Population Density in Hiroshima and Nagasaki Before the Bombings in 1945: Its Measurement and Impact on Radiation Risk Estimates in the Life Span Study of Atomic Bomb Survivors

Web Table 1. Pre-Bombing Population Distribution in Urban Regions Based on 1945 (Hiroshima: June; Nagasaki: July) Rice-Rationing Figures.

Distance From Hypocenter, km	Population Count[a]	Urban Area[b]		Population Density,[c] people/km^2
		mi^2	km^2	
Hiroshima	255,260	11.2	29.0	8,800
0–0.500	6,230	0.17	0.44	14,150
0.501–1.000	24,950	0.67	1.74	14,378
1.001–1.500	45,270	1.26	3.26	13,872
1.501–2.000	67,900	1.92	4.97	13,654
2.001–2.500	30,600	1.94	5.02	6,090
2.501–3.000	30,600	1.81	4.69	6,527
3.001–4.000	29,400	2.43	6.29	4,671
4.001–5.000	20,310	1.00	2.59	7,842
Nagasaki	195,290	5.50	14.2	13,709
0–1.000	30,900	1.15	2.98	10,374
1.001–1.500	14,320	0.62	1.61	8,918
1.501–2.000	6,550	0.44	1.14	5,748
2.001–2.500	6,800	0.30	0.78	8,752
2.501–3.000	21,160	0.66	1.71	12,379
3.001–5.000+[d]	115,560	2.33	6.03	19,149

[a] Population counts were obtained from the published Joint Commission report (1, p. 84).
[b] Urban area in mi^2 was obtained from Volume VI of the declassified Joint Commission report (Hiroshima: p. 12; Nagasaki: p. 86).
[c] To calculate population density, we divided the population count by the urban area in mi^2 and converted the result to km^2 (1 $mi^2 \approx 2.59$ km^2).
[d] The published Joint Commission report provides population counts within 3.001–4.000 km and 4.001–5.000 km from the hypocenter in Nagasaki (1, p. 84). However, Volume VI of the declassified Joint Commission report (p. 86) provides the urban area within 3.001–5.000+ km from the hypocenter; the urban area within 3.001–4.000 km and 4.001–5.000 km from the hypocenter is unknown. Therefore, we calculated population density for 3.001–5.000+ km, and applied the estimated density to 3.001–5.000 km from the hypocenter.

Note: survivors located outside an urban region but within 5 km of the hypocenter, as well as survivors located beyond 5 km, were assigned the average population density in rural Japan according to the February 1944 national census: 116 people/km^2 (2, p. 36).

Web Appendix

METHODS

In this section, we provide additional details on the stratification of person-year tables and the parameterization of excess relative risk (ERR) models for mortality and solid cancer incidence.

Mortality

The table of case counts and accrued person-years was stratified by city (Hiroshima, Nagasaki), ground distance from the hypocenter (with cut-points at 0.5, 1, 1.5, 2, 2.5, 3, 4, and 5 km), located in an urban region (yes, no), sex (male, female), age at exposure (5-year intervals from 0–69 years, or ≥70 years), attained age (5-year intervals from 5–99 years, or ≥100 years), calendar year (5-year intervals from 1950–2000, or 2001–2003), DS02R1 weighted absorbed colon dose (with cut-points at 0.005, 0.02, 0.04, 0.06, 0.08, 0.1, 0.125, 0.15, 0.175, 0.2, 0.25, 0.3, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2, 2.5, and 3 gray), and total shielded kerma (0–4, >4 gray). A value for population density was assigned to a stratum based on city, ground distance from the hypocenter, and location in an urban region (Web Table 1).

Piecewise-constant hazard models related the rate of all-cause and solid cancer mortality λ to the background rate λ_0 and an ERR ρ as a function of radiation dose d (3):

$$\lambda = \lambda_0\{1 + \rho(d)\}.$$

Sex-specific background rates and ERRs, indexed by a superscript $S = \{M, F\}$ for males and females, respectively, were estimated using interaction terms:

$$\lambda^S = \lambda_0^S\{1 + \rho^S(d)\}.$$

Sex-specific background rates were adjusted for (log) attained age a, centered at 70 years, using quadratic regression splines with knots at 40 and 70 years, and age at exposure e, centered at 30 years and scaled by 10 years, using quadratic regression splines with knots at 30 and 50 years:

