# Recent Studies at RERF

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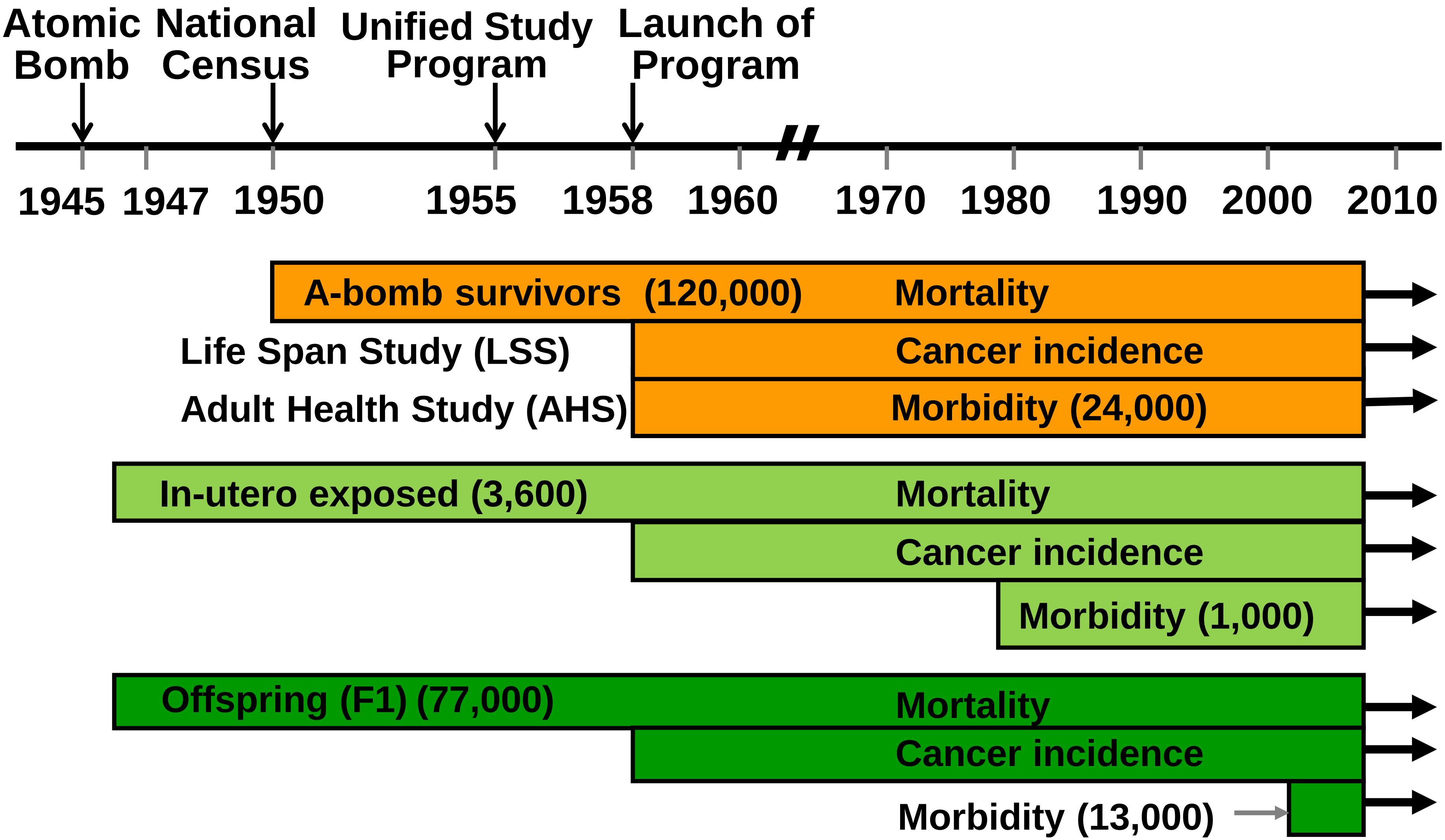
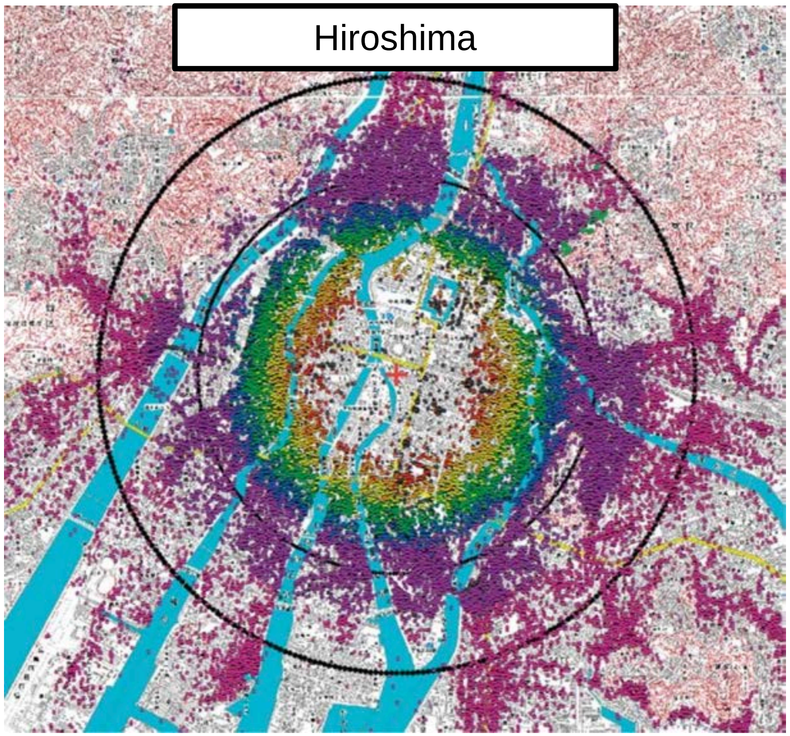
**Chief of Research**
**Vice-Chairman**

