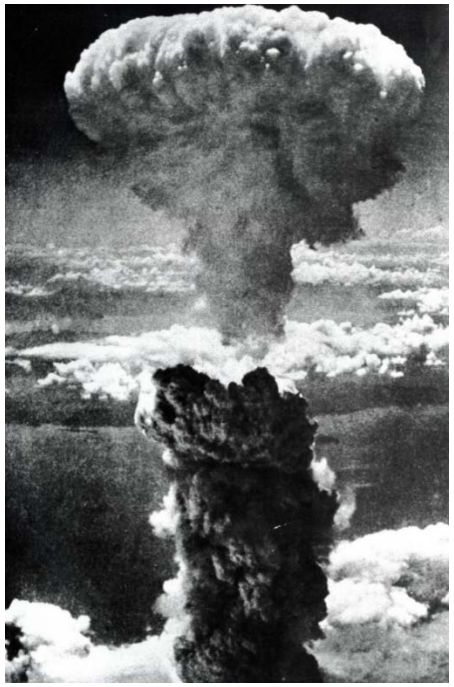


Mortality of individuals exposed to atomic bomb radiation *in utero*: 1950-2012

Hiromi Sugiyama

Department of Epidemiology, Radiation Effects Research Foundation

Commemorating the 75th Anniversary of the Atomic Bombings,
Studies on Radiation Health Effects at the Radiation Effects Research Foundation, Japan

Background
Methods
Results
Discussion

Cohort of individuals exposed to the atomic bombings *in utero*

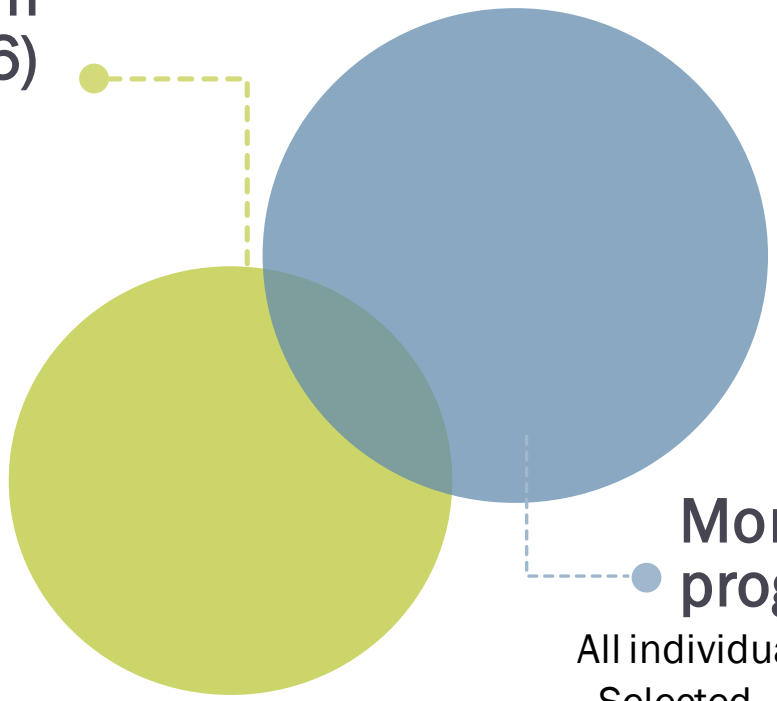
Clinical study program (n=1,606)

Alive as of October 1, 1950
Lived in Hiroshima or Nagasaki.

All individuals exposed within 2,000 m.
Selected
- those exposed between 3,000 m and 4,999 m
- those who were located beyond 10,000m.

(matched by sex and month of birth.)

Followed-up (clinically):
1959-1965 (19 years old)



Sources:
Birth Reports
Master File of ABCC
1960 National Census

Mortality study program (n=2,802)

All individuals exposed within 1,500m.
Selected
those exposed beyond 1,500m
(matched by sex and month of birth.)

