Assessing lead time bias due to mammography screening on estimates of loss in life expectancy

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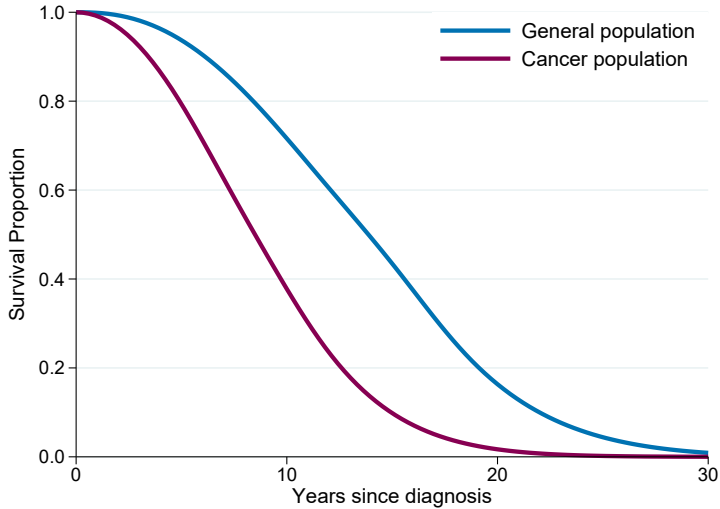
15th September 2022

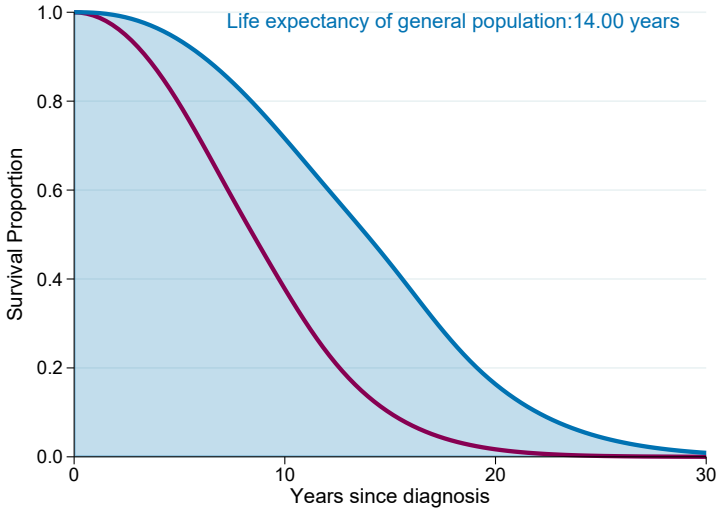
Loss in life expectancy

Loss in life expectancy (LLE) due to a cancer diagnosis is defined as the difference between the life expectancy of the general population and the life expectancy of the cancer population (with similar characteristics).

Loss in life expectancy



Loss in life expectancy



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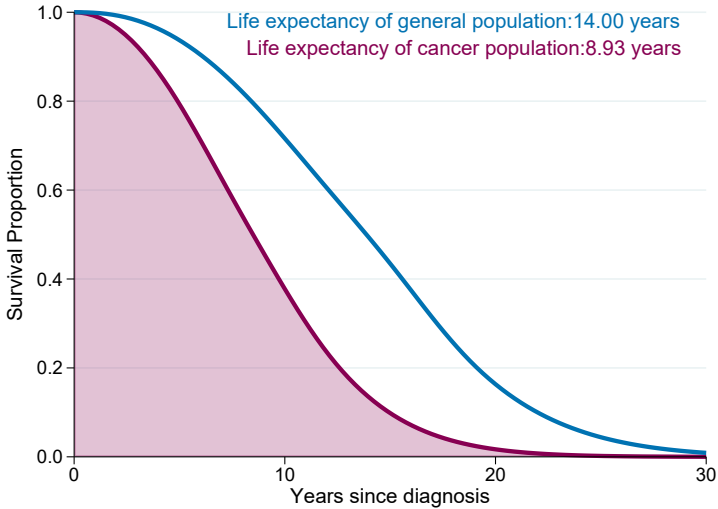

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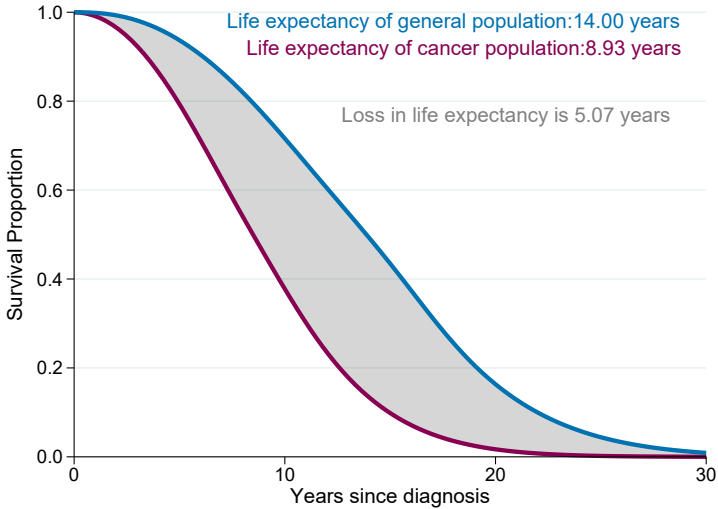


Why use loss in life expectancy?

