Modelling cancer risk: regional and socioeconomic disparities

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Modelling, Measurement and Management of Longevity and Morbidity Risk

- Major research programme funded by the Actuarial Research Centre running from 2016 to 2021
- Significant supporting funding from the Society of Actuaries and the Canadian Institute of Actuaries
- Themes
  - Development of new single and multi-population models for mortality and new sub-population mortality datasets
  - Drivers of mortality and cause of death analysis
  - Longevity risk management
  - **Stochastic models for critical illness insurance**
    Joint work with:
    Dr E Dodd (Southampton U), Prof A Cairns (HWU)

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Research objectives

1. Focus on all-cancer, lung, bowel, prostate, and breast cancer rates
2. Analyse and model incidence/mortality rates to identify
   - temporal trends
   - variation by region and deprivation
3. Quantify the impact of diagnosis delays on mortality

   – also linked to delays relating to Covid-19
4. Project cancer rates in future years

Cancer data

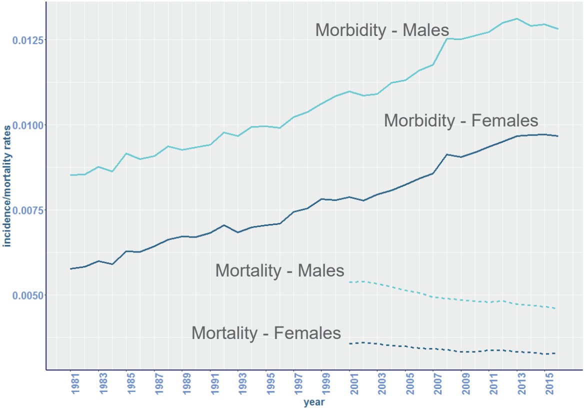
Cancer registration and deaths data
England: Office for National Statistics (ONS)

- Age groups: 0, 1-4, 5-9, ..., 95+

  Age-standardised results, based on the European Standard Population (ESP) 2013
- Gender
- Years: 2001 - 2017 (also some data since 1981)
- Income Deprivation (ID) decile

  1: most deprived; 10: least deprived
- Regions of England: North East, North West, Yorkshire and the Humber, East Midlands, West Midlands, East, London, South East and South West

All-cancer incidence, mortality
Age standardised rates (no modelling)



- Based on European Standard Population (ESP) 2013
- Increasing trends for morbidity incidence
- Decreasing trends for mortality

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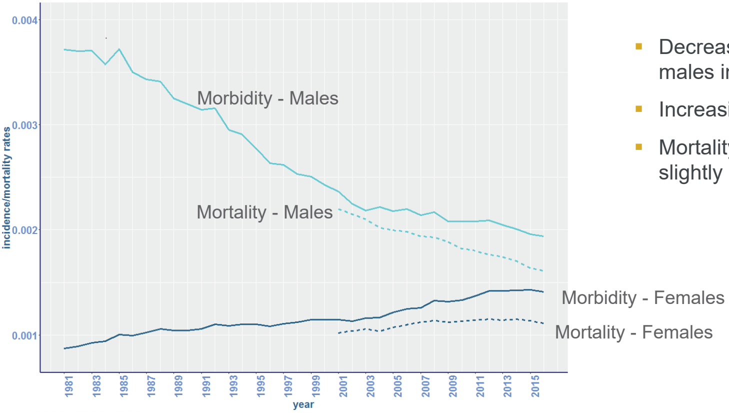
Notable exception in trend:

Lung cancer
Age standardised rates (no modelling)



- Decreasing trend for males incidence
- Increasing for females
- Mortality rates only slightly lower

Regional and/or socioeconomic differences in cancer rates?

- How big is the gap?
- Is it getting better? Worse?

We need modelling - to account for uncertainty and noise.

Stochastic modelling

- How do rates depend on risk factors?