Followed-up:
1945 (birth) or 1960 - present

Results from the clinical cohort and mortality cohort

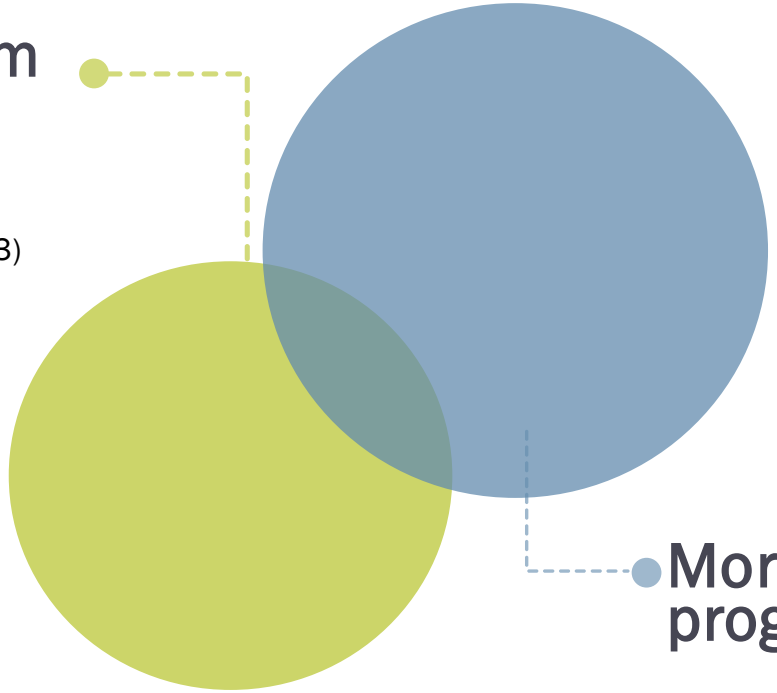
Clinical study program

- Small head size
- Mental retardation

(Otake and Shull. Int J Radiat Biol. 1993)

12才の標準児童（左側）と15才8ヶ月の小頭症児童（右側）（長崎大学医学部附属原爆被災学術資料センター「長崎原子爆弾の医学的影響」より転載）

原爆放射線の人体影響改訂第2版



Mortality study program

Socioeconomic survey in 1964

- High frequency of low birth weight
- High frequency of individuals who lost one or both parents

(Kato and Keehn. ABCC TR 13-66. 1966)

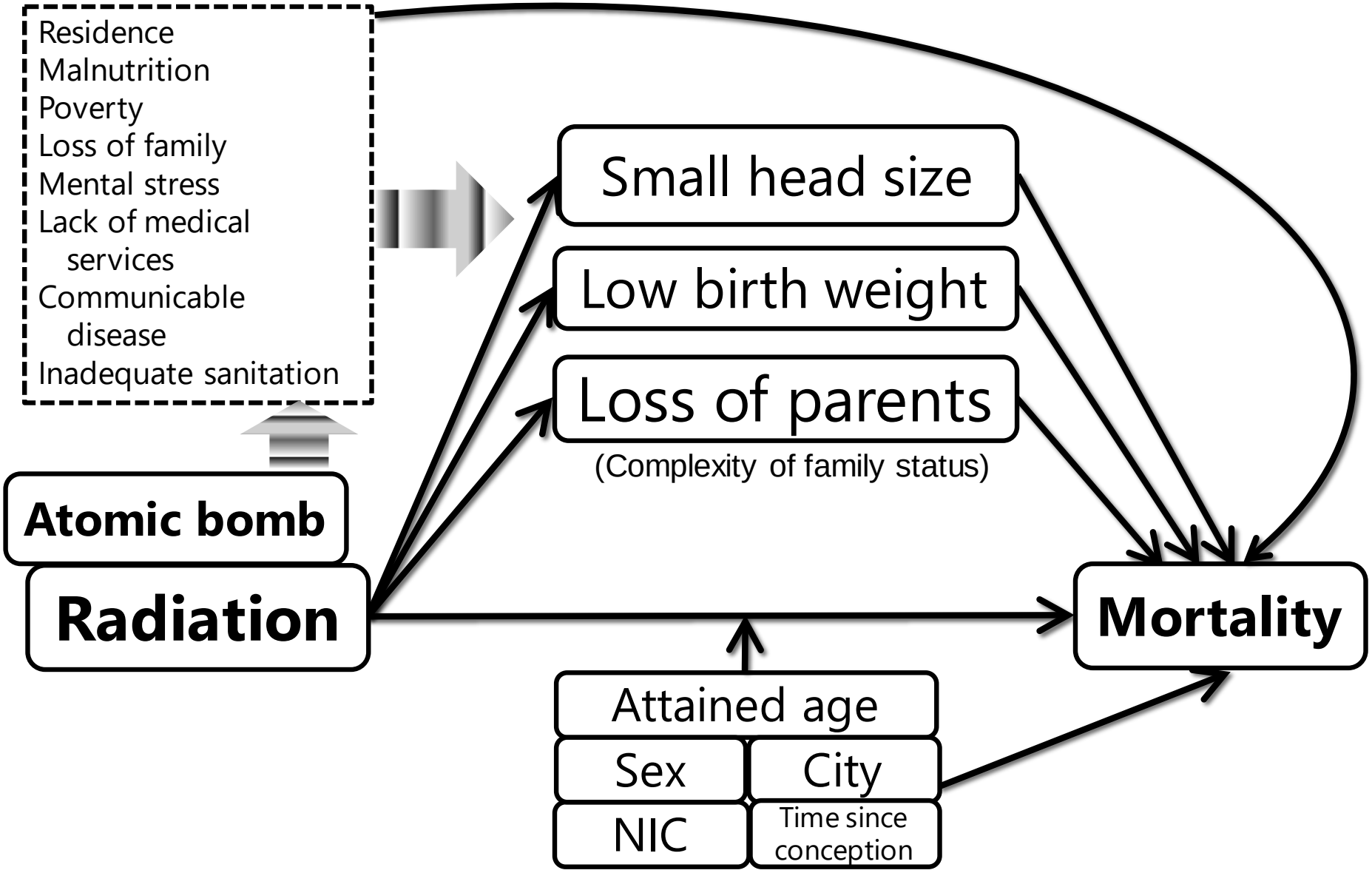


Figure 1. Potential relationships among radiation, observed and unobserved factors and mortality are illustrated. Solid lines indicate observed variables and dashed lines indicate unobserved variables.

