TABLE 6
Parameter Estimates of the Dose–Response Models for Excess Relative Risk (ERR) for all Solid Cancer in the Full Dose Range and for the Range of 0–2 Gy

	Full			<2 Gy		
Dose range model[a]	**L**[b]	LQ	Q	L	**LQ**	Q
β_1: linear	**0.42**	0.36	–	0.44	**0.22**	–
β_2: quadratic	**–**	0.038	0.22	–	**0.18**	0.33
Effect modification						
σ: sex (female = 1; male = −1)	**0.34**	0.35	0.40	0.28	**0.29**	0.29
τ: age at exposure (year)	**–0.035**	–0.034	–0.035	–0.033	**–0.034**	–0.035
υ: attained age (log(age/70))	**–0.86**	–0.86	–0.90	–0.84	**–0.89**	–0.97
Deviance	18301.2	18300.4	18324.9	17557.3	17551.6	17557.2
df	53147	53146	53147	49577	49576	49577
Test (vs. LQ model)	$P = 0.36$	–	$P < 0.001$	$P = 0.02$	**–**	$P = 0.02$

Note. Bolded columns are the selected models.

[a] The ERR model was defined as $\lambda_0(c,s,b,a)$ $[1 + \rho(d) \cdot \exp(\tau\, e + \upsilon \ln(a)) \cdot (1 + \sigma\, s)]$, where d is colon dose, s is sex, b is birth year, e is age at exposure, and a is attained age. $\rho(d)$ was $\beta_1 d$ for the linear model, $\beta_1 d + \beta_2 d^2$ for the linear-quadratic model, and γd^2 for the quadratic model. τ, υ and σ are coefficients for effect modification.

[b] L: linear, LQ: linear-quadratic, Q: quadratic.

model with effect modification by age at exposure and attained age. The sex-averaged excess death rate of all solid cancer was 26/10,000 person-years per Gy under the same conditions. The second important finding is that those who were exposed at younger ages had a higher relative risk for cancer death; e.g., the sex-averaged ERR of solid cancer deaths was 0.83 at age 70 in those who were exposed at 10 years of age compared with 0.30 in those exposed at age 40. For solid cancers the relative risk declined with increasing attained age of the subjects as well as years after the bombing, although, importantly, the excess absolute rates continued to increase with attained age and the rates were higher in those exposed at younger ages among those with the same attained age. These findings suggest that young people are more sensitive to radiation than older people, possibly at the initiation stage in carcinogenesis at the time of exposure, and imply an overall increase in lifetime risk for those exposed at younger ages.

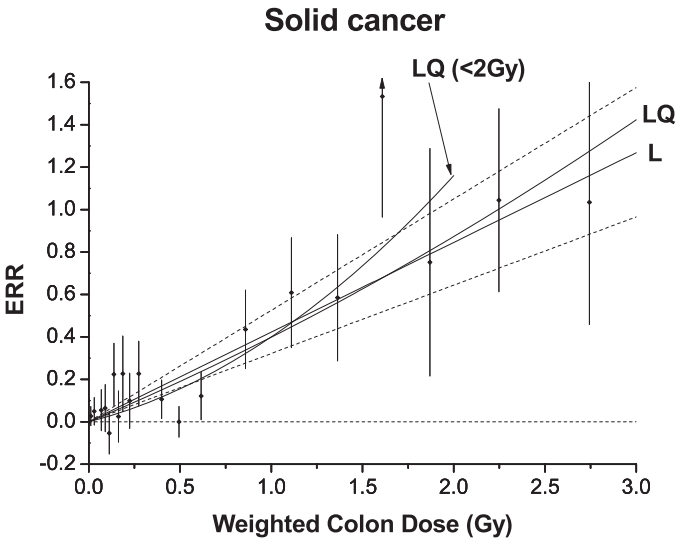

FIG. 4. Excess relative risk (ERR) for all solid cancer in relation to radiation exposure. The black circles represent ERR and 95% CI for the dose categories, together with trend estimates based on linear (L) with 95% CI (dotted lines) and linear-quadratic (LQ) models using the full dose range, and LQ model for the data restricted to dose <2 Gy.

