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The Lesser Evil: Plutonium-239 or Uranium-235? A Study on F0 Atomic Bomb Survivors

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Abstract

'All models are wrong, but some models are useful.' Radioactivity is a life-detrimental exposure that increases individuals' susceptibility to cancer onset. The plasticity of the rate of aging $d(\log \mu(x))/dx$ has never been formally addressed, as it has been casually inferred as mortality rate $\mu(x)$ or risk $\log \mu(x)$. The mortality schedule of irradiated F0 atomic bomb survivors in Hiroshima (U-235) and Nagasaki (Pu-239) at age exposure 40 - 45 (ATE45) can unveil the characteristics of hazard trajectories by isotope type and dosimetry. Based on the advantage derived from background radiation, an alternative population was employed during the comparative study. A dose-dependent relationship between radioactive isotope types and the rate of aging was presented in the frailty framework; *γ-Gompertz-Makeham*. A pseudo-benefit initial mortality risk by distance to the epicenter was also observed among 0-5mGy survivors, suggesting that selection for mortality was determined by stringency from impact and frailty from natural selection. Furthermore, the standardized mortality ratio suggests Pu-239 has a more drastic effect on age-specific mortality trajectory than U-235; 0-5mGy, *Pu-239* 11%(M) 37%(F); *U-235* 4%(M) 0.5%(F). Upon intense radiation exposure, variation in the human rate of aging exists within a 10-km radius from the epicenter, and gender sensitivity may be a significant contributor to mortality selection.

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Introduction

Population dynamics are changing. Life-detrimental risk exposures identified in epidemiological studies have shown that the risk for mortality can be altered by exposure dosage. Few researchers will doubt that once the magnitude of mortality risk is elevated, the rate of aging must be accelerated. In radiation studies, the quadratic equation has been the preferred choice to measure the dose-response relationship. However, it is still unknown whether humans, who are relatively larger in body size compared to laboratory test animals, have the physiological capacity to recover upon radiation exposure. If such beneficial recovery for longevity were to occur, the radioactive dose-response and its lower limits to manipulate the rate of aging $d(log(\mu(x)))/dx$, and age-specific mortality rate from the norm have yet to be identified.

Herein, the life tables of atomic bomb survivors in Hiroshima and Nagasaki were addressed to examine whether exposure to radioactive isotopes can alter the age-specific mortality trajectory and the rate of aging. The difference in the characteristics of the radioactive isotopes Uranium-235 (U-235; Hiroshima) and Plutonium-239 (Pu-239; Nagasaki) that were detonated over the two prefectures in Japan during the end of the Second World War could lead to differences in age-specific mortality trajectories and to persist in its life-detrimental effects across all age groups [1-4].

An extensive amount of literature has presented that the original cohorts *F0* of atomic bomb survivors experienced a remarkable recovery and their remaining life expectancy was at a one-year difference from the general population in Japan [5]. Background radiation exists on Earth, specifically for U-235 [6]. Therefore, my analytical study shows the exceptional case whereby mortality derived from background radiation can be taken as an advantage during comparative analysis. Due to the lagged time interval from exposure to data collection, heterogeneity is taken as an interest as the completion of the frail-robust proportion in the population had to be distinctly different from our usual analytical work and interpretation.

Results

Selection: Stringency and Frailty for Mortality

The conventional approach to addressing research hypotheses concerning risk exposure is to measure the outcome of interest through the passage of time and age; logistic and survival regression models. Age-specific mortality trajectory of a univariate parametric frailty model, which is rarely presented in scientific literature, has limitless potential for a better understanding not only of the population's mortality dynamics but also of the data recorded across calendar years. Unobserved heterogeneity, also known as the frailty component, measures the presence of variables that were left unobserved or not recorded due to emergency or impromptu exposures such as nuclear accidents. The frailty component γ has to be a positive random variable indicator, as negative frailty would lead to non-senescence mortality, which is not representative of the already known human mortality dynamics. If the frailty component is not adjusted during survival and life-table analyses, the obtained risk and parameter estimates can be misleading during data interpretation.

