Considerable amount of data on low-dose radiation (LDR) health effects is indeed available, as it has been studied for a long time. But, there is still disagreement in the scientific community with two opposing views:

– The linear no-threshold (LNT) model
  • Endorsed by advisory bodies
  • Accepted and used by regulatory agencies.
– Radiation Hormesis
The persistence of the low-dose radiation cancer risk controversy, after so much study, is of very much concern since:

- Actions taken based on the wrong hypothesis can be very harmful, as such actions can increase rather than decrease cancer risk.

Hence *the* most important research need is to resolve the low-dose radiation cancer risk controversy.
What is the effect of low-dose radiation on cancer?

To understand this, we need to first understand what causes cancers.

The prevalent model of cancer is the somatic mutation model of cancer, and we have been fighting the war on cancer based on this model. Is this model valid? Are cancerous mutations the primary cause of cancers? No, since almost everyone has cancerous or pre-cancerous mutations (covert cancers) but lifetime risk of being diagnosed with cancer is only ~30%. (Greaves, 2014).

If mutations are not the primary cause of cancers, what is?
What is the Primary Cause of Cancer?

The tremendous increase in cancers when the immune system is suppressed indicates immune suppression may be the primary cause of most cancers. Hence, an alternative model of cancer is the Immune Suppression Model of Cancer. 

(See “Changing the Paradigm of Cancer Screening, Prevention, and Treatment”, Doss, Accepted for publication in Dose-Response, 2016)
### Evidence supporting the immune suppression model of cancer

<table>
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<th>Evidence</th>
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<tr>
<td>Immune system response reduces rapidly with age (<a href="#">Levin, 2012</a>) and cancer risk rises rapidly with age (e.g. <a href="#">WHO</a>), Females have stronger immune system than males (<a href="#">Furman, 2014</a>) and have lower risk of cancer compared to males (<a href="#">Siegel, 2015</a>), Allergy sufferers have overactive immune system and have lower risk of cancer (<a href="#">Wang, 2005</a>), Breastfeeding enhances immune system in infants (<a href="#">Turfkruyer, 2015</a>) and it reduces childhood leukemias (<a href="#">Amitay, 2015</a>), Exercise (<a href="#">Woods, 2009</a>) and infections (<a href="#">Karbach, 2012</a>) stimulate the immune system and reduce cancers (<a href="#">Orsini, 2008</a>, <a href="#">Richardson, 1999</a>), High-dose radiation (<a href="#">Liu, 2003</a>), cigarettes (<a href="#">Stämpfli, 2009</a>), and alcohol (<a href="#">Molina, 2010</a>) suppress the immune system and they all increase cancer risk (<a href="#">Ozas, 2012</a>, <a href="#">Stämpfli, 2009</a>, <a href="#">Nelson, 2013</a>).</td>
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</table>
Effect of low-dose radiation on the immune system

The DNA Damage Response Arouses the Immune System (Gasser and Raulet, 2006)

Up-regulation of Rae1 and other ligands of the NKG2D receptor. Activates NK cells.

LNT model supporting publications (e.g. BEIR VII Report) ignore or dismiss the importance of the immune system in preventing cancers and the enhancement of the immune system from low-dose radiation.

The enhanced immune system response would reduce cancers.
Increased DNA Damage Observed Shortly After Five Minutes of Vigorous Exercise or Low-dose Radiation Exposure

![DNA Damage from Five Minutes of Exercise](image1)

* Significant increase compared to Rest (P < 0.05)

**Fig. 1.** DNA Damage from Five Minutes of Exercise (Data from Fogarty, 2011)

**Fig. 2.** Cancer mortality rate ratio as a function of total physical activity (Data from Orsini, 2008)

Vigorous exercise reduces cancer mortality significantly. The benefit from exercise is due to the enhanced defenses.

Even five minutes of vigorous exercise resulted in increased DNA damage.

Since vigorous exercise reduces cancers, it would be extremely unwise to not exercise based on the observed DNA damage from vigorous exercise. **BEIR VII Report** has used similar logic to raise concerns about the DNA damage from low-dose radiation and has dismissed the beneficial effects of enhanced defenses.
What does the evidence say regarding the cancer risk of LDR?
Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries


Canadian data are clearly inconsistent with most other data.

BEIR VII Report, instead of asking for a re-examination of the Canadian data, utilized these results to support the LNT model in an Addendum to the Report which was already finalized.

