RESEARCH ACTIVITIES OF EPIDEMIOLOGY IN JAPAN

A Long-Term Cohort Study of the Atomic-Bomb Survivors

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The Atomic Bomb Casualty Commission (ABCC), the predecessor of the Radiation Effects Research Foundation (RERF), was established in 1947 to conduct long-term, comprehensive epidemiological and genetic studies of the atomic-bomb (A-bomb) survivors. Today this study still depends upon the voluntary cooperation of several tens of thousands of survivors of the bombings of Hiroshima and Nagasaki. An in-depth follow-up study of mortality in the study population of 120,000 persons, including A-bomb survivors and controls, has continued since 1950. The study of tumor incidence was initiated through record linkage with a tumor registry system in Hiroshima and Nagasaki in 1958. In the same year, biennial medical examinations of 20,000 individuals began. Follow-up studies also have been conducted on in-utero-exposed persons and first-generation offspring of the survivors. On the basis of these studies spanning nearly half a century, we know that the occurrence of leukemia and cancers associated with A-bomb radiation is higher than among the non-exposed. Among the A-bomb survivors, radiation cataracts, hyperparathyroidism, delayed growth and development, and chromosomal aberrations also occur more often. However, to date no evidence exists of genetic effects in the children of A-bomb survivors. It should be kept in mind that such study results could never be obtained without the cooperation of A-bomb survivors. *J Epidemiol*, 1996 ; 6 : S95-S105.

atomic-bomb survivors, cohort study, late health effects, radiation

Throughout human evolution, man has been continually exposed to small quantities of cosmic and terrestrial radiation emanating from the natural background. However, most of the radiation exposures that now pose health hazards are from manmade sources, with a notable exception of radon exposure. Only a century has passed since the discovery of X rays by Wilhelm Roentgen in 1895 and that of radium by Marie Curie in 1898. The past 100 years saw a rapid expansion in the use of radiation for both peaceful and military purposes. On the one hand, the use of radiation and radionuclides for medical purposes has led to immense saving of human lives and nuclear electric power generation has become an important part of the modern life in many parts of the world. On the other hand, the widespread use of radiation also has justifiably given rise to public concerns about the health hazards of radiation exposures. An accident of the Chernobyl nuclear power plant in 1986 has, primarily because its magnitude, reinforced fears against radiation on an internationally scale. This accident resulted from human error rather than an act of war. The

first military use of a nuclear weapon in Hiroshima and Nagasaki in 1945 led to exposure of large populations to a massive amount of radiation. A half century later, countless atomic bomb survivors still suffer from or anxiously living in constant fear of the late effects of radiation exposure. Although systematic efforts to follow up the Chernobyl-affected populations have proved quite formidable, the long-term follow-up of the atomic survivors in Hiroshima and Nagasaki has been and continues to be the source of the most comprehensive knowledge on the human health effects of radiation exposure. Here we will summarize this unprecedented long-term prospective study.

BACKGROUND

In August of 1945, atomic bombs (A-bombs) were detonated over the cities of Hiroshima and Nagasaki. Although the two bombs differed in their composition, about 50% of the total released energy was in the form of blast and 35% in thermal

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rays, but, unlike conventional bombs, 15% of the energy released was in radiation, the source of acute and late health effects among A-bomb survivors¹⁾. An attempt to estimate numbers of acute deaths and the extent of injuries after the bombings is greatly complicated by the massive destruction and chaotic conditions that followed after the bombings. However, it is estimated that approximately 330,000 people lived in Hiroshima at the time of the atomic bombing ; of these, approximately 110,000 people died by the end of December 1945, and approximately 80,000 sustained some kind of injury. In Nagasaki, approximately 70,000 of the 250,000 people residing there at the time of the bombing (ATB) died by the end of December 1945, and 80,000 sustained injuries. Instantaneous and acute deaths thus accounted for about one-third of the total populations of both cities.¹⁾ Those who survived were to carry with them an increased risk of cancer and other delayed health effects for many subsequent years and possibly throughout the life.

