The effect of the COVID-19 health disruptions on breast cancer risk: A semi-Markov modelling approach

Dr. Ayşe Arık

Department of Actuarial Mathematics and Statistics, Heriot-Watt University, and the Maxwell Institute for Mathematical Sciences, UK

joint work with Andrew Cairns, Erengul Dodd, Angus S Macdonald, and George Streftaris

Funding from:
Predictive Modelling for Medical Morbidity Risk Related to Insurance – SoA
Estimating The Impact Of The COVID-19 Pandemic On Breast Cancer Deaths - An Application On Breast Cancer Life Insurance – SCOR Foundation for Science

HERIOT WATT UNIVERSITY SOCIETY OF ACTUARIES SCOR FOUNDATION FOR SCIENCE

Outline

Motivation

Breast cancer (BC) is

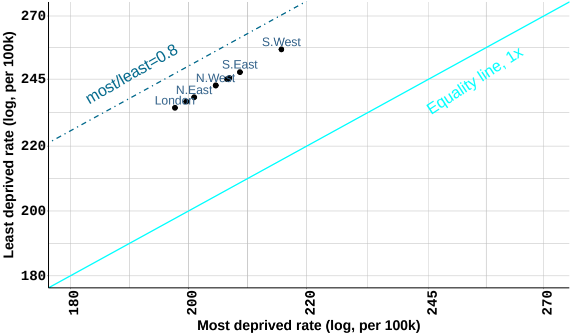
- **the most common** cancer diagnosed in women
- **one of the leading causes** of death for women

Investigate 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

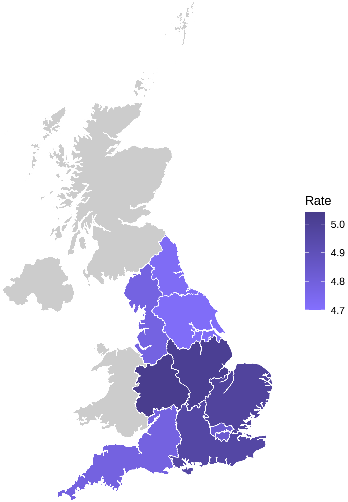
Projection of BC mortality into the future

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 - 2018

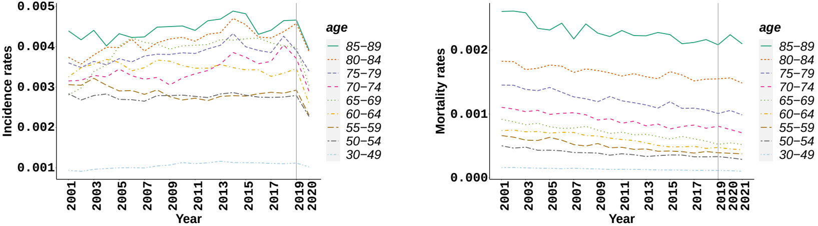


✓Rate is per 10K
✓Deprivation is not significant

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

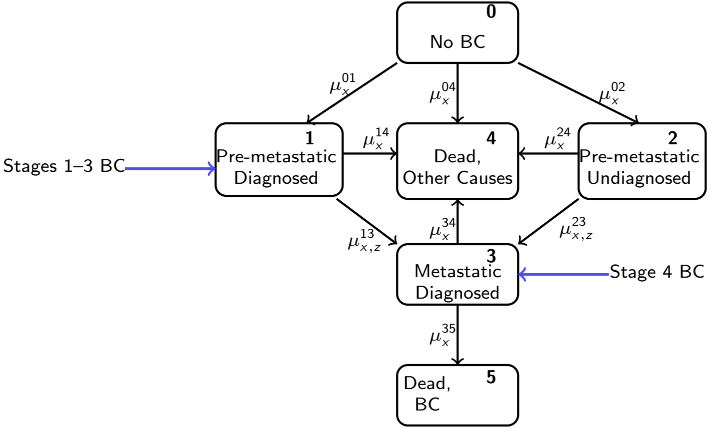
BC incidence and mortality in England: COVID years



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



- 'Dead from BC' is only accessible from 'Metastatic Diagnosed'
- Onset of BC remains unchanged $\Rightarrow \mu_x^{01} + \mu_x^{02} = \mu_x^{*}$
- Treatment is available in 'Pre-metastatic Diagnosed'
  NOT in 'Pre-metastatic Undiagnosed' $\Rightarrow \mu_{x,z}^{13} < \mu_{x,z}^{23}$

