAC, 1993). Kirchner (1990) has stated that such a system would need to have regard to the following factors in addition to simple ICRP radiotoxicity\(^ {13, 14}\), nuclide transport and cycling in the biosphere, nuclide pathways to humans, nuclide fractions ingested or inhaled, organic binding, and nuclide decay chains and their decay products. Few of these factors are presently accounted for in official models of radiation risks. The result is that much uncertainty surrounds the dose estimates from internal radiation as discussed in the CERRIE report in 2004.

(c) Radiation’s Effects

16. Exposures to ionising radiation have two main types of effects:

   (a) cell-killing at higher doses and

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\(^{11}\) because imbalances of electrical charges give the nuclei too much energy

\(^{12}\) a radionuclide is an element which is radioactive, ie gives off radiation

\(^{13}\) Radiotoxicity means the hazard associated with inhaling or ingesting or absorbing via skin a radioactive gas or liquid or solid

\(^{14}\) Simple ICRP radiotoxicity means the ICRP’s dose conversion factors for radionuclides (expressed as Sv per Bq). These factors are in most cases judged to be inadequate ie too low.
(b) probabilistic\textsuperscript{15} (also termed stochastic\textsuperscript{16}) from lower doses

17. Examples of cell-killing include erythema (skin reddening), skin burns, nausea, vomiting, dizziness, all occurring within a few hours or days. At higher doses, eye cataracts, severe skin burns, and hair loss occur. At very high doses, loss of consciousness, coma and eventual death within a few days or weeks can occur, depending on the level of medical care.

18. Examples of probabilistic effects are cancers, genetic mutations and cardiovascular diseases: these can have long latency periods lasting years or decades. The latency period is the time for the radiation’s probabilistic effects to start to occur. After then, cancers will continue to arise sometimes for very long periods. For example, excess thyroid cancers are still occurring among the survivors of the Hiroshima and Nagasaki bombings in Japan in 1945, more than 60 years later (Imaizumi et al, 2006). The rate at which they arise depends on the initial dose.

19. The latter, slower, effect means that radiation results in an increased probability of cancer. Put simply, one doesn’t get a worse cancer but getting a cancer becomes more likely. Radiation exposures are therefore like cigarette smoking: not everyone who smokes will get cancer, but the more one smokes the greater one’s chance of getting a cancer. Some government sources and reports in the media have found it difficult to grasp or to accept the slower, later effect, however it is by far the more significant one.

(d) Cancer

20. Cancer is the name for a large group of diseases which are very common and often fatal. For example, according to the UKCRC, half of UK people born after 1960 will be diagnosed with cancer during their lifetimes.

21. Cancer results when a single stem cell\textsuperscript{17} is damaged so that it fails to respond to signals telling it to stop dividing. As a result, the stem cell and its descendants divide continuously producing a mass of cells, ie a tumour, which if untreated can be fatal. The type of cancer depends on which organ the stem cell is found. Most stem cells are found in the gut lining, bone marrow and skin, but they are to be found in every organ of our bodies.

22. In adults, the production of new cells is closely controlled and just keeps pace with cell loss. This means that stem cells divide only when new cells are needed; if new cells are not needed, the division of stem cells is prevented by signals from nearby cells. However, sometimes this control mechanism doesn’t work and a cancer results.

\textsuperscript{15} probabilistic means we cannot be certain about these effects but we can judge whether or not they are likely, and act accordingly.
\textsuperscript{16} stochastic means having a random probability distribution that may be analysed statistically but may not be predicted precisely.
\textsuperscript{17} stem cells proliferate indefinitely to produce more of the same stem cell and other cells at the same time. For example, when a bone marrow stem cell reproduces, it creates a bone marrow cell AND another stem cell.
23. For some adult cancers, as many as five or more separate DNA mutations may be needed for a cancer to result, but in childhood tumours, fewer are needed. The need for several mutations explains why cancers often appear several years after the original exposure. An initial exposure to radiation (or other agent) causes only the first of several mutations which are required, with the other mutations being caused in later years most likely by our continual exposure to background radiation. This does not occur with childhood cancers whose aetiology\(^{18}\) is still poorly understood and is discussed below.

24. Blood cancers include leukemias and are characterized by an abnormal increase in the numbers and sizes of white blood cells. They do not result in tumours but in large numbers of deformed blood cells (see figure below) which are unable to carry out their normal functions of protecting us against bacterial and viral infections.

The figure below shows bone marrow cells (stained violet) exhibiting acute lymphocytic leukemia amongst normal (stained buff) white blood cells.

25. The numbers and types of cancer in the UK caused by radiation (see Parkin and Darby, 2011) are now monitored by the new UK Health Security Agency (UKHSA) formed in April 2021. This government agency is responsible for health protection and infectious disease capability, and is an executive agency of the UK Government’s Department of Health and Social Care.

26. Previously, radiation matters had been covered by the National Radiological Protection Board set up in the 1950s, then by the Health Protection Agency, then by Public Health England, then by the short-lived National Institute for Health Protection. It is submitted that these continually-changing and increasingly short-lived organisational labels do not instil confidence that proper attention is being devoted to public health matters, particularly to radiation risks, in the UK. Regardless of these agency labels, the reality is that Government support for public health matters (including attention to radiation issues) was systematically reduced over the past two decades. In addition, many local authorities have been forced to dismiss their public health staffs because of severe cuts in central Government funding. The

\(^{18}\) aetiology means the cause or causes of a disease or condition.
Covid-19 pandemic has certainly changed attitudes to public health but whether this means that more attention and staffing will be given to radiation issues remains to be seen. It is worrisome, for example, that little, if any, radiation expertise exists within the Government’s Department of Health and Social Care.

(e) Leukemia/Lymphoma Types

27. Leukemias are cancers of blood-forming cells. Leukemia types are first divided into acute and chronic forms. Acute leukemia means the rapid increase of immature (malignant) blood cells which results in the bone marrow being unable to produce healthy blood cells. Due to their rapid accumulation, many cells enter the bloodstream and spread to other organs. Immediate treatment is required. Acute leukemia is the most common form of leukemia in children. Chronic leukemia means the increase of mature, abnormal, white blood cells over months or years. Whereas acute leukemia must be treated immediately, chronic forms are usually monitored for some time before treatment. Chronic leukemia mostly occurs in older people not children.

28. Secondly, leukemias are divided according to which kind of blood cell is affected, either lymphocytic (lymphoblastic) or myeloid (myelogenous). In the former, the cancer occurs in marrow cells that form lymphocytes, ie infection-fighting cells. In myeloid leukemias, the cancer occurs in cells that form red blood cells, some other types of white cells, and platelets. Combining these two classifications provides a total of four main categories as follows:

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytic</td>
<td>Acute lymphocytic leukemia (ALL)</td>
<td>Chronic lymphocytic leukemia (CLL)</td>
</tr>
<tr>
<td>Leukemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myeloid leukemia</td>
<td>Acute myelogenous leukemia (AML)</td>
<td>Chronic myelogenous leukemia (CML)</td>
</tr>
</tbody>
</table>

29. Most of the literature on childhood leukemia concerns acute lymphocytic leukemia which this report will consider. However one study (Puumala et al, 2015) has examined acute myeloid leukemia. The two types are similar in their effects: differences between the two appear to be matters of degree rather than types.

(f) Radiation Risks

30. Radiation protection, it is necessary to quantify (ie, put numbers on) radiation’s health risks, but we shall see that this is easier said than done. For example, the International Commission on Radiological Protection (ICRP) - an unofficial trade body for radiation whose recommendations are influential among some western Governments - currently expresses

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19 the word “risk” can either mean the hazard(s) from a particular activity or agent, or the probability of this hazard occurring. In many cases, people use the word to mean both. In this report, we use the term to mean probability.
the risk of a fatal cancer arising in all persons from low-LET\textsuperscript{20} radiation as 5\% per sievert (a measure of the amount of radiation: abbreviation = Sv). What this means is this. If, say, 100 adults were each exposed to 10 millisieverts (mSv) of radiation, then 5\% (ie 5) of them would die from cancer.

31. The 5\% per Sv risk is important as many Governments use it in drawing up their dose limits, release limits, and codes of practice. However many problems exist with the current risk estimate, not the least of which is that it has been in effect for more than five decades during which new data and information (US National Research Council, 2006) indicate that it should be revised upwards. Another major problem is that it is a single estimate — see Appendix G.

32. Radiation’s effects depend on many factors including
   a) Dose
   b) Age at time of exposure, including in utero exposures
   c) Age at time of analysis
   d) Gender
   e) Genetic predisposition
   f) Whether internal or external radiation
   g) What endpoint is used, eg just cancer
   h) Whether fatalities or incidence is used
   i) The kind of radiation – eg whether gamma rays or alpha particles, and
   j) The organs exposed – eg whether bone marrow or liver or lungs etc

33. Official models address the first and last two factors and partly address (h) but not the rest. It is recommended that official agencies should try to address the remaining factors: questions will remain to the extent that they do not. Also see discussion in Appendix G.

34. For example, we know that age at time of exposure – the subject of this report on children - is an important factor for determining radiation risks. See chart on page 52. But, as we shall see, age is poorly addressed in official recommendations and limits, no matter which country is examined. For example, there are no official limits published for radiation exposures to boys and girls, or to women members of the public, in the UK or US. In the US and UK, legal provisions exist for women employees who indicate they are pregnant.

35. Other problems remain with how we estimate (a) actual exposures (ie doses) to radiation and (b) its hazard (ie the number of cancers). The final risk to people is the product of these two factors (ie dose times cancers per unit dose). For more detail, see Appendix B which considers additional problems with radiation risks and Appendix C which considers why the system used for assessing chemical risks is considerably safer than that for radiation risks.

36. Numerical risks from radiation are derived from two main sources (a) cellular studies and animal experiments, and (b) epidemiology, ie studies of ill health in human populations.

\textsuperscript{20} low LET means low Linear Energy Transfer. Gamma rays and many beta particles are classified as low LET as they deposit relatively small amounts of energy along their paths.
One of the most influential of the latter studies is the Life Span Study (LSS) of the survivors of the atomic bombs dropped on Japan in 1945 (Ozasa et al, 2012).

(g) The Life Span Study (LSS)

37. The LSS study was set up in 1951 and continues to this day. Its findings constitute the main basis for assessing radiation risks in the system of radiation protection developed by the International Commission on Radiological Protection (ICRP, 2007). However, the LSS survivors were exposed to high-energy gamma rays and neutrons lasting a fraction of a second from the bomb blasts, whereas common occupational and environmental exposures involve protracted exposures to mainly alpha and beta particles at low dose-rates. The use of the LSS study for determining the risks from the latter exposures remains a contentious issue - see Appendix D below on DDREF.

(h) The INWORKS studies

38. More recently, the much larger\(^{21}\) International Nuclear Workers’ Study (INWORKS) of workers in France, United Kingdom, and United States (Hamra et al, 2016) examined associations between low dose-rate radiation and mortality from leukemia/lymphoma (Leuraud et al, 2015), circulatory disease (Gillies et al, 2017), and solid cancers (Richardson et al, 2018).

39. The main conclusion from these three studies is that their risk estimates are broadly similar to the LSS risk estimates (NCRP 2018a; Berrington de Gonzalez et al, 2020). But the INWORKS studies are now the preferred source for deriving radiation risks to adults and are important for the reasons set out below. These reasons apply to the pioneering Leureud et al (2015) study but the other two INWORKS studies have broadly the same findings.

40. The INWORKS study

   a. provided “strong evidence of a dose-response relationship between cumulative, external, chronic, low-dose, exposures to radiation and leukemia”.
   b. confirmed radiation risks even at very low dose rates (average = 1·1 mGy per year).
   c. unlike the LSS study, it observes risks at low dose rates rather than extrapolating them from high dose rates.
   d. found risks do not depend on dose rate thus contradicting the ICRP’s use of a Dose and Dose Rate Effectiveness Factor (DDREF) which acts to reduce by half the ICRP’s published radiation risks. (see Appendix D)
   e. found radiogenic leukemia risks decline linearly with dose, contradicting earlier studies suggesting a lower, linear-quadratic relationship for leukemia.
   f. strengthened the Linear No-Threshold (LNT) model of radiogenic risks, as it now applies to leukemias as well as solid cancers. and
   g. found no evidence of a threshold below which no effects are seen
   h. and the solid cancer study (Richardson et al 2018) found a trend of increasing risk of solid cancer by attained age.

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\(^{21}\) Over ~300,000 workers as opposed to ~85,000 in the LSS
41. The main findings from the Leuraud et al study (2015) are shown in graph 1.

