Estimating the impact of the COVID-19 pandemic on breast cancer deaths among older women

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Outline

Purpose of the study

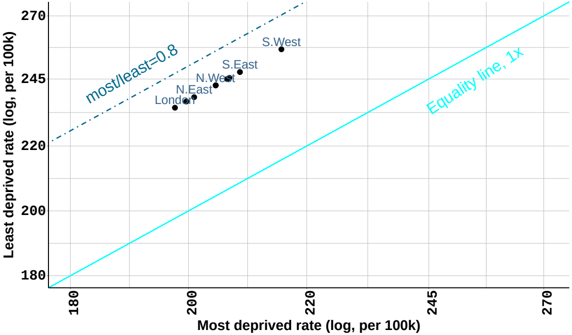
Breast cancer (BC) is

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

Investigate BC rates in the presence of:

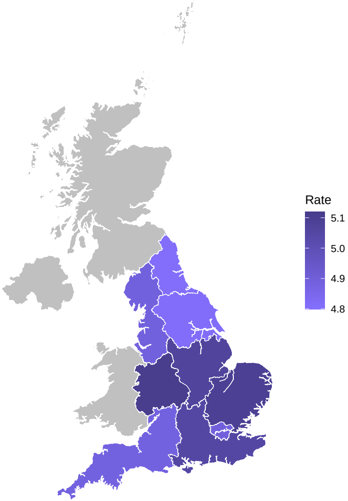
- major disruptions to health services, particularly caused by a catastrophic event, e.g. the COVID-19, preventing or delaying the diagnosis of BC

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

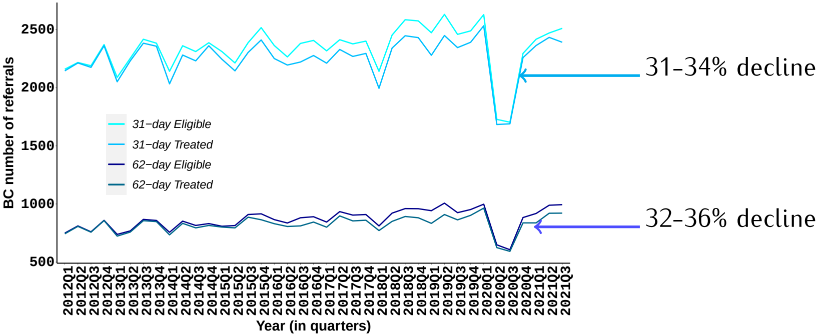


✓Rate is per 10K
✓Deprivation is not significant

What insights we gain from BC data

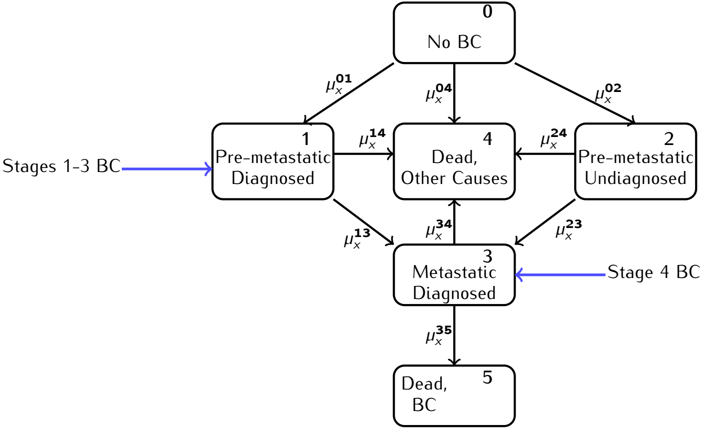
- **Socio-economic differences** are less relevant as compared to, e.g., lung cancer incidence/mortality
- **Not** (easily) controllable or preventable risk factors
- **Regional inequality** exists but relatively low
  - High BC screening awareness
  - National BC screening programme for ages 47-73
-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