To provide continuity, the methods of analysis and risk indicators are the same as those in previous reports since 1987 (*2, 10*). In a previous report, mortality data up to 2000 were examined for changes in the estimated risk of radiation due to changes in dosimetry between DS86 and DS02 (*4*). In that report the estimates of solid cancer risk per unit radiation dose decreased about 8% due to the upward revision in the γ-ray dose estimates (*4*). The ERR/Gy for all solid cancer decreased from 0.45 based on DS86 to 0.42 based on DS02 for 1950–2000 (*4*). The estimates of ERR/Gy and modifiers for solid cancer in this study (Table 4) were similar to those in the latter report (*4*). The effect-modification results showed substantially similar tendencies to previous estimates using DS86 and less follow-up time (*2,5*).

Effect modification was evaluated for the ERR (Table 4) and EAR (Table 5) models. The ERR estimates were

TABLE 7
Change in Dose–Response Curvature For Excess Relative Risk (ERR) of Solid Cancer in The range of 0–2.0 Gy by Observation Period

	1950–1985	1950–1995	1950–2003
Curvature (θ)[a]	0.20	0.40	0.81
95% CI[b]	(−0.23, 3.2)	(−0.09, 3.2)	(0.08, 8.6)
Significance (P)[c]	0.50	0.16	0.02

[a] The ERR model was defined as $\lambda_0(c,s,b,a)$ $[1 + \beta_1(d + \theta d^2) \cdot \exp(\tau\, e + \upsilon \ln(a)) \cdot (1 + \sigma\, s)]$ separately for each period of analysis, where d is colon dose, s is sex, b is birth year, e is age at exposure, and a is attained age. τ, υ and σ are coefficients for effect modification.

[b] Confidence interval.

[c] Likelihood test.

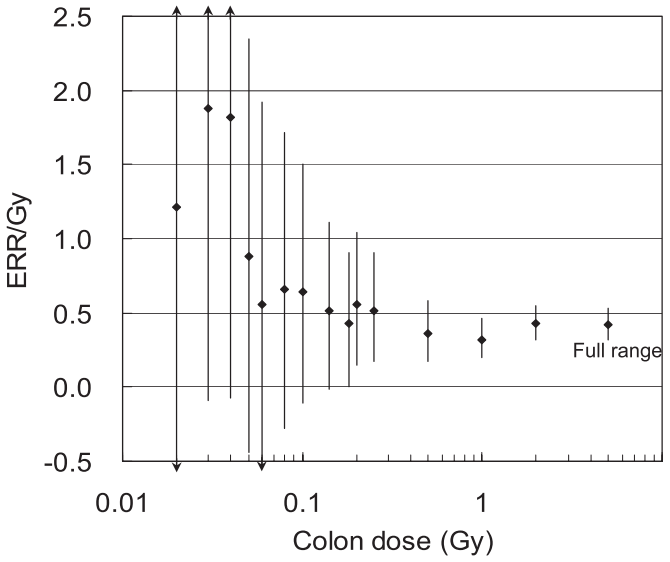

FIG. 5. Excess relative risk per Gy (ERR/Gy) for all solid cancer for selected dose ranges. The figure shows the ERR/Gy and 95% CI for a dose range from zero to a given dose based on the linear model for the full data that allowed for different ERRs below and above the given dose and taking radiation effect modifiers as common to the two dose ranges. The increased ERR/Gy in the low-dose levels less than 0.1 Gy corresponds to the estimates of ERR higher than the expected linear line in Fig. 4.

TABLE 8
Excess Relative Risk (ERR) Estimates per Gy for Noncancer Deaths, 1966–2003

Cause of death	Number of deaths	ERR/Gy[a]	(95% CI[b])	*P*
Noncancer disease[c]	25,618	0.13	(0.08, 0.18)	<0.001
Circulatory disease	14,586	0.11	(0.05, 0.18)	<0.001
Respiratory disease	4,190	0.23	(0.11, 0.36)	<0.001
Digestive disease	2,226	0.20	(0.05, 0.38)	0.009
Genitourinary disease	951	0.18	(−0.06, 0.46)	0.15
Infectious disease	781	–0.03	(−0.22, 0.23)	>0.5
Other disease	2,884	0.03	(−0.11, 0.19)	>0.5

[a] ERR was estimated using the linear dose model, in which city, sex, age at exposure, and attained age were included in the background rates, but not allowing radiation effect modification by those factors.
[b] Confidence interval.
[c] Non-neoplastic blood diseases were excluded from noncancer diseases.

substantially higher for women than men, but the EAR estimates were not. This appears to be a function of the fact that the background mortality rates of cancer were substantially higher in men than in women in this cohort. Similarly, it was observed that cancers having a low background mortality rate tend to have a relatively high ERR, and vice versa. The gender similarity in EAR estimates suggests that the excess of deaths due to radiation is mostly constant in rate rather than in ratio (i.e., more additive than multiplicative) to the background cancer rates. This interpretation is consistent with the differences in ERR between sites of cancer mentioned above.