Graph 1: Relative Risk of Acute Lymphatic Leukemia (all ages)

![Graph 1: Relative Risk of Acute Lymphatic Leukemia (all ages)](image)

42. A recent exhaustive review (Hauptmann et al, 2020) of the INWORKS studies examined possible sources of bias\(^{22}\) and confounding\(^{23}\). It concluded that the new epidemiological studies directly support the conclusion of excess cancer risks from low doses of ionising radiation, with little evidence of bias and confounding. Furthermore, the magnitude of the cancer risks from these low exposures was statistically compatible with the dose-related cancer risks of the atomic bomb survivors. This is similar to the findings of Berrington et al (2020) who reviewed the INWORKS studies using specialist statistical and epidemiological methods to look for evidence of bias and found none.

**(i) The Linear No-Threshold (LNT) Model of Radiation’s Effects**

43. By using the INWORKS results, we now have reliable data to derive the levels of risks from radiation exposures to adults down to about 50 mSv or so. To estimate risks at even lower doses we have to use computer models which extrapolate risks down to very low doses close to zero. Various models exist – see graph 2 below.

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\(^{22}\) statistical bias occurs when a model or statistic is unrepresentative of the population being studied: several sources of bias can occur, eg selection bias

\(^{23}\) Confounding occurs when an extraneous factor causes inaccuracy in the estimated measure of an association, eg smoking in a lung cancer study
The most common and widely-accepted model is the Linear No-Threshold (LNT) model – shown by the solid blue line in the above graph. This posits that biological damage from radiation is linearly related to the amount of exposure and is always harmful, i.e. it has no threshold below which no effects exist. In other words, there is no “safe” dose of radiation. Although different (i.e. largely political) views exist on the validity of the LNT, we shall see that a great deal of scientific evidence supports it. This includes epidemiological evidence from background radiation, from medical exposures, and most important from the recent INWORKS series of occupational studies discussed above. Readers should be aware that, as we are all exposed to small amounts of background radiation (discussed below), there is, in practice, no such thing as zero dose, as shown in the graph above. However it is commonly used to provide a theoretical datum point for use in estimating the shape of dose response curves.

On the other hand, some observers consider that the LNT should not be used but this has been refuted by many observers including Crowley et al (2015). Some reports even consider that exposures to low radiation levels are beneficial and protect the human body against deleterious effects of high levels of radiation. This is termed the hormesis model but the conclusion from the latest independent evidence cited in this video and many other studies is that hormesis is of little, if any, relevance when considering radiation risks.

When we come to childhood exposures and their risks, the graphic below from Goddard (2016) usefully plots the results from three recent epidemiology studies on to one graph. It clearly shows that the LNT model is a good fit for the dose-response relationship for
children. It also shows that childhood risks extend down to below 10 mSv, contrary to suggestions that no risks exist below 100 mSv.

(j) Authoritative Views on LNT

47. Four older international official reviews: US NCRP Report No 136 (2001), National Academy of Science BEIR VII (2006) ICRP 99 (2006) and UNSCEAR (2008) all stated the LNT was the most prudent model for radiation protection purposes. For example in 2006, the chair of BEIR VII, Professor Richard R. Monson, associate dean for professional education and professor of epidemiology, at the Harvard School of Public Health, Boston US stated "The scientific research base shows that there is no threshold of exposure below which low levels of ionizing radiation can be demonstrated to be harmless or beneficial".

48. In 2009, UK and US scientists (Little et al, 2009a) examined the matter in considerable detail. They discussed (i) the degree of curvature in the cancer dose response within the Japanese atomic bomb survivors and other groups, (ii) the consistency of risks between the Japanese and other low-dose cohorts, and (iii) biological data on mechanisms. They also concluded linearity was "the best bet". Also in 2009, the head of the US Environmental Protection Agency’s radiation section reviewed the matter in an influential article. He stated "Although recent radiobiological findings indicate novel damage and repair processes at low doses, LNT is supported by data from both epidemiology and radiobiology. Given the current state of the science, the consensus positions of key scientific and governmental bodies, as well
as the conservatism and calculational convenience of the LNT assumption, it is unlikely that EPA will modify this approach in the near future” (Puskin, 2009).

49. This conclusion was validated by the US NCRP in 2018. The NCRP’s Committee stated that the available epidemiological data were broadly supportive of the LNT model and that no alternative dose-response relationship appeared more pragmatic or prudent for radiation protection purposes.

(k) Conclusion re LNT

50. Regardless of a few differing views on LNT (mostly from the US), the reality is that most concepts used in radiation protection today throughout the world are fundamentally based upon it. For example, the LNT underpins the concepts of absorbed dose, effective dose, committed dose, and the use of dose coefficients (ie Sv per Bq of a radionuclide). It also allows radiation doses (i) to be averaged within an organ or tissue, (ii) to be added from different organs, and (iii) to be added over time. LNT also permits annual dose limits; the practice of optimization -ie comparison of practices; radiation risk assessment at low and very low doses; individual dosimetry with passive detectors; collective dose, and dose registers over long periods of time. The LNT also underpins all legal regulations in radiation protection in the UK and in the rest of the world. Indeed, if the LNT were not used, it’s hard to imagine current radiation protection systems existing at all. However this statement should not be construed to mean that the LNT is used because it’s convenient: the LNT is used because the scientific evidence for it is comprehensive and cogent.

(I) Dose and Dose Rate Effectiveness Factor (DDREF)

51. A second important issue in radiation protection is the rather strange hypothesis of a reduction of radiation-associated cancer risk per unit dose at low doses and low dose-rates (Jacob et al, 2009; Rühm et al, 2015a, b). Such a hypothesis was derived in the past from old observations in laboratory cell studies and animal experiments of lowered effects from low doses compared to high doses, and from low dose-rates compared to high dose-rates. The result was that the observed risks from the (high dose, high dose-rate) LSS studies were arbitrarily halved by the ICRP in its system of radiation protection by its introduction of a so-called “dose and dose-rate effectiveness factor” (DDREF) (ICRP 2007).

52. However this practice is profoundly unconservative24 and is in breach of the Precautionary Principle discussed below. It also has been shown to be incorrect by the INWORKS studies (Leureud et al, 2015) which observed that the risks from occupational exposures at low doses and low dose-rates were similar in size to those from the Japanese high dose, high dose-rate exposures. Therefore, the INWORKS studies proved there was no reduction in risk at low doses and low dose rates.

53. In fact, the evidence from INWORKS has now been compared to LSS in several recent reviews of the epidemiological evidence on DDREFs (Shore et al, 2017; Hoel, 2018; Kocher et al, 2018; Wakeford et al, 2019; and Leuraud et al, 2021). These influential reviews also do

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24 Does not err on the side of caution
25 Excluding data from the unreliable Mayak workers’ study
not support the conclusion of a reduction of risk at low dose-rates and instead point to the conclusion that DDREFs should not be used. The ICRP is currently reviewing relevant cellular, animal, and human studies on the matter (Rühm et al., 2018). A new approach for estimating low dose-rate radiation exposure may well emerge from the literature (Chadwick, 2017).

54. Indeed, the WHO in its report (2013) on health effects from the exposures at Fukushima explicitly stated that DDREFs should be avoided. It stated “The question therefore arises as to whether the risk estimates for the atomic bomb survivors are applicable to populations that have accumulated radiation doses on the order of 100 mGy or below over a long time. Thus far, radiobiological research has provided ambiguous answers to this question. Based on the findings of the two meta-analyses discussed above (74,92), which showed similar risks for protracted and acute exposures, the Human Risks Assessment Expert Group considered it prudent to base risk calculations on models derived from the atomic bomb survivors’ cohort without applying any modification factor for low dose or low dose rate. This decision, which represents a departure from standard practice in radiation risk assessment, was not unanimous as two members (out of 13) expressed a dissenting opinion.”

55. Cancer is by far the most studied effect of radiation, but other effects have been observed to occur, such as increased risks of coronary heart disease, arteriosclerosis26, atherosclerosis27, and strokes28, collectively termed cardiovascular disease (CVD). Strokes occur as a result of blood supplies to the brain being cut off or restricted and are usually included in studies and data on CVD.

56. Until the mid-1960s, heart tissue had been thought to be relatively radio-resistant. Even as late as the 1980s, the issue of whether radiation exposure led to CVD was controversial and the relationship was not confirmed until the late 1990s. It is now well established (Little MP et al, 2008; Kreuzer et al, 2015) that cardiovascular risks are raised after moderate exposures to radiation. In fact, these risks act to limit the survival times of cancer patients after radiation therapy treatment (Heidenreich and Kapoor, 2009).

57. Various theories exist to explain how radiation causes CVD, but no definite consensus exists at present. However these diseases have longish latency periods, do not appear to have a threshold, and are progressive. In other words, they have similar characteristics of stochastic radiogenic cancer effects.

58. Hildebrandt (2010) has stated “In recent years, there is growing epidemiological evidence of excess risk of late occurring cardiovascular disease at much lower radiation doses and occurring over much longer intervals after radiation exposure without a clear-cut threshold. ... The mechanisms of radiation-induced vascular disease induction are far from

26 arteriosclerosis is the thickening, hardening and loss of elasticity of artery walls. This restricts the blood flow to organs and tissues and leads to severe health risks
27 atherosclerosis is a specific form of arteriosclerosis in which an artery wall thickens as a result of invasion of white blood cells and proliferation of intimal smooth muscle cells creating a fibro-fatty plaque
28 stroke occurs when low blood flow (often from atherosclerosis) to the brain results in damage and death to brain cells. Strokes are often fatal: essentially from brain malfunction.
being understood. However, it seems to be very likely that inflammatory responses are involved. If ... inflammatory response is ... the most likely cause of radiation-induced cardiovascular disease after low exposures, this ... implies a role for non-targeted radiation effects.” If the latter point about non-targeted\textsuperscript{29} effects is correct, this could be significant for low-dose CVD effects, as they could be greater than we currently think (Kadhim et al, 2013).

59. Kreuzer et al (2015) stated that evidence is emerging that low radiation doses could increase the long-term risk of cardiovascular disease. “This would have major implications for radiation protection with respect to medical use of radiation for diagnostic purposes and occupational or environmental radiation exposure. Therefore, it is of great importance to gain information about the presence and possible magnitude of radiation-related cardiovascular disease risk at doses of less than 0.5 Gy”. Other studies have found indications of increased CVD risks at low doses. For example, Bruno et al (2013) found an “early peculiar pattern of pre-clinical vascular involvement” after radiation exposures which supported the view that low-level radiation contributed to cardiovascular disease.

(n) Quantitative Risks of CVD

60. An older but large study of Chernobyl emergency workers (Ivanov et al, 2000) showed increased risks of cardiovascular disease which were statistically significant. The ERR/Sv was 0.54 (95% CI 0.18–0.91), i.e. four times higher than the heart disease risk found in the atomic bomb survivors study. More recently, Shimuzu et al, 2010) indicated linear, possibly linear quadratic, dose-effect relationships among the Japanese bomb survivors down to about 0.1 Gy, although the precise relationship at lower doses remained unclear. They concluded that stroke and heart disease combined now account for about one-third of the radiation-associated excess deaths – as does cancer in the atomic bomb survivors. In other words, radiogenic stroke and cardiovascular disease risks are in the same league as radiogenic cancer risks and should be taken into consideration by radiation authorities in setting limits to radiation exposures. For stroke, their estimated excess relative risk per gray was 0.09 (95% confidence interval 0.01 to 0.17, P=0.02) using the LNT model. For heart disease, the estimated excess relative risk per gray was 0.14 (0.06 to 0.23 P<0.001). A linear model provided the best fit, suggesting excess risks at very low doses although the dose-response effect between 0–0.5 Gy was not statistically significant.

61. Buzunov et al (2013) estimated circulatory system disease death rates in people living in contaminated areas in Ukraine after Chernobyl between 1988 and 2010. They found that the increases in CVD death rates were statistically significant in the higher dose cohort (21–51 mSv) compared with a lower dose cohort (5.6–20 mSv). Mortality from circulatory diseases was higher among males than females. It is interesting that increased CVD deaths were seen at such low doses. As for coronary heart disease, Krasnikova and Buzunov (2014) observed statistically significant increases in risks in 8,600 male Chernobyl clean-up workers at doses as low as 0.15 Sv. For the 0.15–0.25 Gy dose group, the RR was 5.6 (95% CI 2.5–15.9) i.e. a 4.6 fold increase. A recent study (Little et al, 2020) confirmed the existence of CVD from radiation exposures but indicated that the dose-response curvature for radiogenic circulatory disease

\textsuperscript{29} meaning that radiation’s effects are not on the DNA molecule
may be inverse, although there were substantial uncertainties. This is the subject of current studies.

62. It is recommended that further studies be carried out on radiogenic cardiovascular diseases. As current radiation dose limits in use around the world are based on cancer risks alone, it is recommended that, as a precautionary step, these should be tightened (ie reduced) by a factor of 2 to take into account CVS and stroke risks.
Part 2: Cancer Risks in Infants and Children

(a) Introduction

63. Childhood cancers are different from adult cancers. They act differently to the way they do in adults and are found in different organs than those found in adults. In general terms, tumours in children often grow more quickly and spread to other parts of the body faster. They look different under the microscope and respond differently to treatments. Children are more likely to develop leukemia and lymphoma than adults.