- Transition characterised by underlying rate $\theta_{g,r,a,d,t}$
- $\theta_{g,r,a,d,t}$ depending on **g**ender, **r**egion, **a**ge, **d**eprivation, **t**ime
- Quantify uncertainty (probability intervals)

Bayesian models for incidence and mortality rates

$$C_{a,t,d,g,r} \sim \text{Poisson}(\theta_{a,t,d,g,r} \; E_{a,t,d,g,r})$$
$$\theta_{a,t,d,g,r} \sim \text{Lognormal}(\mu_{a,t,d,g,r}, \sigma^2)$$
$$\mu_{a,t,d,g,r} = \boldsymbol{\beta}' \boldsymbol{X}$$
$$\boldsymbol{\beta}\text{'s} \sim \text{Normal}(0, 10^4) \quad \textbf{[vague priors for risk factor effects]}$$
$$\sigma^2 \sim \text{Inv.Gamma}(1, 0.001)$$

- $C_{a,t,d,g,r}$: number of cancer registrations/deaths of a given malignant neoplasm at age a in year t for gender g in deprivation level d and region r
- $E_{a,t,d,g,r}$: mid-year population estimates
- $\theta_{a,t,d,g,r}$: incidence/mortality rates of a given malignant neoplasm
- $\boldsymbol{X}$: vector of covariates: age, year, deprivation, gender, region, average age-at-diagnosis + appropriate interaction(s)
- $\boldsymbol{\beta}$: vector of coefficients

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Model selection

1. Bayesian variable selection methodology used

2. Chooses the **best** model for

$$\mu_{a,t,d,g,r} = \beta' \boldsymbol{X}$$

according to model fitting criteria

(here marginal likelihood & deviance information criterion)

3. Results suggest that all main variables (age, time, deprivation, gender, region) are important for all-cancer and life-style cancers, i.e. lung and bowel cancer

   - deprivation is not important for breast and prostate cancer mortality

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Change points

- Allow change point(s) in time trends (and age)
  - E.g. different trend after new health/screening policy introduced
  - or after a certain age
- Changepoint analysis, based on BIC, is considered for detection of changes

$$\mu_{a,t,d,g,r} = \beta_0 + \beta_1 \text{ year} + \dots$$

may become

$$\mu_{a,t,d,g,r} = \beta_0 + \beta_{1,1} \text{ year}_{<2006} + \beta_{1,2} \text{ year}_{\geq 2007} + \dots$$

Which factors (significantly) affect rates?

- Age: higher rates at older ages
- Time:
  - higher incidence in more recent years (for most types)
  - lower mortality
- Gender: higher rates for men
- Region?

  Deprivation?

Impact of income deprivation on lung cancer incidence (women)

Poll:

Q: The difference between rates for most and least deprived is

(a) **negligible**: mostly noise;

(b) significant: higher rates for **most** deprived and **getting wider** over time;

(c) significant: higher rates for **most** deprived, but **getting narrower** over time.

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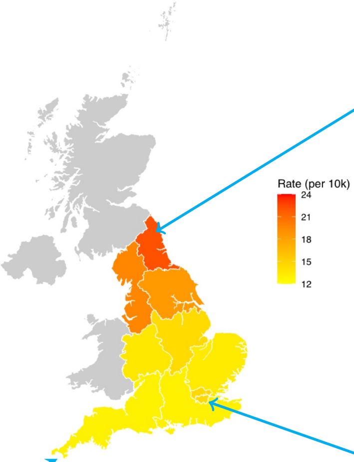
Regional variation in lung cancer incidence - Females, 2017

N.East:40% excess

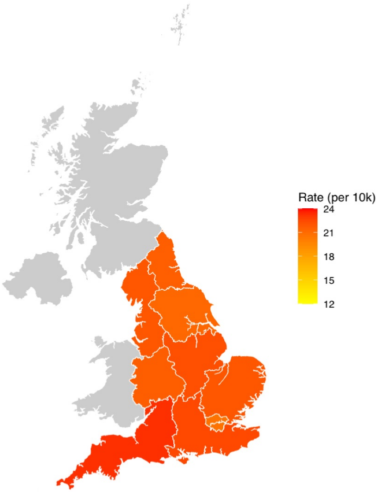


- Regional effect compared to average
- North v. south?