Age at exposure is an important modifying factor in radiation-induced carcinogenesis. Both the ERR and the EAR were higher for younger ages at exposure (Tables 4 and 5, Figs. 2 and 3). However, other reports [for example, the BEIR VII and UNSCEAR 2006 Reports (*6, 23*)] have indicated that the ERRs for those exposed at age 60 years or older were similar to or higher than risks for those exposed at age 40 or 50 years, especially for cancer incidence data (*5, 21, 22*). The nonparametric category-specific estimates of age-at-exposure effects on all solid cancer mortality risk in the current study were similar to the corresponding figures reported by Walsh (*22*), in which an increased risk at an old age at exposure was less remarkable than in the figure reported by Preston *et al.* (*5*).

The linear dose–response relationship provided the best fit to the solid cancer data across the entire dose range in this study, but significant upward curvature was observed over the truncated dose range of 0–2 Gy (Table 7), which had been hinted at in previous reports (*4, 5*). DDREF is defined by dividing the slope of a nonlinear function at low-dose levels by the slope of the extrapolated linear nonthreshold function based on the whole dose range (*23*), so that this upward curvature may imply a DDREF greater than one. However, the dose–response slope was nominally higher at doses below 0.1 Gy than it was overall or for the dose range 0–2 Gy (Fig. 5). The apparent upward curvature appears to be related to relatively lower than expected risks in the dose range 0.3–0.7 Gy (Fig. 4), a finding without a current explanation. A recent paper (*24*) compared the risk of cancer mortality and incidence in 12 studies of low-dose-rate, moderate-dose exposure (mostly external) with those values in the LSS. The ERR per dose for each study was calculated using the same gender distribution, average age at exposure, and average attained age as in the LSS. The expected DDREF based on the ratio of ERR per dose in those studies to that in the LSS appeared to be close to 1.0, nominally lower than the factors suggested by BEIR VII (1.5) (*23*) and ICRP (2.0) (*25*). However, the number of examined studies was limited to the publication period of 2002–2007 with conditions allowing calculation of the values matching the LSS (*24*), so the arguments are still controversial.

The high risks per unit dose observed in the low-dose range are difficult to interpret. One suggestion was that cumulative exposures to diagnostic medical radiation over the many years of follow-up may have reached a considerable proportion of the estimated individual A-bomb doses at the low-dose levels (*26*). However, to impact the ERR estimates, medical exposures or other sources of exposure, including fallout and residual radiation, would have to have preferentially exposed subjects with very low doses. In the LSS, zero-dose subjects were located at around 4 km or farther from the hypocenter while the subjects with doses of up to 50 mGy were located around the range of 2 to