Background

Methods

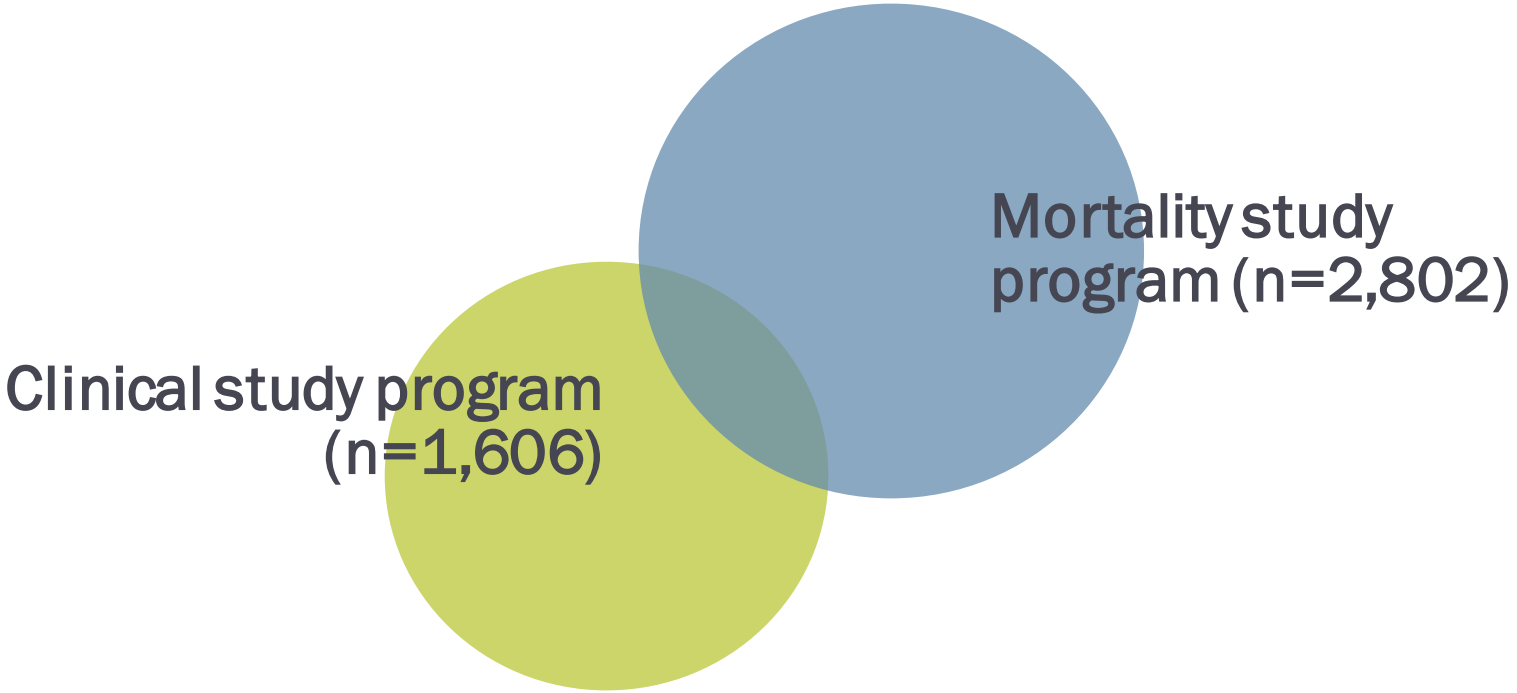
Results

Discussion

Methods

- *In utero* cohort (n=3,638)

  Those exposed to atomic bomb radiation in mother's womb, who were born after the bombing through May 31, 1946.