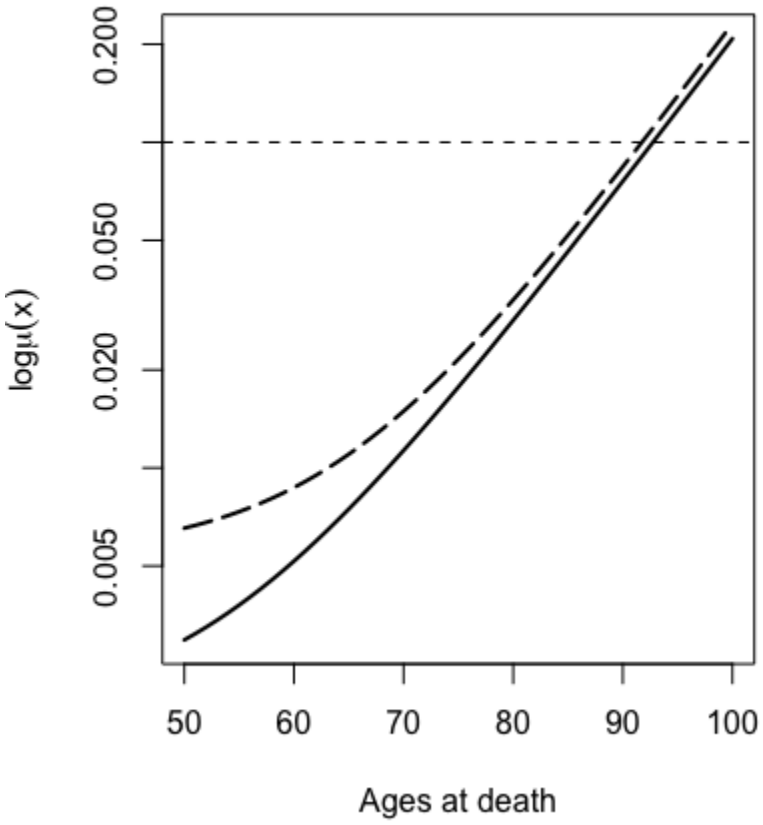
Survivors from the nuclear impact must have undergone a stringent selection for mortality, which was unlikely to be dependent on age and gender, as the proximity to the epicenter would be the main contributor to the likelihood estimation for immediate deaths by instantaneous high radiation exposure and nuclear impact. Subsequent selection for mortality was subject to survivors' vitality robustness to overcome the life-detrimental lagged effects from inhaled and

ingested radioactive isotopes, and their protective shield material types and distance to the epicenter at the time of exposure to account for instantaneous dose exposure.

Distance: Heterogeneity Ruse

Rather than solving the mortality dynamics of irradiated survivors through a theoretical and simulated approach, **Figure 1** presents the fitted mortality of a parametric frailty model *γ-Gompertz-Makeham*; recently coined as the logistic-typed mortality hazard **Equation 1: Methods section**, and its pseudo-benefit of initial mortality risk by dosimetry; 0-5 mGy, <3 km and 3 – 10 km to the epicenter; N.B: 1 Gray (G) = 1,000 mGy; 1 G = 100 rad. Survivors located <3 km experienced a more stringent selection for mortality, as only robust survivors managed to enter the Life Span Study (LSS) in 1950, a pre-set conditional survival probability for recruitment resulting in a lower magnitude for mortality than 3 – 10 km survivors. Survivors who were situated farther away received a lower nuclear impact, hence the proportion of frail to robust survivors was greater in comparison to <3 km survivors at LSS recruitment. It is a heterogeneity ruse from the obtained estimates, but a logical reasoning based on the distance to nuclear impact and conditional survival probability.

