Examining breast cancer risk during COVID-19: Insights from semi-Markov modelling

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Motivation

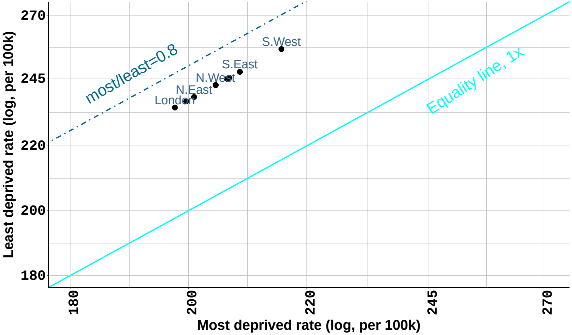
Breast cancer (BC) as it is

- **the most common** cancer diagnosed in women
- **one of the leading causes** of death for women
- one of the most **common** conditions amongst critical illness insurance (CII) claims, e.g. 44% of female CII claims in 2014 in the UK

Investigating BC rates in the presence of:

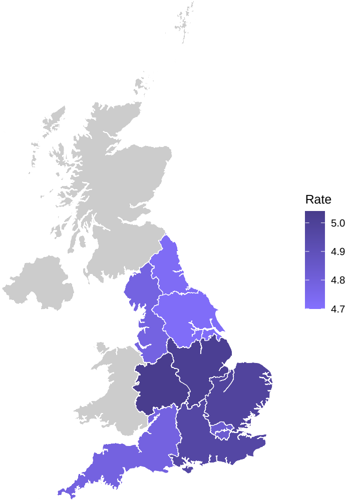
- major disruptions to health services, particularly caused by a catastrophic event, e.g. the COVID-19, preventing or delaying the diagnosis of BC

Most v. least deprived by region: BC incidence in England - 2017



- Not a life-style cancer
- Rates for least deprived higher (higher screening?)
- Less regional variation as compared to, e.g., lung cancer

Regional variation:
BC mortality in England - 2019

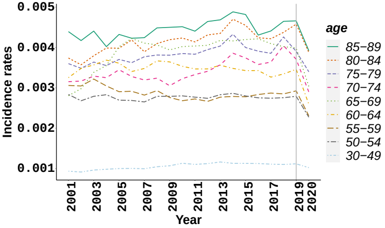


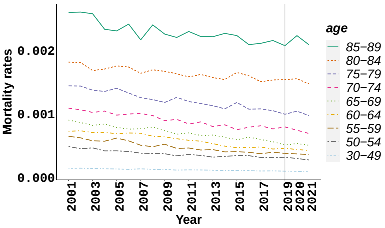
✓Rate is per 10K
✓Deprivation is not significant

What insights we gain from BC data

- **Socio-economic differences** are less relevant as compared to, e.g., lung cancer incidence/mortality
- **Not** (easily) controllable or preventable risk factors
- **Regional inequality** exists but relatively low
  - High BC screening awareness
  - National BC screening programme for ages 47–73
- The availability of BC screening is crucial for early diagnosis, as BC can be curable

BC incidence and mortality in England: COVID years

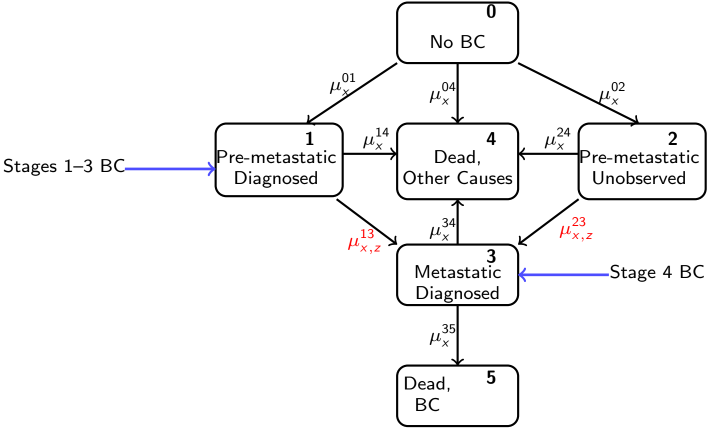




Incidence (left) v. Mortality (right)

- A significant decline in BC incidence, as low as 25% at ages 60–64, in 2020 as compared to the same period in 2019
- An increase in BC mortality from ages 65+, as high as 7%, in 2020 as compared to the same period in 2019

Multi-state model for BC transitions: semi-Markov model



- Duration dependence in 'Pre-metastatic Diagnosed' and 'Pre-metastatic Unobserved'