Methods

- Radiation dose
  - DS02R1 mother's weighted absorbed uterine dose

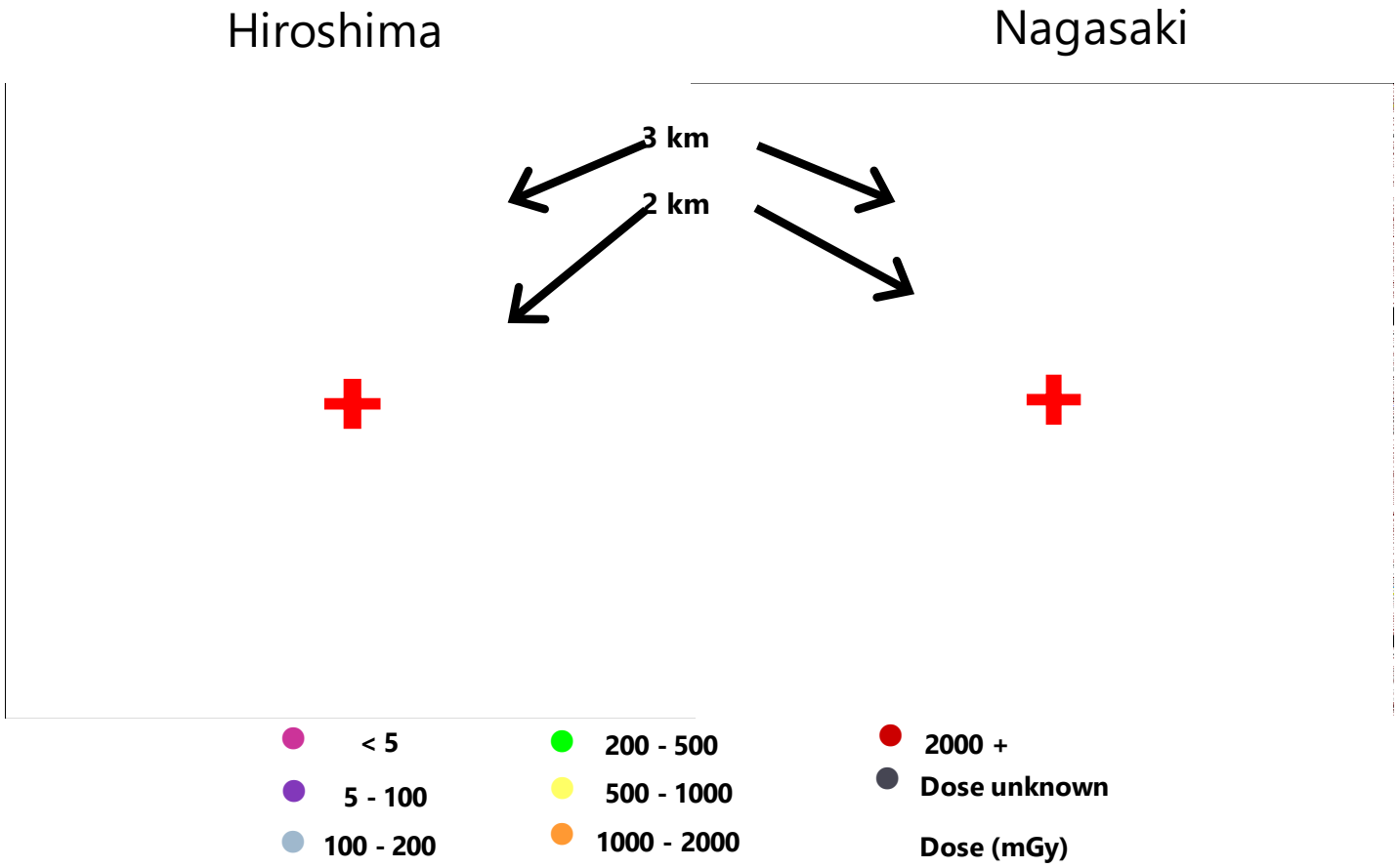


Figure 2. Distribution of location at time of bombing and radiation dose among *in utero*

Method

- Follow up: 1950-2012
  - Start of follow-up:
    - October 1, 1950
    - July 1, 1959 ← Clinical cohort members
    - October 1, 1960 ← 1960 National Census
  - End of follow-up
    - Vital status: Japanese family registry system (*koseki*)
    - Underlying cause of death based on death certificates

Method

- Subjects for analysis (n=2,463)
  - Excluding
    - ineligible cases (*koseki* unknown, foreign nationality) (n=82)
    - mother's absorbed radiation dose unknown, (n=879)
    - those who died before the start of follow-up (n=214)

Statistical analysis 1

Association between radiation and potential mediators

Logistic regression, multinomial logistic regression

- Response:
  1) Birth weight (≧2500g, <2500g, unknown, no information)
  2) Head size (Normal head size or small head size)
  3) Father's survival status (alive, dead, or no information)
  4) Mother's survival status (alive, dead, or no information)

  "dead" includes divorce, disappearance, or unknown
- Risk factor: Radiation dose

  Adjusted for city, sex, source of cohort, NIC (whether subject in city or not at the time of bombing), and trimester at the time of bomings