$$\begin{aligned}\log \lambda_0^S = {} & \alpha_0^S + \boldsymbol{\alpha}_1 + \boldsymbol{\alpha}_2 \\ & + \alpha_3^S \log\left(\frac{a}{70}\right) + \alpha_4^S \left\{\log\left(\frac{a}{70}\right)\right\}^2 + \alpha_5^S \left\{\log\left(\frac{a}{70}\right)\right\}^2 \times [a > 40] + \alpha_6^S \left\{\log\left(\frac{a}{70}\right)\right\}^2 \times [a > 70] \\ & + \alpha_7^S \left(\frac{e-30}{10}\right) + \alpha_8^S \left(\frac{e-30}{10}\right)^2 + \alpha_9^S \left(\frac{e-30}{10}\right)^2 \times [e > 30] + \alpha_{10}^S \left(\frac{e-30}{10}\right)^2 \times [e > 50].\end{aligned}$$

We selected zero-dose survivors within 5 km of the hypocenter as the reference group (4). The parameters in $\boldsymbol{\alpha}_1$ included an interaction between a binary variable for city (Nagasaki versus Hiroshima) and a binary variable for ground distance (>5 km versus ≤5 km):

$$\begin{aligned}\boldsymbol{\alpha}_1 = {} & \alpha_{11}[\text{City = Nagasaki}] \\ & + \alpha_{12}[\text{City = Hiroshima}] \times [\text{Distance > 5 km}] \\ & + \alpha_{13}[\text{City = Nagasaki}] \times [\text{Distance > 5 km}].\end{aligned}$$

Models were fit with and without adjustment of the background rate λ_0 for population density p. Population density was included as a linear term in the background model. We also included an interaction between population density and a categorical variable for age at exposure (<10 years, 10–14 years, 15–29 years, ≥30 years) in the background model:

$$\boldsymbol{\alpha}_2 = \begin{cases} \alpha_2 p \\ \alpha_{21}\, p \times [e < 10] + \alpha_{22}\, p \times [10 \le e < 15] + \alpha_{23}\, p \times [15 \le e < 30] + \alpha_{24}\, p \times [e \ge 30] \end{cases}.$$

Radiation ERRs were parameterized as a function of weighted absorbed colon dose d with effect modification by (log) attained age a, age at exposure e, and an indicator of total shielded kerma k > 4 gray to account for dose-estimation errors at high doses. In the presence of effect modification, the dose-response functions $\{\rho^M(d), \rho^F(d)\}$ parameterized the ERR among males and females, respectively, exposed to a radiation dose with a total shielded kerma ≤4 gray at an age of 30 years and who achieved an attained age of 70 years. For both all-cause and solid cancer mortality, we fit a sex-averaged linear dose-response model:

$$\rho^S(d) = \beta_1 d \times \exp\left\{\gamma_1 \log\left(\frac{a}{70}\right) + \gamma_2\left(\frac{e-30}{10}\right) + \gamma_3[k > 4]\right\} \times \delta S.$$

Statistical code for fitting these ERR models to the Life Span Study mortality data is available at www.rerf.or.jp/library/dl_e/lss14.html.

Solid cancer incidence

The table of case counts and accrued person-years was stratified by city (Hiroshima, Nagasaki), ground distance from the hypocenter (with cut-points at 0.5, 1, 1.5, 2, 2.5, 3, 4, and 5 km), located in an urban region (yes, no), sex (male, female), age at exposure (5-year intervals from 0–69 years, or ≥70 years), attained age (5-year intervals from 10–84 years, or ≥85 years), calendar year (1958–1960, 1961–1965, 1966–1970, 1971–1975, 1976–1980, 1981–1985, 1986–1987, 1988–1990, 1991–1995, 1996–1998, 1999–2000, 2001–2004, or 2005–2009), DS02R1 weighted absorbed colon dose (with cut-points at 0.005, 0.02, 0.04, 0.06, 0.08, 0.1, 0.125, 0.150, 0.175, 0.2, 0.25, 0.3, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2, 2.5, and 3 gray), and total shielded kerma (0–4, >4 gray). A value for population density was assigned to a stratum based on city, distance from the hypocenter, and location in an urban region (Web Table 1).