Figure 1. Pseudo-benefit of initial mortality risk

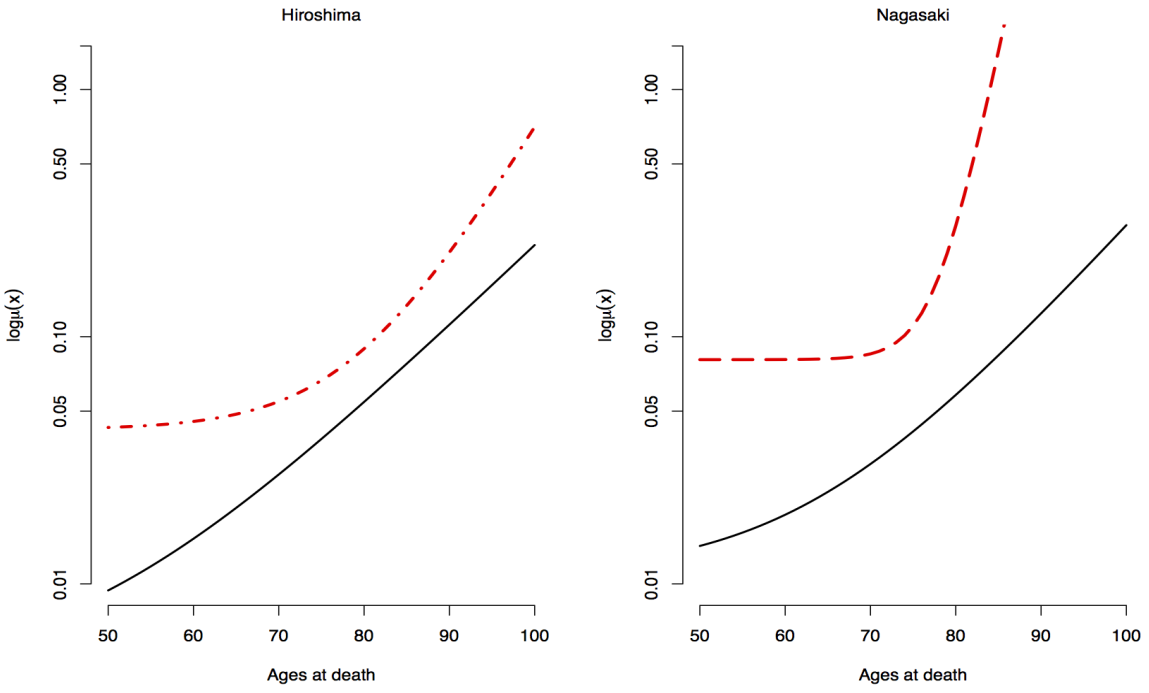


0 – 5mGy Hiroshima females age at exposure 40 – 45 (ATE 45) adjusted for unobserved heterogeneity; *i.e.*, standard individual hazard. Solid line: <3km; Dashed line: 3 - 10km to the epicenter. Horizontal dashed line indicates mortality at 10%; the difference in life expectancy is at one year. Refer to **Supplementary Materials Table S1** for MLE parameter estimates and 95% confidence intervals.

Dose: Two Ends of the Scale

The second analytical procedure is to determine the rate of aging $d(\log(\mu(x)))/dx$; the faster the rate of aging, the steeper the hazard slope on a semi-logarithmic plot; $\log \mu(x)$. Regardless of the distance to the epicenter, survivors who had received the same radioactive dosage presented the same rate of aging, as shown in **Supplementary Materials Table S1**; this converged to parallel lines in **Figure 1**. The mortality 'hump' was attributed to the constant term, *Makeham*, in the parametric hazard function; <3km and 3-10km in **Figure 1**. The rate of aging was then further examined by dosage; extreme and low dosage; **Figure 2 and Supplementary Materials Table S2 *b-estimates***. From the diverging hazard lines of Pu-239 and U-235 age-specific mortality trajectories, my finding shows that the rate of aging of the survivors is determined by and dependent on the dose; **Figure 1** and **Figure 2**. Extreme radioactive dosage accelerates the rate of aging.

