PCN450

FITTING A MIXTURE MODEL OF CANCER EXCESS MORTALITY RATES WITH A TRANSFORMATION STEP, TO CANCER RELATIVE SURVIVAL DATA.

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Objectives:
Mixture models that include a curable and incurable fraction improve the fitting of mortality models to data. However, some cancers display transformational step changes in mortality rates. Sometimes this is due to transformations in the cancer itself such as in chronic myeloid leukaemia, but sometimes occurs when resistance to treatment develops, or when treatment options become exhausted. **Here we test a modified mixture model to include a transformational step to calculate the excess mortality in specific cancers over time from diagnosis using relative mortality statistics, in order to improve the success rate of fitting.**

Methods:
- Relative survival data from the SEER database was used covering a wide range of specific cancers at different ages and stages.
- We introduce a logistic function to a mixture model that includes, curable and incurable fractions, in addition to a model of rising mortality with time to represent the unmodified natural history of the cancer, along with a counterfactual model of decreasing mortality with intervention, to model step changes in mortality rates in specific cancers.
- The transformational step is represented as a logistic function representing a scalar variable applied to a parallel model of mortality that supplements excess mortality after a certain time-point.

Results:
Using the examples of chronic lymphoid, chronic myeloid leukaemia and others, we demonstrate the failure to successfully fit a simple mixture model in comparison to successful fitting with the modified mixture model.

- Examining the graphs of excess mortality on chronic myeloid leukaemia (*Figures 1, 2 and 3*), we can see there is a general pattern of an increase in mortality around the fourth of fifth year. This may reflect treatment failures, or, in the case of CML, blast transformation in those with the Philadelphia chromosome.

Figure 1. Excess mortality hazard rates for chronic myeloid leukaemia

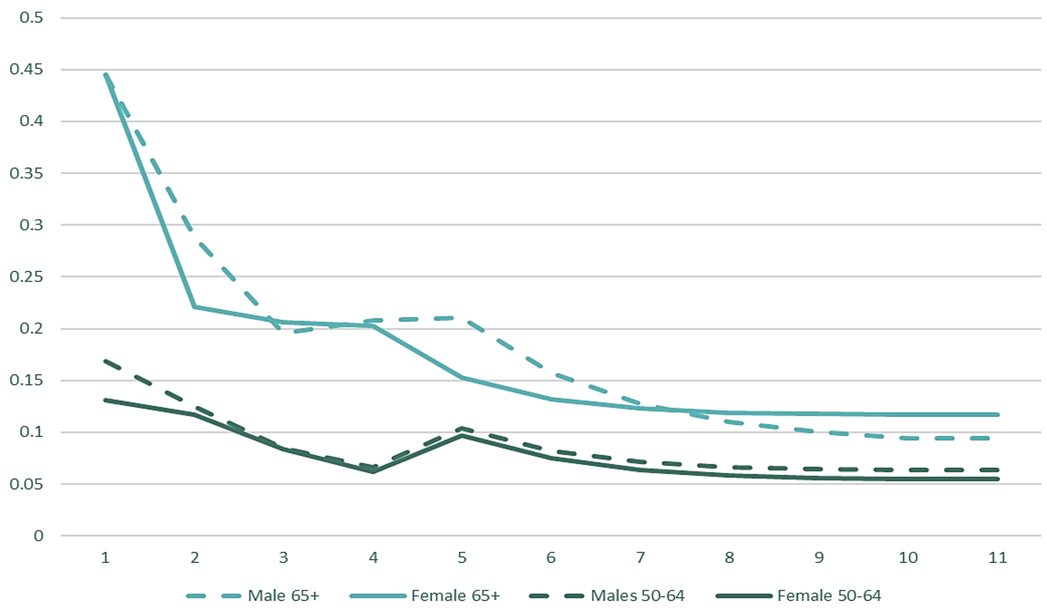


Figure 2. Excess mortality from chronic myeloid leukaemia in 50 to 64-year-old males in the US SEER data