THE EVOLUTION OF ABCC AND RERF

The Atomic Bomb Casualty Commission (ABCC) was established in Hiroshima in 1947 and in Nagasaki in 1948 by the US National Academy of Sciences (National Research Council (NAS-NRC) based on President Harry Truman's directive to initiate long-term comprehensive epidemiological and genetic studies of the A-bomb survivors^{2,3)}. The Japanese National Institute of Health under the Ministry of Health and Welfare (MHW) joined this program 1 year later to assist in the studies and improve the cooperation of the survivors^{2,3)}. The Radiation Effects Research Foundation (RERF) results from the reorganization in 1975, which placed the entire program under the equal sponsorship of the United States and Japan. The RERF oversight bodies are the MHW and NAS under contract with the US Department of Energy. What is remarkable is the continuing cooperation received from the A-bomb survivors, which has enabled the conduct of this long-term ongoing research program.

STUDY OBJECTIVES

The overall objective of ABCC/RERF research is to assess medical and biological effects of radiation on humans, with a view to contributing to the health and welfare of the A-bomb survivors and to the enhancement of the health of all humankind. The epidemiologic objective is to determine the nature and magnitude of health risk associated with exposure to A-bomb radiation. Although these general program objectives have remained unchanged over the years, research emphases and foci have evolved reflecting the progress made in various scientific disciplines and techniques as well as changing societal needs. For example, the objective of risk assessment changed from the early attempt to identifying specific diseases associated with radiation to quantitative charac-

terization of risk as it is affected by host factors. More recently, newly developed biological techniques enable us to gain possible mechanistic insights. The soundness of the original study design and the unified approach have been essential in maintaining the principal objectives intact during the rapid progress in related disciplines.

STUDY METHODOLOGY

Denominator and numerator information is essential in conducting epidemiological research. The study population must be clearly defined, and the amount of exposure to a given factor (in this study, radiation dose) or factors for each study subject must be known. It is also necessary to obtain accurately the health information and the cause of death of each person. The ABCC research program was initiated in 1947. Among the most important studies undertaken during the earliest ABCC years was a large-scale study on genetic effects. Studies of the atomic bomb survivors were carried out by different investigators, each using their own population, with little significant findings except for the early excess in leukemia. In the mid-1950, the ABCC research was reviewed by a committee headed by Thomas Francis, epidemiologist. This committee recommended a Unified Study program, under which all studies be carried out in fixed samples with prospective long-term mortality, pathology and clinical follow-up serving the major components⁴⁾. All subsequent ABCC/RERF studies have been and continue to be undertaken in the framework of fixed cohort samples, perhaps one of the most important reasons for the productiveness of ABCC/RERF research.

Study Populations

The major ABCC-RERF cohort samples for investigating the late effects of A-bomb radiation are survivors of the A-bombings and those exposed in utero. Those born to parents one or both of whom were exposed to the A-bombings are another study sample (Fig. 1)^{1-3,5)}.

A-bomb survivors : The population of atomic bomb survivors used in ABCC/RERF studies of the long term effects of radiation on mortality and cancer incidence is a cohort that includes about 93,000 people who were in the city at the time of the bombs and who were resident in Hiroshima or Nagasaki on October 1, 1950. The sampling frame is a total of some 284,000 survivors enumerated by a nationwide survey of the atomic bomb survivors conducted at the 1950 National Census. The LSS cohort includes most survivors within 2.5 km of the bomb hypocenters who lived in Hiroshima or Nagasaki in 1950 and who met certain conditions considered favorable for follow-up and a sample of survivors, comparable in size and matched by sex and age, who were within 2.5-10 km of the hypocenters. The cohort also includes another group of 27,000 people whose family register was in one of the cities and who lived in Hiroshima or Nagasaki in the early 1950's

Figure 1. Atomic Bomb Casualty Commission-Radiation Effects Research Foundation study cohorts

but were not in the city at the time of the bombs⁵). This latter group is not usually included in analyses because of data suggesting that there are socioeconomic differences from the survivor population. This population is formally known as the Life Span Study (LSS) cohort. Roughly half of the survivors within 2 km are included in the LSS, although this estimate is not precise. Periodical analyses of the LSS mortality have resulted in a series of reports since 1950⁶⁻⁸). More recently, it became possible to analyze LSS cancer incidence data through the Hiroshima and Nagasaki tumor registries, and results of the first comprehensive analyses have been published⁹⁻¹¹).