Figure 2. Diverging age-specific mortality trajectories of extreme- and low-dosage in Nagasaki (Pu-239) and Hiroshima (U-235) of males at ATE 45 situated <3km to epicenter



An acceleration in the rate of aging and an elevated magnitude for mortality risk for extreme-dosage atomic bomb survivors in the two prefectures. Hazard lines were adjusted for unobserved

heterogeneity, *i.e.*, standard individual hazard. Refer to **Supplementary Materials Table S2** for estimated parameters and 95% confidence intervals.

Although extreme radioactive dosage accelerates the rate of aging and an accelerated failure time (AFT) hazard shape should be a more reasonable presentation, if the human physiological recovery and selection for mortality of irradiated survivors were efficient, the conditional survival probability for LSS should have given ample time for normalization towards a Gompertzian fit and a convergence in the hazard lines between low and extreme irradiated survivors. AFT survivors would have experienced mortality before the initiation of LSS. Therefore, the attained convergence of the optimized parameters during MLE is a phenomenon that I consider unusual.

Radioactive Isotopes Characteristics

The predominant public health concern lies in the low-dosage irradiated survivors and in identifying the vitality threshold from minute contamination exposure in the event of an emergency in nuclear power plants: Lowest Observed Effect Level (LOEL) and Frank Effect Level (FEL). Pu-239 is capable of attracting more of its kind to the site of an infected minor cut wound, and upon the inhalation of Pu-239 dust particles, Pu-239 resides in the respiratory system for decades [7]. Irradiated survivors by isotope types are thereby likely to experience different risks for the onset of specific cancer types [1,2]. Similar to Pu-239, U-235 has a tendency to be deposited and to persist in the bones of irradiated survivors, and depending on its path of entry, the risk for cancer types increases; *e.g.*, ingestion of radioactive contaminated water increases the likelihood of urinary bladder cancer [8].

Standardized Mortality Ratio & RA Fisher's Investigation Approach

The Lesser Evil

Though Pu-239 and U-235 are radioactive isotopes, atomic bomb survivors who were exposed at high dosage levels had a faster rate of aging compared to the low-dosage groups. It is of curiosity to distinguish which of the two isotopes is less detrimental and if a logical explanation can be derived based on information from the survivors' life tables and age-specific mortality trajectories.

For a comparative approach of radioactive effects on all-cause mortality, the usual protocol would be to first examine the age at exposure (ATE) by isotope type and in accordance with its age-specific mortality trajectory by prefectures and nationwide. However, the demographic composition at the site of each nuclear impact and the demographic structure of the two prefectures were likely to be very different before the destruction. Young healthy Japanese males were recruited to join the armed forces, thereby offsetting the sex ratio from expected mortality dynamics; **Supplementary Figure S1**. The Pu-239 designed bomb 'Fat Man' was detonated over an industrial district in Nagasaki; a hotspot for a higher proportion of males to females in the field of engineering and mechanical production. According to the literature, there was no survivor within a 1.6-km radius of the epicenter [3,9]. Certainly, there is no hesitation to conclude that exposure to a nuclear impact has a profound effect on mortality, but devastation from the lagged effects of the two radioactive isotopes, particularly contamination at minute dosages, is a considerable concern in the event of a nuclear emergency. This further illustrates the analytical preference for ATE 40-45, for the numbers of survivors were adequate for a parametric fit.

Age-specific mortality trajectory of low-dosage Pu-239 LSS males exhibits a faster rate of aging than U-235 irradiated males at <3km to the epicenter; **Figure 2**. For the validation of the

outcome, if Pu-239 has a detrimental effect on longevity and the rate of aging, its effects will sustain beyond 3km from the epicenter; 3-10km. Therefore, to achieve a fair comparison with the same demographic composition, the respective mortality imprint of Pu-239 and U-235 survivors was imposed onto an alternative population in Japan that is renowned for its long life expectancy. According to the calendar survival follow-up of the life tables, Okinawa is the preferred, and possibly the most suitable, alternative reference population as only robust atomic bomb survivors were recruited for the LSS in Nagasaki and Hiroshima. The standardized mortality ratios were obtained by introducing suitable notations for mortality analyses; **Table 1 & Methods Section**.