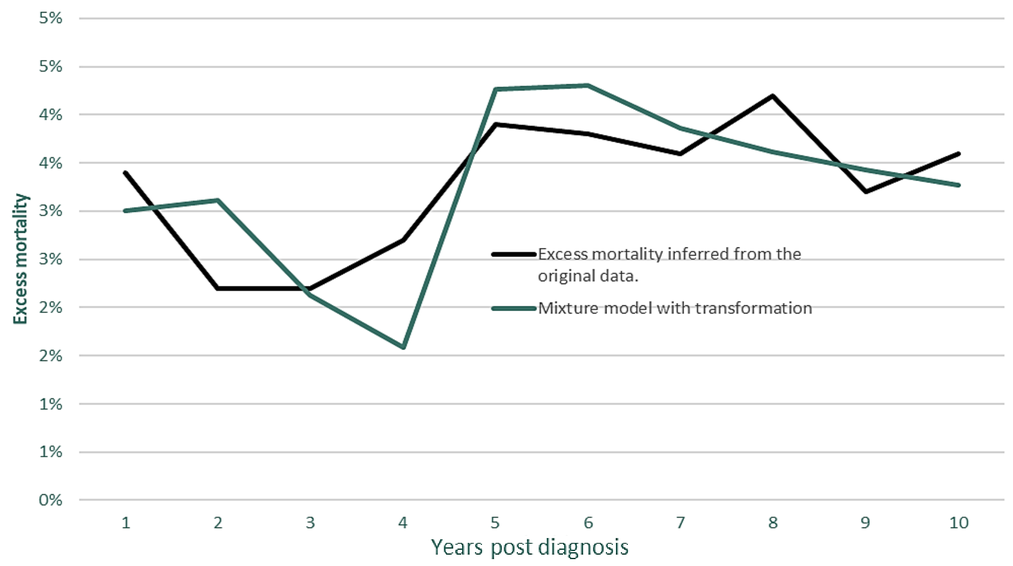
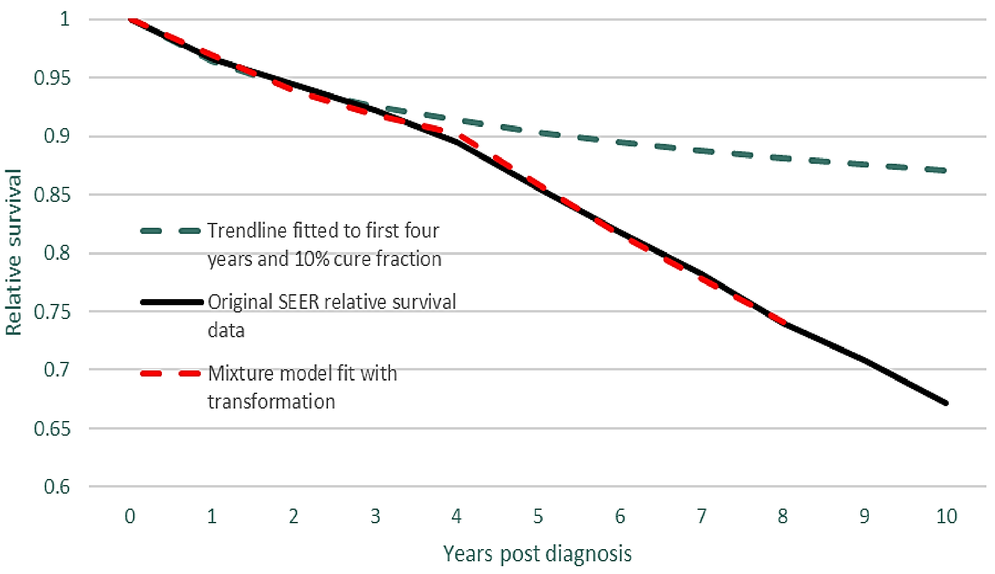


Figure 3. Relative survival from chronic myeloid leukaemia in 50 to 64-year-old males in the US SEER data



The Crystallise cancer model was chosen and has the following form:

$$H_c = Excess\ hazard_{cancer} = -\ln(1-(1-Q_c).F_c)$$
$$Q_c = Unmodified\ initial\ mortality_{cancer} = 1 - e^{-T_c.\kappa.(t+d)}$$
$$F_c = Uncured\ fraction_{cancer} = \beta + e^{-\lambda.t}.(1-\beta)\quad T_c = Transformation\ scalar_{cancer} = 10 - 9/(1+e^{5.t-\pi})$$

Where: c = cancer; d = average delay in diagnosis from inception of cancer; κ = unmodified mortality growth rate; β = is the total curable fraction of all cancer; t = time in years since diagnosis; π = is number of years to a mortality rate transformation

Conclusions:
Introduction of a transformation model within a standard mixture model may improve fitting of excess mortality models to relative survival data when there are transformation step changes in mortality with time from diagnosis.

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