64. Radiation risks for children are often based on adult risks, but this is poor practice. For example, a 2018 policy statement from the American Academy of Pediatrics stated “That children are not little adults is, perhaps, a self-evident fact, but one that is often overlooked. Small children breathe more air, drink more water and eat more food per unit of body weight than an adult. Therefore, if what they breathe, drink or eat is contaminated with radioactive material... they will get a larger dose than a similarly situated adult.”

65. Radiation risks in boys and girls are relatively poorly studied, even though they are more sensitive to radiation than adults. The first exposures for which data were collected specifically on children were from the atomic bombs dropped on Japan in 1945 (Folley et al, 1952). Later, Hsu et al (2013) re-examined the databases from the LSS studies and observed elevated risks of childhood leukemia. Cardis and Hatch (2011) observed that children exposed to radiation from the Chernobyl nuclear accident in 1986 had elevated risks of thyroid cancer (14). Fairlie (2016) showed a range of diffuse ill-health effects in children arising from Chernobyl’s radioactive fallout.

66. Children whose mothers received abdominal X-rays during pregnancy (that is, children who were exposed before birth) increased their risk of leukemia after their births (Stewart et al, 1956). Other studies (Carroquino et al, 1998; Wild and Kleinjans, 2003) have indicated that children are more susceptible to cancer than adults. Richardson RB (2009) observed that infants30, and in particular neonates31, have much greater sensitivity to internal contaminants than older children.

67. The reports of the US BEIR V Committee (1990) and the US BEIR VII Committee (2006) assessed mortality data from solid cancer among the Japanese A-bomb survivors exposed as children (0-14 years). They estimated that children were around 10 times more sensitive to radiation than middle-aged adults: leukemia mortality showed less variation with age. The figure below is constructed from data in the BEIR VII Report (2006). It shows that young girls below 5 years are about twice as radiosensitive as young boys of the same age.

30 under one year
31 within the first month of life
Figure. Lifetime attributable risk of radiation-induced cancer mortality as a function of age at exposure for males (blue – solid) and females (red - dotted) from data in table 12D-2 (page 311) in NAS BEIR VII (2006). These are combined estimates based on relative and absolute risk transport and have been reduced by a DDREF of 1.5, except for leukemia, which is based on a linear-quadratic model.

65. In 2007, the UN’s World Health Organisation (WHO, 2007) published a major (351 pages) review on the health risks to infants and children from exposures to chemicals. This comprehensive report was drafted by a team of 11 US and Canadian academics and scientists. It was published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organization and the World Health Organization. The report contains a wealth of detail on the anatomical, mental, physiological, nervous, and developmental differences between adults on the one hand and infants/children on the other. No analogous report exists for exposures to radiation, although it would be useful for one to be written and published by the WHO.

66. Various reasons have been mooted as to why radiation risks are likely to be higher in infants (aged 0-1) and children (aged 1-14) than in adults. These include

   a) they contain a higher proportion of growing organs and tissues (ie proliferating cells) than adults
   b) they have a greater proportion of their life span in which the potential cancers can be expressed
   c) older animal experiments generally confirm that the risk of cancer from intakes of carcinogens is greatest in utero and in infancy
d) as regards internal exposures from intakes of radionuclides, their smaller bodies lead to higher concentrations of becquerels\textsuperscript{32} inhaled or ingested. This is a major reason for the elevated ICRP dose coefficients (Sv/Bq) for nuclides in infants and children\textsuperscript{33}.

e) growth in infants and children result in the incorporation of nuclides into long-lived cells in brain and bone and into highly-preserved molecules eg DNA and RNA. At present, ICRP risk models do not account for growth, and its rudimentary tritium and carbon-14 models do not model uptakes in brain and bone.

67. Official bodies dealing with radiation do not, in either general or specific terms, publish separate guidance or advice for children’s exposures. The UN’s WHO has published (no date) a series of 41 training slides on the theme of Children and Radiation. The ICRP (1989, 1996) has published extensive lists of age-dependent dose conversion factors (Sv per Bq) for thousands of radionuclides. However these long lists of unexplained numbers are of little help to health scientists and the public as the ICRP gives no advice as to what these numbers mean or how to apply them. It also refrains from giving information on additional protection for children (or other vulnerable groups) against radiation exposures - except for stable iodine prophylaxis in case of a radiological accident.

68. The UN’s International Atomic Energy Agency (IAEA) which is responsible for promoting nuclear power has at least published maximum radionuclide contamination levels\textsuperscript{34} for various\textsuperscript{35} radionuclides\textsuperscript{36} in infant foods, milk and drinking water. These are 10% of the maximum levels in foodstuffs for general consumption, which implies that the infant/adult risk ratio is 10 for the ingestion of beta-emitters\textsuperscript{37} and alpha-emitters\textsuperscript{38} in food and drink.

69. Richardson RB (2009) investigated the added risks from internal radiation to children compared with adults. He pointed out that, to assess their health risks, one has to multiply their exposure (ie estimated dose in mSv) by the hazard (ie fatal cancer risk per mSv). For infants (up to one year), he stated that internal doses (in mSv) from ingestion of radionuclides were approximately 10 times higher than in adults, varying with the radionuclide. In addition, for metabolic reasons, the hazard coefficients (Sv per Bq) for radionuclides in infants were also approximately 10 times\textsuperscript{39} greater than in adults. This meant the total health risks of internal radionuclides in infants were approximately $10 \times 10 = 100$ times greater than in adults. These increased risks for infants are inadequately taken into consideration by radiation protection authorities in the UK or US.

(b) Cancer rates in UK Children

\textsuperscript{32} A becquerel (Bq) is a unit of radioactivity meaning one nuclear disintegration per second

\textsuperscript{33} for example, a 1 Bq intake by a 3-month-old baby will have a 12-fold greater specific activity than the same intake by an adult (ratio of body masses - 73 kg/6.0 kg) if homogeneous distributions in both were assumed.

\textsuperscript{34} In kBq per Kg

\textsuperscript{35} I-131, Am-241, Pu-239, Pu-239, Pu-240 and Pu-242

\textsuperscript{36} Radionuclides are radioactive elements which emit radiation when they decay

\textsuperscript{37} Radionuclides which emit beta particles when they disintegrate

\textsuperscript{38} Radionuclides which emit alpha particles when they disintegrate

\textsuperscript{39} Dose coefficients for a 3-month-old were 2–56 times more for ingestion and 2–12 times more for inhalation than those for adults
Cancer (excluding benign, brain, CNS and intracranial tumours) is the most common cause of death in children accounting for a fifth of all deaths in boys and girls aged 0-14 in the UK.[1-3] Despite this, deaths from cancer are still relatively rare in children, amounting to less than one per cent of all cancer deaths. [4-6] The peak rate of childhood cancer with almost half (46%) of all cases is among children aged 0-4. All data here are from the Office for National Statistics, the General Register Office for Scotland and the Northern Ireland Statistics and Research Agency.

(c) Cancer Incidence in UK Children

The annual UK incidence rate of cancer in children aged <15 is 150 per million children. This rate has been increasing over the past few decades: between 2015-2017, cancer incidence in UK children increased by 10% (12% in girls and 8% in boys). See chart 2 below. It is not really known why these increases are continuing, nor why they are greater among girls than boys. Interestingly, similar increasing incidences of childhood cancer are also occurring in the US (Kriebel et al, 2016).

These observed numbers translate to a risk of a child being diagnosed with cancer before the age of 15 of about 1 in 500. This is made up of 1 in 1,600 for leukemia (ie “one-third of the overall risk of cancer”), 1 in 2,200 for a brain or spinal tumour and 1 in 1,100 for all other cancers combined. As above, these numerical risks have also been increasing.

Between 2015-2017, the annual number of cancer cases in UK children (0-14) was 1,878. This number has increased by 15% since the early 1990s. Chart 2 shows the increasing incidence rates for child cancers between 1993 and 2016.

Chart 2. Children's Cancer Incidence Rates, Ages 0-14, UK, 1993-2016

Data were provided by the National Cancer Registration and Analysis Service (part of the former Public Health England), through the Office for Data Release, November 2019. Also by ISD Scotland April 2019. And by the Welsh Cancer Intelligence and Surveillance Unit, Health
(d) Cancer Mortality (Deaths) in UK Children

74. On the other hand, in the recent past, childhood mortality rates have declined markedly due to improved treatment regimes. For example, over the decade 2008-2018 (the last period for which UK statistics are available), mortality rates for cancers in children decreased by 25%. See Chart 1 below. Cancer deaths among children (aged 0-14) now account for fewer than 1% of all cancer deaths in the UK (2015-2017): 43% in girls and 57% in boys. In absolute numbers, between 2015 and 2017, the annual number of cancer deaths among UK children (0-14) was 236, whereas the annual number of new cases in UK children was 1,878 in the same period. Nevertheless, in relative terms, the annual number of 236 cancer deaths in children is still about 6 times greater than the 39 children who died in UK road accidents in 2019.

75. Although death rates have thankfully been declining, the side effects of treatment, the secondary cancers, and the emotional and financial costs to children and their families are reasons why we should not settle for improved medical care, but continue to focus on primary prevention of this disease.

76. The above data were obtained from the following agencies:
   a. National Cancer Registration and Analysis Service (part of former Public Health England),
   b. Information Services Division Scotland
   c. Welsh Cancer Intelligence and Surveillance Unit, Health Intelligence Division, Public Health Wales

Chart 1. Children's Cancers Mortality Rates per Million Population, UK, Ages 0-14, 1971-2018
(e) Cancer Types

77. As shown in the UKCRC pie chart, below, 21% of childhood cancer deaths are from leukemias, 35% are brain and CNS tumours, and 44% are from other cancer types. Frequent single diagnoses are acute lymphoblastic leukemia, astrocytoma⁴⁰, neuroblastoma⁴¹, non-Hodgkin lymphoma⁴², and nephroblastoma⁴³ (Kaatsch 2010). Leukemia is the most common childhood cancer, accounting for nearly a third of all cases (31% and 29% in boys and girls, respectively) in Great Britain between 2006 and 2008.

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⁴⁰ Astrocytoma is a type of cancer that forms in the brain or spinal cord. Astrocytoma begins in cells called astrocytes that support nerve cells.

⁴¹ Neuroblastoma is a rare type of cancer that mostly affects babies and young children. It develops from specialised nerve cells (neuroblasts) left behind from a baby's development in the womb.

⁴² Non-Hodgkin lymphoma is a group of blood cancers that includes all lymphomas except Hodgkin lymphomas. Symptoms include enlarged lymph nodes, fever, night sweats, weight loss and tiredness. Hodgkin lymphoma is a relatively aggressive cancer but can be relatively easily treated.

⁴³ Nephroblastoma, also known as Wilm's tumour, is the most common renal tumour affecting children. It accounts for around 5% of childhood cancers.
(f) Causes of Childhood Cancer

78. Childhood cancer has no single cause and it is not known why it occurs in any individual case. Possible causes of childhood cancer have been studied for decades, but apart from radiation, few risk factors with strong links exist (Spector et al, 2015). Confirmed clinical and epidemiologic associations explain less than 10% of cancer incidence in children, leaving 90% of cases without a clear etiology. (Spector et al, 2015). Germ-line mutations are thought to be involved in only about 5% of childhood leukemias (more in AML than ALL) (Brison et al, 2015).

79. Little evidence exists to support viral causation, unlike in animals. Other environmental factors for which some evidence exists include non-ionising electromagnetic radiation and electric fields, although their mode of action remains unclear. See Appendix A. As stated above, there is no single cause for childhood leukemia and for most individuals a combination of factors appears to be necessary - all involving environmental interactions (Eden, 2010).

80. In recent years, non-radiation causes of childhood cancer have also been identified. Epidemiological evidence has emerged that the following chemical exposures: pesticides, traffic-related air pollution, and paints and solvents, are associated with leukemias, brain tumours and lymphomas. Danyshc et al (2016) observed that maternal proximity to major roadways in Texas US was positively associated with their babies having central nervous system (CNS) tumours. Mothers living ≤500 meters from a major roadway were 31% (95% CI: 1.0, 1.8) more likely to have offspring with a CNS tumour and 3.1 times (95% CI: 0.9, 10.4) ore likely to have offspring with an ependymoma – a special type of brain cancer - compared to
mothers living >500 m from the nearest major roadway. Also, Ribeiro et al (2021) found a positive association between traffic and NO$_2$ levels in São Paulo in Brazil with Hodgkin lymphoma and lymphoid leukemia among children. The ERRs for lymphoid leukemia were 1.21 (95% CI: 1.06, 1.39) for traffic density and 1.38 (95% CI: 1.13, 1.68) for NO$_2$. Finally, Yan et al (2020) observed associations between indoor air pollution and childhood acute leukemia in Shanghai, China. The pollutants with positive findings were styrene, butyl alcohol, chlorinated hydrocarbons and other volatile organic compounds (VOCs). The authors stated that VOC exposures were associated with elevated risks of childhood acute leukemia.