S.West:18% lower

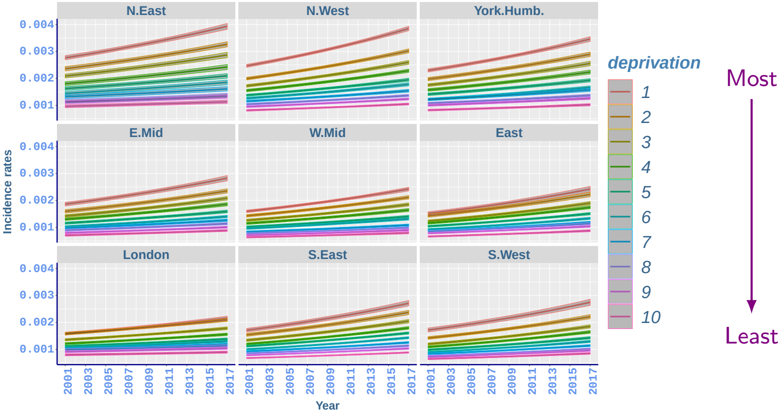
London:about average

Regional variation in breast cancer incidence - 2017



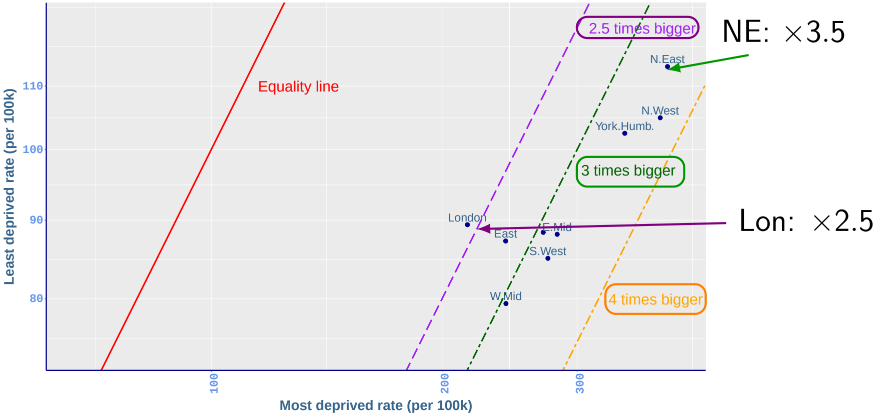
- Not a life-style cancer
  - Regional variation much lower

Deprivation inequality in cancer rates
Lung cancer incidence - Females, 2001-2017



- Higher rates for most deprived (1)
- Deprivation gap getting wider **[Poll answer: (b)]**
- Inequalities more evident in northern regions

Most v. least deprived by region
Lung cancer incidence - Females, 2017



- Rates for **most deprived** much higher
- Regional variation

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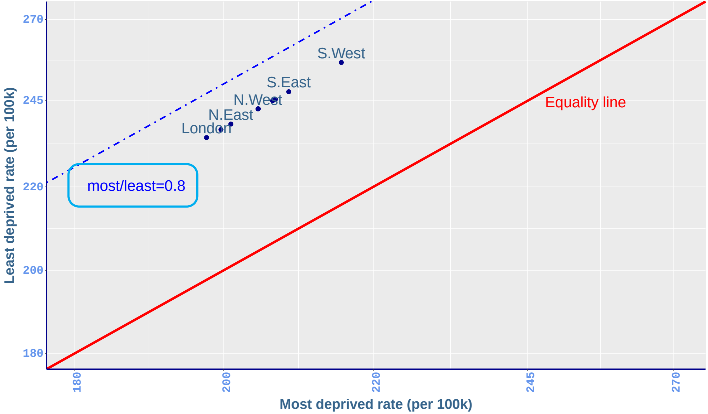
Most v. least deprived by region
Breast cancer incidence - 2017