# Long-term Epidemiological Studies of Atomic Bomb Survivors and Their Offspring



# Conclusive Results at Higher Doses

- Non-selectively exposed population with rapidly decreasing doses by distance
- Little chance for bias or confounding by major cancer risk factors
- Highly significant risks by dose for all solid cancers in aggregate




Cullings, et al. *Health Physics*, 2017;112:46-97

# Dose by Sex, City, and Age at Exposure

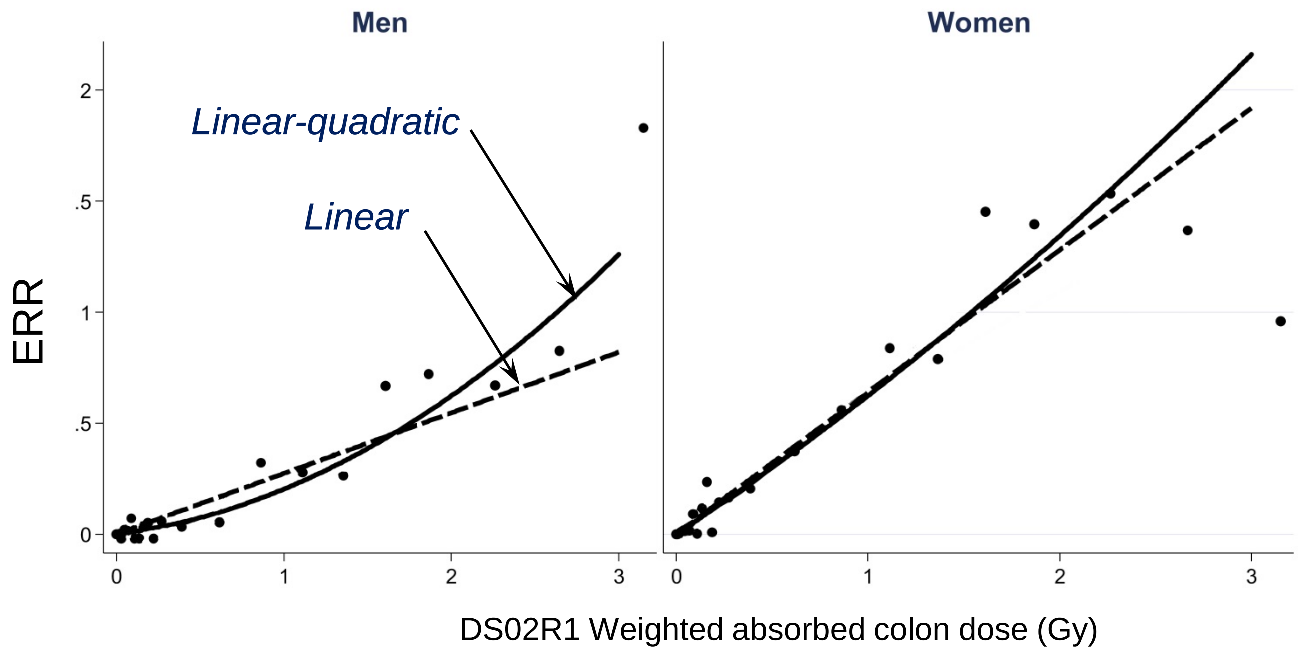
**TABLE 2**
**Distribution of Weighted Absorbed Colon Dose by Sex, City and Age at Exposure: LSS Solid Cancer Incidence Cohort, 1958–2009**

| | Eligible LSS members[a] | Subjects with known dose (%) | No. of subjects (%) per DS02R1 colon dose indicated | | | | | Dose unknown |
|---|---|---|---|---|---|---|---|---|
| | | | NIC | 0–0.005 Gy | 0.005–0.5 Gy | 0.5–1 Gy | ≥1 Gy | |
| Sex | | | | | | | | |
| Male | 45,864 | 42,910 (100) | 10,488 (24) | 14,574 (34) | 15,608 (36) | 1,282 (3) | 958 (2) | 2,954 |
| Female | 66,053 | 62,534 (100) | 14,751 (24) | 21,404 (34) | 23,423 (37) | 1,854 (3) | 1,102 (2) | 3,519 |
| City | | | | | | | | |
| Hiroshima | 76,549 | 73,401 (100) | 19,249 (26) | 20,087 (27) | 30,556 (42) | 2,100 (3) | 1,409 (2) | 3,148 |
| Nagasaki | 35,368 | 32,043 (100) | 5,990 (19) | 15,891 (50) | 8,475 (26) | 1,036 (3) | 651 (2) | 3,325 |
| Age at exposure (years) | | | | | | | | |
| <10 | 23,562 | 22,708 (100) | 4,995 (22) | 7,928 (35) | 8,909 (39) | 505 (2) | 371 (2) | 854 |
| 10–19 | 25,442 | 23,079 (100) | 5,878 (25) | 7,973 (35) | 7,750 (34) | 892 (4) | 586 (3) | 2,363 |
| 20–29 | 15,352 | 14,251 (100) | 3,675 (26) | 4,718 (33) | 5,070 (36) | 478 (3) | 310 (2) | 1,101 |
| 30–39 | 16,642 | 15,838 (100) | 4,034 (25) | 5,127 (32) | 5,953 (38) | 418 (3) | 306 (2) | 804 |
| 40–49 | 16,877 | 16,074 (100) | 3,727 (23) | 5,472 (34) | 6,067 (38) | 504 (3) | 304 (2) | 803 |
| ≥50 | 14,042 | 13,494 (100) | 2,930 (22) | 4,760 (35) | 5,282 (39) | 339 (3) | 183 (1) | 548 |
| Total | 111,917 | 105,444 (100) | 25,239 (24) | 35,978 (34) | 39,031 (37) | 3,136 (3) | 2,060 (2) | 6,473 |

*Note*. NIC = not in either city.
[a] Alive and not known to have cancer as of the start of follow-up.