Statistical analysis 2

Association between radiation exposure and mortality

- Outcomes: Solid cancer deaths, non-cancer disease deaths, and external cause of deaths
- Poisson regression, individual person-years data
  - Basic ERR model

$$\lambda = \lambda_0(c, s, a, src, c*nic, tri)\,[1+\rho(d)]$$

  - Full ERR model

$$\lambda = \lambda_0(c, s, a, src, c*nic, tri, bw, s*h, fs, ms)\,[1+\rho(d)]$$

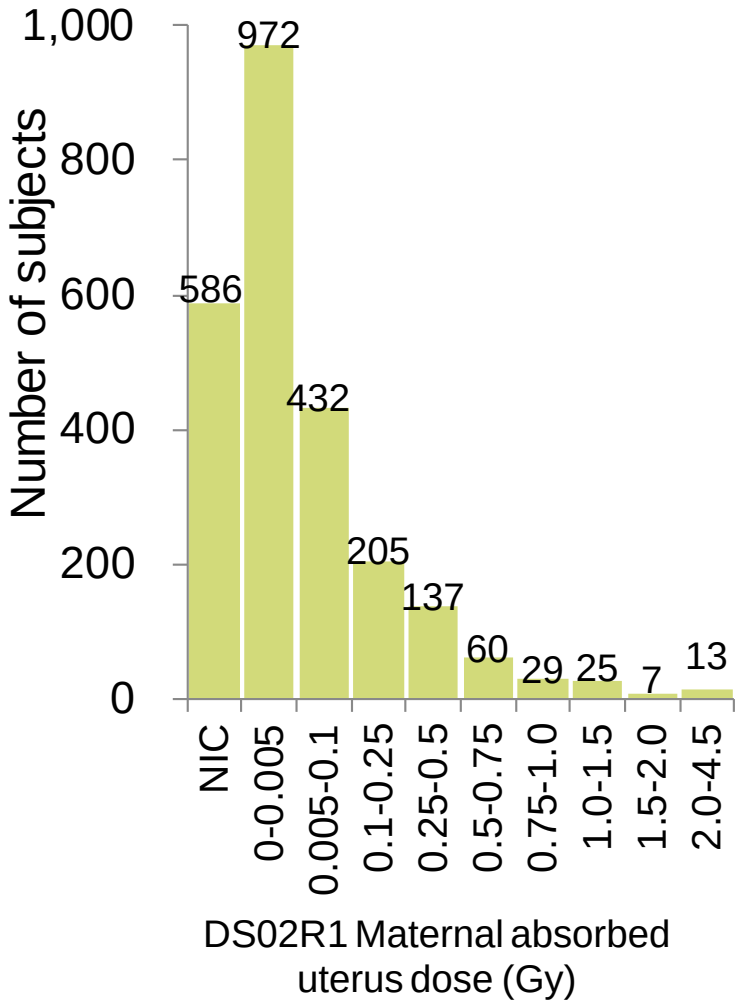
c: city
s: sex
a: attained age
src: source of cohort
nic: whether subject in city or not at the time of bombing,
tri: trimester

bw: birth weight (normal, low, unknown, no info.)
h: head size (small, normal head size)
fs: father's' survival status (alive, loss, no info.)
ms: mother's survival status (alive, loss, no info.)
d: DS02R1 mothers' absorbed uterus dose (Gamma+10*neutron)