Pu-239 exhibits excess deaths in both genders, and its effects persist at low dosage. This analytical approach can be considered avant-garde because the mortality imprint by isotope type was introduced to a non-exposed and healthy population but representative of the atomic bomb survivors' robustness during mortality selection. Background radiation of U-235 serves as an inference point for Hiroshima low-dosage survivors (0-5 mGy) and a validation of Okinawa's suitability as the alternative reference population.

Table 1. Standardized mortality ratio of U-235 and Pu-239 ATE45 mortality imprint on males and females residing in Okinawa between 1975 and 1979

	Hiroshima (U-235)	**Nagasaki (Pu-239)**
<3km from epicenter of Okinawa		
Males		
Low	1.040±0.024	1.111±0.024
Extreme	1.743±0.030	3.613±0.043
Females		
Low	1.005±0.025	1.370±0.030
Extreme	3.932±0.050	1.518±0.031
3 – 10km from epicenter of Okinawa		
Males	1.073±0.024	1.030±0.023
Females	1.194±0.028	1.160±0.027

If there were excess deaths from the radioactive isotope, the standardized mortality ratio would be $\bar{h} > 1.0$. When $\bar{h} = 1.0$, there is no excess death, and when $\bar{h} < 1.0$, there is beneficial risk exposure on mortality; $\bar{h}$ ± standard error (SE).

Gender Sensitivity Towards Isotope Types

Though Pu-239 has a more drastic effect on overall mortality than U-235, an intriguing finding at extreme dosages suggests that there is a gender discrepancy from radioactive-isotope type; **Table 1**. Extreme Pu-239 appears to have a stronger impact on males than on females, and on the contrary, extreme U-235 dosage exhibits a higher excess death rate among females. The proposed hypothesis for this phenomenon would be that extreme dosage Pu-239 survivors were mostly infected through cut wounds and the respiratory tract, and a higher prevalence of tobacco smoking in males could have contributed to a less favorable survival outcome than in females. U-235 adheres to the infected survivors by anchoring to the kidneys and urinary tract [6]. The possibility of such gender discrepancy for excess deaths under U-235 extreme doses may be due to the anatomical differences between males and females. This hypothetical explanation may be

challenging to determine or prove as the assessment of gender differences by radioactive isotopes is very limited in epidemiological studies, *e.g.*, survival profiles or health outcomes of nuclear power plant workers, as the lack of statistical power limits gender stratification or comparative analysis. Aside from cancer survival outcomes by gender, discussion on radiation sensitivity between the two genders remains limited [10]. The interaction and effects of isotope type by gender require a more detailed investigation using individuals' survival profiles from a prospective study.

Discussion and Conclusion

The challenge in this analysis is to distinguish the following two elements: stringency for mortality from radioactivity effects on frailty $Z(x)$ and the naturally occurring force of mortality $\mu(x)$, whereby $Z(x)$ contributes an important role in its equation during mortality selection over calendar time and age. Application of parametric frailty survival models permits $Z(x)$ to be a rank indicator for the gradient of robustness or vitality in the population [11]. Frail individuals will have a higher Z-value compared to robust individuals. Though gender and age can be confounders in the investigation of survival outcomes from radiation-dose exposure, immediate casualties from nuclear impact were unlikely to be selective for gender and age.

Heterogeneity is the predominant reason why we are witnessing changes in population dynamics and the deceleration in the improvement of life expectancy. If members of the population were exposed to the same life-detrimental measures, such as a radioactive dose, it would be within our logical acceptance that a distribution exists to determine the pace of the selection process. Some individuals may have underlying diseases prior to risk exposure and would then be considered frail individuals to be swiftly expired from the population, while a handful of robust individuals would then age over calendar time to reach the presumed normal or non-exposed mortality rate of the general population. Although this analytical study may be the first to present evidence of all-cause mortality on the rate of aging and risk for mortality by isotope type, there is at least one previous publication that has suggested the existence of heterogeneity by dose-response and survival by ATE among atomic bomb survivors [12].