# All Solid Cancer Incidence, LSS, 1958-2009

Adjusted for smoking, At age 70, Exposed at age 30




Sex-averaged ERR/Gy=0.47 (95% CI: 0.39, 0.55), f/m=1.81

No. of cases= 10,473 (m), 12,065 (f)

No threshold dose observed

Lowest range of a significant dose response was 0-100 mGy

Radiation risk was not confounded by smoking habits in general

Grant, et at. *Radiat Res*, 2017

# Cancer Radiation Risks: 1958-2009

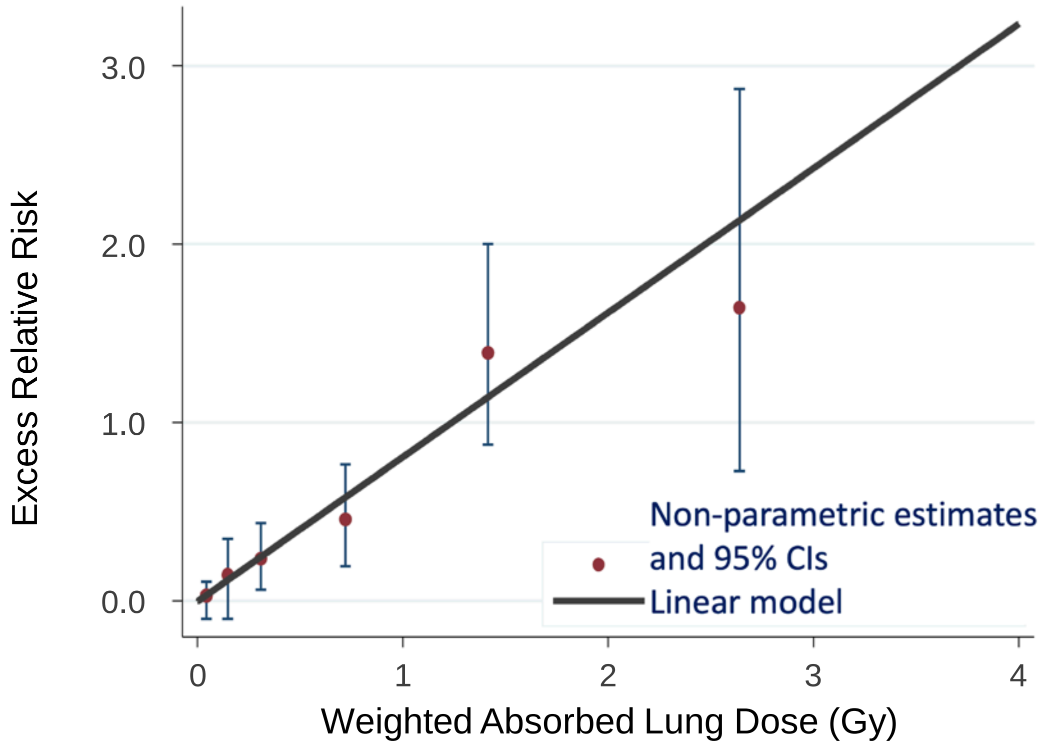
- Since the last report (through 1998), the surviving population has decreased from 52% to 37%;
  - 5,090 new solid cancer cases were observed
  - 22,538 total solid cancer cases observed (1958-2009)
  - 992 cancers associated with radiation exposure
  - Among those with more than 5mGy of exposure, 10% of all cancers were associated with radiation exposure
- Most important finding: single acute exposure increases solid cancer risks for life
- Shape of dose response more curvilinear since the last report but significant elevated risks still evident in low dose range (0-100 mGy)

# Less Certainty at Lower Doses

- Despite large size of LSS, statistical power is limited at lower doses
- Less accuracy of dose parameters at longer distances
  – Proximal survivors had detailed shielding histories; distal survivors had fewer interviews
- Medical exposures and/or residual radiation exposures become larger compared to direct exposure from bombs
- Higher probability of bias/confounding factors associated with survivors' geospatial distribution (affects background rates)
  – Socio-economic factors
  – Urban/rural differences

# Lung Cancer Incidence
# LSS, 1958-2009

Cases: 1,445 (male); 1,002 (female)



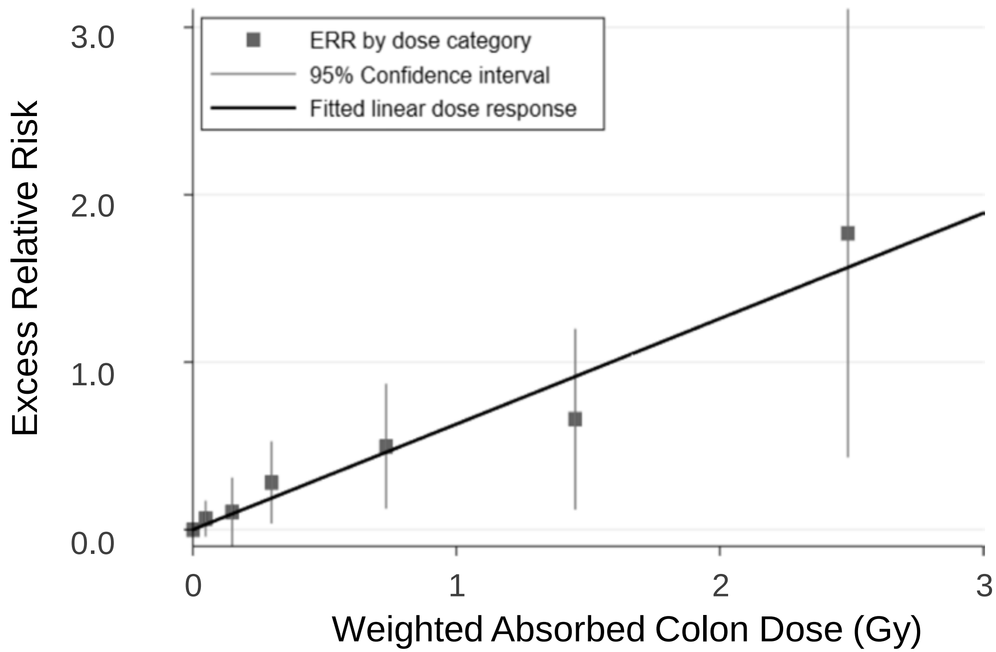

11% of all solid cases

Sex-averaged, attained age 70, age-at-exposure=30, adjusted for smoking

Cahoon *et al.*, Rad. Res. 2017; 187:513-537

# Colon Cancer Incidence LSS, 1958-2009

Cases: 782 (male); 1,132 (female)