A convenient parametrisation of the model

From

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

we can write

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

α : level of BC diagnoses

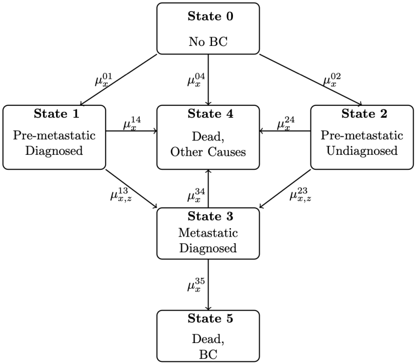
Also we assume

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

β : availability of BC treatment

Transitions to death due to other causes from all 'live' states are equal to μ_x^{04}

$$\mu_x^{14} = \mu_x^{24} = \mu_x^{34} = \mu_x^{04}$$

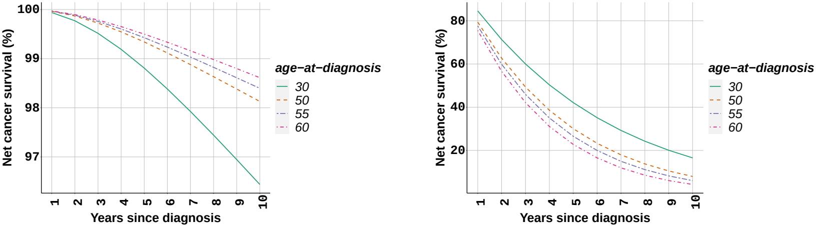


BC semi-Markov model: pre-Covid rates

Age	μ_x^{01}	μ_x^{04}	μ_x^{35}
30–49	0.00086	0.00084	0.16739
50–54	0.00224	0.00228	0.24005
55–59	0.00233	0.00363	0.24005
60–64	0.00282	0.00588	0.28060
65–69	0.00318	0.00952	0.28060
70–74	0.00280	0.01643	0.36002
75–79	0.00311	0.02987	0.40000
80–84	0.00338	0.05496	0.49711
85–89	0.00362	0.10112	0.50000

- μ_x^{01} : ONS/NHS Digital data, 81% of new BC registrations, England, 2001–2019
- μ_x^{04} : ONS data, deaths from other causes, England, 2001–2019
- $\mu_{x,z}^{13}$: Average metastasis rates per 1000 person-years (Colzani et al., 2014)
- μ_x^{35} : BC deaths by age within 12 months after Stage 4 BC diagnosis (Zhao et al., 2020)

BC net survival: 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 semi-Markov 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}	
	α	65–84	85–89
April–Nov. 2020	0.8	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

Occupancy Probabilities										
	From State 0						From State 1		From State 3	
Age	${}_5p_x^{00}$ (%)	${}_5p_x^{01}$ (%)	${}_5p_x^{02}$ (%)	${}_5p_x^{03}$ (%)	${}_5p_x^{04}$ (%)	${}_5p_x^{05}$ (%)	${}_1p_x^{15}$ (%)	${}_5p_x^{15}$ (%)	${}_1p_x^{35}$ (%)	${}_5p_x^{35}$ (%)
Pre-pandemic calibration										
65–69	93.09	1.47	0.68	0.31	4.29	0.16	0.16	5.98	24.36	74.15
70–74	90.49	1.22	0.57	0.23	7.32	0.16	0.20	6.82	30.02	81.25
75–79	85.07	1.31	0.61	0.24	12.59	0.19	0.22	6.97	32.56	82.61
80–84	75.07	1.26	0.59	0.20	22.66	0.21	0.26	7.21	38.26	84.79
85–89	59.71	1.07	0.50	0.17	38.36	0.19	0.25	6.29	37.65	79.54
Pandemic scenario										
65–69	92.73	1.42	0.70	0.32	4.66	0.17	0.16	5.96	24.36	74.03
70–74	89.90	1.18	0.58	0.24	7.93	0.17	0.20	6.79	30.00	81.03
75–79	84.09	1.25	0.62	0.24	13.60	0.20	0.22	6.91	32.53	82.24
80–84	73.42	1.20	0.59	0.21	24.36	0.22	0.26	7.10	38.20	84.15
85–89	57.53	1.00	0.49	0.17	40.61	0.20	0.25	6.12	37.55	78.56

- 3–6% decline in age-specific, ${}_5p_x^{01}$, ‘Pre-metastatic Diagnosed’
- 3–5% increase in, ${}_5p_x^{03}$, ‘Metastatic Diagnosed’ (Vulnerability? Higher deaths from BC and other causes?)

Changes in BC pre- v. post-pandemic

	Additional deaths		YLL		AC in BC mortality from (%)			
	Dead (Other)	Dead (BC)	Dead (Other)	Dead (BC)	Pre-metastatic Diagnosed		Metastatic	
	State 4	State 5	State 4	State 5	State 1		State 3	
Pre-pandemic calibration v. Pandemic scenario					1 year	5 year	1 year	5 year
65–69	363	10	7010	193	0.00	−0.02	0.00	−0.12
70–74	607	9	9293	138	0.00	−0.03	−0.02	−0.22
75–79	1012	10	11770	116	0.00	−0.06	−0.03	−0.37
80–84	1699	9	14340	76	0.00	−0.11	−0.06	−0.64
85–89	2253	6	13158	35	0.00	−0.17	−0.10	−0.98