The Adult Health Study (AHS) population was established as a subset of the LSS sample, comprising 20,000 individuals : 5,000 exposed within 2 km from the hypocenter with acute radiation symptoms ; 5,000 exposed within 2 km from the hypocenter with no acute radiation symptoms ; 5,000 exposed at distances beyond 3 km from the hypocenter ; and 5,000 who were in neither Hiroshima nor Nagasaki ATB⁵). Since 1958, biennial examinations have been conducted on this population to study the morbidity status of the A-bomb survivors. Currently, the 19th cycle of examinations is underway^{12,13}).

In utero-exposed survivors : A long-term mortality follow-up has also been conducted in a cohort of about 2,800 in-utero exposed survivors. In a separate but largely overlapping cohort of 1,100 individuals has been included in the AHS clinical program^{5,14,15}).

Current analyses of mortality and cancer incidence data among the in-utero exposed persons make use of data from a combined clinical and mortality cohort.

Children of A-bomb survivors : A mortality follow-up has been undertaken of about 77,000 persons consisting of those born to parents at least one of whom was exposed and age and sex-matched comparison groups. A cytogenetics study was initiated in 1967 on 45,000 individuals, and a biochemical genetics study was initiated in 1975 on 33,000 members of this population. In 1985, a DNA study was initiated on 3,300 individuals^{5,16}).

Dosimetry

Individual radiation dose estimates for study participants, though costly and laborious, are essential for risk assessment. During the first decade of the ABCC research, no individual dose estimates were available and analyses were based on comparisons by distance from the hypocenter. This was satisfactory for the purpose of screening for specific diseases associated with radiation exposure, but not for assessing the magnitude of risk. Over the years ABCC-RERF has devoted extensive resources to dosimetry, and this work still continues. To estimate radiation doses, the type and quantity of radiation released by A-bombs must be known and how it was attenuated by distance from the hypocenter and shielding. In the

ICHIBAN study conducted in the United States^{17,18)}, a tower 465 m in height, with a nuclear reactor mounted at the top, was built in the Nevada. Japanese houses were shipped from Japan, and tests were repeated, beginning in 1962, to obtain data needed to estimate radiation attenuation by distance from the reactor and shielding by the Japanese houses. In addition, interviews of survivors were conducted from 1954 to 1965 to determine the distance from hypocenter and exposure conditions for each A-bomb survivor. All this information has been re-evaluated periodically during the last 40 years, resulting in the present system known as Dosimetry System 1986 (DS86)^{18,19)}.

While individual physical dose estimates form the basis of all RERF studies, research on developing biological dosimeters has recently become more active. Frequencies of stable chromosomal aberrations in lymphocytes have long been known to be a reliable measure of levels of past radiation exposure²⁰⁾. More recently, glycophorin A assays, a measure of somatic mutations in erythrocytes, and electro-spin resonance measurements of tooth enamel tissue have been added to the list of biological dosimeters for radiation exposure^{21,22)}.

Morbidity and Mortality Follow-Up

After establishing the study population, the denominator, and estimating the individual doses of study subjects, it is necessary establish long-term plans for obtaining the numerator data on such endpoints as health conditions and causes of death, as they occur. The major endpoint data obtained in the ABCC-RERF epidemiological follow-up studies include : (1) mortality data based on death certificates (DC) ; (2) tumor and tissue registry cancer incidence data; and (3) periodical (biennial) medical examination data. Until 1978, autopsy data were also obtained for a subset of the population through an active autopsy procurement.

Mortality data : The mortality follow-up of the ABCC (RERF cohort studies has been greatly facilitated by access to the koseki or official family registration records in Japan. By checking koseki records every 2-3 years, virtually complete ascertainment of vitas status of cohort members is achieved regardless of where they live in Japan. More than 99% of deaths are ascertained, and underlying causes of death are identified from death certificates.

The accuracy of cause of death as recorded on DC is an obvious concern. Tables 1 and 2 present data on several measures of accuracy of DC diagnoses for various disease categories using autopsy findings performed at ABCC-RERF^{23,24)} as the standard. The accuracy of DC diagnoses clearly differ by disease. While the agreement between DC and autopsy diagnoses is rather high for cancer as a group or leukemia, it is rather lower when specific cancer sites are concerned. The agreement is particularly poor for less accessible cancer sites such as the liver and pancreas. The agreement for non-cancer diagnoses is generally quite low. Mortality also is a poor endpoint for cancers and other diseases with low fatality.

Systematic and continuing collection of morbidity data is difficult for a large cohort population. It is also essential that quality of morbidity data be defined in risk assessments. For cancer risk assessment, tumor registry-based incidence data have been found to be more informative than DC-based mortality data for certain types of tumor (Table 3). For diseases other than cancer, the Adult Health Study as described below provide longitudinal clinical data.