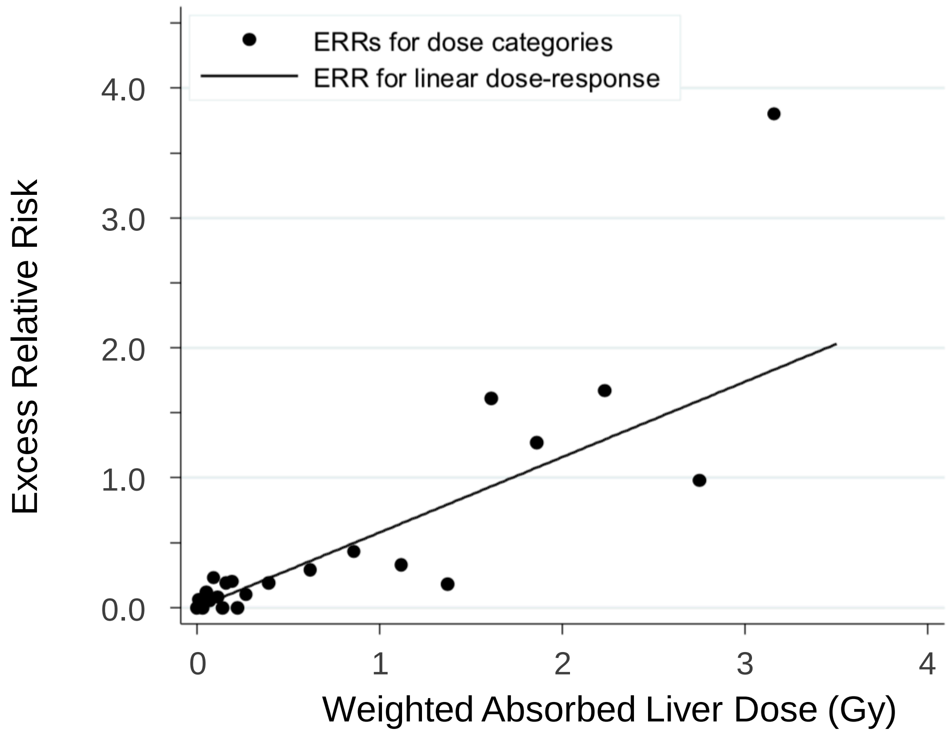

9% of all solid cases

Sex-averaged, attained age 70, age-at-exposure=30, adjusted for smoking, alcohol, meat, BMI

Sugiyama *et al.*, Int. J Can. 2019; doi:10.1002/ijc.32275

# Liver Cancer Incidence
# LSS, 1958-2009

Cases: 1,445 (male); 1,002 (female)