Piecewise-constant hazard models related the rate of first primary solid cancer λ to the background rate λ_0 and an ERR ρ as a function of radiation dose d (5):

$$\lambda = \lambda_0\{1 + \rho(d)\}.$$

Sex-specific background rates and ERRs, indexed by a superscript $S = \{M, F\}$ for males and females, respectively, were estimated using interaction terms:

$$\lambda^S = \lambda_0^S\{1 + \rho^S(d)\}.$$

Sex-specific background rates were adjusted for (log) attained age a, centered at 70 years, using quadratic regression splines with a knot at 70 years, and age at exposure e, centered at 30 years and scaled by 10 years, using linear and quadratic terms:

$$\begin{aligned}\log \lambda_0^S &= \alpha_0^S + \boldsymbol{\alpha}_1 + \boldsymbol{\alpha}_2 \\ &\quad + \alpha_3^S \log\left(\frac{a}{70}\right) + \alpha_4^S\left\{\log\left(\frac{a}{70}\right)\right\}^2 + \alpha_5^S\left\{\log\left(\frac{a}{70}\right)\right\}^2 \times [a > 70]\end{aligned}$$

$$+ \alpha_6^S \left(\frac{e-30}{10}\right) + \alpha_7^S \left(\frac{e-30}{10}\right)^2.$$

We selected zero-dose survivors within 5 km of the hypocenter as the reference group (6). The parameters in $\boldsymbol{\alpha}_1$ included an interaction between a binary variable for city (Nagasaki versus Hiroshima) and a binary variable for ground distance (>5 km versus ≤5 km):

$$\begin{aligned}\boldsymbol{\alpha}_1 = {} & \alpha_{11}[\text{City = Nagasaki}] \\ & + \alpha_{12}[\text{City = Hiroshima}] \times [\text{Distance > 5 km}] \\ & + \alpha_{13}[\text{City = Nagasaki}] \times [\text{Distance > 5 km}].\end{aligned}$$

Models were fit with and without adjustment of the background rate λ_0 for population density p. Population density was included as a linear term in the background model. We also included an interaction between population density and a categorical variable for age at exposure (<10 years, 10–14 years, 15–29 years, ≥30 years) in the background model:

$$\boldsymbol{\alpha}_2 = \begin{cases} \alpha_2 p \\ \alpha_{21}\, p \times [e < 10] + \alpha_{22}\, p \times [10 \le e < 15] + \alpha_{23}\, p \times [15 \le e < 30] + \alpha_{24}\, p \times [e \ge 30] \end{cases}.$$