Tumor registry data : Recognizing the need of cancer incidence data for the follow-up of the A-bomb survivors, ABCC in collaboration with the local medical associations started tumor registries in Hiroshima and Nagasaki in 1957 and 1958, respectively. These were the first population-based tumor registries in Japan. The Hiroshima and Nagasaki tumor registries also provide linkage with the ABCC/RERF study samples pro-

Table 1. Accuracy of Death Information Obtained by ABCC-RERF
- Comparison of Death Certificate Diagnosis with Autopsy Diagnosis-

Cancer site	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
All	75.7	96.9	90.9
Stomach	70.6	98.4	82.4
Colon	44.2	99.7	63.9
Liver	55.0	98.8	34.4
Pancreas	33.9	99.7	55.9
Breast	75.7	100.0	96.6
Female genital	67.3	99.6	80.9
Male genital	16.0	99.9	50.0
Urinary	48.0	99.7	63.2
Hematopoietic	68.4	99.7	80.7

Ron E et al : *Epidemiology* 5 : 48-56, 1994.

Table 2. Accuracy of Death Information Obtained by ABCC-RERF
- Comparison of Death Certificate Diagnosis with Autopsy Diagnosis -

Non-cancer diseases	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
Stroke	67.0	84.3	39.8
Heart	33.7	90.0	51.7
Respiratory	23.3	94.9	28.4
Digestive	51.4	95.7	47.1
Urinary	19.0	98.7	23.8
Nutritional Endocrine	41.7	98.1	21.0
Hematopoietic	43.8	99.5	21.9

Ron E et al : *Epidemiology* 5 : 48-56, 1994.

viding the monitoring of incident cases in the cohorts^{9,10}.

Advantages of the cancer incidence data include accuracy of diagnosis and coverage of low mortality cancers. Shortcomings are high costs for supporting an adequate number of skilled personnel for data collection and management. Since there are no nationwide cancer incidence data, a considerable number of the RERF cohort members who have migrated out of the tumor registry's catchment area poses another problem. The quality of the cancer incidence data can be measured in several ways (Table 3)⁹. Table 3 shows the percentage of diagnoses based on DC only, mortality/incidence ratio, and the rate of histological verification. The overall quality of the data as judged by these conventional indices is good, although the quality is slightly poorer for certain cancers, e.g., liver cancer (Table 3)⁹.

Medical examination data : Biennial medical examinations have been carried out among the AHS subcohort for more than 30 years. A wide variety of information has been collected including data on diseases other than cancer, low-mortality cancers, and other clinical data, such as biochemical and physical measurements as well as information on factors that might

confound the effects of radiation. These provide a unique opportunity to study longitudinal clinical data from one of the longest continuing observations of a large-size defined population. Incompleteness in longitudinal data can occur as result of participants missing certain examination cycles, and this could be a course of unknown bias associated with long-term follow-up and nonresponders. In order to maintain a high participation rate, the AHS program includes regular day visits to the clinic, night clinics, and home visits (Fig. 2). As a result, strikingly high response rates have been maintained over an extended period of time²⁵.

Fig. 3 shows the longitudinal trend in participation by birth cohort 1958-1988. Despite some fluctuation, participation has remained at the level of 70%-90% up to 70 years of age. The participation rate differs by age, as it rapidly decreases after 70 years of age. Now that the average age of AHS participants is 64.3 years, the ongoing biennial examination system will cease to be an efficient way to collect information in the near future²⁵. A comprehensive surveillance system incorporating hospital surveys and other means was introduced to the AHS program in 1995²⁶. Although differences in participation rates according to radiation dose could possibly be a source of bias,

Table 3. Accuracy of Cancer Incidence Data Obtained by ABCC-RERF
- Life Span Study : 1958-1987-

Cancer site	Number of cases	DCO (%)	M/I	HV (%)
Stomach	2,658	14.1	0.70	72.8
Colon	457	9.2	0.53	80.7
Liver	585	32.8	1.05	38.8
Pancreas	240	17.1	0.91	55.0
Lung	872	18.3	0.85	69.4
Breast	529	1.9	0.27	95.1
Uterine cervix	553	0.9	0.16	96.7
Thyroid	225	3.1	0.20	93.3

DCO : Death certificate only, M/I : mortality to incidence ratio, HV: histological verification.