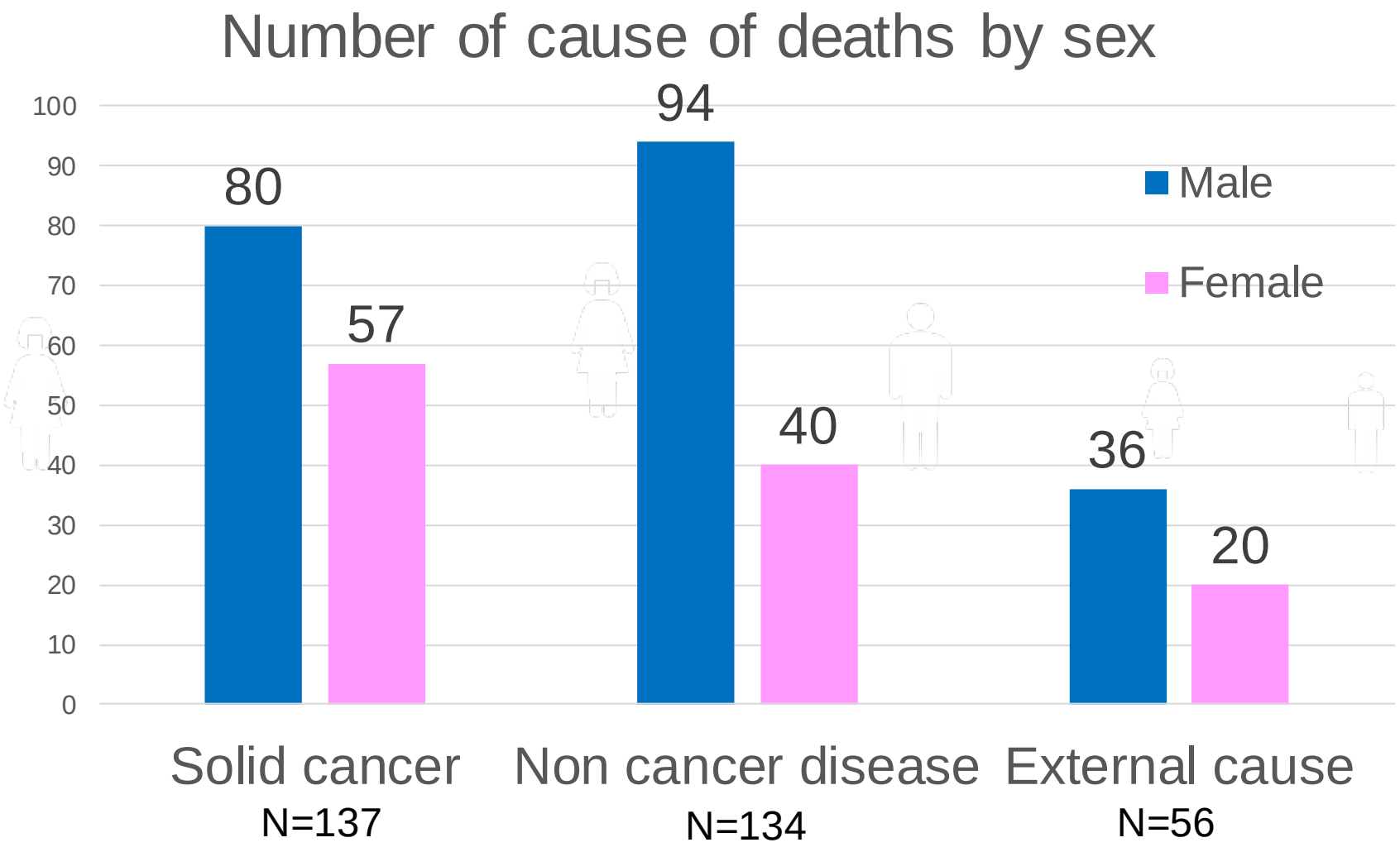
Background
Methods
Results
Discussion

Characteristics of subjects

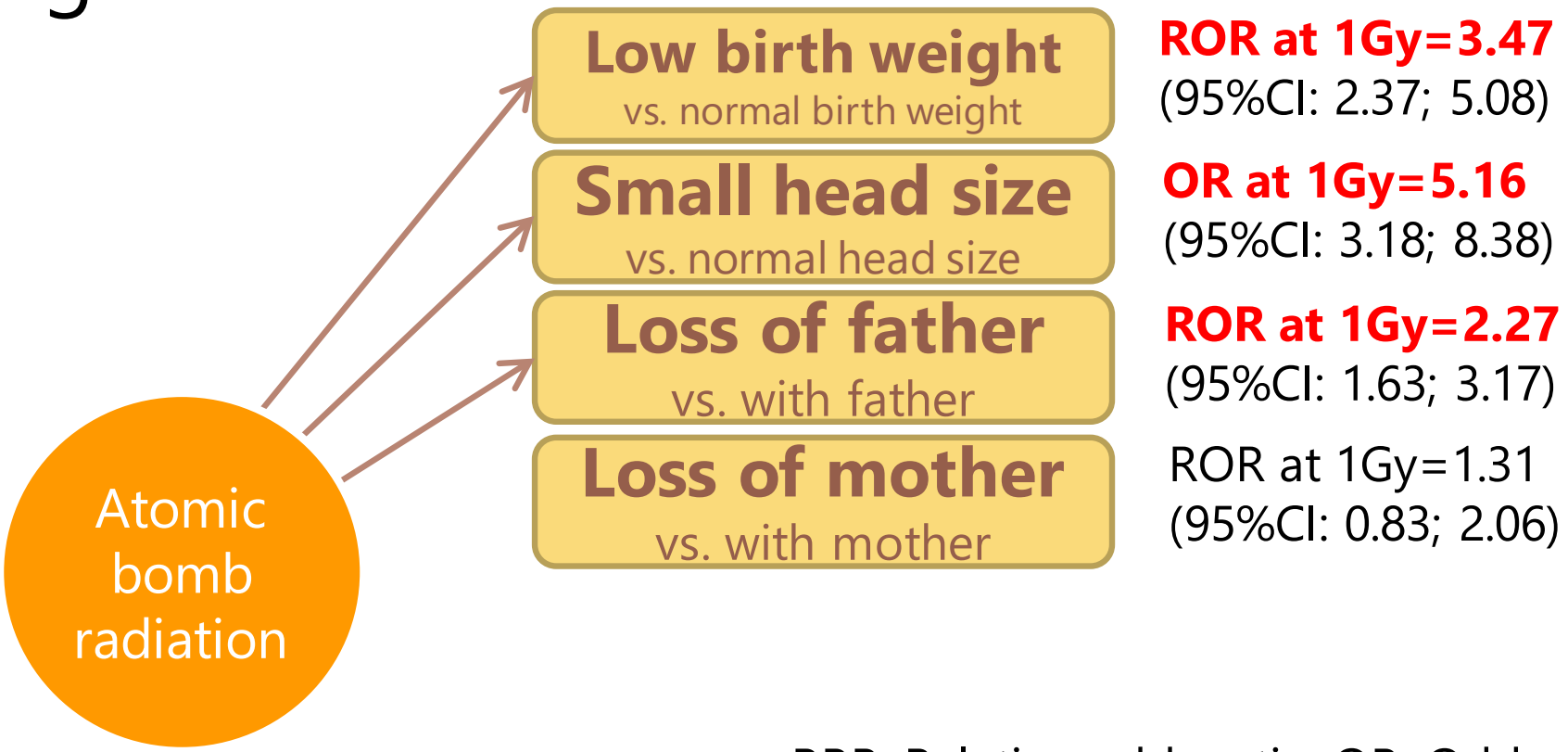
		Numbers (%)	
Sex	Male	1,217	(49.4%)
	Female	1,249	(50.7%)
City	Hiroshima	2,048	(83.1%)
	Nagasaki	418	(17.0%)
Cohort	Birth record	1,218	(49.4%)
	Master file	953	(38.6%)
	1960 Census	295	(12.0%)
Birth weight	≧2500g	1,956	(79.3%)
	<2500g	206	(8.4%)
	Unknown	105	(4.3%)
	No information	199	(8.1%)
Head size	Male, small head size	31	(2.5%)
	Female, small head size	30	(2.4%)