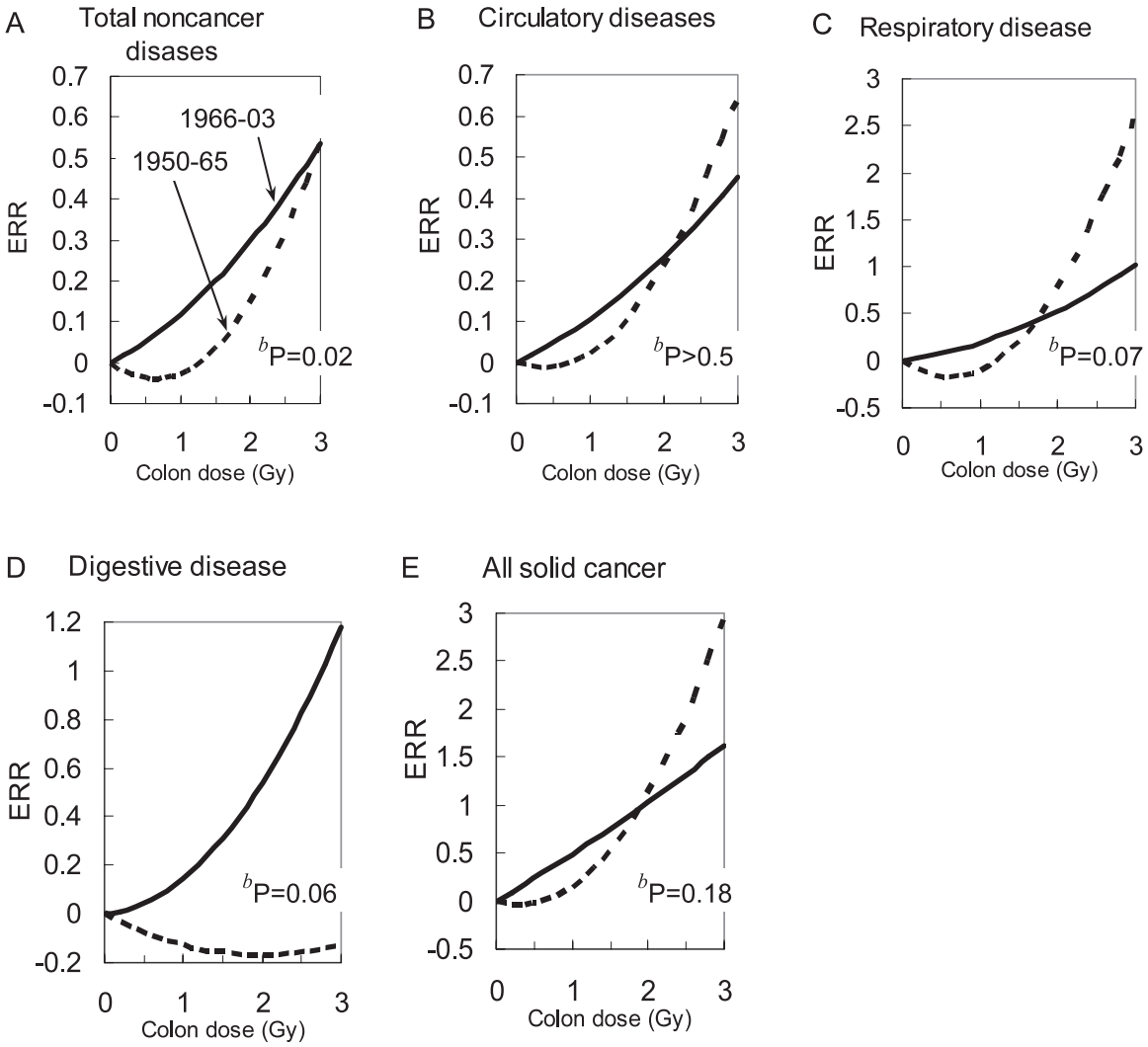

FIG. 6. Comparison of dose–response curve[a] for early period (1950–1965, shown with dashed line) and for late period (1966–2003, shown with solid line) from noncancer diseases (based on LQ without any effect modification) and all solid cancer (based on LQ with effect modifications). [a]Based on the ERR model defined as the linear-quadratic model without effect modifications for noncancer diseases: $\lambda 0(c,s,e,a)$ [1 + $\beta_1(d + \theta d^2)$], and the model with effect modifications for all solid cancer: $\lambda 0(c,s,e,a)$ [1 + $\beta_1(d + \theta d^2) \cdot \exp(\tau e + \upsilon \ln(a)) \cdot (1 + s s)$], where d is colon dose, s is sex, e is age at exposure, and a is attained age. The figure for all solid cancer shows the sex-averaged estimates for $e = 30$ years and $a = 70$ years. [b]Significance of the difference between the two curves.

TABLE 9
Observed and Excess Deaths from Solid Cancer and Noncancer Diseases

			Solid cancer			Noncancer diseases[b]		
Colon dose (Gy)	Number of subjects	Person-years	Number of deaths	Number of excess cases[a]	Attributable fraction (%)	Number of deaths	Number of excess cases[b]	Attributable fraction (%)
<0.005	38,509	1,465,240	4,621	2	0	15,906	1	0
0.005–	29,961	1,143,900	3,653	49	1.3	12,304	36	0.3
0.1–	5,974	226,914	789	46	5.8	2,504	36	1.4
0.2–	6,356	239,273	870	109	12.5	2,736	82	3.0
0.5–	3,424	129,333	519	128	24.7	1,357	86	6.3
1–	1,763	66,602	353	123	34.8	657	76	11.6
2+	624	22,947	124	70	56.5	221	36	16.3
Total	86,611	3,294,210	10,929	527	4.8	35,685	353	1.0

[a] Based on the ERR model was defined as the linear model with effect modification: $\lambda_0(c,s,b,a)[1 + \beta_1 d \cdot \exp(\tau e + \upsilon \ln(a)) \cdot (1 + \sigma s)]$.
[b] Non-neoplastic blood diseases were excluded from noncancer diseases.