Mabuchi K et al : *Radiat Res* 137 : S1-S6, 1994.

Figure 2. Types of examination chosen by participants, according to age (Adult Health Study, 1986-1988)

Figure 3. Secular changes in participation rate by birth cohort (Adult Health Study, 1958-1988)

this has not been observed to date²⁷⁾.

STUDY RESULTS

Fifty years have passed since the atomic bombings in Hiroshima and Nagasaki. During these years, cancer has been

among the prominent health effects of radiation exposure. The most striking are the temporal trends of cancer and leukemia risks and their patterns that are modified by host factors. The latest cancer mortality data, covering the period from 1950 through 1990, show that among 50,000 survivors with significant exposure to radiation (>0.01 Sv), a total of 176 leukemia

Table 4. Number of Deaths due to Malignant Neoplasm
- Life Span Study : 1950-1990 -

	Total number of deaths	Estimate number of deaths due to radiation	% of deaths attributable to radiation
Leukemia	176	86	49%
Other types of cancer	4687	341	7%
Total	4863	427	9%

* For the 50,000 RERF study members with doses greater than 0.5m Sv.
This includes about half of all survivors with such exposures.

Figure 4. Cancer deaths among survivors with significant exposures* by decade

deaths and 4,687 deaths from cancer other than leukemia (mostly solid cancers) occurred²⁸. As shown in Table 4, 86 (49%) of the leukemia deaths and 341 (7%) of deaths from other cancers are estimated to be due to radiation.

It is noteworthy that most of the excess risk of leukemia, especially among people exposed as children, occurred in the early years of the follow-up, with a peak excess risk around 5-10 years after the bombings. The number of excess leukemia cases has continued to decline over the years. On the other hand, the excess risk for other cancers, which began to appear 5-10 years after exposure, still continues today and it seems likely that it will persist throughout the lifetime of the survivors (Fig. 4). With 85% of the LSS subjects exposed at young ages (<30 years) being still alive, a further follow-up is essential for risk assessment as these survivors enter ages in which natural cancer risk is increased.

A-bomb radiation has been shown strongly to be associated with a variety of diseases and conditions. Specific health effects revealed by the ABCC-RERF long-term epidemiological study are summarized in Table 5. Strong evidence on radiation effects has been obtained for leukemias (excluding chronic lymphocytic leukemia and adult T-cell leukemia), several major types of cancer (female breast, thyroid, colon, stomach, lung, liver, bladder, skin and ovary)^{6,8,11,29,30} radiation cataract³¹, and hyperparathyroidism^{32,33}, delayed growth and development³⁴, chromosomal aberrations of lymphocytes²⁰,

and somatic mutations of erythrocytes²¹. In-utero exposure has been associated with microcephaly and mental retardation³⁵. A relationship with radiation also has been observed, with less certainty, with cancers of the esophagus and salivary glands^{6,8,11}; total mortality^{6,7}; cardiovascular diseases³⁶⁻³⁸; thyroid diseases^{13,39,40}; decreased PHA response of lymphocytes⁴¹ and chromosome aberrations of lymphocytes⁴² among those exposed in utero. In addition, an excess risk of benign tumors recently has begun to be observed in A-bomb survivors, with a significant increase in uterine myoma^{12,13}, benign tumors of the digestive organs, especially of the stomach⁴³, the thyroid³⁹ and the ovary⁴⁴. The long-term follow-up study also has demonstrated that in the exposed group the serum cholesterol level is significantly elevated and that psychological effects among the survivors are stronger the closer they were to hypocenter^{45,46}.

No clear relationship to A-bomb radiation exposure has been observed with chronic lymphocytic leukemia and adult T-cell leukemia³⁰, and infertility in A-bomb survivors⁴⁷. Also the aging of survivors has not been accelerated by A-bomb exposure⁴⁸. Among their children congenital abnormalities⁴⁹ and genetic effects¹⁶ have not been demonstrated.