81. In adults, lifestyle-related risk factors, such as smoking, obesity, lack of exercise, poor diet, and alcohol play major roles in promoting cancer, but these are considered unimportant in childhood cancers partly because most of these factors do not apply to children and partly because such cancers take several years or decades to appear. Similarly most childhood cancers are not caused by inherited DNA changes. Known agents exist such as infections, chemicals and previous cancer treatments, but most children with cancer aren’t affected by any of these. And most children who are affected by them, don’t go on to develop cancer (Buffler et al, 2005) and (Brisson et al, 2015).

**In utero exposures**

82. According to Professors Rössig and Jürgens (2008) and Professor Eden (2010), molecular studies have revealed the pre-natal origin of many childhood leukemias: they are caused by the malignant transformation of blood-forming cells in embryos and fetuses *in utero*. They state their current models indicate that a first mutation *in utero* causes a pre-leukemic stem cell clone which, after the baby is born, progresses to full-blown leukemia after receiving further genetic hits. This two-stage model is shown in figure 4 below.

83. The pre-natal and post-natal events involved in leukemogenesis in children are not fully understood: the available evidence is discussed in Appendix E. Professors Rössig and Jürgens (2008) added that, although genetic predisposition and specific environmental exposures may account for individual cases, the bulk of childhood leukemias cannot be explained by these factors.

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44 the creation of leukemic cell clusters
84. According to Wiemels (2012) about 80% of acute leukemias are precursor-B cells in origin. The higher incidence of the most common leukemias in affluent societies, as well as the age peak of 2–5 years, suggest a contributory role of socio-economic factors. A plausible mechanism for malignant progression (ie the second hit) of pre-leukemic clones in children was an abnormal immune-response during delayed exposure to common infections. However for the first initiating stage, it was likely that multiple factors were involved and that exposures during embryonal and fetal stages are most likely implicated.

85. More recently, Marcotte et al (2021) discussed this matter in more detail. The authors concluded that “More than 70% of infant leukemia cases and >40% of ALL cases diagnosed age 1–9 years contain cytogenetic profiles that have been found to occur in utero through backtracking and twin studies and have been positively identified in newborn blood spots.” Although they did not allocate these cytogenetic changes to radiation specifically, they stated that radiation was an accepted cause of leukemia and “no other environmental risk factors have emerged as definitively causal”.

86. From the above cellular evidence, the epidemiological evidence discussed below, together with the deficiencies in current modelling and radiation dosimetry applied to children, including in pre-natal period, this report suggests that about half of infant and childhood leukemias arise from radiation exposures in utero.

87. To date, few clear preventative measures for childhood leukemias have emerged, except the complete avoidance of first trimester X-rays or CT scans in pregnancy; a healthy diet with adequate oral folic acid intake both in preconception and in early pregnancy; breast feeding; and the early exposure of children to other children outside the home to facilitate stimulation and maturation of their immune systems.

(g) Radiation and Leukemia

88. Belson et al (2007) have extensively reviewed possible risk factors for childhood leukemia. Exposure to radiation was the only well-established cause of leukemia, and of solid cancers for that matter. It has been clear for many years that childhood leukemia is closely associated with radiation, the increased risk being expressed as a temporal wave with time since exposure. Inter alia, childhood leukemias have been observed (Wakeford, 2013) in

- studies of children treated with radiotherapy,
- studies of childhood leukemia after fetal exposure to diagnostic x-rays,
- large studies of leukemia following CT scans of young people, and
- large studies of background y-radiation and childhood leukemia

(h) In utero Exposures to Radiation

89. It is necessary to discuss the issue of risks to babies arising from in utero exposures to radiation as an extensive literature exists on the matter. It is clear that in utero exposures to

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45 immature cells which arise from blood forming stem cells in red bone marrow
46 in the first 3 months of pregnancy
diagnostic radiation result in increased incidences of cancer in the babies born afterwards (Linet et al, 2009). Increased leukemia risks in embryos and fetuses exposed to diagnostic X rays of pregnant women were first observed in 1956 by Alice Stewart in the Oxford Study of Childhood Cancers (OSCC) (Stewart et al, 1956). Her team detected a statistically-significant ~40% increase in paediatric cancer risk after abdominal exposures to doses as low as 5 to 10 mGy\(^{47}\). Her findings were subject to much medical opposition and criticism at the time (Greene, 2017).

90. However her team’s findings have been validated and accepted (Doll and Wakeford 1997), partly due to later case–control studies which also found that X-ray examinations of the abdomen of pregnant women produced similar increases in leukemia risk in their babies (Boice and Miller, 1999; Doll and Wakeford, 1997).

91. Wakeford and Little (2003) reviewed risk coefficients for childhood cancer after intrauterine radiation and concluded that the consistency of the cancer risk coefficients found in the Oxford Study of Childhood Cancers and the Japanese bomb cohort irradiated \textit{in utero} supported a causal explanation of the association between childhood cancer and antenatal X-ray examinations observed in case-control studies. This implied that doses to the fetus \textit{in utero} of ~10 mSv or lower discernibly increased the risk of subsequent childhood cancer.

92. The authors also asked why there was an absence of childhood cancers among the Japanese children irradiated \textit{after birth} in contrast to the significant excesses found in \textit{in utero} exposure studies \textit{before birth}. They hypothesised this was due to the cells from which the cancers originated being sensitive to radiation only \textit{in utero} and not after birth. No explanation was offered as to why this should be the case. One possible explanation is that post-natal blood-forming cells are increasingly protected from external background radiation by the denser bone material from the calcium supplied after birth in maternal milk.

93. The fact that \textit{in utero} exposures to radiation cause defects in subsequent infants and children means that radiation should be classified as a teratogenic agent, like thalidomide. The main difference is that with thalidomide the effects –malformations – were immediately apparent at birth whereas with radiation the effects – mutations in blood-forming tissues- are not apparent at birth, and only become so in later months and years. Unfortunately the ICRP (2007) still judges that, following prenatal exposure, cancer risk in embryos fetuses “will be similar to that following irradiation in early childhood”.

\(^{47}\) equivalent to mSv for this discussion
Part 3: Sources of Radiation Exposures to Children

94. The main sources of radiation to children in the UK are medical exposures, background radiation and industrial sources. Other minor sources do exist such as airport scanning devices, tanning parlours, and long-haul air flights, but these are not thought at present to constitute major problems in terms of their low collective doses to women and children.

A. Medical Exposures to Radiation

(a) Introduction

95. Radiation exposures to children from medical procedures are especially worrying as clinicians are sometimes unaware that children are considerably more sensitive than adults to radiation-induced cellular damage (Hall, 2002). Children can be exposed to both diagnostic medical radiation from CT scans and X-rays, from nuclear medicine, fluoroscopy, and to treatment radiation, eg radiation therapy for cancers.

96. Radiotherapy can involve very large doses of radiation – see table 1 on page 6 above. This is considered problematic in children who receive radiotherapy for cancer as they may suffer many ill effects (Erdmann et al, 2021). For example, they run greater risks of developing chronic health conditions (Oeffinger et al, 2006) and developing secondary cancers (Meadows et al, 2009) than adults similarly treated.

97. Sinorello et al (2010) in a relatively large (~3,000 subjects) cohort study observed that, when girls with cancer were treated with uterine and ovarian radiation therapy, this resulted in increased numbers of serious adverse effects when they later had children. In particular, uterine and ovarian radiation at doses >10 Gy in girls and non-pregnant women significantly increased the risks (RR = 9.1) of stillbirth and neonatal death when they later became pregnant. For young girls treated before puberty, radiation of the uterus and ovaries at doses as low as 1.00–2.49 Gy still significantly increased the risk of stillbirth or neonatal death (RR = 4.7) when they became pregnant later in life. The authors concluded that when young women with cancer were given pelvic radiation therapy before puberty, then “careful management was warranted of their later pregnancies”.

98. Women alone are about twice as radiosensitive as men but this is not recognised in official models for radiation protection which, rather incredibly, still focus solely on men (Olson, 2019).

(b) Computed Tomography (CT) Scans

48 CT = Computed Tomography is a computerized x-ray imaging procedure in which a beam of x-rays is aimed at a patient and quickly rotated around the body, producing signals that are processed by the machine’s computer to generate cross-sectional images or “slices” of the body.

49 Nuclear medicine imaging is a method of producing images by detecting radiation from different parts of the body after a radioactive tracer is given to the patient.

50 Fluoroscopy is a type medical imaging that uses a continuous X-ray image of organs on a TV monitor.

51 Radiation therapy uses very high doses of intense gamma radiation to kill cancer cells.
As diagnostic CT scans are the largest medical sources of radiation in Western developed countries (COMARE, 2014), and because 11% of all CT examinations in Europe are paediatric (Bernier et al, 2019), they will be discussed at most length in this report (Kesminiene and Cardis, 2018).

In 2001, a landmark article by (British) Professors Brenner and Hall at Columbia University in the US alerted the world to the potential problems of increasing pediatric exposures from CT scans (Brenner and Hall, 2001). CT scans deliver doses of radiation that are several hundred times (Linet et al, 2009) greater than conventional x-rays depending on the target organ(s). This property has led to major increases in the per person radiation dose from medical sources (Linet et al, 2012).

Professor Hall (2002) stated that “It is clear that children are ten times more sensitive than adults to the induction of cancer. An abdominal CT scan in a young girl results in a risk of fatal cancer later in life that amounts to about one in a thousand. This risk to the individual is small, and readily balanced by the medical benefits. The public health problem is, however, significant when the small individual risk is multiplied by the 2.7 million such procedures then performed annually in the US. Every effort is needed to minimize doses by an appropriate choice of peak kilovoltage (kVp) and milliampere-seconds (mAs), and at the same time to urge a more selective use of pediatric CT.”

Hall and Brenner (2008) stated that the rapid increase in the number of CT scans both in the US and the UK fuelled concerns about future cancer consequences. In their 2008 article, they stated that statistics indicated a 20-fold increase in the US and a 12-fold increase in the UK in CT usage since 1988 with the per person CT usage in the US being about five times that in the UK. In both countries, most of the collective dose from diagnostic radiology came from high-dose procedures such as CT scans, interventional radiology and barium enemas.

In the US, Hall (2009) estimated that the then annual collective dose from such procedures was 930,000 person Sv. If we apply a commonly-accepted fatal cancer risk factor of 10% per Sv to this number, we can estimate that over 90,000 fatal cancers annually would result in the future in the US. This is considered a high price to pay for such medical diagnostic procedures, even if the clinical advantages were large. Between 2001 and 2020, Professors Brenner and Hall rigorously pursued this important matter – see their many references at end. It is considered that these British professors should be given greater recognition for their pioneering work in alerting the medical world to the dangers of pediatric imaging.

In the UK, according to the Government’s COMARE Committee (2014) the use of CT scans had expanded “dramatically” and CT scans were now the largest contributor to UK patient doses from all medical uses of radiation. No recent data on the collective doses from CT scans are presently available in the UK, although ideally these should be collected and published.

It is necessary to assess the degree to which CT scans are linked with subsequent cancer increases. A number of earlier cohort studies (Bailey et al, 2010; Krille et al, 2011; Meulepas et al, 2014; Journy et al, 2014; and Miglioretti et al, 2013) indicated possible associations. More recently, four larger studies (Pearce MS et al, 2012; Mathews et al 2013;
Berrington et al, 2016; and Huang et al 2016) showed statistically-significant associations between the numbers of CT scans and increased cancer risks. In more detail, Mathews et al (2013) reported a significant dose–response relation over the range from zero to more than three CT scans, with an increase in the cancer incidence rate ratio, relative to controls, of 1.16 for each additional CT scan. This relationship is shown in the figure below. Berrington et al (2016) found statistically significant dose-response relationships not only for leukemia in relation to cumulative red bone marrow dose from CT scans, but also for brain tumours in relation to cumulative brain dose.

Chart. Risk vs Numbers of CT scans

Chart from Mathews et al (2013). Cancer incidence rate ratios for all cancers in individuals who received CT scans vs those who did not. The right most data point refers to ?3 CT scans, with the mean number of CT scans being 3.5. The data shown here are for a lag period (exclusion period before cancer diagnosis) of 1 year; similar results were reported9 for lag periods of 5 or 10 years. Reproduced with permission from BMJ Publishing Group and originally published in9. CI, confidence interval.

(c ) Major European Study: EPI-CT

106. The” EPidemiological study to quantify risks for paediatric Computerized Tomography and to optimize doses” (EPI-CT) is a retrospective European study (Bernier et al, 2019) set up in 2011 to provide direct estimates of risk of solid tumours and leukaemia among children and young adults who had undergone CT scans in France, Germany, The Netherlands, Norway, Spain, Sweden and the UK. Over one million cases have been examined of which one third were children under 5 at the time of their scans. The EPI-CT study is still continuing as more
cancers will be expressed in future years. EPI-CT manuscripts on brain cancer and other solid cancer risks should be submitted for publication in June 2021.