4 km. Thus, with such a large geographical distribution, differential exposures to additional radiation sources seem implausible, although we have insufficient information about fallout or residual radiation to completely rule out this possibility.

Potential causes other than radiation include selection bias due to early mortality prior to study initiation in a manner that correlates with dose (e.g., high doses among urban people and lower doses among rather rural people) (*1, 2, 5, 27, 28*). Suggestively lower baseline mortality has been shown in the low-dose but relatively proximal survivors compared to the more distant survivors, which suggests that sociodemographic factors such as urban-rural differences may be more important than dose-based selection effects (*1, 2, 27, 28*). However, sociodemographic selection effects might have weakened because of modernization of the Japanese lifestyle over the decades. The issues related to the influences of dose, latency and sociodemographic-lifestyle factors on mortality from noncancer diseases in the LSS require further investigation.

A variety of studies of risks for site-specific cancers from external exposure to low-LET (linear energy transfer) radiation are documented in the UNSCEAR 2006 Report (*6*). Most studies were based on either subjects with high-dose radiation such as radiotherapy or radiation workers with low-level exposures. Thus the LSS is often thought to provide the most reliable estimates of radiation effects because of its large size, wide range of relatively precise individual doses, observation of numerous diseases, and long follow-up period. Cancers of the esophagus, stomach, colon, lung, breast, ovary and bladder and transitional cell carcinoma of kidney, pelvis and ureter are thought to be associated with low- and high-dose radiation based on the LSS and other studies (*6*). A strong interaction between radiation and smoking was observed in the risk of lung cancer (*29*), so high ERRs of smoking-related cancers might be partly due to such an interaction. Rectal cancer is thought to be inducible after high-dose radiotherapy exposures (*6*), but no association has been observed among the LSS. On the other hand, an association of liver cancer with radiation exposure has not been demonstrated in studies of medical and occupational exposure to low-LET radiation, while the LSS showed a significant increase in risk (*6*). It is inconclusive whether there was a synergism between HCV infection and radiation (*30*) or independent effects by each of them (*31*). Cancers of the pancreas, prostate and uterine cervix are not thought to be associated with radiation (*6*), which is consistent with the results of this study. Uterine corpus and kidney parenchymal cancers are possibly associated with a high-dose radiation exposure (*6*), but this association was not observed in this study.

Most excess cases of leukemia occurred shortly after the atomic bombings, even before the beginning of the LSS (*32*), and a modestly elevated risk has continued at a low level over the last several decades (*1, 7*). In this study, the estimated ERR at 1 Gy for total leukemia was 3.1 (95% CI: 1.8, 4.3) using a linear-quadratic model without effect modification, based on 313 cases, which is similar to a recent, more detailed leukemia report (*7*). An analysis of malignant lymphoma mortality in the LSS was conducted recently based on the subset of males of working age at the time of the bombing (*33*). The present study similarly found an excess for males [ERR/Gy of 0.70 ($P = 0.02$)] but no association for women [ERR/Gy $= -0.18$ ($P = 0.33$)]. We have no explanation for the disparity between the male and female results and believe the radiation effect should be interpreted cautiously due to both the gender disparity and the diversity of malignancies under the rubric of lymphoma. Earlier LSS reports of multiple myeloma mortality (*34*) did not show statistically significant excesses. But, based on hematologically reviewed incident cases from leukemia registries and tumor registries, Preston *et al*. (*35*) showed an ERR/Gy $= 0.25$ ($P > 0.5$) based on 30 first primary cases with shielded kerma under 4 Gy and ERR/Gy $= 0.9$ ($P = 0.02$) after adding seven cases of second primaries and those with shielded kerma >4 Gy. In the present study (all with bone marrow doses $\leq$4 Gy), ERR/Gy of multiple myeloma was 0.11 ($P > 0.5$) in males and 0.86 ($P = 0.04$) in females based on 34 and 59 cases, respectively.