In epidemiology, strength of the association is an important factor in estimating the causal relationship. For cancer deaths, Fig. 5 shows the strength of association for specific diseases and A-bomb radiation⁶. The relative risk (RR) of site-specific

Figure 5. Relative risk of death due to cancer at major sites (1 gray radiation exposure, Life Span Study, 1950-1985)

cancer death at 1 Gy is 4.92 and the highest is for leukemia (95% confidence interval : 3.89-6.40). The RR of other cancers ranges from 1.5 to 2.0 (Fig. 5). Even when a significantly higher frequency of any health abnormality is observed, one should not immediately conclude that it is due to radiation. Assumption of a causal relationship must be judged according to consistency, strength, specificity, temporal relationship, and coherence of the association⁵⁰. Furthermore, observation of a statistical relationship between cancer mortality and radiation by itself does not mean that all cancers observed in A-bomb survivors can be attributed to A-bomb radiation since many environmental carcinogens other than radiation exist. The extent of the involvement of radiation in the development of cancer among A-bomb survivors has been calculated as what is called the attributable risk (AR). The AR of leukemia at 1 Gy is as high as 55.4%, showing the remarkable contribution of radiation, whereas the AR of cancers other than leukemia is only 7.9%. By specific site, the AR is relatively high for breast cancer and urinary tract cancer, at 22.1% and 22.7%, respectively (Fig. 6)⁶.

Public Health Implications of the A-Bomb Studies

The ABCC-RERF studies have contributed to the establishment of the governmental program aimed at the welfare for A-bomb survivors, including the recently revised compensation measures. In addition, the ABCC-RERF epidemiological studies have been the major source of information used by leading national and international organizations to establish radiological protection standards for workers and the public. National and international organizations that incorporate ABCC(RERF) results into their advisories include the International Commission on Radiological Protection (ICRP), the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), and the US National Academy of

Sciences(Advisory Committee on the Biological Effects of Ionizing Radiations (BEIR)^{2,51-53}).

What We Have Learned from This Long-Term Epidemiological Study

Through the voluntary cooperation of the A-bomb survivors and countless others in the communities of Hiroshima and Nagasaki, the ABCC-RERF epidemiological study has continued for nearly half a century. An unprecedented historical event produced a unique follow-up response among many groups. The local medical societies, national and local governmental agencies (which have permitted access to the Japanese family registry system or koseki for death ascertainment) and the dedication of research staff have been key to the success of this long-term study.

An important limitation of the ABCC-RERF studies is that the cohort of A-bomb survivors was not established until several years after the bombings and thus does not include those who died before 1950. It has been suggested that particularly radiosensitive persons died during the 5 years after the A-bombings, leaving a more-radioresistant group upon which ABCC-RERF has focused for 5 decades. However, study after study has failed to show any difference in the radiation sensitivity of the A-bomb survivors' cells as a function of radiation dose². Whenever possible, after a radiation-exposure incident, the study populations should be established immediately.

Biennial physical examinations, the core of the ABCC-RERF clinical adjunct to the tumor and tissue registry data acquisition, have resulted in intervals when no information is collected. To collect some of this "missing" information-especially as the participation among elderly A-bomb survivors decreases, a morbidity/mortality surveillance system has been introduced belatedly into the Adult Health Study. In retrospect, annual examinations would have been useful.

Table 5. Summary of Late Health Effects of Atomic-bomb Radiation

1. Strong association
Leukemia and other malignant tumors
Cataract
Hyperparathyroidism
Delayed growth and development (expose when young)
Chromosomal aberrations, somatic mutations
Microcephaly and mental retardation (in-utero exposed)
2. Weak association
Some malignant tumors
Noncancer mortality
Thyroid and some other diseases
Certain changes in immunity
Total solid tumors and chromosome aberrations (in-utero exposed)

Figure 6. Attributable Risk of Death from Cancer among A-bomb Survivors (1 gray radiation exposure, Life Span Study, 1950-1985)

CONCLUSION

We have summarized briefly the longest epidemiological study of a radiation-exposed population—the ABCC-RERF Life Span Study and its subcohort, the Adult Health Study. The association of radiation exposure with leukemia and cancer has been established during 5 decades of data collection among A-bomb survivors and a control population, leading to understanding of the nature and magnitude of risk associated with radiation. However, much more can be learned from further follow-up of the survivors and their children. Furthermore, it analyses of the LSS mortality and incidence data have recently shown an apparent excess in diseases other than cancer, such as cardiovascular disease among the survivors. This important finding must be studied further. The continued voluntary participation of the A-bomb survivors is essential to these ongoing efforts. As RERF scientists, we cannot adequately express our

gratitude to the A-bomb survivors who continue to entrust vital information into our care.

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