Survivors who were at close proximity to the epicenter would have experienced a more intense selection for mortality, and their natural-occurring $Z(x)$ had to be modified, leaving the robust survivors to be selected for mortality by radiation dose, not by age. Hence, the approach to further consider the non-recorded deaths from 1945-1950, prior to LSS data collection, is to make a reasonable assumption that despite the high stringency for mortality selection <3km from the epicenter, a frailty distribution must exist among robust survivors and the selection for mortality had occurred at a much faster pace for 3 – 10 km survivors. However, the obtained estimates from the parametric frailty model suggest that exposure to the isotopes has reduced the intended heterogeneity component to a negligible measurement; **Supplementary Materials Tables S1 - S3**. Although estimated parameters in the frailty models attained convergence, the lack of heterogeneity suggests that before the construction of the life tables, all significant covariates were already adjusted for, or the effects of radioactive isotopes (U-235 and Pu-239) had caused such destruction that the physiological recovery processes were exactly the same among long-term robust survivors.

Normalization of hazard risk from exposure can occur in humans, and such a phenomenon is often observed upon successful smoking cessation. For example, a lower prevalence of hypertension and an improvement in cardiac health among smokers were reported in studies concerning smoking bans in public premises [13-15]. The human body is programmed to repair damage that has occurred in the cells and organs. Genetic studies have also shown that there are regular checkpoints in the cells to detect errors during the synthesis of deoxyribonucleic acid (DNA) and the availability of adult stem cells to regenerate and replace old and worn-out cells.

Failure of the repair-replace mechanisms can cause irreversible damage, such as spontaneous mutations that may lead to the onset of specific cancer types [16-20]. It is often under extreme conditions, and usually induced through the means of toxicity, that the physiological system is not able to overcome the impromptu surge of damage required for repair [21]. This study has shown that LSS survivors who had survived extreme radioactive exposure did not experience a normalization in their age-specific mortality trajectory and rate of aging, **Figure 2**.

Background radiation of U-235 exists at approximately 0.72%, and, similar to Pu-239, the isotope is capable of undergoing a continuous fission chain reaction; under the right conditions, the chain reactions produce nuclear power [22]. It was within my expectation that survivors exposed to U-235 at low dosages of 0-5 mGy did not present notable excess deaths, and this finding further supports Okinawa as the reference group for comparative analyses; **Table 1**. One of the key findings in this study is that Pu-239 at a minute dosage is capable of increasing mortality by 37% in females and 11% in males. Pu-239 has also increased the rate of aging of male survivors in Nagasaki. Based on my findings, there is a variation in the rate of aging among survivors living in an environment containing higher background radiation or who were exposed to a Pu-239 nuclear impact, and such stochasticity in survivors' rate of aging persists at a 10 km radius from the epicenter; **Supplementary Figure S2**, **Table S3**.

Atomic bomb survivors are unique members of the population who show that the rate of aging and the magnitude of risk for mortality can be subjected to manipulation by dose-response risk exposure. Using conventional epidemiological methods and a demographic approach, my study presents an avant-garde approach to obtaining the rate of aging of atomic bomb survivors from their complex mortality schedule. My findings support the aging hypothesis proposed by Sir Peter Medawar that damage accumulation can be augmented in the presence of DNA mutagens; *e.g.*, radiation, and the ability to repair such instantaneous damage declines with increasing age [23]. Further analytical work is required, specifically, entropy for the observed rise in pseudo-benefit for initial mortality risk, and on the effects of entropy among irradiated individuals during early survival time, which is not captured in the LSS F0 generation. A study in this area of research has the potential to address mortality and frailty selection among the oldest old – centenarians and super-centenarians, which is a time-pressing issue in Japan and global aging.

Methods

The Life Span Study Report 14 (LSS) is the life-table survival follow-up of cancer and non-cancer mortality of atomic bomb survivors in Nagasaki and Hiroshima between 1950 and 2003 [4]. Survival follow-up of the LSS study was restricted to the main generation (F0) of survivors with age at exposure (ATE) between 0 and 75 in the year of the nuclear impact, 1945; **Table 2**.