In this overview, risk of noncancer diseases was reported using a broad classification of disease types. The elevated risk of diseases of the blood and blood-forming organs may be genuinely due to the effects of radiation or to possible misdiagnoses of hematopoietic malignancies as non-neoplastic conditions, since many death certificates were completed without intensive investigations as to the cause of death (*8*). The risk of circulatory diseases was significantly higher. This is important because circulatory diseases are the leading cause of death in developed countries (*6*); detailed results for circulatory disease deaths among the LSS have been reported elsewhere (*36*). The risk of respiratory diseases was also significantly elevated due to the increased risk of pneumonia and influenza, which constituted 63% of the deaths from respiratory diseases. However, characteristics of pneumonia and influenza appeared to be different between the periods of observation; namely, it was associated with acute epidemics in the early period but was more likely to be associated with terminal diseases among the elderly in the more recent period. Hence a problem in interpreting pneumonia and influenza deaths is that they may be associated with other concurrent or underlying diseases. Although digestive diseases showed an association with radiation during 1966–2003, liver cirrhosis, which constituted 43% of digestive disease deaths during that period, did not show any increased radiation risk. Therefore, further detailed analyses of both respiratory and digestive diseases are planned. There was no association of radiation dose and death due to external causes or to infectious/parasitic diseases.

The strengths of this LSS mortality study are, as stated previously (*2, 4, 34*), (1) a large, representative sample across all age groups of A-bomb survivors who were alive

in 1950, using stratified sampling to enrich the higher-dose portion of the sample, (2) reasonably precise estimates of individual doses, (3) a wide range of doses in the cohort, (4) complete ascertainment of mortality and cause of death using the *koseki* system, and (5) a long observation period with a large number of deaths. Those strengths provide a high-quality, informative epidemiological study.

A potential limitation of the LSS was that the subjects were the ''survivors'' of physical injuries and burns from the A-bomb explosion and biological injuries due to deterministic radiation effects. Additional stressors included poor nutrition and bad hygienic conditions in Japan in the postwar period. Those conditions might have led to early mortality and hence selective exclusion of vulnerable people, including vulnerability to radiation, from the available subjects in 1950. Nevertheless, the stochastic late health effects such as cancer development are not likely to be affected by such selection bias, which is supported by the negligible discrepancies in the dose–response curves between the early and late periods for all solid cancer (Fig. 6). A careful analysis of this phenomenon would require breakdowns by period, cancer site and other factors. Another unavoidable exclusion is that perhaps an appreciable number of leukemia cases occurring before 1950 were lost to the study (*32*). On the other hand, the significant discrepancy between the early and late calendar periods for noncancer diseases ($P = 0.02$) implies a potential selection bias for noncancer diseases as a whole. The discrepancy was not observed in circulatory diseases, while borderline differential patterns were observed for respiratory and digestive diseases. More detailed analyses are required.

In conclusion, the risk of death from malignant neoplasms in most sites and selected noncancer diseases increased in a dose-dependent fashion among LSS subjects over the period 1950–2003. The relative risk of radiation for solid cancer was largest among those exposed at young ages. The results of this study, which extended the observations for 6 years, are consistent with previous reports and continue to show increased cancer risks throughout the survivors' lifetimes. Since epidemiological evaluation can be done only after the development of outcomes, we sincerely pay our respects to those who have died. It would be our pleasure if clarification of late health effects of A-bomb radiation could offer fundamental information for the survivors' welfare. Clearly the LSS will continue to provide increased precision in risk estimation and additional information regarding risk modification by other factors, as 42% of the survivors in LSS subjects overall, and 80% of those who were exposed to radiation at the age of 20 years or younger, were still alive at the end of follow-up in 2003.

ACKNOWLEDGMENTS

The Radiation Effects Research Foundation (RERF), Hiroshima and Nagasaki, Japan is a private, non-profit foundation funded by the Japanese Ministry of Health, Labour and Welfare (MHLW) and the U.S. Department of Energy (DOE), the latter in part through DOE Award DE-HS00000031 to the National Academy of Sciences. This publication was supported by RERF Research Protocol RP 1–75. The views of the authors do not necessarily reflect those of the two governments.

Received: March 23, 2011; accepted: November 28, 2011; published online: December 15, 2011

