Reviewer’s report

Title: Environmental radon exposure and breast cancer risk in the Nurses' Health Study II

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Reviewer: William Field

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R. William Field, PhD, MS - Reviewer

Review: "Environmental radon exposure and breast cancer risk in the Nurses' Health Study II".

Thank you for the opportunity to review the paper, "Environmental radon exposure and breast cancer risk in the Nurses' Health Study II". The availability of an existing prospective cohort allows a cost-effective opportunity to study potential causal associations between environmental exposures and various adverse health outcomes. A nested case control study performed within the cohort would potentially help address some of the limitations of radon exposure assessment.

Abbreviated line-by-line feedback (comments and suggested edits) follow:

The Introduction needs substantial editing. The information offered regarding the effects radon and its decay products can have on DNA is somewhat fragmented throughout the introduction. Since the estimated dose to the breast from inhalation or ingestion of radon and its decay products (See referenced Kendall study and ICRP data) is low, additional information would be helpful to support the biological plausibility of a causal relationship between protracted radon exposure and breast cancer.

Line 28-30 - Radon, a type of ionizing radiation, and its progeny are primarily inhaled and can deliver a radiation dose to breast tissue, where they may continue to decay and emit DNA damage-inducing particles.

* Radon is radioactive gas, not a type (e.g., alpha, beta, etc.) of radiation

* Suggest using "decay products" instead of progeny

* The radon decay products that deliver the majority of the dose to the lung are polonium 218 and 214. These two decay products have a rather short half-life. Which decay products are deposited in the breast or body that continues to irradiate the breast?

Line 33-34 - County-level radon exposures were linked with geocoded residential addresses updated throughout follow-up.
It is important to note that the radon data (even the Lawrence Berkeley National Laboratory U.S. radon exposure model) are based primarily on short term charcoal-based radon measurements and do not necessarily represent radon exposure for an individual within the county. I would suggest either stating (throughout the paper) that average county-level radon concentrations (or estimated exposure depending on data source) were linked ……

Line 59-64 - However, the relationship between radon, a type of ionizing radiation and International Agency for Research on Cancer (IARC) Group 1 human carcinogen [10], and breast cancer has not been well characterized.

See previous comment about type of radiation

Suggest stating potential causal relationship

Not well characterized? Where has it been characterized?

Line 61-62 - Radon is a naturally occurring radioactive gas forming from the decay of uranium and thorium, found in air, soil, rocks, and water.

It may be helpful to state uranium-238 and thorium-230 since there is a separate thorium (thorium-232) decay series.

Line 65-67 - Approximately 6% of U.S. homes have radon levels above the Environmental Protection Agency (EPA) action level of 400 Bq/m3 at which remediation is recommended [13].


Line 67-69 - Radon decays into its progeny (e.g., polonium-218), both of which can enter the human body primarily through inhalation, emitting radiation in the form of alpha particles, beta particles, and/or gamma rays.

Does "both" refer to radon and decay products?

Inhalation of polonium 218 and polonium 214 are of radiogenic significance to the lung, but is inhalation a substantial source of exposure to the breast? Some groundwater sources have very high radon concentrations. Does ingesting water in these high waterborne radon areas present a greater risk than inhalation in regard to the breast. Radon is lipophilic so ingestion of radon in water results in a small radiation dose to the breast (see references below).


Although there is strong biological plausibility that radon exposure could influence breast carcinogenesis, few epidemiologic studies have been conducted.

* The introduction does not provide evidence of "strong" biological plausibility.

* Additional information would be helpful to the reader regarding estimated doses to the breast from inhalation (potential translocation of radon decay products?) and ingestion of radon (and decay products) to determine likelihood (e.g., study power, etc.) of detecting a causal association if one existed.

Not sure that any descriptions of the case study and ecologic studies are useful other than references.

However, to date, no prospective epidemiologic study has been conducted.

* Not only cohort study, but also include case-control studies. A case-control or nested case control study may have greater internal validity especially with exposure information at the individual level.

I may have missed it, but was there any verification that the breast cancers were primary cancers?

Not sure of the utility of including hydraulic fracturing "treatments". Very little scientific evidence to conclude that hydraulic fracturing affects residential radon concentrations. Including this variable detracts from the overall analyses.

However, some women residing in certain parts of the Western U.S. may be exposed to relatively higher levels of radon compared to women living in other regions, as parts of the Western U.S. are near active faults (e.g., San Andreas Fault) characterized by anomalously high radon emissions [50]. High radon concentrations are correlated with seismic activity, as the release of trapped radon from rocks may precede seismic events [51]. The impact of residential proximity to active fault systems .................

This line of reasoning is a stretch in the reviewer's opinion and does not add to the interpretation of the paper. Heterogeneity of radon concentrations within a county reduces the overall validity of using aggregated average short term radon concentrations as a surrogate measure of radon exposure.
Line 279 - The impact of residential proximity to active fault systems as well as regional differences in exposure due to time spent indoors, individual-level housing characteristics (e.g., presence of basements), and remediation practices should be examined in future studies.

* Aggregate radon short term radon exposure data cannot replace year-long individual level radon measurements on each level of the home that are linked with the retrospective mobility (e.g., time spent on different levels of the home, outside the home, etc.) of the subject. Time spent outside varies by region (e.g., IA versus CA).

Line 291-294 - The radon exposure data used in this study were collected during the mid- to late-1980s. We assumed radon levels remained consistent over time and calculated exposure measurements using updated address information throughout follow-up.

* While many new homes had AC installed in the 1960s (https://energy.gov/articles/history-air-conditioning), retrofitting of homes for central AC and the increased use of window AC continued through and after the 1980s. The switch from window fans to AC substantially increased yearlong radon concentrations in many regions after the 1980s.

Line 303-305 - We objectively assessed radon exposure using a metric created from short- and long-term radon monitoring surveys, utilized in previous epidemiologic studies examining cancers [53].

* Using the metric from a previous study is not necessarily a strength. The use of a sensitivity analyses could be considered a strength.

Line 309-310 - Updated address information beginning in 1989 provided an opportunity to reconstruct historical radon exposure, which allowed us to evaluate long-term radon exposure and breast cancer incidence.

* Estimate long term exposure? Please explain in more detail how you can evaluate long term radon "exposure" based on short term average radon measurements (e.g., no individual level data). You discussed limitations of radon measurements in limitations section. I would suggest not trying to state it is a strength. The reference to using a method like the Turner et al. study does provide some support for its usefulness to estimate radon exposure over aggregated counties and perhaps should be mentioned earlier under Method justification.

One concluding comment. It is noteworthy that several studies have described the occurrence of an inverse association in the U.S. between county average radon concentrations and estimated county smoking rates that can lead to residual confounding if not adjusted for adequately. Unfortunately, adjustment of confounding at the aggregate level is difficult.

See:


Again, thank you for the opportunity to review the paper.

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