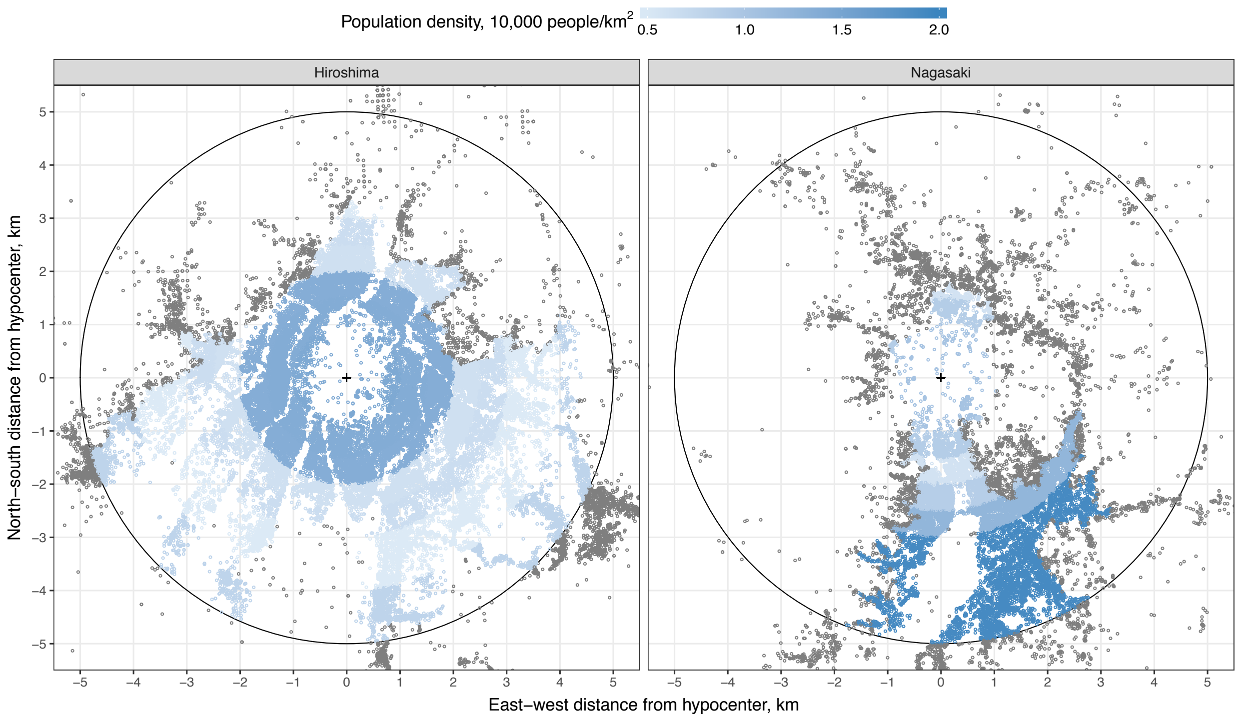
Radiation ERRs were parameterized as a function of weighted absorbed colon dose d with effect modification by (log) attained age a, age at exposure e, and an indicator of total shielded kerma $k >$ 4 gray to account for dose-estimation errors at high doses. In the presence of effect modification, the dose-response functions $\{\rho^M(d), \rho^F(d)\}$ parameterized the ERR among males and females, respectively, exposed to a radiation dose with a total shielded kerma ≤4 gray at an age of 30 years and who achieved an attained age of 70 years. We considered two radiation dose-response models: a sex-averaged linear dose-response model:

$$\rho^S(d) = \beta_1 d \times \exp\left\{\gamma_1 \log\left(\frac{a}{70}\right) + \gamma_2\left(\frac{e-30}{10}\right) + \gamma_3[k > 4]\right\} \times \delta S;$$

and a sex-specific linear-quadratic dose-response model:

$$\begin{aligned}\rho^M(d) &= (\beta_1^M d + \beta_2^M d^2) \times \exp\left\{\gamma_1^M \log\left(\frac{a}{70}\right) + \gamma_2\left(\frac{e-30}{10}\right) + \gamma_3[k > 4]\right\}, \\ \rho^F(d) &= (\beta_1^F d + \beta_2^F d^2) \times \exp\left\{\gamma_1^F \log\left(\frac{a}{70}\right) + \gamma_2\left(\frac{e-30}{10}\right) + \gamma_3[k > 4]\right\}.\end{aligned}$$

Curvature in the radiation dose-response was defined as the ratio of the coefficient for the quadratic dose term to the coefficient for the linear dose term (i.e., β_2^M/β_1^M). Statistical code for fitting these ERR models to the Life Span Study solid cancer incidence data is available at www.rerf.or.jp/library/dl_e/lssinc17e.html.