REFERENCES

1. Beebe GW, Ishida M, Jablon S. Studies of the mortality of A-bomb survivors. 1. Plan of study and mortality in the medical subsample (Selection 1), 1950–1958. Radiat Res 1962; 16:253–80.
2. Preston DL, Shimizu Y, Pierce DA, Suyama A, Mabuchi K. Studies of mortality of atomic bomb survivors. Report 13: Solid cancer and noncancer disease mortality: 1950–1997. Radiat Res 2003; 160:381–407.
3. Young R, Bennett B, editors. DS02: A revised system for atomic bomb survivor dose estimation. Hiroshima: Radiation Effects Research Foundation; 2006.
4. Preston DL, Pierce DA, Shimizu Y, Cullings HM, Fujita S, Funamoto S, et al. Effect of recent changes in atomic bomb survivor dosimetry on cancer mortality risk estimates. Radiat Res 2004; 162:377–89.
5. Preston DL, Ron E, Tokuoka S, Funamoto S, Nishi N, Soda M, et al. Solid cancer incidence in atomic bomb survivors: 1958–1998. Radiat Res 2007; 168:1–64.
6. United Nations Scientific Committee on the Effects of Atomic Radiation. Effects of ionizing radiation. UNSCEAR 2006 Report, Volume 1. New York: United Nations; 2008.
7. Richardson D, Sugiyama H, Nishi N, Sakata R, Shimizu Y, Grant E, et al. Ionizing radiation and leukemia mortality among Japanese atomic bomb survivors, 1950–2000. Radiat Res 2009; 172:368–82.
8. Beebe GW, Kato H, Land CE. Studies of the mortality of A-bomb survivors. 6. Mortality and radiation dose, 1950–1974. Radiat Res 1978; 75:138–201.
9. Kato H, Johnson KG, Yano K. Mail survey on cardiovascular disease study, Hiroshima-Nagasaki. ABCC TR 19-66. Hiroshima: Atomic Bomb Casualty Commission; 1966.
10. Preston DL, Kato H, Kopecky KJ, Fujita S. Studies of the mortality of A-bomb survivors. 8. Cancer mortality, 1950–1982. Radiat Res 1987; 111:151–78.
11. Cullings HM, Fujita S, Funamoto S, Grant EJ, Kerr GD, Preston DL. Dose estimation for atomic bomb survivor studies: Its evolution and present status. Radiat Res 2006; 166:219–54.
12. Manual of the international statistical classification of diseases, injuries and causes of death: 7th revision (ICD-7). Geneva: WHO; 1957.
13. International classification of diseases, revision 8 (ICD-8). Geneva: WHO; 1967.
14. International classification of diseases, ninth revision (ICD-9). Geneva: WHO; 1977.
15. International classification of diseases, tenth revision (ICD-10). Geneva: WHO; 1993.
16. Pierce DA, Stram DO, Vaeth M. Allowing for random errors in radiation dose estimates for the atomic bomb survivor studies: Its evolution and present status. Radiat Res 1990; 123:275–84.
17. Breslow NE, Day NE. Statistical methods in cancer research, Vol. II. The design and analysis of cohort studies. IARC Scientific Publications No. 83. Lyon: International Agency for Research on Cancer; 1988.
18. Shimizu Y, Pierce DA, Preston DL, Mabuchi K. Studies of the mortality of atomic bomb survivors. Report 12, Part II. Noncancer mortality: 1950–1990. Radiat Res 1999; 152:374–89.
19. Preston DL, Lubin JH, Pierce DA, McConney ME. Epicure users guide. Seattle: Hirosoft International Corporation; 1993.

20. Akaike H. A new look at statistical model identification. IEEE Trans Automat Control 1974; 19:716–23.

21. Little MP. Heterogeneity of variation of relative risk by age at exposure in the Japanese atomic bomb survivors. Radiat Environ Biophys 2009; 48:253–62.

22. Walsh L. Heterogeniety of variation of relative risk by age at exposure in the Japanese atomic bomb survivors. Radiat Environ Biophys 2009; 48:345–7.

23. National Research Council, Committee on the Biological Effects of Radiation. Health risks from exposure to low levels of ionizing radiation (BEIR VII Phase 2). Washington, DC: National Academies Press; 2006.

24. Jacob P, Rühm W, Walsh L, Blettner M, Hammer G, Zeeb H. Is cancer risk of radiation workers larger than expected? Occup Environ Med 2009; 66:789–96.

25. The 2007 recommendations of the ICRP – Publication 103. Annex A. Biological and epidemiological information on health risks attributable to ionising radiation. Ann ICRP 2007; 37:137–246.

26. Yamamoto O, Antoku S, Russell WJ, Fujita S, Sawada S. Medical X-ray exposure doses as possible contaminants of atomic bomb doses. TR 16–86. Hiroshima: Radiation Effects Research Foundation; 1986.

27. Cologne JB, Preston DL. Longevity of atomic-bomb survivors. Lancet 2000; 356:303–7.

28. 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; 80:491–6.

29. Furukawa K, Preston DL, Lönn S, Funamoto S, Yonehara S, Matsuo T, et al. Radiation and smoking effects on lung cancer incidence among atomic bomb survivors. Radiat Res 2010; 174:72–82.