- 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' and 5–8% increase in 'Dead from Other Causes' for women, with 'No BC' at time zero, across different ages over 5 years
- Absolute change (AC) in BC mortality is less than 1%

Years of life expectancy lost (YLL) from a given cause is:

$$\text{YLL}^{\text{cause}}_{x,t} = D^{\text{cause}}_{x,t} e_x$$

where $D^{\text{cause}}_{x,t}$ is age- and type-specific additional deaths; and

e_x is defined using standard life tables

Sensitivity analysis

- Sensitivity analysis is carried out, all else equal, with
  - $\alpha = 0.4$ and $\alpha = 0.8$ (lower v. higher BC diagnoses)
  - $\beta = \frac{1}{5}$ and $\beta = \frac{1}{10}$ (worse v. better BC treatment)
  - μ_x^{35} is 20% lower and higher than the pre-pandemic level (lower v. higher BC deaths)

- Consistent results in relation to relative changes in BC mortality and deaths from different causes, under pre- and post-pandemic scenarios

A projection model:
BC mortality in England, 2001–2018

$$D_{a,t,r} \sim \text{Poisson}(\theta_{a,t,r}\ E_{a,t,r})$$
$$\theta_{a,t,r} \sim \text{Lognormal}(\mu_{a,t,r}, \sigma^2)$$
$$\mu_{a,t,r} = \beta_0 + \beta_{1,a} + \beta_{2,t} + \beta_{3,r}$$
$$\sigma^2 \sim \text{Inv.Gamma}(1, 0.1)$$
$$\beta_0,\ \beta_1,\ \beta_3 \sim \text{Normal}(0, 10^4)$$ [vague priors for risk factor effects]

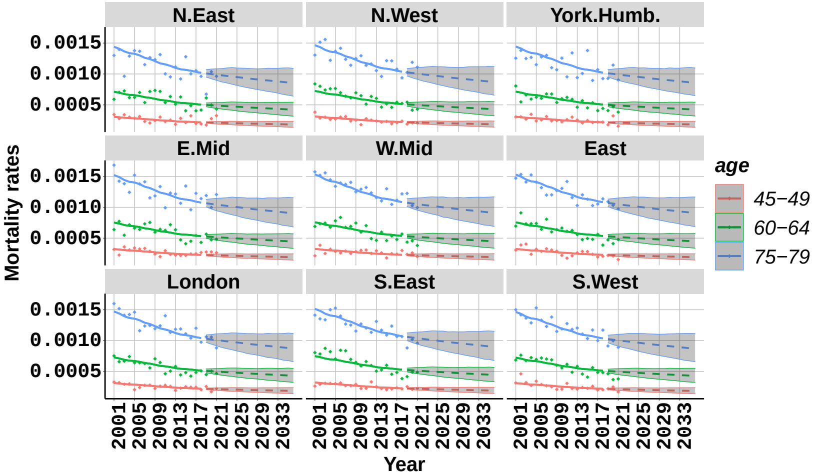
Add random walk with drift for 'period' effect:

$$\beta_{2,t} = \text{drift} + \beta_{2,t-1} + \epsilon_t$$
$$\text{drift} \sim \text{Normal}(0, \sigma^2_{\text{drift}})$$
$$\epsilon_t \sim \text{Normal}(0, \sigma^2_{\beta_2})$$
$$\sigma^2_{\beta_2} \sim \text{Inv.Gamma}(1, 0.001)$$

for $t = 2001, 2002, \ldots, 2018$, where $\hat{\sigma}^2_{\text{drift}} = \frac{\hat{\sigma}^2_{\beta_2}}{2018-2001}$

- $D_{a,t,r}$: number of cancer deaths at age a in year t for region r
- $E_{a,t,r}$: mid-year population estimates

Projected mortality:
BC mortality - women, ages 45–79, 2001–2036



- Decreasing trend over time
- Projected rates for youngest & oldest screening age groups NOT overlapping

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
- As compared to the pre-pandemic scenario
  - 3–6% increase in deaths from BC and 5–8% in 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
- Less than 1% change in net single premiums when key transition rates are defined including COVID years
- Projection for BC mortality shows persistent age gap
- Duration dependence matters in actuarial applications
- Measuring parameter and model uncertainty?

More details in:

1. Arık, A., Cairns, A., Dodd, E., Macdonald, A.S., Shao, A., Streftaris, G. Insurance pricing for breast cancer under different multiple state models, working paper.
2. 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, https://arxiv.org/abs/2303.16573.
3. 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.
4. 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.
5. Arık, A., Dodd, E., Streftaris, G. Cancer morbidity trends and regional differences in England - a Bayesian Analysis, PLOS ONE, 2020.

Thank You!

Questions?

E: A.ARIK@hw.ac.uk
W: https://researchportal.hw.ac.uk/en/persons/ayse-arik