- Rates for **least deprived** higher
- No regional variation

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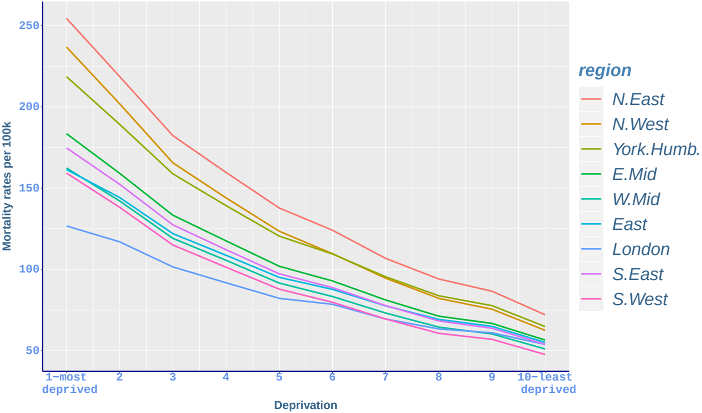
Mortality modelling

Modelling mostly the same as for incidence

Focus on:

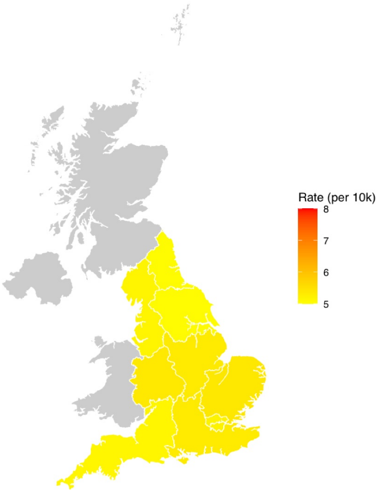
- deprivation and regional differences
- impact of diagnosis delays on mortality
- projection

Deprivation inequality in cancer rates
Lung cancer mortality - Females, 2017



- Higher rates for most deprived (1)
- Inequalities more evident in more deprived groups

Regional variation in breast cancer mortality - 2017



- Deprivation is not-significant

Impact of diagnosis on mortality

Early cancer diagnoses plummeted in England during Covid pandemic

Official figures spark fears that patients may miss out on treatment until it is too late

Denis Campbell
Wed 5 May 2021 19.45 BST

▲ The number of people in England diagnosed with stage one cancer was down 33% in March-June 2020 compared with a year earlier. Photograph: Alamy Stock Photo

The number of people being diagnosed with cancer early in England has plummeted during the Covid pandemic, sparking fears that many will only be treated when it is too late to save them.

✓Estimate average age-at-diagnosis, AAD, with incidence data

✓Include AAD as a factor in mortality model

$$\text{AAD}_{t,d,g,r} = \frac{\sum_a \hat{\theta}_{a,t,d,g,r} E_a^{\text{std}} a}{\sum_a \hat{\theta}_{a,t,d,g,r} E_a^{\text{std}}}$$

E_a^{std} : exposures at age a in the ESP 2013

$$\text{AAD}_{d,g,r} = \frac{\sum_t E_{t,d,g,r} \text{AAD}_{t,d,g,r}}{\sum_t E_{t,d,g,r}}$$

$E_{t,d,g,r}$: original exposure aggregated over age

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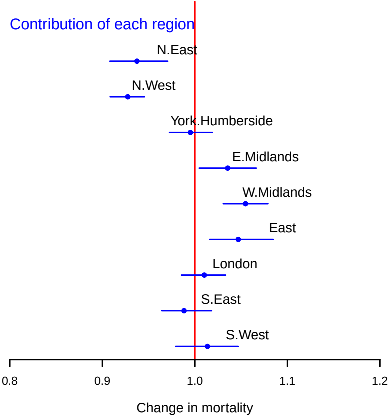
Impact of diagnosis on mortality by region
All cancers - Males

- Impact of age-at-diagnosis compared to the mean level across regions (set to 1)
- N.West: significantly lower effect
- East: significantly higher effect
- London: not significantly different from the average