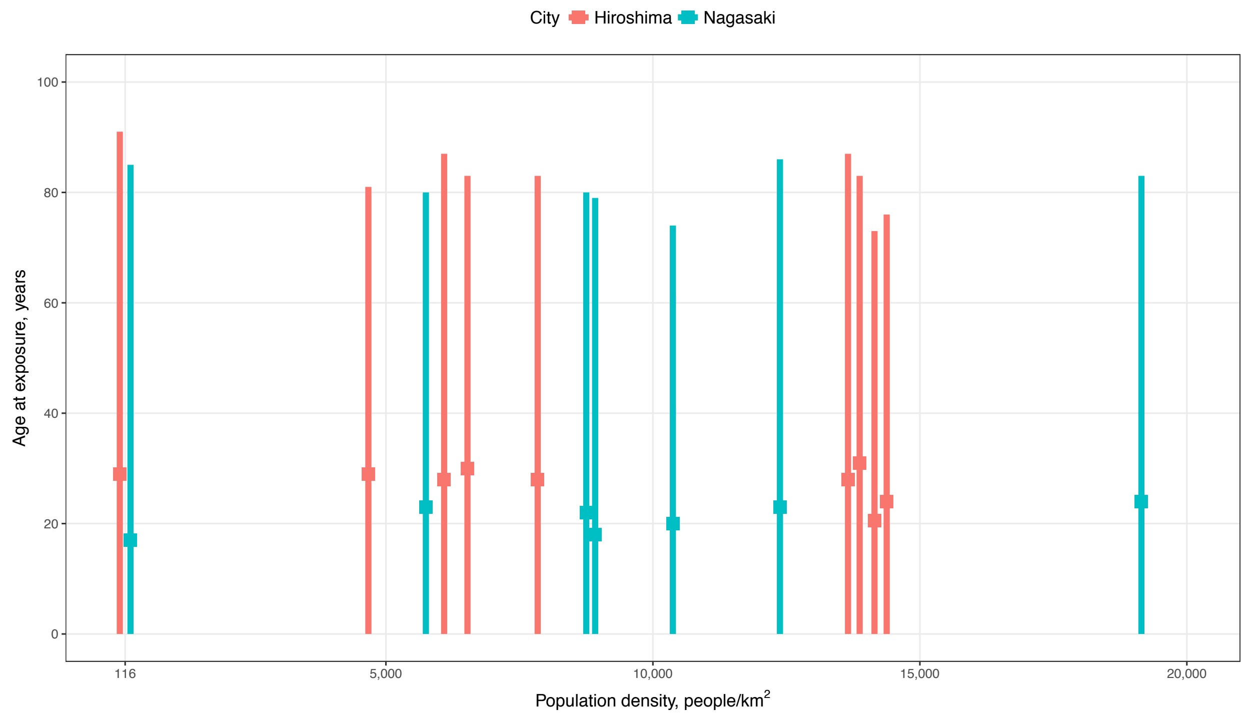
Web Figure 1. Locations of atomic bomb survivors enrolled in the Life Span Study, Hiroshima and Nagasaki, Japan. Survivors located in an urban region within 5 km of the hypocenter were assigned the population density for that region (points with a blue gradient). Survivors located outside an urban region but within 5 km of the hypocenter, as well as survivors located beyond 5 km, were assigned a population density of 116 people/km^2 (gray points).

Web Table 2. Demographic Characteristics Among Atomic Bomb Survivors Stratified by Location, Life Span Study, Hiroshima and Nagasaki, Japan.

	Distance ≤5 km Inside Urban Region	Distance ≤5 km Outside Urban Region	Distance >5 km	P[a]
Hiroshima	(n = 55,136)	(n = 2,439)	(n = 4,412)	
Female, %	59.0	57.6	57.7	0.12
Age, years[b]	29 (14, 45)	32 (13, 48)	28 (13, 45)	<0.001
Nagasaki	(n = 22,351)	(n = 6,955)	(n = 2,448)	
Female, %	57.0	59.8	55.9	<0.001
Age, years[b]	22 (12, 42)	16 (7, 41)	17 (8, 40)	<0.001

[a] Obtained from Pearson's chi-squared test or Kruskal-Wallis rank-sum test.

[b] Median (inter-quartile range).