30. Sharp GB, Mizuno T, Cologne JB, Fukuhara T, Fujiwara S, Tokuoka S, et al. Hepatocellular carcinoma among atomic bomb survivors: significant interaction of radiation with hepatitis C virus infections. Int J Cancer 2003; 103:531–7.

31. Ohishi W, Fujiwara S, Cologne JB, Suzuki G, Akahoshi M, Nishi N, et al. Impact of radiation and hepatitis virus infection on risk of hepatocellular carcinoma. Hepatology 2011; 53:1237–45.

32. Folley JH, Borges W, Yamawaki T. Incidence of leukemia in survivors of the atomic bomb in Hiroshima and Nagasaki, Japan. Am J Med 1952; 13:311–21.

33. Richardson D, Sugiyama H, Wing S, Sakata R, Grant EJ, Shimizu Y, et al. Positive associations between ionizing radiation and lymphoma mortality among men. Am J Epidemiol 2009; 169:969–76.

34. Pierce DA, Shimizu Y, Preston DL, Vaeth M, Mabuchi K. Studies of the mortality of atomic bomb survivors. Report 12, Part I. Cancer: 1950–1990. Radiat Res 1996; 146:1–27.

35. Preston DL, Kusumi S, Tomonaga M, Izumi S, Ron E, Kuramoto A, et al. Cancer incidence in atomic bomb survivors. Part III. Leukemia, lymphoma and multiple myeloma, 1950–1987. Radiat Res 1994; 137 Suppl:S68–97.

36. Shimizu Y, Kodama K, Nishi N, Kasagi F, Suyama A, Soda M, et al. Radiation exposure and circulatory disease risk: Hiroshima and Nagasaki atomic bomb survivor data, 1950–2003. BMJ 2010; 340:b5349.

APPENDIX
Classification of Cause of Death in This Report

	Edition of International Classification of Diseases (ICD) and applicable years			
	ICD-7 1950–1968	ICD-8 1969–1978	ICD-9 1979–1997	ICD-10 1998–2003
Neoplasm	140–205, 210–239, *251*	140–239	140–239	C00–C97
All solid cancer	140–199	140–199	140–199	C00–C80
Esophagus	150	150	150	C15
Stomach	151	151	151	C16
Colon	153	153	153	C18
Rectum	154	154	154	C19–C20
Liver	155 (0, 8), 156	155, 197.8	155 (0, 1, 2)	C22 (0–4, 7, 9)
Gallbladder	155.1	156	156	C23, C24
Pancreas	157	157	157	C25
Other digestive system	158, 159	158,159	158,159	C26, C48
Lung	162 (0, 1, 8), 163	162	162	C33, C34
Breast	170	174	174,175	C50
Uterus	171, 172, 174	180, 182.0, 182 (9)	179–180, 182	C53, C54, C55.9
Ovary	175	183	183	C56, C57 (0, 1, 2, 3, 4)
Prostate	177	185	185	C61
Bladder	181	188	188	C67
Kidney parenchyma	180	189	189	C64
Renal pelvis, other urinary tract	180	189 (1, 2)	189 (1, 2)	C65, C66
Other solid cancer	Others in 140–199	Others in 140–199	Others in 140–199	Others in C00–C80
Leukemia	204	204–207	204–208	C91 (0–3, 5, 7, 9), C92 (0–5, 7, 9), C93, C94 (0–3, 7), C95
Malignant lymphoma	200–202, 205	200–202	200–202	C81–C85, C91.4, C96
Multiple myeloma	203	203	203	C88. (7, 9), C90
Other neoplasms	210–239, 251	208, 210–239	210–239	C94.4, D00–D48, Q85.0
Non-neoplastic diseases				
Blood disease	290–299, 468 (0, 1, 2)	209, 280–289	280–289	D50–D75, D77, C94.5
Circulatory disease	330–334, 400–467, 468.3	390–458	390–459	I00–I99, G45, M30
Respiratory disease	240–241, 470–527	460–519	460–519	J00–J64, J66–J99, R09.1
Pneumonia and influenza	480–493	470–486	480–487	J10–J18
Digestive disease	530–587	520–571	520–571	K00–K92
Liver cirrhosis	581	571	571	K70, K73, K74
Genitourinary disease (*additional for female)	590–617, 620–637*	580–607, 610–629*	580–608, 610–629*	N00–N50, N60–N98*
Infectious Disease	001–138	000–136	001–139	A00–A32, A35–B99, D86, J65, M35.2
External causes	N800–N999	N800–N999	800–999	S00–T98