- LLE is a real-world measure that captures the cancer impact on the entire remaining lifespan.
- It can help us address useful questions:
  - Quantify the impact a cancer diagnosis has on a patient's life expectancy
  - Quantify disease burden in the society
    - "How many life-years are lost due to the cancer?"
    - "How many life-years are lost due to cancer by socioeconomic group?"

LLE across population groups - Sweden

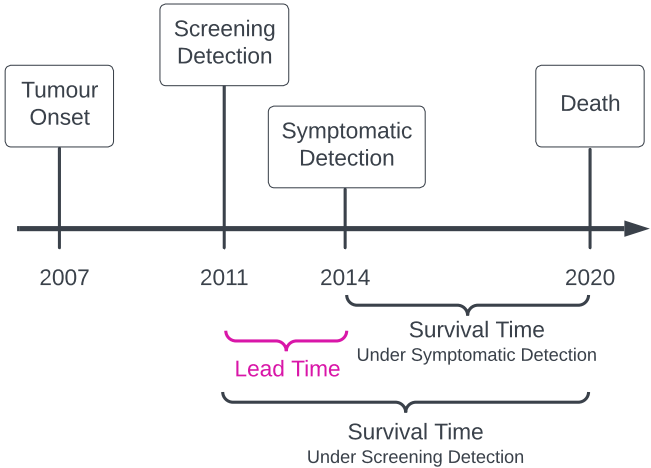
Age (years)	Education group	Life years lost (95%
		Study population
45	Low	9.90 (8.46,11.33)
	Medium	9.69 (8.76,10.62)
	High	9.11 (8.10,10.13)
55	Low	5.42 (4.85,5.99)
	Medium	5.27 (4.78,5.76)
	High	5.03 (4.52,5.54)
65	Low	2.81 (2.53,3.08)
	Medium	2.69 (2.44,2.93)
	High	2.86 (2.54,3.18)
75	Low	2.28 (2.12,2.44)
	Medium	1.89 (1.74,2.05)
	High	2.11 (1.88,2.33)

Bower H, Andersson TM, Syriopoulou E, Rutherford MJ, Lambe M, Ahlgren J, Dickman PW, Lambert PC. Potential gain in life years for Swedish women with breast cancer if stage and survival differences between education groups could be eliminated - Three what-if scenarios. Breast 2019, 45:75–81.

Motivation - Why are there differences in LLE?

- Many factors have been suggested as potential drivers for the observed differences e.g. stage at diagnosis, differential treatment, lifestyle, comorbidities, health-seeking behaviours, …
- Screening (and lead time bias) may also drive part of the differences.
- The uptake of screening varies vary across socioeconomic groups, even in in countries where screening programmes are available on a national level.
- Are LLE estimates affected by lead time bias?

Lead time


Tumour Onset
Screening Detection
Symptomatic Detection
Death
2007
2011
2014
2020
Survival Time
Under Symptomatic Detection
Lead Time
Survival Time
Under Screening Detection

Assessing the impact of lead time bias

- Screening can affect survival times both through real improvements in survival as well as artificial increase (lead time bias) in survival times.
- Partitioning the effect of screening into these two components is challenging as it would require knowledge of what would have happened in the absence of screening.
- We use a simulation-based approach informed by Swedish cancer registry data which uses a natural history model developed in a Swedish setting*.

*Andersson TM, Rutherford MJ, Humphreys K. Assessment of lead-time bias in estimates of relative survival for breast cancer. Cancer Epidemiology 2017, 46:50–56.

Simulation

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- tumour growth (and time at symptomatic detection) was simulated from a natural history model developed in a Swedish setting[**]

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For individuals with onset of breast cancer:

- tumour growth (and time at symptomatic detection) was simulated from a natural history model developed in a Swedish setting[**]
- time to death was then generated as the minimum between:
  - time to death due to cancer
  - time to death due to other causes

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Screening scenarios

We also imposed a mammography screening programme with individuals invited to screening every second year for ages 40 –74.

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- Screening sensitivity
  - Low
  - Moderate
  - High
- Screening attendance
  - Perfect – everyone attends all screening visits
  - Imperfect
    - 80% of the individuals attend each scheduled screen visit with a probability of 0.9
    - 20% of the individuals attend each scheduled screen visit with a probability of 0.15

Lead time bias

We compare

- LLE estimates calculated in the absence of screening (*actual* value)
- LLE estimates when screening is imposed

with the only difference that screen detected tumours result in an earlier diagnosis.