A convenient parametrisation of the model

The onset of BC is

$$\mu_x^{01} + \mu_x^{02} = \mu_x^*$$

where we can write

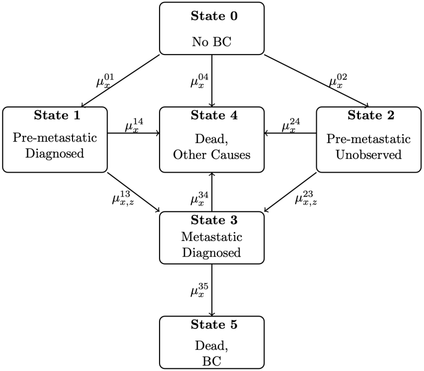
$$\mu_x^{01} = \alpha\, \mu_x^*$$
$$\mu_x^{02} = (1 - \alpha)\, \mu_x^*, \qquad 0 < \alpha < 1$$

α : % of diagnosed BC cases

Assume

$$\mu_{x,z}^{13} = \beta\, \mu_{x,z}^{23}, \qquad 0 < \beta < 1$$

β : developing metastatic BC in the absence of treatment



Modified Kolmogorov equations: semi-Markov model

$$\frac{d}{dt}\,{}_tp_x^{00} = -\,{}_tp_x^{00}\left(\mu_{x+t}^{01} + \mu_{x+t}^{02} + \mu_{x+t}^{04}\right)$$

$$\frac{d}{dt}\,{}_tp_x^{01} = {}_tp_x^{00}\,\mu_{x+t}^{01} - {}_tp_x^{01}\;\mu_{x+t}^{14} - \int_{u=0}^{t} {}_up_x^{00}\;\mu_{x+u}^{01}\;{}_{t-u}p_{[x+u]}^{11}\;\mu_{[x+u]+t-u}^{13}\;du$$

$$\frac{d}{dt}\,{}_tp_x^{02} = {}_tp_x^{00}\,\mu_{x+t}^{02} - {}_tp_x^{02}\,\mu_{x+t}^{24} - \int_{u=0}^{t} {}_up_x^{00}\;\mu_{x+u}^{02}\;{}_{t-u}p_{[x+u]}^{22}\;\mu_{[x+u]+t-u}^{23}\;du$$

$$\frac{d}{dt}\,{}_tp_x^{03} = \int_{u=0}^{t} {}_up_x^{00}\;\mu_{x+u}^{01}\;{}_{t-u}p_{[x+u]}^{11}\;\mu_{[x+u]+t-u}^{13}\;du +$$

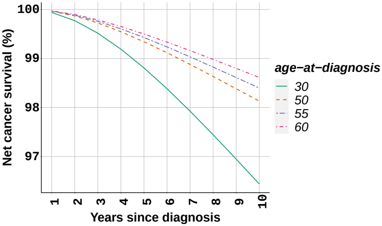
$$\int_{u=0}^{t} {}_up_x^{00}\;\mu_{x+u}^{02}\;{}_{t-u}p_{[x+u]}^{22}\;\mu_{[x+u]+t-u}^{23}\;du - {}_tp_x^{03}\left(\mu_{x+t}^{34} + \mu_{x+t}^{35}\right)$$

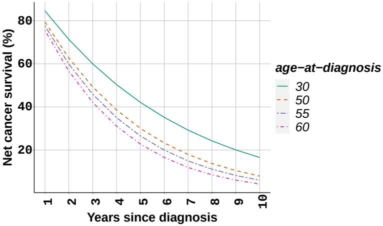
$$\frac{d}{dt}\,{}_tp_x^{04} = {}_tp_x^{00}\,\mu_{x+t}^{04} + {}_tp_x^{01}\,\mu_{x+t}^{14} + {}_tp_x^{02}\,\mu_{x+t}^{24} + {}_tp_x^{03}\,\mu_{x+t}^{34}$$

$$\frac{d}{dt}\,{}_tp_x^{05} = {}_tp_x^{03}\,\mu_{x+t}^{35}$$

- $\mu_{x,u}^{13} = \mu_{[x]+u}^{13}$ and $\mu_{x,u}^{23} = \mu_{[x]+u}^{23}$ with select attained age $[x]$ and duration u
- Differential equations involve integration over duration u

BC net survival, semi-Markov model: pre-Covid rates





Pre-metastatic BC (left) v. Metastatic BC (right)

- Baseline scenarios are carried out for women when $\alpha = 0.6$ and $\beta = \frac{1}{7}$
- Net Survival: **ONLY** consider 'Dead, BC' as cause of death **AFTER** BC diagnosis
- An unusual age pattern in pre-metastatic BC net survival
- Lower metastatic BC net survival at older ages

For a woman aged x, diagnosed with pre-metastatic BC, BC survival in t years:

$$\frac{1 - {}_tp_x^{14} - {}_tp_x^{15}}{1 - {}_tp_x^{14}}$$

BC model - COVID scenario

In order to quantify the impact of COVID-19 on BC mortality at older ages, we have

- Excess deaths from other causes,
  i.e. increase in μ_x^{04}
- Decline in BC diagnosis,
  i.e. slowdown in μ_x^{01} and increase in μ_x^{02}