Changes in BC during COVID: referrals in Scotland



- A significant decline in BC referrals during COVID-19 in Quarters 2-3 2020 as compared to the same period in 2019
- A significant fall, 19%, in BC registrations between April - December 2020 (PHS, 2021)

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' $\Rightarrow \mu_x^{13} < \mu_x^{23}$

A convenient parametrisation of the model

Due to the assumption relating to an unchanged overall onset of BC

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

we can write

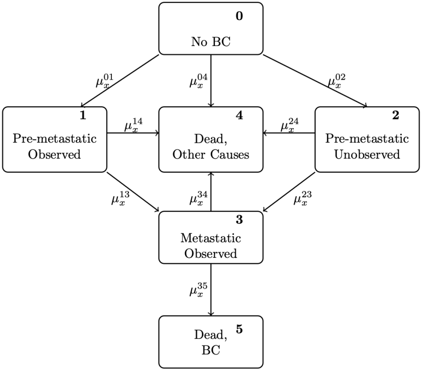
$$\mu_x^{01} = \alpha\, \mu_x^*$$
$$\mu_x^{02} = (1-\alpha)\, \mu_x^*, \qquad 0 < \alpha < 1$$

Also we assume

$$\mu_x^{13} = \beta\, \mu_x^{23}, \qquad \beta < 1$$

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

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



Calibration of the Markov model

- Based on available ONS data and published clinical studies
- 500,000 women in 'No BC' at time zero, taken as January 1, 2020
- 100,000 women in each age group 65-69, 70-74, …, 85-89
- Additional deaths, absolute changes (AC) in BC mortality, years of life expectancy lost (YLL) with

$$\text{YLL}_t^{\text{cause}} = \sum_x D_{x,t}^{\text{cause}} L_x$$

where

- $D_{x,t}^{\text{cause}}$ is age-specific additional deaths
- L_x is defined using standard life tables

BC Markov model: pre-Covid rates

Age	μ_x^{01}	μ_x^{04}	μ_x^{13}	μ_x^{35}
65–69	0.00361	0.00867	0.01954	0.28060
70–74	0.00268	0.01516	0.01954	0.36002
75–79	0.00310	0.02779	0.01954	0.40000
80–84	0.00302	0.05416	0.01954	0.49711
85–89	0.00472	0.09857	0.01954	0.50000

- μ_x^{01} : BC registrations by age and stage for women in the east of England between 2006-2010 (Rutherford et al. 2013, 2015); ONS data, the east of England
- μ_x^{04} : ONS data, the east of England, 2006-2010
- μ_x^{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 Markov model - COVID scenarios

In order to quantify the impact of COVID on BC mortality, we have

- **Scenario 1:** Excess deaths from other causes by a factor of
  - 1.13 for ages 65-84 and 1.12 for ages 85+ bw April 2020 - Nov 2021
  - 1.10 for ages 65-84 and 1.09 for ages 85+ bw Nov 2021 - Dec 2022
  - 1.07 for ages 65-84 and 1.06 for ages 85+ in 2023
  - 1.04 for ages 65-84 and 1.03 for ages 85+ in 2024
- **Scenario 2:** Scenario 1 + Decline in BC diagnoses
  - Slowdown in μ_x^{01} by 20% bw April - Dec 2020
  - Increase in μ_x^{02} to keep the onset of BC, μ_x^*, unchanged

BC Net Survival: pre-Covid rates

	'Pre-metastatic Observed'			'Metastatic Observed'		
Age	1-year (%)	5-year (%)	10-year (%)	1-year (%)	5-year (%)	10-year (%)
			ONS approach			
65–69	99.75	95.57	87.58	75.45	24.10	5.70
70–74	99.69	94.81	86.06	69.60	15.86	2.44
75–79	99.66	94.37	84.91	66.70	12.49	1.48
80–84	99.58	93.42	82.29	60.12	7.00	0.45
85–89	99.57	92.81	78.89	59.36	5.94	0.30
			Our model			
65–69	99.75	95.64	87.95	75.53	24.59	6.04
70–74	99.69	94.95	86.81	69.77	16.53	2.73
75–79	99.66	94.66	86.38	67.03	13.53	1.83
80–84	99.59	94.06	85.59	60.83	8.33	0.69
85–89	99.59	94.05	85.57	60.65	8.21	0.67