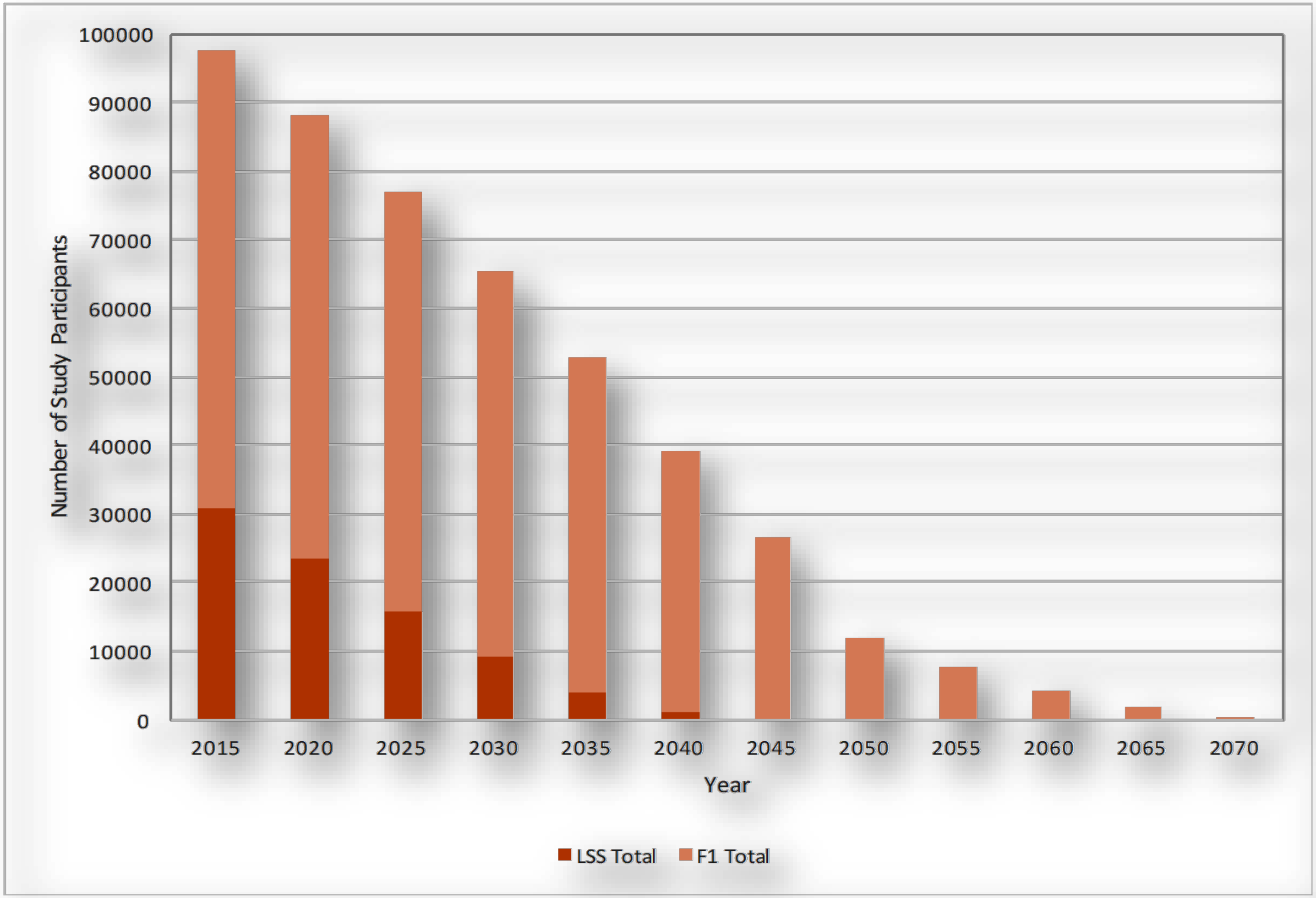



8% of all solid cases

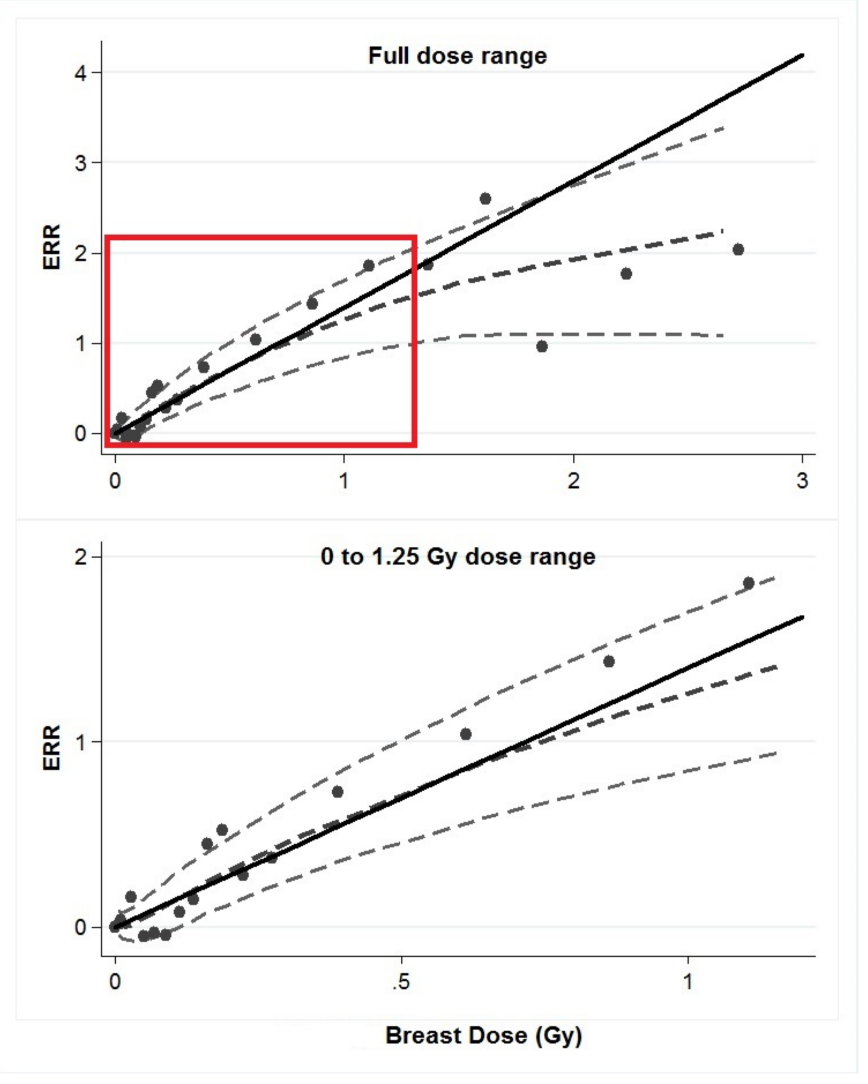
Sex-averaged, attained age 70, age-at-exposure=30, adjusted for smoking, alcohol, BMI