Survivors in the two prefectures were categorized according to DS02 radiation measurement-weighted colon dose levels. In this study, a specific focus was placed on the comparative analysis between low and extreme dosages; 0 - 5 mGy and 1500 - 3000+ mGy, respectively. If radioactive isotopes alter the rate of aging and mortality trajectory of survivors, a distinct difference between low and extreme dosages by distance to the epicenter would be the expected finding. Among the low radiation dose group, survivors were further categorized by distance to the epicenter; <3 km and 3 - 10 km. Survivors who were situated 3 - 10 km from the epicenter were only exposed to a total radioactive dosage of 0 - 5 mGy.

Due to the demographic disproportion in gender-specific and age structure of Japan, and the aftermath of the nuclear impact in the two prefectures, this article presents mortality trajectories of atomic bomb survivors of ATE 40 – 45 (ATE45), *i.e.*, cohorts born between 1900 and 1905, and all presented mortality trajectories were fission core- and gender-specific; **Supplementary Figure S1**. ATE45 had sufficient survival profiles to achieve an adequate parametric fit using

MLE. Population registries and records in the two prefectures were mostly destroyed during the Second World War. Hence, cohort life tables collected prior to the nuclear impact were considered unreliable. In this comparative analysis, an alternative baseline hazard (*h0*), also known as the reference group in epidemiological studies, had to be defined. Due to the pre-set conditional survival probability for survivors to be recruited in the year 1950 to LSS, a comparison must be made to a very robust alternative population; members of a population that experience long life expectancy. A comparison to the general population in Japan by nationwide or to the respective prefectures will generate a misleading outcome and will draw erroneous conclusions of dose-dependent radiation exposure on the risk for mortality. The alternative reference population used in this analysis was Okinawa, a prefecture that is renowned for its long life expectancy in Japan and worldwide. Data was obtained from the National Institute of Population and Social Security Research, Japan; life tables available between 1975 and 2012 [24].

Table 2. Characteristics of atomic bomb survivors in Hiroshima and Nagasaki from 1950 to 2003, Life Span Study

Prefecture	**Hiroshima (N= 58,494)**		**Nagasaki (N = 28,117)**	
Distance	< 3km (N= 42,388)	3-10km (N= 16,106)	< 3km (N= 18, 680)	3-10km (N=9,437)
Males (%)	40.5	42.1	40.8	43.4
Died (%)	60.6	61.3	53.3	54.3
Dose, mGy (N, %deaths)				
Low	5,591 (60.9%)	16,106 (61.3%)	7375 (52.4%)	9,437 (54.3%)
Moderate	26,911(59.1%)	-	8,008 (54.1%)	-
High	9103 (63.9%)	-	2967 (52.1%)	-
Extreme	783 (68.2%)	-	330 (62.7%)	-
Age at Exposure, ATE (N, %deaths)				
0 - 20	15,883 (19.6%)	6,028 (20.7%)	9,023 (20.5%)	4,462 (19.9%)
20 - 40	11, 985 (67.7%)	4,555 (68.6%)	4,463 (65.4%)	2,159 (66.5%)
40 – 45 (ATE45)	3,625 (98.2%)	1,303 (98.8%)	1,241 (99.3%)	638 (98.7%)
45 - 50	3,467 (99.9%)	1,331 (99.6%)	1254 (100%)	645 (100%)
50 - 55	979 (99.9%)	2,575 (100%)	953 (100%)	523 (100%)
55 - 60	2014 (100%)	776 (99.9%)	724 (100%)	416 (100%)
60 - 70+	562 (100%)	1411 (100%)	491 (100%)	276 (100%)

DS-02 weighted colon dose radioactive measurements expressed in mGy were categorized as low (0-5 mGy); moderate (5-175 mGy); high (175-1500 mGy); extreme (1500-3000+ mGy). *N.B.:* Percentages or crude numbers as shown are not an indication of the total number of casualties that occurred before the 1950 LSS.