107. To date, among the national studies, the UK data have shown a dose-response relationship between CT-related dose and CNS tumours and leukaemia in exposed children (Pearce et al, 2012) and young adults (Berrington de Gonzalez et al, 2016) but not for Hodgkin lymphoma (Berrington de Gonzalez et al, 2017).

(d) Confounding by Indication

108. The issue of confounding by indication (ie that the observed increases in cancers following scans may be partly caused by the illness prompting the scan in the first place) has been extensively discussed and examined in the above studies. A French cohort study, (Journey et al, 2015) showed the impact of this, if it existed, was small. This was consistent with an earlier case-control study (Knox et al, 1987) of pre-natal x-rays which showed that adjusting for maternal illnesses during pregnancy only reduced the risk of subsequent childhood cancers by 13% overall.

109. Other scientists have in fact shown the opposite, ie that cancer-predisposing health conditions instead of being confounders are really effect-modifiers. (Cardis and de Basea, 2015; Journey, 2015; Muirhead, 2015). In other words, the unadjusted risks found by various large cohort studies above are in fact reasonable (and unconfounded) estimates of the true risk. The issue of confounding by indication is discussed at length by Bernier et al (2019).

110. The most recent meta-analysis of 24 studies (Abalo et al, 2020) on CT exposures found pooled excess relative risks of leukemias of 26.9 per Gy and of brain tumours of 9.1 per Gy. These are substantial risks which should addressed by medical authorities in all Western developed countries.

111. In the past, increases in childhood cancers due to exposures from medical radiation especially from CT scans were an issue on which views were polarised. More recently with the evidence from large-scale studies, there has been a gradual acceptance that increased cancer risks from CT scans clearly do exist. It is interesting to see the parallels between the controversies over diagnostic X-rays in the 1950s/1960s, and nowadays over CT scans.

112. Thankfully, greater emphases are now being placed on newer equipment and better procedures and protocols designed to lower patient doses. For example Brenner (2012a) has stated that it is likely that at least 25% of CT scans were unnecessary, ie clinically unhelpful, in that they could either be replaced with alternative techniques (ultrasound and Magnetic Resonance Imaging (MRI)) or be avoided entirely. The use of clinical decision rules for CT scans is also a good way to slow down the increase in CT usage. Similar sentiments have been expressed by Metayer et al (2016).
(B) Background Radiation

113. Many people give little thought to background radiation, perhaps because it is considered largely unavoidable, but it merits greater attention as it actually causes many cancers. For example, Parkin et al (2010) have estimated that it is the cause of about one in five radiation-induced cancers in UK adults, almost half of which are leukemias.

114. In the UK, the former NRPB in 1994 calculated (using the linear-no-threshold hypothesis and a 5% per Sv risk factor in the then UK population of 55 million) that the average UK background dose rate of 2.5 mSv/a resulted in about 6,000 to 7,000 cancer deaths per year, i.e., about 5% of annual UK cancer deaths (Robb, 1994). If we update this calculation to 2021 using a current accepted risk factor of 10% per Sv and the UK population of 68 million and an average dose of 2.7 mSv/a, then background radiation would account for about 18,000 cancer deaths - about 11% of the 166,000 UK cancer deaths each year.

115. Some scientists point to viruses, bacteria and chemicals as alternative causes of cancer. For example, as regards traffic pollution, it has been known since at least the 1990s (Seaton et al, 1995) that, overall, daily mortality rates increase as the concentration of small particles in the air rises. Clearly, these factors will have effects but background radiation is constant not episodic: it exists 24 hours a day, 365 days a year for all of our lives, unlike the above agents.

116. Background radiation also has adverse effects on women’s fertility. Girls are born with their lifetime supply of eggs, as they are not replenished if killed or damaged. For this reason, women aged over ~40 years are not recommended to have babies, as their stocks of egg cells will have been exposed to ~40 mSv of background gamma radiation during their lifetimes. This will have killed some of their egg cells and damaged some of the remainder. This observation is supported by older mammal studies which show decreases in fertility after relatively low doses of radiation: older cell studies support this view as well. Of course, we cannot test this proposition in humans, but it would be strange if human egg cells were to be radio-resistant: humans are generally more radio-sensitive than other mammals (Fairlie, 2007).

117. On average, the estimated annual dose to adults from background radiation in the UK is 2.7 mSv. See table below on doses in 2010 attributable to background radiation in the UK. Of this figure, about 60% (1.7 mSv) arises from internal radionuclides and about 40% from external radiation (1 mSv).

118. Radon (Rn-222) and thoron (Rn-220) are radioactive gases which occur naturally in the air and when their atomic nuclei disintegrate they emit alpha particles – a form of radiation. In addition, their numerous daughters are highly radioactive and more hazardous than the parents. These progenies are found in outdoor air at low levels, but can sometimes build up to high levels indoors. Because they are naturally-occurring, it is difficult and/or expensive to control exposures from them.
<table>
<thead>
<tr>
<th>Source</th>
<th>Average annual dose (μSv)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Natural</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cosmic</td>
<td>330</td>
<td>12</td>
</tr>
<tr>
<td>Gamma</td>
<td>350</td>
<td>13</td>
</tr>
<tr>
<td>Internal</td>
<td>250</td>
<td>9.5</td>
</tr>
<tr>
<td>Radon(^b)</td>
<td>1300</td>
<td>50</td>
</tr>
<tr>
<td><strong>Artificial</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical (diagnostic only)</td>
<td>410</td>
<td>15</td>
</tr>
<tr>
<td>Occupational</td>
<td>6</td>
<td>0.2</td>
</tr>
<tr>
<td>Fallout</td>
<td>6</td>
<td>0.2</td>
</tr>
<tr>
<td>Discharges</td>
<td>0.9</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Consumer products</td>
<td>0.1</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td><strong>Total (rounded)</strong></td>
<td><strong>2700</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>


\(^a\) the term ‘dose’ means ‘effective dose’ which is derived from the absorbed dose (in joules per kilogram) and then multiplying it by a weighting factor to take account of the type of radiation involved. For sources that do not involve a uniform dose to the whole body, the doses to specific organs are further weighted according to factors recommended by the International Commission on Radiological Protection (ICRP, 2007).

\(^b\) assuming that living for a year in a home with a long-term average radon gas concentration of 20 Bq m\(^{-3}\) gives rise to a dose of about 1300 μSv.

**a. Sources of Background Radiation**

119. Thorne (2003) gave more details on the sources of background radiation as follows
- External gamma radiation from soil (mainly from K-40, Ra-226) (~20% of total)
- External cosmic radiation (photons, muons, neutrons) (~17%)
- Ingested (or internal) radionuclides (K-40, H-3, C-14) (~12%)
- inhaled Rn-222, Rn-220 and their decay products (~50%)

**b. Increased Cancers from Background Radiation**

120. Exposures to low-level background radiation are ubiquitous, leading to a steadily accumulating dose received by red bone marrow (RBM) from cosmic ray and terrestrial sources of penetrating radiation, as well as from radionuclides taken into the body through inhalation and ingestion of various naturally-occurring radioactive materials. Standard risk models predict that RBM doses from background radiation will induce some cases of leukemia, especially among children.
121. To investigate this, Little et al (2009) estimated that the annual RBM dose received by a 10-year-old UK child was about 1.2 mSv, of which around 45% was from radionuclides in food and drink, about 45% from cosmic rays and terrestrial external sources of γ-rays, and approximately 10% from the inhalation of radon and thoron and their radioactive decay daughters. From this dose, they estimated that about 20% of childhood leukemia cases in the UK was caused by background radiation. Later they refined (Little et al, 2009) their estimate to 15%. The slightly lower proportion was largely due to the lower high-LET dose in the first year of life.

122. In their later (Kendall et al, 2013) study, the same authors concluded that these statistically-significant raised risks reflected a real effect of natural background gamma radiation on childhood leukemia risks. Their study therefore supported the application of radiation-induced leukemia risks from high doses and high dose rates to protracted RBM gamma-ray doses of about 1 mGy per year. This was relevant to practical radiological protection in, for example, CT scans. The results of their study directly contradicted the idea that there were no adverse radiation effects, or might even be beneficial effects, at these very low doses and dose-rates.

Graph 4

In graph 4 above reproduced from the Kendall et al (2013) study, the x-axis represents cumulative gamma ray doses in mGy. The red line shows not merely a linear but a slightly supralinear curve fitted to the data. The small dotted lines mark the 95% confidence interval.

123. Previous studies had provided some suggestive evidence for the influence of background radiation on childhood leukemia risk (Little, 1999). A case–control study in Denmark (Raaschou-Nielsen et al, 2008) found an association between domestic radon exposure and childhood acute lymphoblastic leukemia. The authors concluded that about 9% of childhood acute lymphoblastic leukemia cases in Denmark were attributable to radon exposures. An ecological correlation study in France (Evrard et al, 2006) also showed a significant positive association of childhood leukemia with residential radon exposure, but not with background γ-radiation. However, neither the Danish nor the French study used individual dose measurements. A recent meta-analysis summarised data from ecological and case–control studies on radon exposure and childhood leukemia, and showed an increase in leukemia rates with increasing radon exposure (Tong et al, 2012).
124. As for brain/CNS tumours, Baraganza et al (2012) found elevated risks for these were consistently observed in relation to background exposures, but the strength of this association varied across cohorts. Generally, radiation was more strongly associated with risk for meningioma compared with glioma. The positive association between radiation exposure and glioma risk was stronger for younger vs older people. The authors did not observe effects by varying sex, age at exposure, time since exposure, or attained age. Also, Del Risko et al (2014) found an elevated risk for childhood cancers in the central nervous system, although the increase was not statistically significant, i.e., there was a >5% possibility that the observed increase was due to chance.

125. In a nationwide Swiss cohort study, Spycher et al (2015) investigated whether the incidence of childhood cancer was associated with background radiation from terrestrial gamma and cosmic rays. Among 2,093,660 children included at census, 1,782 incident cases of cancer were identified including 530 with leukemia, 328 with lymphoma, and 423 with cancer of the central nervous system (CNS). Hazard ratios for each millisievert increase in cumulative dose of external radiation were 1.03 (95% CI: 1.01, 1.05) for any cancer, 1.04 (95% CI: 1.00, 1.08) for leukemia, 1.01 (95% CI: 0.96, 1.05) for lymphoma, and 1.04 (95% CI: 1.00, 1.08) for CNS tumours. Adjustment for a range of potential confounders had little effect on the results. The study concluded that background radiation contributed to the risk of cancer in children, including leukemia, lymphoma and CNS tumours. In a similar Finnish nationwide study, Nikkila et al (2015) found statistically significant increases in leukemia amongst children aged 2 to 6, which they said provided further support to the view that low doses of background radiation increased the risk of childhood leukemia.

c. Difficulties with older Epidemiology Studies

126. It is necessary to state that older epidemiological studies were often a poor tool for discovering the adverse effects of radiation exposures. They were often descriptive (i.e., ecological) rather than the better case-control or cohort studies. Some studies suffered from poor case identification, non-uniform registration, variable or uncertain diagnostic criteria and uncertainties in the uniformity of data collation. Predicted excess deaths were often uncertain due to confounding factors, competing causes of death and the use of different risk projection models.

127. Especially in the past, many studies were too small with the result that they each showed a few extra cases which proved little. Meta-studies which group together such studies in order to strengthen their statistical significance are a solution, but relatively few were carried out. In addition, various agents can produce bias in studies. For example, smoking and alcohol cause major increases in overall mortality, morbidity, and cancer and other diseases.

128. The conclusion is that many factors have to be taken into account in assessing the findings of epidemiology studies. We needed to slightly lower our expectations about

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52 A meningioma is a tumour that forms on membranes covering the brain and spinal cord just inside the skull.
53 A glioma is a tumour that starts in the non-neuronal cells of the brain and the spine.
54 numbers of deaths
55 numbers of cases of the illness
epidemiology in general, and to interpret the findings of all epidemiology studies with considerable care.

129. That said, in recent years, the quality of epidemiology studies has been improving, especially as regards their larger sizes, rigorous attention to controls and to possible confounding factors, use of statistical tests (see Appendix F), treatments of uncertainty and their analyses of previous studies and the various factors involved in possible causalities. For example, the INWORKS studies considered above are marked improvements over studies pre-2000. In addition, the recent exhaustive epidemiology study by Wakeford and Bithell (2021) on childhood leukemia increases following in utero exposures sets a high bar for future studies in this area to match.

130. It is concluded that background radiation is associated with childhood leukemias/lymphomas and brain/CNS cancers. This conclusion comes partly from theoretical dosimetric studies but mainly from the recent strong epidemiological evidence.