Screening might also result in improved survival outcomes of patients but here the actual survival time was not changed for screen detected cases.

- We want to isolate the impact of lead time bias!

Descriptives - Proportion screen detected

Attendance	Screening	Number diagnosed	% screen detected	Lead time (mean)
Perfect	Low	2999 (2901 – 3098)	35.2 (33.7 – 37.1)	2.01 (1.83 – 2.22)
Perfect	Moderate	3028 (2925 – 3136)	45.1 (43.2 – 47.1)	2.45 (2.27 – 2.64)
Perfect	High	3062 (2959 – 3171)	53.0 (51.0 – 54.9)	2.98 (2.80 – 3.22)
Imperfect	Low	2988 (2887 – 3075)	27.1 (25.1 – 28.8)	1.98 (1.74 – 2.27)
Imperfect	Moderate	3010 (2904 – 3106)	35.3 (33.7 – 36.8)	2.42 (2.22 – 2.67)
Imperfect	High	3035 (2928 – 3143)	42.1 (40.6 – 44.0)	2.93 (2.71 – 3.19)

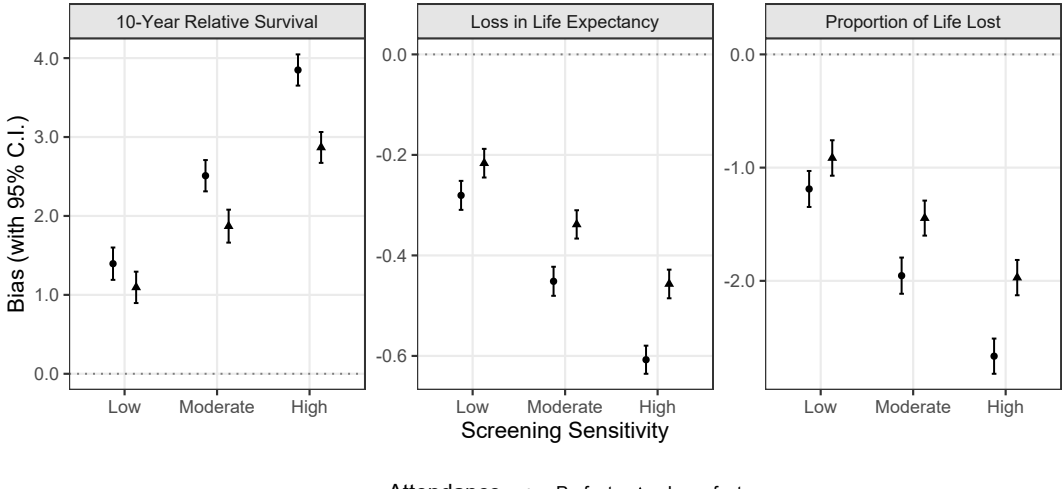
Averages (with 2.5 and 97.5 percentiles) based on 200 simulations

Estimates 10-year RS, LLE and PLL

Attendance	Screening	10-Year RS	LLE	PLL
—	None	50.96 (48.18 – 54.04)	8.08 (7.62 – 8.50)	44.13 (41.58 – 46.39)
Perfect	Low	52.35 (49.36 – 55.44)	7.80 (7.37 – 8.20)	42.95 (40.56 – 45.13)
Perfect	Moderate	53.47 (50.72 – 55.91)	7.63 (7.24 – 8.00)	42.18 (39.95 – 44.21)
Perfect	High	54.81 (52.27 – 57.50)	7.48 (7.08 – 7.89)	41.47 (39.29 – 43.73)
Imperfect	Low	52.05 (49.29 – 54.91)	7.87 (7.45 – 8.29)	43.22 (40.84 – 45.56)
Imperfect	Moderate	52.83 (49.69 – 55.65)	7.74 (7.33 – 8.16)	42.69 (40.37 – 44.95)
Imperfect	High	53.83 (51.24 – 56.47)	7.63 (7.20 – 8.07)	42.16 (39.88 – 44.65)

Averages (with 2.5 and 97.5 percentiles) based on 200 simulations

Bias


10-Year Relative Survival
Loss in Life Expectancy
Proportion of Life Lost
Bias (with 95% C.I.)
4.0
3.0
2.0
1.0
0.0
-0.2
-0.4
-0.6
-1.0
-2.0
Low
Moderate
High
Screening Sensitivity
Attendance
Perfect
Imperfect

Conclusions

- Lead time bias may affect estimates of LLE and PLL.
- It is important to carefully consider the impact of lead time bias when reporting differences across population groups.

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- It is important to carefully consider the impact of lead time bias when reporting differences across population groups.
- Our simulation is a simplification of the real world!
- You can read more about this work at:
  Syriopoulou E, Gasparini A, Humphreys K, Andersson T M, Assessing lead time bias due to mammography screening on estimates of loss in life expectancy. Breast Cancer Res 24, 15 (2022).