Pandemic period	μ_x^{01}/μ_x^{02}	μ_x^{04}	
		65–84	85–89
April–Nov. 2020	20% decline in α	1.13	1.12
Dec. 2020–Nov. 2021	1	1.13	1.12
Dec. 2021–Dec. 2022	1	1.10	1.09
Jan.–Dec. 2023	1	1.07	1.06
Jan.–Dec. 2024	1	1.04	1.03

Short-term implications up to 5 years

Semi-Markov (S-M) Model v. Markov (M) Model

- 1–3% increase in, ${}_5p_x^{02}$, in 'Pre-metastatic Unobserved', under M pre- v. post-pandemic calibrations

  AND

  less than 2% under S-M

- 3–6% decline in age-specific, ${}_5p_x^{01}$, 'Pre-metastatic Diagnosed'

- 3–5% increase in, ${}_5p_x^{03}$, 'Metastatic Diagnosed', under M

  AND

  less than 4% increase under S-M

  (Vulnerability? Higher deaths from BC and other causes?)

Changes in BC pre- v. post-pandemic

	Excess deaths, per 100K				Years of Life Expectancy Loss			
Age	Dead (Other)		Dead (BC)		Dead (Other)		Dead (BC)	
	State 4		State 5		State 4		State 5	
	M	*S-M*	M	S-M	M	*S-M*	M	*S-M*
65–69	363	*363*	8	10	7000	*7010*	152	*193*
70–74	607	*607*	7	9	9298	*9293*	113	*138*
75–79	1011	*1012*	8	10	11762	*11770*	92	*116*
80–84	1699	*1699*	7	9	14342	*14340*	63	*76*
85–89	2253	*2253*	5	6	13158	*13158*	29	*35*

- 100,000 women in each age group, in 'No BC' at time zero, taken as January 1, 2020
- 3–6% increase in 'Dead from BC' in the semi-Markov (S-M) model;

  5–8% increase in the Markov (M) model;

  5–8% increase in 'Dead from Other Causes' for women, with 'No BC' at time zero, across different ages over 5 years

Sensitivity analysis

- Change in % of diagnosed BC cases (α) under the semi-Markov model

  pre- and post-pandemic calibrations

  - 40% $\Rightarrow$ 3% increase in BC deaths
  - 80% $\Rightarrow$ 9–12% increase in BC deaths

- Change in the rate of developing metastatic BC in the absence of treatment (β)

  - 5 times higher $\Rightarrow$ 2–5% increase in BC deaths
  - 10 times higher $\Rightarrow$ 3–6% increase in BC deaths

- Change in the level of BC mortality after metastatic BC diagnosis (μ_x^{35})

  - 20% lower OR

    20% higher than the pre-pandemic calibration (baseline scenarios)

  - 3–6% increase in BC deaths

Summary

- More equality in BC as compared to life-style cancers
- A valuable model relating to delays in the provision of BC diagnostic and treatment services
  - Health service provision in different countries in non-pandemic times
  - Impact of a pandemic in different health services
- As compared to the pre-pandemic scenario
  - 3–6% increase in deaths from BC and 5–8% from other causes between ages 65–89
  - Less than a 1% change in the probability of death for women with pre-metastatic BC (${}_5p_x^{15}$)
  - A relatively significant change in the probability of death for women with metastatic BC (${}_5p_x^{35}$) as compared to women with pre-metastatic BC
- Duration dependence matters in actuarial applications
- Measuring parameter and model uncertainty?

Implications of this study

- This study can inform policy makers
  - Implementing evidence-based health interventions
- New medical technologies and early cancer diagnoses improve cancer survival
- Individual level cancer models are relevant to inclusivity and fairness in insurance pricing
- A more detailed modelling framework as compared to one industry-based model (Reynolds and Faye, 2016)
  - Better insights in relation to insurance cash flows: long-term pricing and reserving
- Upcoming pandemics?

More details in:

1. Arık, A., Cairns, A., Dodd, E., Macdonald, A.S., Streftaris, G. The effect of the COVID-19 health disruptions on breast cancer mortality for older women: A semi-Markov modelling approach, Scandinavian Actuarial Journal, 2024.
2. Arık, A., Cairns, A., Dodd, E., Macdonald, A.S., Streftaris, G. Estimating the impact of the COVID-19 pandemic on breast cancer deaths among older women, Living to 100 Research Symposium, 16 February 2023, conference monograph.
3. Arık, A., Dodd, E., Cairns, A., Streftaris, G. Socioeconomic disparities in cancer incidence and mortality in England and the impact of age-at-diagnosis on cancer mortality, PLOS ONE, 2021.
4. Arık, A., Dodd, E., Streftaris, G. Cancer morbidity trends and regional differences in England - a Bayesian Analysis, PLOS ONE, 2020.

Thank You!

Questions?

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