In 2011, CNSC withdrew Canadian data because of faults identified in them, negating the conclusion of the 15-Country Study.
Effect of prolonged low-dose radiation exposures on cancer

Taiwan - Residents of radio-contaminated apartments in Taiwan (Hwang, 2006)
NSWS - Radiation workers in Nuclear Shipyard Worker Study (Sponsler, 2005) This study excluded the possibility of Healthy Worker Effect since the comparison is to non-radiation workers.
British Radiologists - British Radiologists who entered service during the period 1955-1979 (Berrington, 2001)
Mayak - Evacuated residents of villages near Mayak Nulcear Weapons Facility (Kostyuchenko, 1994)

Low-dose radiation exposures have resulted in reducing cancers contradicting the LNT model prediction

BEIR VII Report ignored British Radiologists and Mayak studies which were available at the time of the report. BEIR VIII Scoping meeting in 2014 ignored results from Taiwan and NSWS studies.
Atomic Bomb Survivor Cancer Mortality Data
(the most important data according to BEIR VII Report & others)

Excess Relative Risk rises with dose from 0 to ~0.25 Gy, decreases with dose from ~0.25 to ~0.5 Gy, and then rises with dose, resulting in a significant curvature.

Ozasa et al. state: “The curvature over the 0-2 Gy range has become stronger over time, .................., and has become significant with longer observation”

The significant curvature in the dose-response of the atomic bomb survivor cancer mortality data is inconsistent with the LNT model.

Since Ozasa et al. utilized cancer rates of lowest dose cohorts, extrapolated to zero dose, as the baseline cancer rates in the process of extracting the Excess Relative Risks, and since low radiation doses reduce cancer risk as seen earlier, the baseline cancer rates used would have a negative bias.
Atomic Bomb Survivor Data Corrected for Negative Bias in Baseline Cancer Rate

Correcting for the negative bias in the baseline cancer rate results in a J-shaped dose-response curve consistent with radiation hormesis. (Doss, 2012), (Doss, 2013)

Since the publication of the (Ozasa, 2012) update, many LNT model supporters, have stopped referring to the atomic bomb survivor data when discussing low-dose radiation cancer risk, e.g. Mark Little in his opening statement in Medical Physics “Point/Counterpoint: low-dose radiation is beneficial, not harmful” (Doss, 2013)
Repeated whole-body low-dose radiation treatments (10 cGy X 15 over 5 weeks = 1.5 Gy total) had a cancer therapeutic effect, performing as well as or better than chemotherapy, contradicting the LNT model. There were very few adverse side effects from the low-dose radiation treatments (temporary suppression of blood cells).
Interspersed low-dose radiation treatments to the whole body or half-body (10 cGy x 15 over 5 weeks = total 1.5 Gy) between the standard radiation therapy treatments to the tumor led to better survival and had a cancer therapeutic effect, contradicting the LNT model.
Tissues having \( \sim 0.2 \) Gy radiation dose had reduced second cancers per kg of tissue in comparison to tissues having no radiation dose from the radiation therapy, contradicting the LNT model prediction.
Smoking data at County level were not available. State level data were used to estimate County level data. Led to uncertainties.

Cohen study was criticized for incorrect accounting of Smoking


County level smoking prevalence data are now available, e.g.:
Lung cancer mortality rates were lower in high radon counties in comparison to low radon counties for the same level of smoking. Therefore, confounding by smoking cannot explain the reduction of lung cancers observed in high radon counties. Multiple linear regression of entire dataset confirms the reduction of lung cancers with increasing radon levels.
Radon Levels and Lung Cancer in USA

Higher radon counties (green, yellow, red) correspond to mostly lower rates of lung cancer (blue). Higher lung cancer counties (red) correspond mostly to lowest radon areas (blue).

Radon levels: [http://energy.lbl.gov/ie/high-radon/frac4.htm](http://energy.lbl.gov/ie/high-radon/frac4.htm)

Similar pattern observed for: UK, Canada, Ireland, France, Germany, Spain, Switzerland, Sweden, Portugal.
How about publications that claim increased cancer risk from low-dose radiation?
Publications that claim to support the LNT model

• Have major flaws in study design, data, analysis, and/or interpretation.
• Utilize 90% CI to claim increased cancer risk when 95% CI (which they previously used) would show no increased cancer risk.
• Use evidence that is of marginal significance and do not consider important confounding factors.
• Have insufficient statistics to distinguish between radiation hormesis and LNT models but calculate radiation risk coefficient using a linear model.
• Generally do not discuss other publications that show reduced cancer risk from low-dose radiation.
• Discuss increased cancer risk from a single type of cancer (which could result from chance, considering the lower statistics) while ignoring the overall reduction in cancers.
<table>
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<tr>
<th>Study</th>
<th>Criticism</th>
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<tr>
<td>(Leuraud, 2015), (Richardson, 2015) – INWORKS studies</td>
<td>(Doss, 2015), (Sacks, 2016): Ignored medical radiation dose, which was small compared to occupational dose in early years but was much higher in later years. Used 90% CIs.</td>
</tr>
<tr>
<td>(Kendall, 2013) Childhood Leukemias vs. Natural Background Radiation</td>
<td>(Doss, 2014), (Sacks, 2016): Data are of marginal significance. All cancers RR=1.03 (1.00-1.07 95%CI). Did not consider confounding by breastfeeding &amp; daycare attendance, which result in 20% and 30% cancer reduction respectively.</td>
</tr>
<tr>
<td>(Pearce, 2012) (Mathews, 2013) Cancers following childhood CT scans</td>
<td>(Cohen, 2013), (Walsh, 2014), (Boice, 2015), (Sacks, 2016): Potential for Reverse causation; data not consistent with present knowledge on radiation-induced cancers, not consistent with A-bomb survivor data.</td>
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<tr>
<td>(Hwang, 2008) Taiwan apartment residents</td>
<td>One cancer type had higher incidence (90% CI), quite likely due to chance. (Doss,2013): Reduction of all cancers (95% CI).</td>
</tr>
<tr>
<td>(Schonfeld, 2013) Techa River solid cancer mortality</td>
<td>Statistics not sufficient to determine dose-response shape; LNT model was used for analysis. (Jargin, 2014): Possible medical examination bias in higher dose population.</td>
</tr>
<tr>
<td>(Krewski, 2006), (Darby, 2005) Radon lung cancer</td>
<td>(Fornalski, 2011) : Bayesian analysis of 28 studies shows no dose-dependence can be determined.</td>
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</table>
INWORKS Study of Cancers in Nuclear Industry Workers in USA, UK, and France (Richardson, 2015)