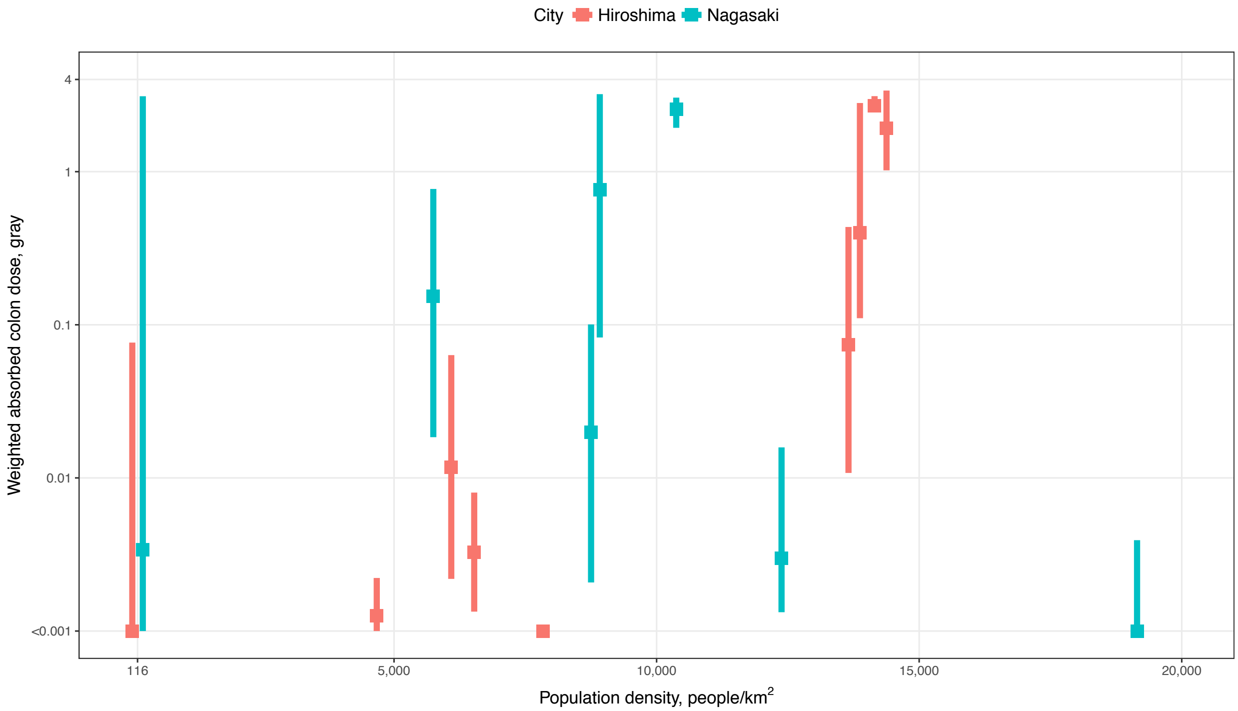


Web Figure 2. Age at exposure versus pre-bombing population density among atomic bomb survivors, Life Span Study, Hiroshima and Nagasaki, Japan. Boxes denote median values; vertical bars extend from the minimum to the maximum value.

Spearman rank correlation

Hiroshima: 0.01

Nagasaki: 0.07



Web Figure 3. Weighted absorbed colon dose versus pre-bombing population density among atomic bomb survivors with known DS02R1 radiation doses, Life Span Study, Hiroshima and Nagasaki, Japan. Boxes denote median values; vertical bars extend from the minimum to the maximum value.

Spearman rank correlation

Hiroshima: 0.83

Nagasaki: −0.34

Web Table 3. Crude Rates for All-Cause Mortality by Weighted Absorbed Colon Dose Among 86,660 Atomic Bomb Survivors With Known DS02R1 Radiation Doses and Stratified by Location, Life Span Study, Hiroshima and Nagasaki, Japan, 1950–2003.

Weighted Absorbed Colon Dose, gray	Distance ≤5 km Inside Urban Region		Distance ≤5 km Outside Urban Region		Distance >5 km	
	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
Hiroshima						
<0.005	15,599	163.8	1,766	176.7	4,408	161.5
0.005–0.099	22,075	154.1	660	141.9	0	
0.100–0.499	10,172	167.2	0		0	
0.500–0.999	2,294	177.0	0		0	
≥1.000	1,518	188.5	0		0	
Nagasaki						
<0.005	12,277	141.7	2,499	123.6	2,446	126.4
0.005–0.099	4,667	150.3	2,257	123.7	0	
0.100–0.499	1,362	141.4	859	127.0	0	
0.500–0.999	901	117.4	188	128.9	0	
≥1.000	507	152.6	205	141.9	0	
Total	71,372	156.2	8,434	136.3	6,854	148.5

[a] Per 10,000 person-years.

Web Table 4. Crude Incidence Rates for First Primary Solid Cancer by Weighted Absorbed Colon Dose Among 80,205 Atomic Bomb Survivors With Known DS02R1 Radiation Doses and Stratified by Location, Life Span Study, Hiroshima and Nagasaki, Japan, 1958–2009.