- Assume 'Dead, BC' to be the **ONLY** cause of death **AFTER** BC diagnosis
- Lower BC cancer net survival at older ages
- **Consistent** results: ONS approach vs. Our model

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

$$\frac{100\% - {}_tp_x^{\mathbf{14}} - {}_tp_x^{\mathbf{15}}}{100\% - {}_tp_x^{\mathbf{14}}}.$$

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	92.92	1.62	0.82	0.26	4.24	0.14	0.25	4.24	24.37	74.17
70–74	90.65	1.17	0.59	0.17	7.30	0.12	0.31	4.82	30.02	81.26
75–79	84.81	1.27	0.64	0.17	12.97	0.14	0.34	4.91	32.54	82.49
80–84	74.38	1.08	0.55	0.13	23.71	0.14	0.40	5.05	38.21	84.45
85–89	58.73	1.35	0.68	0.16	38.89	0.19	0.39	4.45	37.62	79.34
Scenario 2										
65–69	92.57	1.57	0.85	0.26	4.60	0.15	0.25	4.23	24.36	74.04
70–74	90.06	1.13	0.61	0.17	7.90	0.13	0.31	4.80	30.00	81.04
75–79	83.79	1.22	0.66	0.17	14.01	0.15	0.33	4.87	32.51	82.11
80–84	72.66	1.03	0.55	0.13	25.48	0.15	0.40	4.97	38.15	83.78
85–89	56.54	1.26	0.68	0.16	41.16	0.20	0.39	4.34	37.52	78.36

- Baseline scenarios are carried out for $\alpha = 0.6$ and $\beta = \frac{1}{7}$.
- 3–6% decline in 'Pre-metastatic Diagnosed'
- Around 3% increase in 'Pre-metastatic Undiagnosed' (Vulnerability? Higher deaths from BC and other causes?)

Changes in BC pre- vs. 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	
					1 year	5 year	1 year	5 year
Scenario 1								
65–69	358	0	6915	−8	0.00	−0.01	−0.01	−0.13
70–74	606	−1	9273	−10	0.00	−0.02	−0.02	−0.22
75–79	1040	−1	12090	−16	−0.01	−0.04	−0.03	−0.38
80–84	1766	−3	14901	−23	0.00	−0.08	−0.06	−0.67
85–89	2274	−6	13282	−34	0.00	−0.11	−0.10	−0.98
Scenario 2								
65–69	358	9	6912	164	0.00	−0.01	−0.01	−0.13
70–74	605	7	9269	106	0.00	−0.02	−0.02	−0.22
75–79	1039	8	12085	87	−0.01	−0.04	−0.03	−0.38
80–84	1765	6	14894	52	0.00	−0.08	−0.06	−0.67
85–89	2272	6	13270	36	0.00	−0.11	−0.10	−0.98

- Displaced mortality (in the presence of BC) in Scenario 1
- 5–8% increase in both 'Dead from BC' and 'Dead from Other Causes' across different ages in scenarios 1-2
- Absolute change in BC mortality is less than 1%

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

Summary and future directions

- More equality in BC as compared to life-style cancers
- As compared to the pre-pandemic scenario
  - 5–8% increase in deaths from BC across different ages
  - 5–8% increase in deaths from other causes across different ages
  - Less than a 1% increase in the probability of death for women with pre-metastatic BC (p_x^{15})
  - A relatively significant increase in the probability of death for women with metastatic BC (p_x^{35}) as compared to women with pre-metastatic BC
- A more flexible setting using a semi-Markov model
- What are the implications for related insurance products?

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, working paper.
2. 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.
3. 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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