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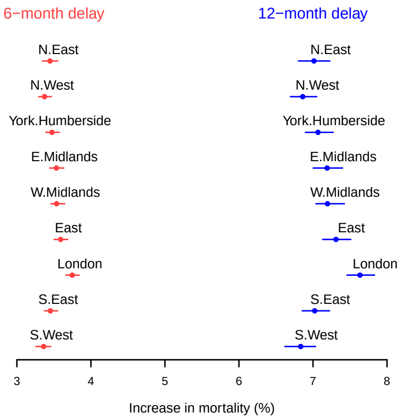
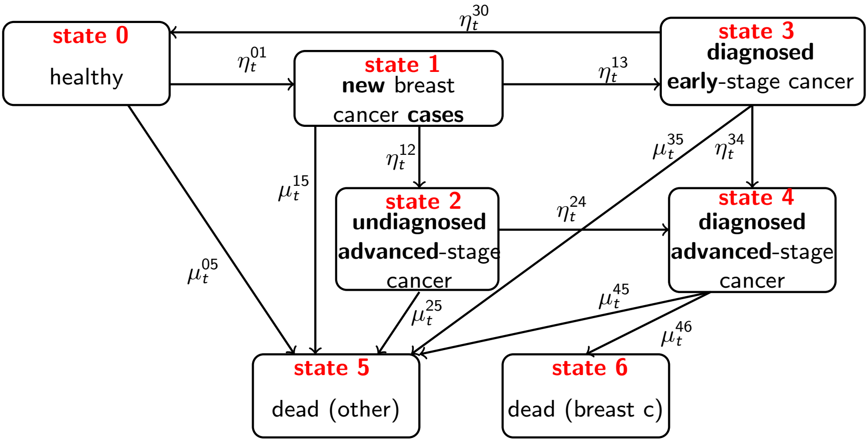
Impact of diagnosis delay on mortality
Lung cancer - Females

Estimate impact of delay in AAD:

- 6-month delay:
  - 3.5% increase in mortality
- 1-year delay:
  - 7% increase in mortality
- Highest impact in London



A Markov model for diagnosis delay - Breast cancer



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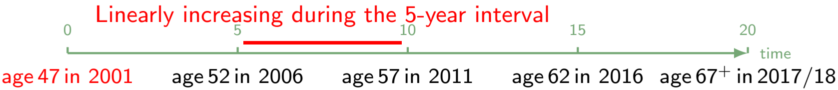
Breast cancer Markov model - A cohort of 100,000 women aged 47 at time zero



1. **Data used:**
   - Breast cancer registrations and deaths (ONS data)
   - Weekly excess deaths in women between 1 April 2020 - 1 July 2021 (PHE data)

2. **Assumptions:**
   - **states 2-4:** Early-stage ≈ 70% All-stage (ONS data, 2012 - 2016)
   - **state 4:** Advanced-stage ≈ 30% Early-stage (O'Shaughnessy, 2005)

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Breast cancer Markov model - COVID-scenarios

1. **No** change in **state 1**

2. A **reduction in cancer registrations** (**state 3**) by

   - **Scenario 1:** 75% for 3 months between April 2020 - June 2020
   - **Scenario 2:** Scenario 1 + 50% between July - September, and 25% for the following 6 months

3. Breast cancer deaths $\approx$ 3.7% All-deaths (PHE, 2017)

   - **state 6:** excess breast cancer deaths $\approx$ 3.7% excess deaths

An illustration for breast cancer Markov model

A cohort of 100,000 people aged 47 at time zero, aged 67 at time 20

	Transition numbers		
state	**Base Scenario**	**Scenario 1**	**Scenario 2**
Healthy	**94279**	**93545**	**93523**
Death (other)	**3813**	4545	4545
Death (breast cancer)	**645**	**652**	**670**

In **Scenario 2:**

- excess number of deaths
  - 25 (**BC, state 6**) - 4%
  - 732 (**Other, state 5**) - 19%
- 10-year net survival rate
  - 91.52% for a woman in (early) state 3 (v. 92.10% in **Base Scenario**)
  - 15.70% for a woman in (advanced) state 4 (v. 19.08%)