90% confidence intervals (CIs) used. Data points have very large errors, and almost all data points are consistent with no increased cancer risk if 95% CI were used. Obtaining shape of dose response from this poor quality data is senseless.

Criticism of the study (Doss, 2015), (Sacks, 2016)
(Pearce, et al, 2012) UK Study:

**Brain Cancers:**
- ERR/Gy for glioma increased with age at exam – this is reverse of prior studies. The risk is expected to decrease for higher ages when brain development nears completion
- ERR/Gy =23 much higher than 0.88, observed in A-Bomb survivors <10 y

**Leukemias and MDS:**
- ERR/Gy Leukemia and Myelodysplastic Disease (MDS) – 36, much higher than 6.5 in A-Bomb Survivors <20y

(Mathews, 2013) Australian Study:

**All cancers:** Risk estimate for All cancers (excluding brain cancers) was 27 vs 3 for A-bomb survivors

**Latency period:** Study of cancers one year after CT scans increased the likelihood of reverse causation

**Implausible tumors associated with CTs:**
Excesses seen for melanoma and Hodgkin’s lymphoma, not known to be associated with radiation, and not for breast cancer, a radiosensitive site

**Inconsistent Age at exposure effect:**
Excess leukemias observed for later age exposure but not for early age

Both studies were subject to reverse causation because of study design. Considering the large inconsistencies with previous studies, the conclusions of these studies are in doubt, and so these studies do not provide evidence for causal link between CT scans and cancers (Boice, 2013). The conclusions of these publications are not credible.
A Bayesian analysis of 28 ecological and case-control studies indicates no conclusion on shape of dose-response can be drawn. The original data span a wide range of dose-response shapes.
Challenge to LNT Model Proponents

1. Explain the significant reduction of cancer mortality rates in atomic bomb survivors as radiation dose increases from ~0.25 Gy to ~0.5 Gy

2. Explain the cancer therapeutic effect of repeated applications of LDR in cancer patients

3. Explain the reduction of second cancers/kg of tissue in radiation therapy patients for tissues with ~20 cGy dose

4. Explain the reduction of cancers with low-dose rate radiation exposures in evacuated residents of villages near Mayak, British Radiologists who joined service between 1955-79, Nuclear Shipyard Radiation Workers, and Taiwan apartment residents

5. Explain the negative correlation universally observed between residential radon levels and lung cancers

6. Stop using obviously faulty data and data that are already discredited because of major flaws.
Overall Conclusion:
Low-dose radiation reduces cancer risk.

But, we have been using the LNT model for radiation safety since the 1950s. What are the consequences of using the LNT model?

A No-Threshold model is intrinsically more dangerous to the public as it inflates the risk by giving significance to unmeasurable changes in risk, thereby inducing governments and the public into fleeing the imagined risk and running into real risk.
LNT model is responsible for ~30% of recent cancer deaths

The war on cancer has not been successful as age-adjusted cancer mortality rates continue to be high in spite of tremendous advances in cancer screening, prevention, and treatment based on the mutation model of cancer.

LNT Model blocked study of radiation hormesis in the 1980s when it was proposed as a method of reducing cancers (Hormesis with Ionizing Radiation, TD Luckey, 1980).

About 30% of cancer deaths in the past few decades could have been avoided if radiation hormesis had been studied in the 1980s & utilized.
Research Needs in the Low-dose Radiation Area

• Prospective studies to resolve the LDR cancer risk controversy
• Prospective studies to optimize cancer prevention from LDR
• Clinical trials of LDR treatments for different types of cancers
• Study of lung cancer rates in residents of radon-mitigated homes, before and after radon mitigation, to determine definitively the effect of residential radon on lung cancers.

Benefits to the Public:

• Significant reduction of cancer mortality rates, much more than has been achieved in the past 50 years
• Eliminate the harm caused by the use of the LNT model in diagnostic imaging, in case of nuclear accidents, dirty bombs, etc.
• Reduced costs for all uses of radiation