(C) Industrial Sources of Radiation

131. Among the risk factors for acute leukemia in children discussed by Belson et al (2007) were radioactive discharges from industrial facilities. About 40 civil and military nuclear facilities exist in the UK as listed in tables A.2.1 and A2.2 in the Appendices of the annual publication Radionuclides in Food and the Environment (RIFE) (Environment Agency, 2019). Although their annual emissions to air and discharges to sea can be quite large, ie up to several terabecquerels56 (TBq = 10^{12} Bq) per year, many are located in rural areas or on the coast, ie remote from highly populated areas. From the RIFE reports, it is noted that nuclear facilities which have been closed for decades still continue to emit large quantities of radioactive tritium (H-3) each year in the form of radioactive water vapour.

a. Childhood Leukemias near Nuclear Facilities

132. In the 1980s and early 1990s, increased incidences of childhood leukemias were reported near several UK industrial facilities (Gardner et al, 1990). Various explanations were offered for these clusters including population-mixing (Kinlen, 2004); an unusual response to infectious diseases in children (Greaves, 2006); genetic predisposition to cancer; or combinations of factors. The UK Government’s Committee on the Medical Aspects of Radiation in the Environment (COMARE 1986; 1988; 1989; 1996) concluded that the cause(s) remained unknown but were unlikely to involve radiation because official estimates for radiation doses from these facilities were too low by orders of magnitude to explain the increased leukemias.

b. German KiKK study

133. The KiKK study (Kinderkrebs in der Umgebung von KernKraftwerken = Childhood Cancer in the Vicinity of Nuclear Power Plants (NPPs)) found a 120% increase in leukemia and

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56 a becquerel is the rate of radioactive decay in a radionuclide = 1 disintegration per second
a 60% increase in all cancers among infants and children under 5 years old living within 5 km of all German NPPs (Kaatsch et al, 2008b; Spix et al, 2008). The increase of risk with proximity to the NPP site, tested with a reciprocal distance trend, was significant for all cancers (p = 0.0034, one-sided), and leukemias (p = 0.0044). A particular increase in embryonal cancers, i.e. cancers in unborn embryos, was observed.

134. KiKK was a large, well-conducted study; its findings are scientifically rigorous; its evidence is particularly strong; and the German Government’s Bundesamt für Strahlenschutz (BfS) which commissioned the study, confirmed its findings. A BfS-appointed expert group stated (BfS, 2008) “The present study confirms that there is a correlation between the distance from the home to the nearest NPP [nuclear power plant] at the time of diagnosis and the risk of developing cancer (particularly leukemia) before the 5th birthday. This study is not able to state which biological risk factors could explain this relationship. Exposure to ionising radiation was neither measured nor modelled.”

135. The KiKK study’s findings reignited the childhood leukemia debate and resulted in Government-sponsored studies in the UK (COMARE, 2011), France (Sermage-Faure et al, 2012) and Switzerland (Spycher et al, 2011). Together with a geographical study from Germany (Kaatsch et al, 2008a) using data from the KiKK study, four datasets existed of similar design and with the same endpoints, distance definitions and age categories. These four studies had very similar findings: leukemia increases within the 5 km zone observed in the four studies are shown in Table 2.

Table 2. Studies of observed (O) and expected (E) leukemia cases within 5 km of NPPs.

<table>
<thead>
<tr>
<th>Country</th>
<th>Observed</th>
<th>Expected</th>
<th>SIR = O/E</th>
<th>90%CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>34</td>
<td>24.1</td>
<td>1.41</td>
<td>1.04-1.88</td>
<td>0.0328</td>
</tr>
<tr>
<td>Great Britain</td>
<td>20</td>
<td>15.4</td>
<td>1.30</td>
<td>0.86-1.89</td>
<td>0.1464</td>
</tr>
<tr>
<td>Switzerland</td>
<td>11</td>
<td>7.9a</td>
<td>1.40</td>
<td>0.78-2.31</td>
<td>0.1711</td>
</tr>
<tr>
<td>France b</td>
<td>14</td>
<td>10.2</td>
<td>1.37</td>
<td>0.83-2.15</td>
<td>0.1506</td>
</tr>
<tr>
<td><strong>Pooled data</strong></td>
<td><strong>79</strong></td>
<td><strong>57.5</strong></td>
<td><strong>1.37</strong></td>
<td><strong>1.13-1.66</strong></td>
<td><strong>0.0042</strong></td>
</tr>
</tbody>
</table>

b acute leukemia cases

136. Körblein and Fairlie (2012) pooled the data from these four studies, and their standardized incidence ratios (SIRs) are shown in the coloured bottom row in Table 2. Their analysis yielded an overall SIR of 1.37 (90% CI: 1.13-1.66, p= 0.0042, one-sided). This pooled analysis provides statistically strong evidence of leukemia increases near NPPs which contradicts several official statements to the contrary.

(c) Increases near NPPs worldwide

137. Laurier and Bard (1999) and Laurier et al (2008) examined the literature on childhood leukemias near NPPs world-wide. The two studies identified a total of over 60 studies. An independent review of these studies (Fairlie and Körblein, 2010) indicated that the large majority (>75%) showed small increases in childhood leukemia but many were not statistically significant. Laurier and Bard and Laurier et al who were mostly employees of the French Government’s Institut de Radioprotection et Sûreté Nucléaire (IRSN), confirmed that clusters
of childhood leukemia cases existed near most NPPs around the world but the authors refrained from drawing any conclusions.

138. On the other hand, Fairlie and Körblein (2010) in their review concluded that the copious evidence indicating increased leukemia rates near nuclear facilities, specifically in young children, was convincing. A pattern of epidemiological evidence world-wide indicated increased childhood leukemia risks near nuclear power plants.

139. This conclusion was supported by two meta-analyses of national multi-site studies. Baker and Hoel (2007) assessed data from 17 research studies covering 136 nuclear sites in the UK, Canada, France, the US, Germany, Japan, and Spain. In children up to nine years old, leukemia death rates were from 5 to 24% higher and leukemia incidence rates were 14-21% higher. However their analysis was later criticised by Spix and Blettner (2009). The second meta-analysis by Körblein (2009) covering NPPs in Germany, France, and the UK also found a statistically significant increased risk of child leukemias near NPPs (RR = 1.33; one-tailed p value = 0.025). Further studies (Guizard et al, 2001; Hoffman et al, 2007) indicated increased leukemia incidences in France and Germany. Very recently, Demoury et al (2021) also found increased child leukemias near Belgian NPPs: the pattern continues.

140. Fairlie (2014) has suggested a hypothesis to explain the discrepancy between the low official estimated doses from NPPs and the observed high risks of leukemias in children nearby. The main points are that

(a) radionuclide emissions from NPPs are not spread throughout the year but bunched into single spikes resulting in considerably higher (x 20) doses to people downwind,
(b) the main risks arose in embryos and fetuses in utero at the time of the emissions,
(c) radiogenic leukemia risks in embryos/fetuses were much higher than predicted by official models,
(d) official dose models were unreliable as they used 5 computer models in sequence with the central values from each model being inserted into the next model then into the next, etc: this resulted in unreliable dose estimates
(e) the product of unreliable dose estimates x unreliable risks explained the discrepancy.
Part 4: Conclusions and Recommendations

Conclusions

Cancer is a serious health concern for us all: according to the UKCRC, about half of all UK people born since 1960 will get cancer. According to ONS data, cancer is the most common cause of death in children 0–14 years of age in the UK. Cancer incidence in children has been slowly but remorselessly increasing in recent decades. This is a matter for some concern as we are unsure as to the reason(s) for this continuing increase.

A growing body of literature (Metayer et al, 2016; Landrigan and Levine, 2020) implicates environmental indoor and outdoor hazards in the aetiology of childhood leukemia specifically, rather than other cancers. But leukemia is the most common cancer in children, representing approximately one-third of all pediatric cancer cases.

The clearest evidence is for radiation, the subject of this report. But exposures to solvents, traffic pollution, pesticides, and tobacco smoke have also demonstrated positive associations with increased risks of childhood leukemia (Metayer et al, 2016).

To protect our children’s health, it would be prudent to establish programmes to reduce exposures to those hazards, especially radiation, which have well-established associations with leukemia rather than to suspend judgment and wait until no uncertainty remains. This is particularly true because other serious health outcomes have been associated with exposures to radiation.

The steady increase in incidence of childhood leukemia in the UK is a strong indicator that its origins are influenced by environmental factors, including radiation exposures. This report clearly indicates that these exposures, especially during early pregnancy and after birth, play important roles in the aetiology of childhood leukemia.

The author has not been able to identify any Government/NHS prevention programmes for childhood leukemia in the UK, although some may exist at local levels. At least one very good example exists in the US (Coalition Against Cancer, 2020). The UK absence of public health prevention is likely due to a lack of consensus at senior levels in public bodies about whether the current evidence, eg on radiation risks, warrants a causative determination (Gee, 2008). However this report indicates copious evidence as to causality: the question remains as to whether public bodies will act upon it to establish prevention programmes for childhood leukemia and by extension for all childhood cancers. It is recommended that they do so.

It is probably the case that political, industrial and institutional factors exist which make unanimous progress towards reducing childhood leukemias difficult, especially during the current Covid pandemic. On the other hand, it could be argued that, due to Covid, there is heightened interest and awareness of public health issues, so now may be a good time to press for prevention programmes for childhood cancer to be set up in the UK.

The frontispiece quote at the head of the Table of Contents of this report is from Cicero (109 - 46 BC). He was a Roman statesman, lawyer, scholar, philosopher and Consul. *Salus populi*
suprema lex esto – the health/welfare of the people is the supreme law, is probably his most famous legal dicta. His words are ubiquitous on courthouses and legislative buildings throughout the world. Cicero did not say that political expediency or vested interests were the supreme law: it was the health and welfare of the people.

With childhood cancer, perhaps it is time to act on his wise words.

Recommendations

A. On cancer risks in children

i. At the outset it is recommended, that the Precautionary Principle (see footnote 59 on page 45) be adopted as a matter of public policy, particularly in assessments of cancer risks. This principle enables decision-makers to adopt precautionary measures when scientific evidence about an environmental or human health hazard is uncertain and the stakes are high. It first emerged during the 1970s and has since been enshrined in a number of international treaties on the environment, in the Treaty on the Functioning of the European Union and the national legislation of certain Member States. The precautionary principle divides opinions. To some, it is unscientific and an obstacle to progress. To others, it is an approach that protects human health and the environment. https://www.europarl.europa.eu/thinktank/en/document.html?reference=EPRS_IDA(2015)573876

ii. Adopting this principle means, inter alia, that that the LNT model for radiation risks should continue to be supported.

iii. Since the last official investigation of childhood cancers was over 20 years ago (Doll et al, 2000), it is recommended that a similar investigation be established soon. In particular, it is recommended that the specific question of why childhood cancers are increasing in the UK and other Western countries should be addressed.

iv. Post-Covid, NHS prevention programme(s) for childhood cancer should be set up in the UK.

v. Since it is relatively clear that a significant proportion (perhaps >50%) of child leukemias arise from radiation exposures in utero, it is recommended that precautionary steps should be taken to protect pregnant women and to increase their rights not to be irradiated. For example, official advice should be issued that pregnant women should not to be subject to radiation exposures from any medical procedures and from airport security devices (unless consented to). Information should be made available about the increased risks to children and their mothers of residing within 5 km of industrial facilities emitting large amounts of radioactivity.

B. On the risks from radiation exposures, the following steps are recommended

vi. A COMARE subcommittee which contains independent (ie non-governmental) experts be established to assess whether the current ICRP radiation risk factors are based on up to date science, and whether they should be increased to give better levels of protection to vulnerable people, including children and women of child-bearing age.

vii. This subcommittee should address the problems with the ICRP’s single risk factor for radiation risks (see Appendix G), and the problems with assessments of radiation dosimetry and hazards set out in Appendix B.
viii. Further studies should be carried out on radiogenic cardiovascular diseases (see para 52 et seq above). As current radiation dose limits in use are based on cancer risks alone, it is recommended that, as a precautionary step, these should be tightened (reduced) by a factor of two to take into account CVS and stroke risks (see Appendix G).

ix. DDREFs should be not be used in the assessment of radiation risks In line with UNSCEAR and WHO views. This means, inter alia, that radiation limits should be tightened by a further factor of two. Ie radiation limits should now be tightened by a factor of four.

x. An NHS committee should be established to determine extent of the exposures to pediatric CT scans. In particular, annual UK data on collective doses and risks from CT scans throughout the UK should be collected and published.

xi. As a precautionary step, all children under 15 should not be given CT scans unless the clinical need for them has been verified by two doctors not known to each other.

xii. A separate report be commissioned on cancer risks to children from exposures to non-ionising radiation, in particular from mobile telephones. In the interim, the Stewart Committee’s advice in 2005 should be adhered to, inter alia, that children under eight should not use mobile phones, and that older children should use them only for texting, not voice calls.

xiii. WHO should commission and publish a report on radiation risks in children analogous to its major 2007 report on chemical risks in children.

xiv. Finally, WHO should draw up a hazard index of radionuclides for use in radiation protection, which takes into account their physical, chemical and biological properties (Kirchner, 1990).
Appendix A: Health Effects of Non-Ionising Radiation

The IARC (2002, 2011) in its Monograph series on Carcinogenic Risks to Humans has classified both power frequency (ELF = Extremely Low Fields) and radio frequency fields (RF) as IARC 2B Possible Carcinogens. See also the IARC conference proceedings on these issues (Baan et al, 2011).