Sadakane *et al., submitted*

# Study Participants in LSS and F1

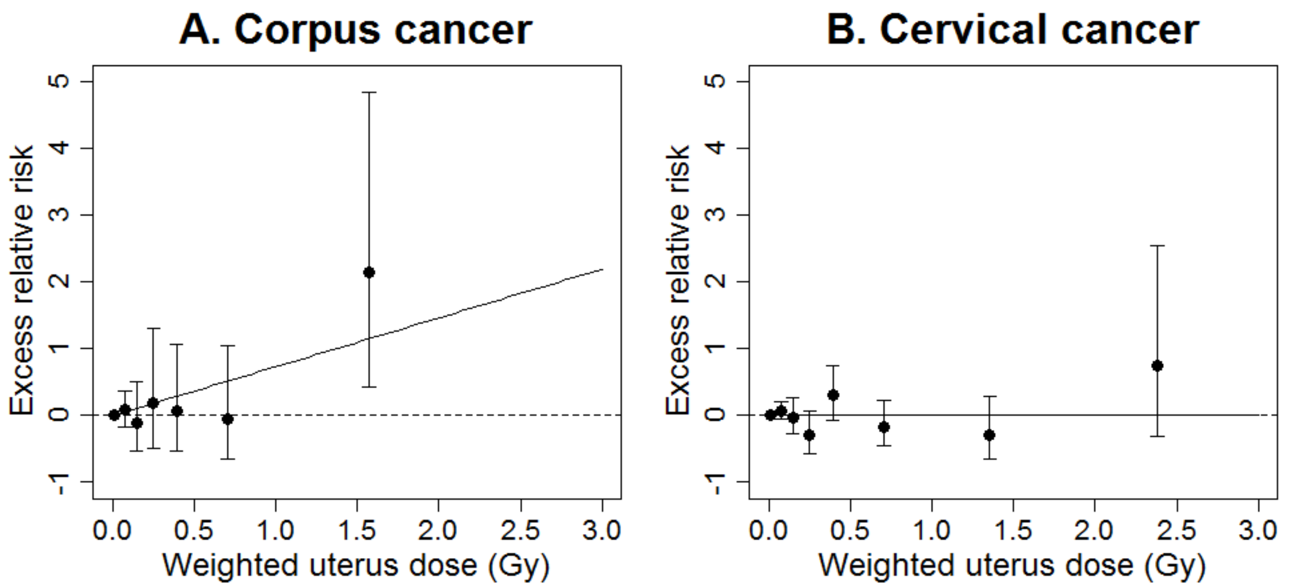


# Breast Cancer
# LSS, 1958-2009




Brenner et al., Rad Res, 2018

# Uterine Cancer
# LSS, 1958-2009



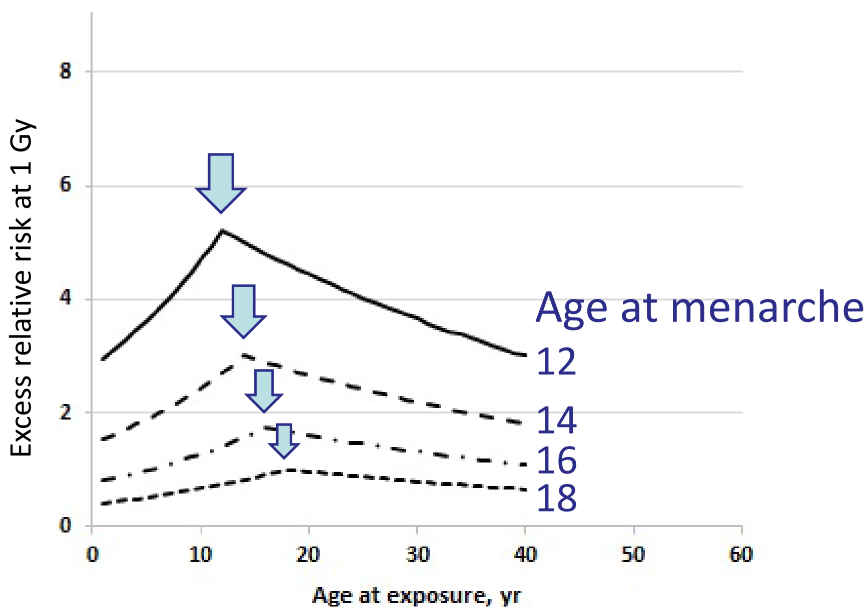

Utada et al., JNCI-CS, 2019

# Effect of Age At Exposure

## Breast cancer

Around menarche

(Brenner et al., Rad Res, 2018)

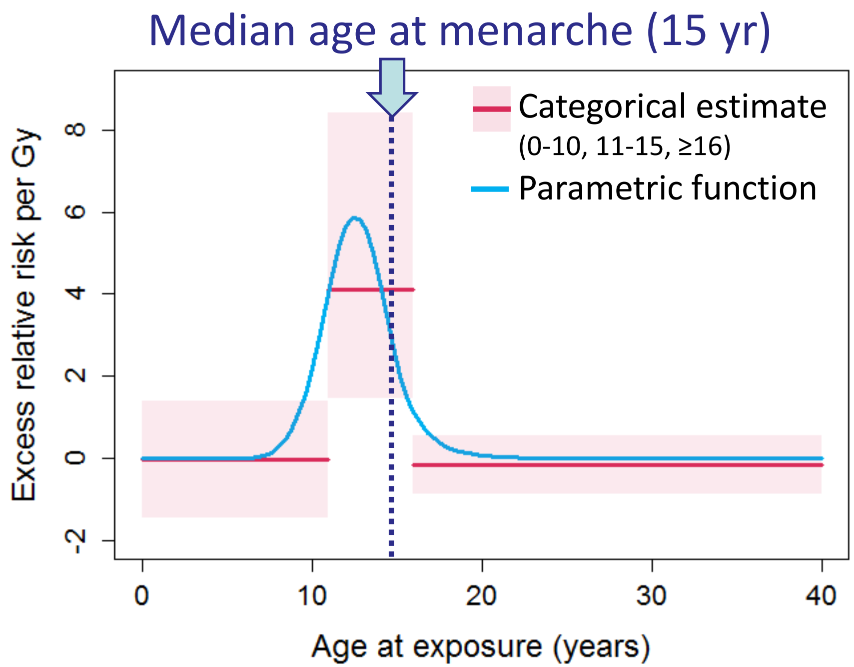



ERR/Gy by age at exposure for several ages at menarche at attained age 50.
Linear spline model with a knot age at menarche.