Total number of deaths=339

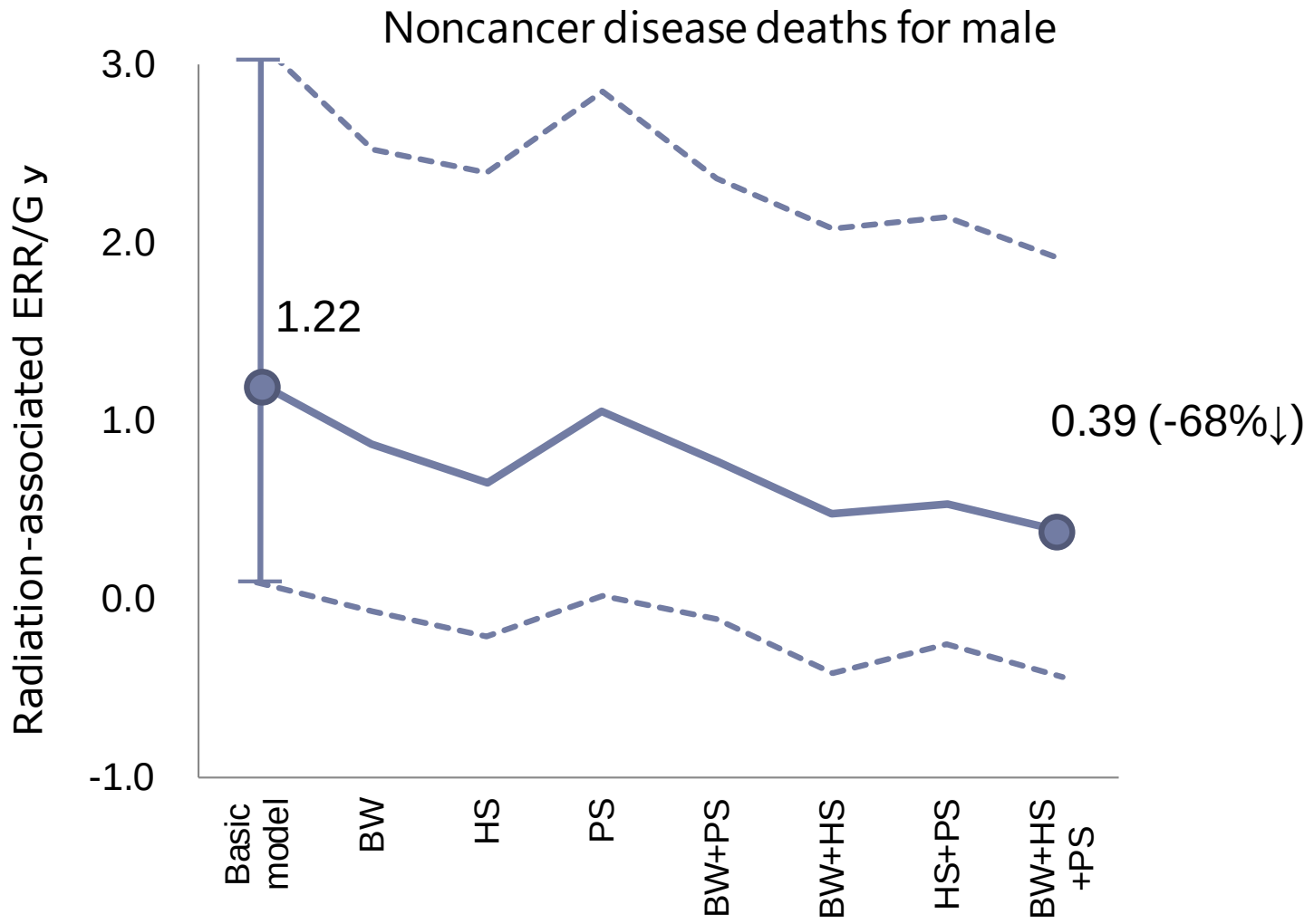


Association between A-bomb radiation and potential mediators based on the logistic and multinomial logistic regression



RRR: Relative odds ratio, OR: Odds ratio

Changes in ERRs adjustment for birth weight (BW), head size (HS) and parents status (PS)



Changes in ERRs for solid cancer deaths

	All attained age	
	Male	Female
Radiation ERR/Gy (95% CI) not adjusted for PMs	-0.18 (<0.77; 0.95)	2.24 (0.45; 5.63)
Radiation ERR/Gy (95% CI) Adjusted for PMs	-0.07 (<-0.82; 1.37)	2.51 (0.53; 6.28)
Relative risk at 1Gy (95% CI)		
Low birth weight to normal birth weight	0.86 (0.44: 1.66)	
Small head size to normal head size	0.61 (0.08; 4.74)	0.76 (0.10; 5.62)
Loss of father to father alive	0.74 (0.45; 1.22)	
Loss of mother to mother alive	1.21 (0.57; 2.57)	

PM: Potential mediator

Changes in ERRs for noncancer disease deaths

	All attained age	
	Male	Female
Radiation ERR/Gy (95% CI) not adjusted for PMs	1.22 (0.10; 3.14)	2.86 (0.56; 7.64)
Radiation ERR/Gy (95% CI) Adjusted for PMs	0.39 (< -0.42; 1.91)	1.48 (-0.05; 4.55)
Relative risk at 1Gy (95% CI)		
Low birth weight to normal birth weight	1.96 (1.18: 3.25)	
Small head size to normal head size	2.16 (0.85; 5.40)	3.02 (1.00; 9.10)
Loss of father to father alive	1.51 (0.99; 2.31)	
Loss of mother to mother alive	1.67 (0.89; 3.16)	

PM: Potential mediator

Changes in ERRs for external cause of deaths

	All attained age	
	Male	Female
Radiation ERR/Gy (95% CI) not adjusted for PMs	0.28 (<-0.60; 2.36)	2.57 (0.20; 9.19)
Radiation ERR/Gy (95% CI) Adjusted for PMs	0.10 (<-0.57; 1.96)	1.38 (<-0.46; 5.95)
Relative risk at 1Gy (95% CI)		
Low birth weight to normal birth weight	1.89 (0.84: 4.22)	
Small head size to normal head size	2.33 (0.48; 11.40)	3.81 (0.81; 17.88)
Loss of father to father alive	1.14 (0.58; 2.26)	
Loss of mother to mother alive	2.54 (1.03; 6.24)	

PM: Potential mediator

Background
Methods
Results
Discussion

- **339 deaths from 1950 to 2012**
  - Solid cancer (n=137), Non cancer disease (n=134), external causes (n=56), lymphohematopoietic cancer (n=8)
  - Childhood cancer (n=1)
- **Low birth weight, small head size, and father's survival status**
  - Radiation dose was positively associated with these factors, but not for mother's survival status.
  - Birth weight:
    - No relationship between radiation dose and birth weight in Chernobyl study (Hatch, et al. Eur J Epidemiol 2017)
    - Other risk factors of low birth weight: food shortage, mental stress, destruction of infrastructure, lack of access to medical services during armed conflict.

Limitations

- Fetal radiation doses by gestational age at the time of bombing were not estimated.
- Lifestyle and socioeconomic status in adult life were not obtained.
- All individuals with small head size are assumed to be included in this study.
- The subjects have been followed since 1950 or later.

Conclusion

Low birth weight
Small head size
Loss of parents

Atomic bomb radiation

External cause
females

Non cancer

Cancer
females

Co-authors: Munechika Misumi[2)], Ritsu Sakata[1)], Alina Brenner[1)], Mai Utada[1)], Kotaro Ozasa[1)]

1) Department of Epidemiology and 2) Department of Statistics, RERF

Acknowledgment

The Radiation Effects Research Foundation (RERF), Hiroshima and Nagasaki, Japan is a public interest foundation funded by the Japanese Ministry of Health, Labour and Welfare (MHLW) and the US Department of Energy (DOE). This publication was supported by RERF Research Protocol 2-61. The views of the authors do not necessarily reflect those of the two governments.