Numerous epidemiologic studies have been conducted to determine whether an association exists between exposure to non-ionising electro-magnetic fields (EMFs) and childhood leukemia. Some have found a small association (Ahlbom et al, 2000; Greenland et al, 2000; Hatch et al, 1998; Rivard and Deadman, 2003; Savitz et al, 1990) while others have not (Kleinerman et al, 2000; Linet et al. 1997; Myers et al, 1990). The inconsistent results of the EMF and childhood leukemia studies may be due in part to differing methods for assessing residential magnetic field exposures and unmeasured EMF characteristics (Bowman and Thomas 2001; Brain et al. 2003; Hardell et al. 1995). Also, investigations of animals with exposure to much higher levels of EMFs than humans have not shown increased risk for hematopoietic neoplasia (Brain et al, 2003).

As regards negative studies, we always should bear in mind the axiom that absence of evidence in a study does not provide evidence of absence (Altman and Bland, 1965). It merely means that the study did not find an association and many reasons could exist for this, eg poor study design, too few cases, confounding factors etc. The corollary is that studies with positive findings are always more informative than those which find no associations.

Ahlbom et al (2000) conducted a pooled analysis of data collected for nine studies. For the 44 children with leukemia and 62 control children with high estimated residential EMF exposure, the estimated summary relative risk was 2.00 (95% CI, 1.3–3.1). Adjusting for potential confounding variables did not appreciably change the results, but selection bias may have accounted for some of the increase. Linet et al (1997) conducted a case–control study with actual measurements of EMFs in the homes of > 1,200 study subjects near the time of their diagnoses of ALL cases. Overall, there was an increased risk of ALL with increasing exposure to residential magnetic fields (OR = 1.24; 95% CI, 0.86–1.79) for the highest exposure category compared with the lowest. Furthermore, no increased risk of childhood leukemia studies may be due in part to differing methods for assessing residential magnetic field exposures and unmeasured EMF characteristics (Bowman and Thomas 2001; Brain et al. 2003; Hardell et al. 1995). Also, investigations of animals with exposure to much higher levels of EMFs than humans have not shown increased risk for hematopoietic neoplasia (Brain et al, 2003).

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In 2005, the UK Government’s Stewart Committee concluded that it was then not possible to say that exposure to RF radiation, even at low levels, was totally without potential adverse health effects. (Chapter 5, paragraphs 6.35–6.42). It recommended a precautionary approach be adopted to the use of mobile phones by children until more detailed and scientifically robust information on health effects became available. The Committee recommended that children under eight should not use mobile phones at all, and that older children should use it for texting, not voice calls.

Pooled analyses have indicated that exposures to high levels of extremely low-frequency-electromagnetic fields are associated with an increased risk of childhood leukemia (Ahlbom et al, 2000; Greenland et al, 2000; IARC, 2002). Methodological issues including possible confounding, selection bias, and measurement errors have been mooted as explanations for this observed association, and animal studies are ongoing to identify possible biological mechanisms (Schuz et al, 2009; Teepen et al, 2012). If the association between extremely low-frequency-electromagnetic fields and childhood leukemia is causal, the overall population attributable risk of cancer has been estimated to be 1.9% (1–4% depending on which countries) (Schuz et al, 2009; Teepen et al, 2012). In 2018, a peer review of a US Government study concluded clear evidence existed that radiation from mobile phones causes cancer in animals. Specifically, it caused heart tissue cancer in rats that was too rare to be explained as a random occurrence.

The most recent very large meta-analysis (Seomun et al, 2021) found statistically significant associations between exposure to ELF-MFs and childhood leukemia. The meta-analysis included thirty studies with 186,223 participants. Children exposed to 0.2, 0.3, and 0.4 microtesla ELF-MFs had respectively 1.26, 1.22, and 1.72 times higher odds of childhood leukemia. All odds were statistically significantly raised.
The rapid recent introduction of 5G technology in the UK will result in increases in non-ionising radiation due to exposures not only from uploading but also from downloading digital files (Velghe et al, 2021). Recent official UK guidance on the matter is sparse, although several studies are continuing. See also the UK Government response to the Stakeholder Advisory Group on extremely low frequency electric and magnetic fields (ELF EMFs) (SAGE) recommendations. Written Ministerial Statement 16 October 2009. Available at: Electromagnetic fields : Department of Health - Public health (nationalarchives.gov.uk)

It is recommended that a separate report be commissioned on cancer risks to children from exposures to non-ionising radiation, in particular from mobile telephones.
Appendix B: Problems with how we estimate exposures to radiation – doses

(a) In all cases, whether from external or internal exposures, “doses” are derived by using models which contain assumptions and uncertainties. That is, all doses are estimates and should be described as such.
(b) The ICRP system of doses uses different effective, equivalent, absorbed doses most of which use the same unit, ie sievert.
(c) The resulting “doses” are perhaps adequate for external exposures but are inadequate for internal exposures.
(d) Large numerical uncertainties exist with estimates of internal doses – see CERRIE (2004) – and should be acknowledged,
(e) Bq/litre and/or Bq/gram concentrations should be used instead of dose for internal exposures.

Problems with how we determine radiation hazard – cancers

I. Observed human risks (ie cancer rates from the LSS study) are arbitrarily halved by a DDREF (dose and dose rate effectiveness factor). This unconservative practice should be abandoned - for many scientific reasons. See para 48 et seq in main report.
II. The hazard (RBE57) of the very common radionuclide, tritium, should be 3 not 1.
III. The hazard (RBE) for common Auger emitters58 (eg Cs-137 via Ba-137m) should be 5 not 1
IV. The ICRP risk model takes into account a nuclide’s dose coefficient, uptake rate, and solubility, but it also should consider its
   • transport and recycling in biosphere;
   • global distribution and resulting collective doses;
   • multiple pathways of exposure, via inhalation, ingestion, skin absorption, and immersion
   • organic binding in biota;
   • long biological half-lives in humans;
   • long radiological half-lives (ie not just 50 years); and
   • long nuclide decay chains with many radiotoxic daughters

Consideration of the two above factors of dose times cancer rates would mean that radiation risks would be increased and that the dose coefficients59 for commonly-mentioned nuclides such as H-3, Rn-222, Ra-226, Cs-137, U-238, C-14, and I-129 would be increased.

57 RBE = relative biological effectiveness of the radiation form under test compared to higher energy X-rays
58 Auger emitters emit large numbers of low-energy electrons which are very damaging to cells
59 Expressed as Sv per Bq
Appendix C: Differences between Chemical and Radiation Risk Assessments

The many questions with radiological risk assessments listed in Appendix B contrast with the conservative, i.e., safer, approach used for chemicals. For example, the Precautionary Principle\(^{60}\) is used repeatedly in chemical risk determinations but is notable by its absence in the assessment of radiation risks. With chemicals, the concentrations at which no adverse effects are observed in animal studies are arbitrarily tightened (usually by factors of 10 or 100) when applied to humans. This means chemical limits are routinely 10 to 100 times safer for humans than those observed in animals.

Why the different approaches?

This intriguing question was addressed by the US EPA in a 13 page report from 1992 which is no longer available but which was reproduced in Appendix 5 of the Ontario Government’s ACES Report “A Standard for Tritium” by the former Advisory Committee on Environmental Standards (ACES, 1994) The latter report is available from the Ontario Drinking Water Advisory Council [www.odcac.gov.on.ca](http://www.odcac.gov.on.ca).

It was also addressed by the report “Assessment and Management of Cancer Risks from Radiological and Chemical Hazards” prepared jointly by the Atomic Energy Control Board, Health Canada and Ontario Ministry of Environment and Energy (AECB, 1997). This is also available from [www.odcac.gov.on.ca](http://www.odcac.gov.on.ca).

These reports concluded that the two different approaches were essentially due to the backgrounds, policies, experiences, and histories of the respective Governmental agencies which set up the standards.

The chemical risk paradigm was largely established in the 1950s and 1960s by doctors and medical officials responsible for protecting public health. On the other hand, the radiation risk paradigm was drawn up by atomic physicists in the 1940s primarily responsible for making nuclear weapons… in a hurry. As a result, reducing risks to workers and the public was apparently a secondary consideration. For example, radiation risks (now defined by the ICRP) were assumed to derive from a single exposure to healthy male adults, and little or no account was taken for chronic exposures or exposures to embryos, babies or pregnant women. This is still the case.

Furthermore when it came to setting the actual risk of fatal cancers (i.e., 0.05 per Sv), no safety factors were built in as routinely occurs with chemicals. Indeed, the risk was arbitrarily halved (i.e., deliberately underestimated) by introducing a DREF (dose reduction effectiveness factor) although this was strongly questioned by radiation biologists at the time. A DREF is still included in ICRP recommendations.

The conclusion is that serious problems still exist with current official methods of estimating radiation doses and its risks which should be addressed by the ICRP.

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60 The [precautionary principle](https://www.europarl.europa.eu/thinktank/en/document.html?reference=EPRS_IDA(2015)573876) enables decision-makers to adopt precautionary measures when scientific evidence about an environmental or human health hazard is uncertain and the stakes are high. It first emerged during the 1970s and has since been enshrined in a number of international treaties on the environment, in the Treaty on the Functioning of the European Union and the national legislation of certain Member States. The precautionary principle divides opinions. To some, it is unscientific and an obstacle to progress. To others, it is an approach that protects human health and the environment.
Appendix D: Absolute and Relative Risks of Radiation

Two methods exist to describe risk: absolute risk and relative risk.

**Absolute risk** is defined as the probability that a person who is disease-free at a specific age will develop the disease at a later time following an exposure to radiation, e.g. the probability of cancer induction following exposure to radiation. The **relative risk** model assumes that radiation increases the existing natural incidence of a cancer: it is expressed as a fraction or multiple of this naturally-occurring background risk. Most advisory publications use relative risk because of its mathematical and statistical advantages when derived from epidemiological studies.

Increases in risk can be expressed in two ways, by addition or by multiplication. For example, if the background risk of a given cancer before a given radiation exposure was, say, 10% and afterwards it is found to be 15%, then the increase can be described as 10% - 15% = 5%: this is the absolute risk. But it can also be described as a 15%/10% = 1.5 fold increase in risk: this is called the relative risk. Both types are used in the literature. There are no hard and fast rules as to which one should be used as far as can be ascertained, except that comparing relative risks from different countries are best avoided as they can have different baseline risks.

Nowadays, the preferred method of citing risks is relative risk: the observed increase in risk when compared to the prevailing (ie background) risk of cancer in a country. For example, according to UK Clinical Research Collaboration (UKCRC) (2020), 50% of people born after 1960 will be diagnosed with some form of cancer during their lifetime. In other words, the baseline risk of getting cancer in the UK is about 50%. If a representative subset of the population were exposed to some added radiation which later resulted in 60% of the subset getting cancer, then the absolute increased risk would be (50%-60%) = 10% and the relative increased risk would be 60/50 = 1.2. For example, the averaged relative risk for solid cancer observed among radiation workers in the above INWORKS studies was 1.29 per Sv of added radiation they received. As it is commonly observed that, on average, about half of all cancer cases are fatal, the risk of a fatal cancer in the UK among people born after 1960 is roughly 25%.

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61 the actual fraction varies with age at exposure (Richardson, 2009).
Appendix E: Enhanced Radiosensitivity of Blood-Forming Cells in embryos and fetuses

Various reports suggest an apparent increased radiosensitivity of pre-natal blood-forming cells in bone marrow and lymphatic tissues. These tissues contain high concentrations of stem cells which are usually rapidly self-replicating. Radiation-induced mutations to these stem cells are hypothesised to result in increased malformation rates of white blood cells. This means that bone marrow is likely to be among the most radiosensitive of embryonic/fetal tissues: this has been hinted at on at least four occasions in previous studies, as shown below.

1. In 1990, after Gardner et al (1990) had published their paternal pre-conception irradiation hypothesis, the BMJ published letters questioning aspects of the hypothesis. A letter by Dr J A Morris (1990) stated that, assuming mutations were the cause of the 10-fold increase in leukemia incidence observed by Gardner’s team, it would require a 100 to 1000-fold increase in the radiation-induced mutation rate if acting on the germ cell; a 10-fold increase if acting on lymphocytes during early extra-uterine life; but only a 1.8-fold increase if acting on lymphocytes throughout intrauterine life. See also Morris (1992). He earlier had stated (1989) the latter seemed the most plausible mechanism even though the exposure pathways were unclear.