## Uterine corpus cancer

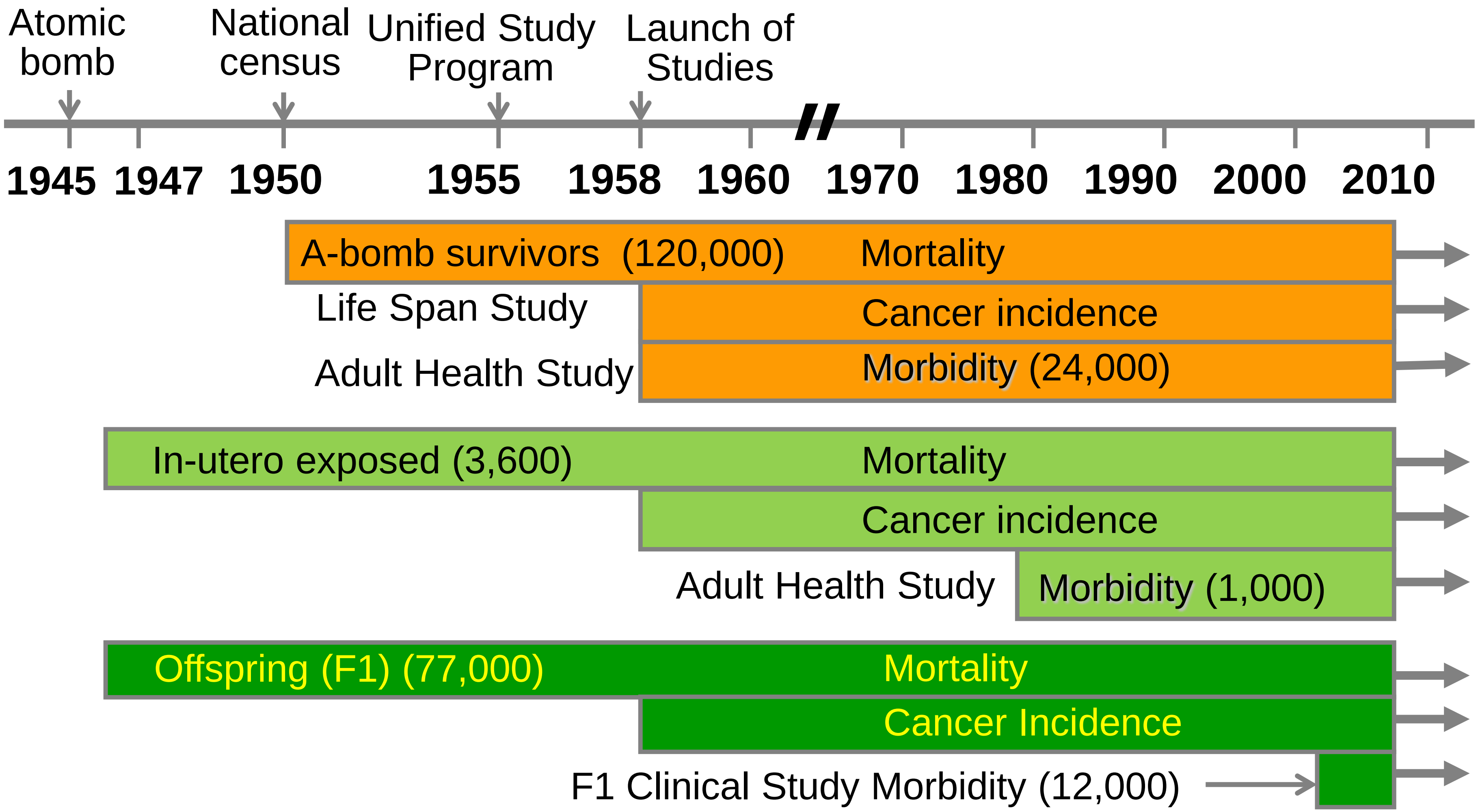
Before menarche

(Utada et al., JNCI-CS, 2019)



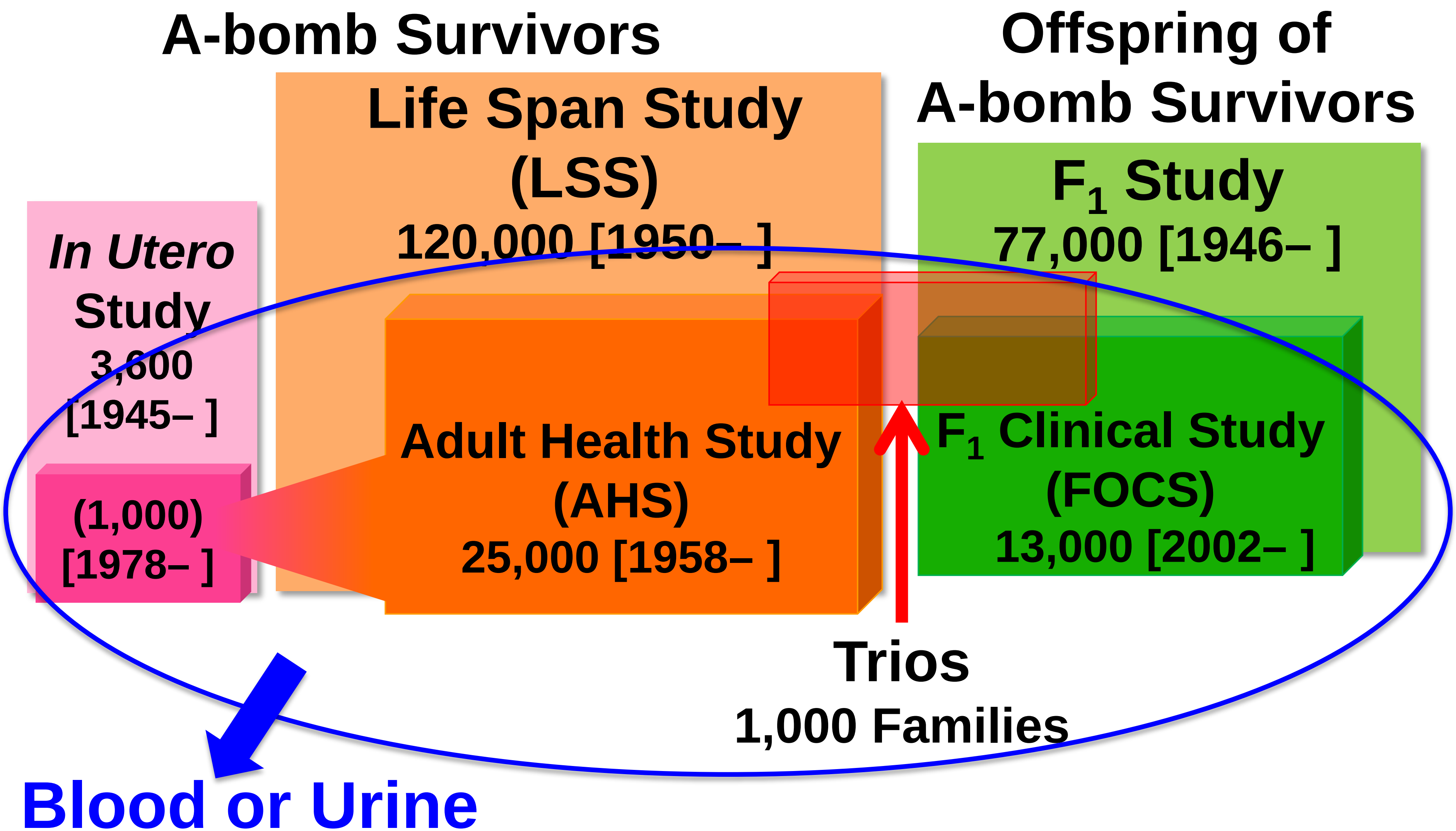

ERR/Gy by age at exposure without effect modification by attained age or age at menarche.
Quadratic spline model with a knot at age 15.