Weighted Absorbed Colon Dose, gray	Distance ≤5 km Inside Urban Region		Distance ≤5 km Outside Urban Region		Distance >5 km	
	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
Hiroshima						
<0.005	14,401	76.9	1,596	64.1	4,090	73.9
0.005–0.099	20,504	70.4	605	62.0	0	
0.100–0.499	9,447	79.1	0		0	
0.500–0.999	2,100	101.6	0		0	
≥1.000	1,409	143.1	0		0	
Nagasaki						
<0.005	11,321	69.0	2,302	57.1	2,268	60.3
0.005–0.099	4,308	74.4	2,094	62.4	0	
0.100–0.499	1,267	81.6	806	72.9	0	
0.500–0.999	863	96.3	173	98.0	0	
≥1.000	464	115.6	187	136.6	0	
Total	66,084	76.4	7,763	64.7	6,358	69.3

[a] Per 10,000 person-years.

Web Table 5: Radiation Dose (Linear-Quadratic Dose-Response Model) and Population Density Associations With Risk of First Primary Solid Cancer Among 80,205 Atomic Bomb Survivors With Known DS02R1 Radiation Doses, Life Span Study, Hiroshima and Nagasaki, Japan, 1958–2009.

	Radiation Dose		Population Density		AIC
Model	Curvature[a]	*P*[b]	RR[c]	95% CI	
Base[d]	1.063	0.003			91,038.9
With density	1.220	0.002	1.010	0.993, 1.026	91,039.5
With density × age	1.180	0.002			91,043.8
<10 years			1.002[e]	0.971, 1.035	
10–14 years			1.021[e]	0.994, 1.049	
15–29 years			1.008[e]	0.987, 1.028	
≥30 years			1.010[e]	0.989, 1.031	

Abbreviations: AIC, Akaike information criterion; CI, confidence interval; RR, relative risk.

[a] Estimated curvature in the radiation dose-response among males, calculated as the ratio of the estimated coefficient for the quadratic dose term to the estimated coefficient for the linear dose term.

[b] Likelihood ratio *P* value for evaluating the null hypothesis that the coefficient for the quadratic dose term among males is equal to 0.

[c] Relative risk of first primary solid cancer per 5,000 people/km^2 increase in population density.

[d] Base model: adjusted for city, distance >5 km, sex, age at exposure, and attained age; effect modification by sex, age at exposure, attained age, and total shielded kerma >4 gray.

[e] Likelihood ratio *P* value for evaluating the null hypothesis of equality in relative risks across age groups (3 degrees of freedom): *P* = 0.64.

Web Table 6. Population Density Associations With Risk of All-Cause Mortality Among 86,660 Atomic Bomb Survivors With Known DS02R1 Radiation Doses and Stratified by Calendar Year, Life Span Study, Hiroshima and Nagasaki, Japan, 1950–2003.

	1950–1957		1958–2003	
Age at Exposure	RR[a]	95% CI	RR[a]	95% CI
<10 years	1.059	0.965, 1.159	1.017	0.983, 1.052
10–14 years	1.226	1.148, 1.305	1.036	1.010, 1.063
15–29 years	1.090	1.042, 1.140	0.985	0.968, 1.003
≥30 years	1.005	0.990, 1.021	0.997	0.987, 1.008

Abbreviations: CI, confidence interval; RR, relative risk.

[a] Relative risk of all-cause mortality per 5,000 people/km^2 increase in population density.

References

1. Oughterson AW, Warren S. *Medical Effects of the Atomic Bomb in Japan*. New York, NY: McGraw-Hill International Book Co, Publishers; 1956.
2. Bureau of Statistics, Office of the Prime Minister. Population census of 1950, volume 1, total population [in Japanese]. http://www.estat.go.jp/statsearch/files?&layout=datalist &toukei=00200521&tstat=000001036869. Published November 20, 1950. Updated June 10, 2014. Accessed January 4, 2018.
3. Ozasa K, Shimizu Y, Suyama A, et al. Studies of the mortality of atomic bomb survivors, Report 14, 1950-2003: An overview of cancer and noncancer diseases. *Radiat Res*. 2012;177(3):229–243.
4. Cologne JB, Preston DL. Impact of comparison group on cohort dose response regression: An example using risk estimation in atomic-bomb survivors. *Health Phys*. 2001;80(5):491–496.
5. Grant EJ, Brenner A, Sugiyama H, et al. Solid cancer incidence among the Life Span Study of atomic bomb survivors: 1958-2009. *Radiat Res*. 2017;187(5):513–537.
6. French B, Cologne JB, Sakata R, et al. Selection of reference groups in the Life Span Study of atomic bomb survivors. *Eur J Epidemiol*. 2017;32(12):1055–1063.