2. A few years later, Lord et al (1992) indicated the same thing when they suggested that embryonic haematopoietic cells could be up to 1,000 times more radiosensitive than post-natal haematopoietic cells. They added that different mechanisms of inducing this damage operated at different embryonic/fetal stages.

3. Ohtaki et al (2004) suggested the same in their study of chromosome translocation frequencies in white blood cells of Japanese A-bomb survivors irradiated in utero. They found that precursor lymphocytes of the fetal haematopoietic system may be highly radiosensitive, perhaps 100 times more so than post-natal lymphocytes.

4. From this study, Wakeford (2008) surmised that radiosensitive primitive cells remain active throughout pregnancy, including during the third trimester but not after birth, although it is not known at present why this should be the case. He stated that mutation of these radiosensitive primitive cells may result in childhood cancers.

This apparent increased radiosensitivity of haematopoietic cells before birth may be a factor in explaining the discrepancy between official dose estimates and observations of increased leukemia risks in studies near some industrial facilities.
Appendix F: Misuse of Statistical Significance Tests in Health Studies

Many epidemiology studies on childhood cancers near industrial sites have dismissed observed increases by stating that such increases were not statistically significant. To give two examples, Bithell et al (2008) and Laurier et al (2008) found increases in child leukemias near UK and French nuclear power plants (NPPs) respectively. However, instead of reporting these increases, the studies incorrectly concluded that there was “no evidence” (Bithell et al) and “no suggestion” (Laurier et al) of leukemia increases near UK and French nuclear reactors, merely because their data lacked statistical significance.

These conclusions were incorrect: the authors should have reported the observed leukemia increases but added there was a >5% probability they could have occurred by chance. In more detail, p values (that is, the probabilities that observed effects may be due to chance) are affected by both the magnitude of effect and the size of study (Whitley and Ball, 2002). This means statistical tests must be used with caution as the use of an arbitrary cut-off for statistical significance (usually p = 5%) can lead to incorrectly accepting the null hypothesis (ie nil effect) merely because it is not statistically significant (Sterne and Smith, 2001): a possible type II error in statistics.

This often occurs in small studies due to their small sample sizes rather than lack of effect (Everett et al, 1998). Axelson (2004) has pointed out that the findings of many epidemiology studies with negative results statistically speaking, are “of questionable validity as they may obscure existing risks”.

On March 20 2019, the British journal Nature published a landmark editorial headlined “It’s time to talk about ditching statistical significance” which argued against the indiscriminate use of statistical testing in health studies. The same edition contained a commentary “Scientists rise up against statistical significance” signed by 853 scientists worldwide with about 80 in the UK. It called for call for an end to the dismissal of possibly crucial effects in health studies through the inappropriate use of statistical testing. The Nature editorial simultaneously reported that US scientists at the American Statistical Association (ASA) had just published a scientific article with the same end. See further discussion here.

The nub of the matter is that, as reported in the Nature editorial, “the rigid focus on statistical significance encourages researchers to choose data and methods ... that yield statistical non-significance for an undesired result ...thereby invalidating any conclusions.” This damning verdict also applies to the undesired result of observed increases in health effects from an epidemiology study.

For decades, some scientists, including those employed at government agencies, have dismissed risk findings in epidemiology studies near nuclear facilities by concluding they showed “no significant” raised risks or that excess risks were “not significant” or similar phrases. Now, in theory, they will not be able to do this as easily as they have in the past as this poor scientific practice has been exposed.
Appendix G: ICRP’s Inadequate Radiation Risk Factor

ICRP’s risk factor for radiation is problematic for several reasons. First, it only refers to fatal, not non-fatal, cancers. Non-fatal cancer remains a very serious matter for children and their families and should not be ignored. The ICRP risk factor also excludes non-cancer effects known to result from radiation exposures, such as cardiovascular diseases, strokes, birth defects, mental ill health, and cataract induction.

It is true that the ICRP, at least in the past, included a small factor for hereditary risk and non-fatal cancer risk (ie with a 1% increase from 5% to 6% per Sv) but this is not considered to fully account for these effects.

Another problem is that the ICRP risk is just for a single year and a lifetime risk should be used. Despite the above shortcomings few, if any, Governmental or international initiatives currently exist to address these shortcomings.

Fatal Cancer Risks

I. The current ICRP risk factor is 0.05 per Sv for radiogenic fatal cancer in adult males. This was established in the late 1960s and has not been updated since then: it is out of date. For example, in 2006, the US National Academy of Science’s BEIR VII report cited fatal cancer risks of 0.11 and 0.13 per Sv for adult US males and females respectively.

II. The ICRP figure of 0.05 per Sv is obtained AFTER the application of the ICRP’s DDREF (dose and dose rate effectiveness factor) of 2. This means that the net risks are halved. But this is wrong - see para 48 et seq above: most international bodies now avoid using DDREFs. If they were discontinued then ICRP’s fatal cancer risk factor would immediately increase to 0.10 per Sv.

III. The ICRP’s risk figure for fatal cancer is unsatisfactory for other reasons. This figure is averaged over all ages and applies only to males. Little account is taken of the higher radio-sensitivities of women and of embryos, fetuses, neonates, babies or children, nor of higher individual radio-sensitivities. See chart on page 52 below.

IV. The ICRP’s risk factor derives from a single exposure and assumes no further exposures will be made. In other areas of toxicity, eg exposures to chemicals, much safer methods and standard-setting approaches are used. With chemicals, the risk is the additional chance of a lifetime exposure to a carcinogen, and usually the figure of 70 years is used for a lifetime, ie a factor of 70 times greater than an annual risk. For example, the US EPA uses lifetime risks for radiation standard-setting purposes. In other words, the ICRP’s risk assumes that people are only exposed once and will not be exposed again. This methodology is not relevant to chronic radiation exposures, eg from background radiation or from environmental (or many occupational) exposures.

V. To take into account higher risks to embryos, fetuses, babies and children, generous precautionary factors are inserted into chemical risks. But with radiation, no such safety factors are built in. Indeed with DDREFs, the exact opposite occurs. It is interesting to ascertain why these differences between chemical and radiation risk-setting approaches exist. This is explained in Appendix C above.

VI. It is recommended that the ICRP should refrain from further use of DDREFs and should adopt a new risk factor of at least 0.11 per Sv (the BEIR VII figure) for fatal cancer risks alone in adult males. It should explicitly acknowledge that this is the risk from a single acute exposure to low-LET radiation and that it only applies to adult males.

VII. Risks will be commensurately higher for adult women. To take them into account, the BEIR VII risk of 0.13 per Sv should be used from NAS Report BEIR VII. To take account of radiation risks to all children aged 1-15, it should be increased by a factor of 10 (See NAS Report BEIR VII, 2007) ie to 1.1 per Sv. To take account of risks to all infants <1, it should be increased by a factor of 100, ie to 11 per Sv (Richardson RB, 2009). See chart below on increasing risks for younger people.

VIII. It is expected that risks will and be progressively higher for neonates62, foetuses and embryos. The ICRP should explicitly recognise that radiation is a potent teratogen and address this matter.

Increasing Risks for Younger People

62 within the first month of life after birth
The chart below shows the lifetime attributable risk of cancer (cases) per Sv, according to age at time of exposure. The chart was created by this report. The data were obtained from Table 12D-1 Lifetime Attributable Risk of Cancer Incidence on page 311 of the BEIR VII report (2006). The BEIR raw data were multiplied by a factor 1.5 to remove the DDREF of 1.5 applied by the BEIR Committee.

This chart shows that risks steadily increase the younger the people are at the time of exposure. It also shows that girls are about twice as radiosensitive as boys. Finally it shows that the ICRP’s fatal cancer risk factor of 5% should not be applied to children and infants, as it seriously underestimates their radiation risks.

Non-Fatal Cancer Risks

Since non-fatal cancers are serious matters for children and their families, and since approximately twice as many cancer cases occur as cancer deaths, it is recommended that a new radiation risk of cancer cases be established of 0.11 x 2 = 0.22 cancer cases per Sv. The above factors would all be increased commensurately.

Non-Cancer Risks

Several recent studies (see para 52 et seq above) have confirmed increased radiogenic risks of cardiovascular disease and stroke. In particular, Shimuzu et al (2010) have indicated stroke plus heart disease combined now account for about one-third of the radiation-associated excess deaths – the same rate as cancer in the atomic bomb survivors. In other words, radiogenic fatal stroke and cardiovascular disease risks are in the same league as radiogenic fatal cancer risks and should now be taken into consideration by radiation authorities in setting limits to radiation exposures.

It is therefore recommended that a new radiation risk of fatal stroke and cardiovascular disease be created of 0.12 per Sv to reflect these newly perceived risks. Since we do not have separate CVS risks for men and women, an average figure is used.
In total, this would mean establishing a new radiation risk factor for adult males for all cancer cases plus all fatal cardiovascular diseases + stroke of 0.11 + 0.22 = 0.33 per Sv with the risks for women and infants, children being increased commensurately. See table below.

**Factors for Radiogenic Risks per Sv (to two significant figures) – as recommended by this report**

<table>
<thead>
<tr>
<th></th>
<th>Adult Men</th>
<th>Adult Women</th>
<th>Children 1-15</th>
<th>Infants Under 1 year</th>
<th>ICRP Risk for fatal cancer in adult males (for comparison)</th>
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<tbody>
<tr>
<td>Fatal Cancer</td>
<td>0.11</td>
<td>0.13</td>
<td>1.1</td>
<td>11</td>
<td>~0.05</td>
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<tr>
<td>Non-fatal Cancer</td>
<td>0.22</td>
<td>0.26</td>
<td>2.2</td>
<td>22</td>
<td>~0.01</td>
</tr>
<tr>
<td>Fatal CVS + Stroke</td>
<td>0.11</td>
<td>0.13</td>
<td>1.1</td>
<td>no data*</td>
<td>nil</td>
</tr>
<tr>
<td><strong>Total risk = Non-fatal cancer plus CVS disease/stroke</strong></td>
<td><strong>0.33</strong></td>
<td><strong>0.4</strong></td>
<td><strong>3.3</strong></td>
<td>no data*</td>
<td>nil</td>
</tr>
</tbody>
</table>

*Few data are available for radiogenic risks of CVS + stroke in children.

It can be seen that significantly increased risk factors are recommended for use in assessing in radiogenic risks in children and women.
### Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ALL</td>
<td>acute lymphocytic leukemia</td>
</tr>
<tr>
<td>AML</td>
<td>acute myelogenous leukemia</td>
</tr>
<tr>
<td>AR</td>
<td>absolute risk</td>
</tr>
<tr>
<td>BEIR</td>
<td>Biological Effects of Ionizing Radiation Committee of US National Academy of Sciences</td>
</tr>
<tr>
<td>BFS</td>
<td>Bundesamt für Strahlenschutz (German Federal Office for Radiation Protection)</td>
</tr>
<tr>
<td>Bq</td>
<td>becquerel</td>
</tr>
<tr>
<td>CERRIE</td>
<td>UK Government Committee Examining the Radiation Risks of Ionising Radiation</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
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<td>CLL</td>
<td>chronic lymphocytic leukaemia</td>
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<td>CML</td>
<td>chronic myelogenous leukaemia</td>
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<tr>
<td>COMARE</td>
<td>UK Government Committee on the Medical Aspects of Environmental Radiation</td>
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<td>CT</td>
<td>computed tomography</td>
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<tr>
<td>CVS</td>
<td>cardiovascular system</td>
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<td>DNA</td>
<td>deoxyribonucleic acid</td>
</tr>
<tr>
<td>DDREF</td>
<td>dose and dose-rate effectiveness factor</td>
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<tr>
<td>EAR</td>
<td>excess absolute risk</td>
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<tr>
<td>ERR</td>
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</tr>
<tr>
<td>Gy</td>
<td>gray</td>
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<td>IAEA</td>
<td>International Atomic Energy Agency</td>
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<td>ICRP</td>
<td>International Commission on Radiological Protection</td>
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<tr>
<td>INWORKS</td>
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<td>KKK</td>
<td>Kinderkrebs in der Umgebung von KernKraftwerken = Childhood Cancer in the Vicinity of Nuclear Power Plants</td>
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<tr>
<td>LNT</td>
<td>Linear No-Threshold</td>
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<tr>
<td>LSS</td>
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<tr>
<td>mSv</td>
<td>millisievert</td>
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<tr>
<td>μSv</td>
<td>microsievert</td>
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<tr>
<td>NHL</td>
<td>non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>OR</td>
<td>odds ratio</td>
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<tr>
<td>OSCC</td>
<td>Oxford Study on Childhood Cancer</td>
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<tr>
<td>p-value</td>
<td>probability value of a result occurring by chance</td>
</tr>
<tr>
<td>RBM</td>
<td>red bone marrow</td>
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<td>RR</td>
<td>relative risk</td>
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<tr>
<td>SIR</td>
<td>standardised incidence ratio</td>
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<tr>
<td>Sv</td>
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