# Epidemiological/ clinical data & biosamples

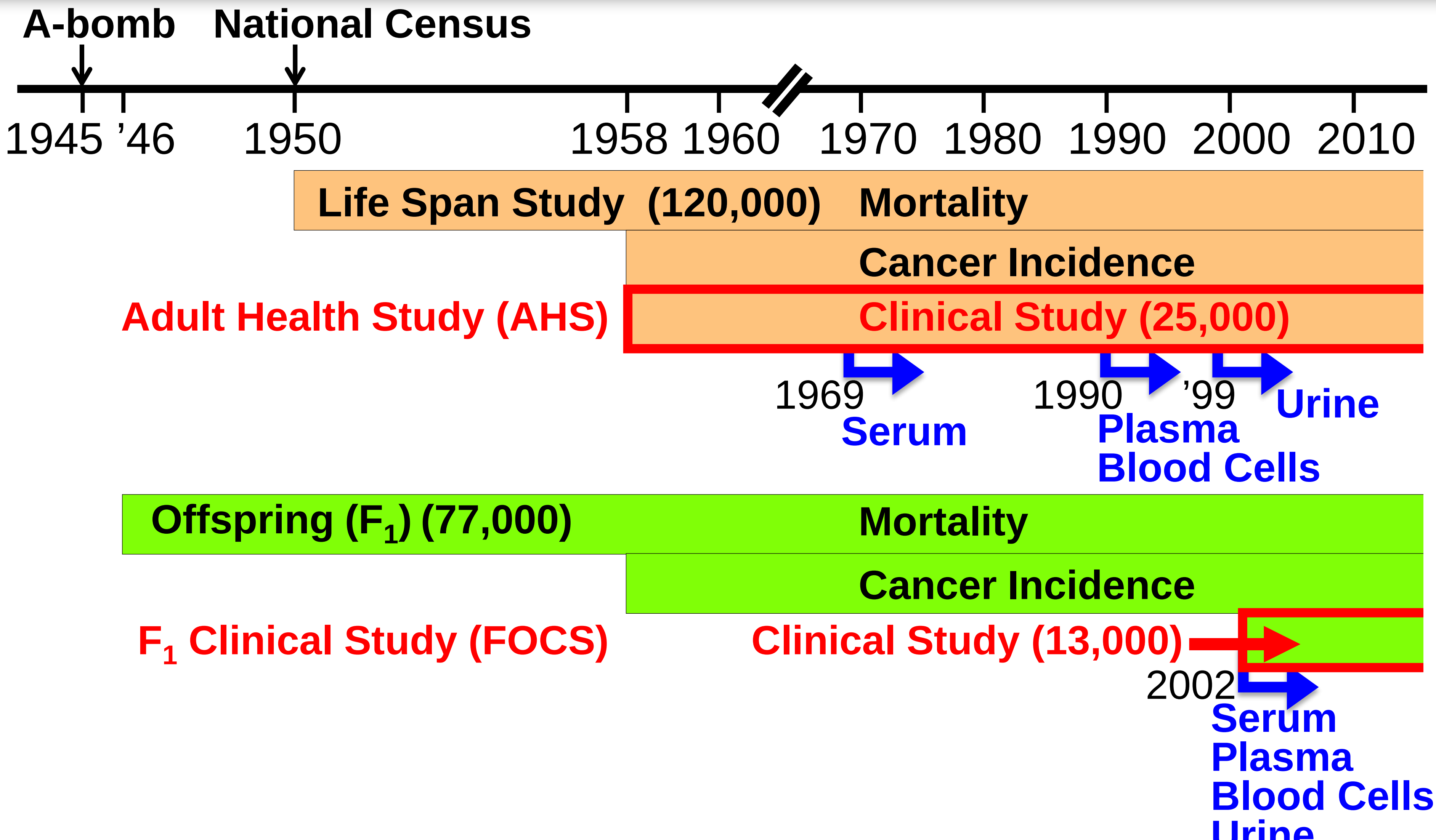



**Accumulation of large epi/clinical data and biosamples**

# RERF Cohorts with Biosamples



# Clinical Studies of A-bomb Survivors and Their Offspring and Biosamples



# Current Holdings of Biosamples – AHS and FOCS –

| Type | Start Year | | Subjects | Tubes | Storage Condition |
|---|---|---|---|---|---|
| | AHS | FOCS | | | |
| **Serum** | **1969** | **2002** | **31,000** | **746,000** | –80°C, 4°C |
| **Plasma** | **1990** | **2002** | **22,000** | **364,000** | –80°C |
| **Blood Cells** | **1990** | **2002** | **21,000** | **266,000** | –80°C |
| | | | | **180,000** | Liquid $N_2$ |
| **Urine** | **1999** | **2002** | **20,000** | **212,000** | –80°C |
| | | | **TOTAL** | **1,768,000** | |

# Summary

Studies to date suggest a linear response at low doses (0-1 mGy) but statistical power is limited in spite of large sample size

Current studies allow the study of the effect of age on sensitivity to carcinogenic effects

In breast and uterine cancer sensitivity is associated with age at menarche

Longitudinally collected biosamples allow the study of early events and underlying mechanisms