

SIMULATION OF SURVIVAL BIAS IN EPIDEMIOLOGICAL SURVEY BY REANALYZING J-EPISODE AND HANFORD WORKERS

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BACKGROUND: Japanese Epidemiological Study on Low-Dose Radiation Effects (J-EPISODE) has high-quality dose data and data on cause of death, as well as lifestyle data such as smoking for a part of it.

Although the inception of radiation exposures began in 1957, the follow-up period of the cohort was 1991 to 2010, which was one of the weaknesses. The average follow-up period was 14 years, the total observation was 3 million person-years, and the population was decreased by 10% at the end of follow-up, indicating that the statistical power was not sufficient. There was also the possibility of a survival bias due to the cohort setting in 1991.

In addition, the new cohort to be set in 2019, which employed opt-in method for informed consent, might have a selection bias, because the subjects are restricted to survivors and consentees might be in good health.

OBJECTIVES: To simulate survival bias by reanalysing J-EPISODE and Hanford workers and assess the possible impact of survival bias.

MATERIALS & METHODS: The micro data set of "Hanford Workers Cohort Study Follow-up Through 1994" at the Comprehensive Epidemiological Data Resources (CEDR) was used for comparison with J-EPISODE.

Mortality of all cancers excluding leukaemia was taken as an end point. Poisson regression was applied for the Hanford male workers and J-EPISODE by changing observation period, to clarify the effects of survival bias.

Also windows approach regarding dose rate and age at exposure was applied for both cohorts, in order to clarify the structure of each cohort and possible causes of survival bias.

RESULTS: The simulation results of estimated survival bias under several assumptions indicated that the directions of the bias were not constant. The possible causes of the differences were discussed in line with birth cohorts and trends of annual exposure dose.

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Simulation of survival bias in epidemiological survey by reanalyzing J-EPISODE and Hanford worker



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Challenges of J-EPISODE

- ✓ Dose records of nuclear workers available since 1957.
- ✓ On the other, follow-up began for survivors from 1991.
- ✓ Possibility of survival bias, because mortality from 1957 to 1990 were not considered for risk estimation (NCRP Commentary No. 27, 2018).
- ✓ Further, a new cohort to be constructed in 2019 will be composed with survivors who consented to the study during 2016-2018.
- ✓ Need to assess direction and magnitude of survival bias.
- ✓ Next data are missing for direct assessment of survival bias.
 - total number of death during 1957-1990
 - death date and cause of death
 - correspondence with dose records

Objectives of the present study

- ✓ To clarify direction and magnitude of survival bias.
- ✓ To clarify factors affecting survival bias.

Materials and Methods

- ✓ Cohort data of Hanford workers provided by DOE, and J-EPISODE
- ✓ Target was all cancer mortality excluding leukaemia
- ✓ Poisson regression was applied.
- ✓ Estimated ERR/Sv for Hanford male workers since time T (T=1975, 1980, 1985 and 1990), assuming that follow-up was carried out for survivors at time T.
- ✓ Estimated ERR/Sv for J-EPISODE since time T (T=2000 and 2005), assuming that follow-up was carried out for survivors at time T.

Profile of J-EPISODE cohort

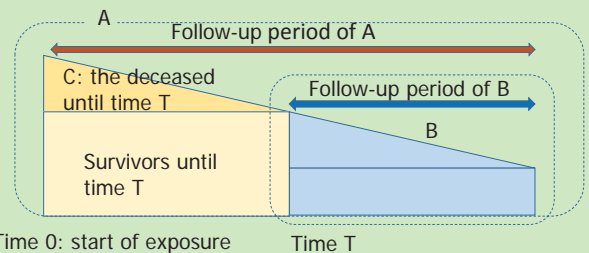
Follow-up period: 1991–2010
 Size: 204,103 male nuclear workers
 Mean age at the end: 55.6 years old
 Total follow-up: 2.89 million person-years
 Mean follow-up: 14.2 years/person
 Mean cumulative dose: 13.8 mSv at the end
 All death: 20,519
 Caused by cancer, excluding leukemia: 7,929

Reanalysis of Hanford workers

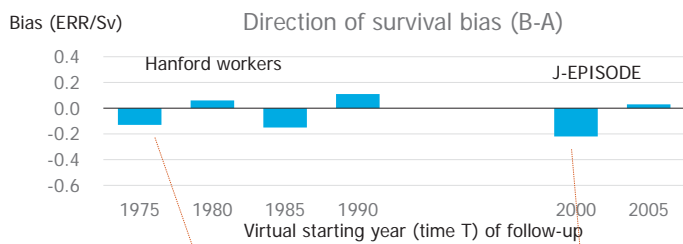
Micro data set of "Hanford Workers Cohort Study Follow-up Through 1994" at the Comprehensive Epidemiological Data Resources (CEDR)
 Restricted to male (19,684 persons).
 Dose data 1944 to 1989 (10-year lag assumption)
 Follow-up period 1944 to 1994
 Cohort definition: hired during 1944 to 1978
 Start of follow-up: 180 days after employment

Definition of survival bias

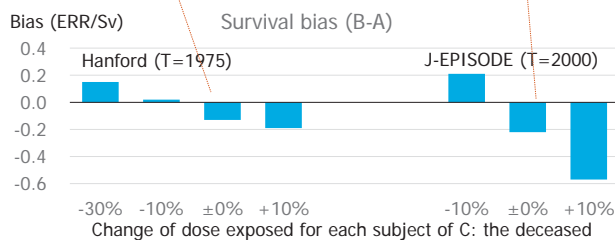
- Survival bias=(ERR/Sv derived from B)-(ERR/Sv derived from A)



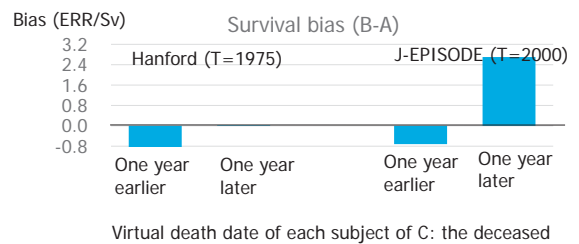
Result I : Direction of survival bias is not constant.



Result II : If dose distribution of the deceased had changed to lower, the survival bias would change to positive direction.



Result III : If mortality by age had changed to higher, that is, death date had become earlier, the survivor bias would change to negative direction.



Results of windows approach by dose rate and age at exposure

- ✓ Might indicated differences of the trends of dose exposure, and structure of birth cohorts.
- ✓ It may have influenced the appearance of survival bias.

Dose rate / age at exposure	ERR/Sv (90% CI) for all cancers excl. leukaemia	
	Hanford (1944-1994)	J-EPISODE (1991-2010)
<5mSv/y	14.8 (6.0, 23.6)	-3.8 (-8, 0.23)
>=5mSv/y	2.23 (0.89, 3.57)	1.59 (0.73, 2.46)
<45years	15.2 (5.34, 25.0)	0.06 (-1.02, 1.19)
>=45years	2.39 (1.01, 3.77)	2.16 (0.91, 3.14)
Total	0.52 (-0.22, 1.25)	1.20 (0.43, 1.96)

Conclusions

- ✓ Direction of survival bias is not constant.
- ✓ If dose distribution of the dead changes to lower, the bias changes to the positive direction.
- ✓ If death rate by age had changed to higher, that is, death date had become earlier, the survivor bias would change to negative direction.

✓ TO DO: Despite lack of death data during 1957-1990, survival bias will be assessed by simulating death data consistent with dose records