A projection model
Lung cancer mortality

$$C_{a,t,d,r} \sim \text{Poisson}(\theta_{a,t,d,r}\ E_{a,t,d,r})$$
$$\theta_{a,t,d,r} \sim \text{Lognormal}(\mu_{a,t,d,r}, \sigma^2)$$
$$\mu_{a,t,d,r} = \beta_0 + \beta_{1,a} + \beta_{2,t} + \beta_{3,r} + \beta_{4,d} + \beta_5 \text{AAD}_{r,d}$$
$$\sigma^2 \sim \text{Inv.Gamma}(1, 0.1)$$
$$\beta_0,\ \beta_1,\ \beta_3,\ \beta_4 \text{ and } \beta_5 \sim \text{Normal}(0, 10^4),$$

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

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

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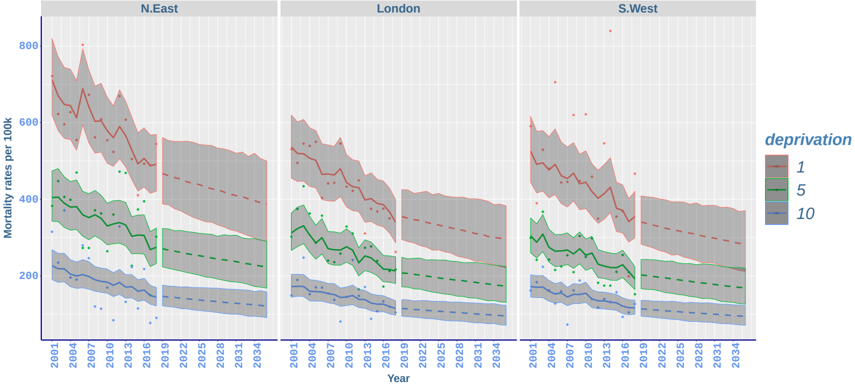
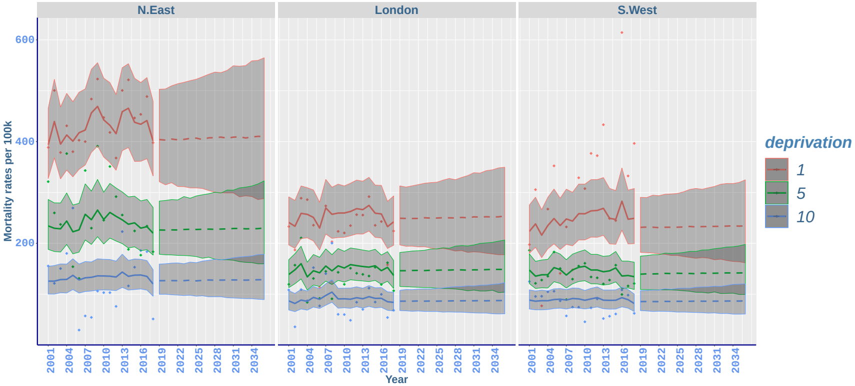
Projected cancer rates (1): men
Lung cancer mortality - age 72, 2001-2035



- Decreasing trend over time
- Projected rates for most & least deprived NOT overlapping

Projected cancer rates (2): women
Lung cancer mortality - age 72, 2001-2035



- Mortality for women *NOT* decreasing
- More uncertainty (compared to men)
  - still rates for most deprived not catching up

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Summary and future directions

1. Regional and socioeconomic gap for cancer rates is widening
    - but not for all cancer types
2. Delay in diagnosis can lead to significant increase in type-specific cancer deaths
3. Projection for lung cancer mortality shows persistent deprivation gap
4. Can public health interventions at regional and deprivation level contribute to lower cancer incidence and deaths?
5. What are the implications for related insurance products?

More details in:

1. 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.
2. Arık, A., Dodd, E., Streftaris, G.. Cancer morbidity trends and regional differences in England - a Bayesian Analysis, PLOS ONE, 2020.

Questions

Comments

The views expressed in this presentation are those of the presenters.