The LSS life-table was constructed based on cohort mortality, *i.e.*, deaths by age at exposure (*dx*), person-years (*Lx*), and the number of survivors (*Nx*). The readily available constructed Okinawa life-table, however, was based on calendar time. The approach to resolve this difference in life-table construction is to reconstruct the life-table of Okinawa to a cohort structure; see **Supplementary Figure S3i and S3ii**. Based on the information provided in the life-tables, the observed mortality can be obtained using $\mu(x) = dx/Lx;$

Rearranging the aforementioned equation to obtain expected deaths if the reference population were to be subjected to the same mortality risk as the exposed population,

$Dx = \mu_{survivors}(x) * Lx_{okinawa}$

Retrieve reference population age-specific death counts from the life-table; $dx_{okinawa}$,

$\hbar = Dx/dx_{okinawa}$

The standard error (s.e.m.) shall hence be,

$$s.e.m = \frac{\sqrt{Dx}}{dx_{okinawa}}$$

The baseline hazard shape of atomic bomb survivors in LSS and Okinawa was first assumed to be a *Gompertz-Makeham* shape, a parametric model which has been shown to fit the general population between ages 30 and 90. The parametric function permits an exponential increase with every unit increment in age,

$$\mu(x) = ae^{bx} + c$$

The presence of unobserved heterogeneity in the population *Z(x)* was then considered in this analysis, which was assumed to be gamma distributed, **Equation 1**. The gamma distribution is an appropriate fit as it converges with the characteristic of an exponentially increasing hazard. The rate of aging is obtained from $d(log(\mu(x)))/dx$, also referred to as the gradient of the age-specific mortality trajectory. Hence, the faster the rate of aging, the steeper the slope of $log(\mu(x))$. **N.B.** Refer to **Supplementary Illustration S1** for the mathematical illustration of initial mortality risk at any given age, *x*; *h0(x)* and $\mu 0(x)$.

Equation 1. Population hazard with a gamma-distributed frailty, *ɣ-Gompertz-Makeham*, also known as the logistic-typed model in mathematical demography, as the *log*-hazard shape bends in accordance with the logistic-shaped function at high ages; $x \geq 95$ in the general population.

$$\mu(x) = \frac{ae^{bx}}{Z(x)} + c = \frac{ae^{bx}}{1 + \frac{a\gamma}{b}(e^{bx} - 1)} + c$$

All estimates were obtained using Maximum Likelihood Estimation (MLE) and attained convergence. Estimates were optimized using the Nelder-Mead method. Analyses were conducted using *R software version 3.2.1* [25]. Presented hazard lines in figures were adjusted for unobserved heterogeneity, and parameter estimates could be inferred from the **Supplementary Materials Section III: Tables S1 – S3**.

As MLE is sensitive to the initial values, each parameter was assigned 50 random numbers, and a combination of these random sets of four parameters was then introduced; *e.g.*, set one: $a = 0.001, b = 0.13, c = 0.0002, \gamma = 0.1$; *set two:* $a = 0.004, b = 0.15, c = 0.0002, \gamma = 0.1$. A total of *6,250,000* four-parameter sets were introduced during optimization to retrieve the best-fitted parameter estimation.

Conflict of interest This hypothesis was first initiated by YL at the Max Planck Institute for Demographic Research, Germany; 1 Konrad-Zuse Strasse, 18057 Rostock, Germany. The analysis and manuscript were completed by YL.

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Figure legends

Figure 1. Pseudo-benefit of initial mortality risk. 0 – 5 mGy Hiroshima females age at exposure 40 – 45 (ATE 45) adjusted for unobserved heterogeneity. Solid line: <3 km; Dashed line: 3 - 10 km to the epicenter. Horizontal dashed line indicates mortality at 10%; the difference in life expectancy is at one year.

Figure 2. Diverging age-specific mortality trajectories of extreme- and low-dosage in Nagasaki (Pu-239) and Hiroshima (U-235) for males at ATE 45 situated <3 km from the epicenter.