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# Loss in life expectancy and gain in life years as measures of cancer impact

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ABSTRACT

There are a broad range of survival-based metrics that are available to report from cancer survival studies, with varying advantages and disadvantages. A combination of metrics should be considered to improve comprehensibility and give a fuller understanding of the impact of cancer. In this article, we discuss the utility of loss in life expectancy and gain in life years as measures of cancer impact, and to quantify differences across population groups. These measures are simple to interpret, have a real-world meaning, and evaluate impact over a life-time horizon. We illustrate the use of the loss in life expectancy measures through a range of examples using data on women diagnosed with cancer in England. We use four different examples across a number of tumour types to illustrate different uses of the metrics, and highlight how they can be interpreted and used in practice in population-based oncology studies. Extensions of the measures conditional on survival to specific times after diagnosis can be used to give updated prognosis for cancer patients. Furthermore, we show how the measures can be used to understand the impact of population differences seen across patient groups. We believe that these under-used, and relatively easy to calculate, measures of overall impact can supplement reporting of cancer survival metrics and improve the comprehensibility compared to the metrics typically reported.

## 1. Introduction

Cancer survival measures are usually calculated from data collected at the population level via cancer registries covering a geographically defined area [1]. The measures used typically attempt in some way to account for mortality due to other causes and thus capture solely the impact of the cancer itself on mortality, prior to converting to the survival scale [1,2]. These type of measures, such as relative survival are typically given at specific timepoints, at say 1-, 5- or 10-years post diagnosis [3,4], and are often averaged in some way across the age profile of patients diagnosed, sometimes weighted to reflect an external standard age distribution [5]. Even though these metrics can be useful for comparing survival across countries or over calendar time, it is difficult to easily comprehend what is meant in terms of the impact on patients' survival prospects.

In this article, we discuss a range of metrics based on the average life expectancy with and without cancer that circumvent a number of the limitations of the traditional metrics. Firstly, they evaluate the impact of cancer across the whole lifetime of a patient [6,7], removing the need to report at specific timepoints. Secondly, measures of life expectancy with and without cancer in unison portray a comparison that helps gauge the actual impact of a cancer diagnosis. Finally, these measures also incorporate, rather than account for, competing mortality and therefore portray the real-world impact of cancer. We will also consider alternative formats of the metric; both the proportion of life lost and also conditional measures to calculate updated impact on a patient's life expectancy.

A number of investigators have tried to quantify the impact of differences between population groups by calculating the deaths that could be avoided at given timepoints post diagnosis if inequalities in relative survival were removed [8–12]. One alternative would be to calculate the life expectancy for cancer patients should the differences in relative survival be removed [12,13]. This gives a measure that expresses the magnitude of the differences using a metric that is tangible; the average life years that could be gained by removing inequities in cancer survival. The paper is structured as follows: firstly, brief details of how the measure is calculated are given, before four related examples are used to illustrate the approach, prior to a discussion of when and where these measures should be utilised in practice to supplement existing metrics relating to survival. We will use data on women diagnosed with: colon cancer (International Classification of Diseases–10 site code: C18), breast cancer (C50), ovarian cancer (C56) and lung cancer (C34) in England to exemplify the approaches. The dataset contains information on tumour site, age, time since diagnosis, as well

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as a categorical variable with a crude measure of deprivation split into five categories based on postcode areas. The data are the same as those used by Syriopoulou et al. [14], but we restrict to a subset of cancer sites to exemplify the approach. We also use a population lifetable specific to England whereby information on all-cause mortality is available stratified by age, sex, calendar year and deprivation group [15].

## 2. Methods and examples

The loss in expectation of life metric is calculated by the difference between the mean survival for people without cancer for a given set of characteristics (e.g. age, calendar year and sex) and the estimated mean survival for people with cancer with the same characteristics. This can be achieved using non-parametric estimates [6] or can be obtained from model-based estimates [7,16]. The mean survival needs to be calculated over a lifetime horizon and therefore extrapolation is often required in order to estimate these quantities. Andersson et al. [7] have developed a model-based approach that involves extrapolating the excess and expected mortality curves in order to estimate the long-term all-cause survival. This approach has been shown to perform well empirically using historical data and has been applied in a number of settings [7,12–14,17]. Further steps can be taken to ensure the estimates are up-to-date by undertaking a period analysis approach [18,19].

The shaded area in Fig. 1 represents the difference in the mean survival for those with and without cancer and quantifies the impact of cancer on life expectancy; this value can be calculated using numerical integration techniques.

## 3. Example 1 – life expectancy as a measure of cancer impact

A simple use of life expectancy measures can be to report the impact of cancer to reflect the accumulation of excess mortality over the lifespan of cancer patients. Fig. 2 give the life expectancy measures across age at diagnosis for the four cancer sites. A 60-year-old female without cancer could expect to live 25 years on average, whilst a 60-year-old female with a diagnosis of colon cancer could expect to live an average of 15 years (see Fig. 2(a)). The impact of cancer on the life expectancy for a 60 year old patient is thus a reduction of 10 years (Fig. 2(b)). As a comparison, for the same aged patient, the loss in life expectancy for lung cancer would be 21.5 years (Fig. 2(b)), highlighting the much

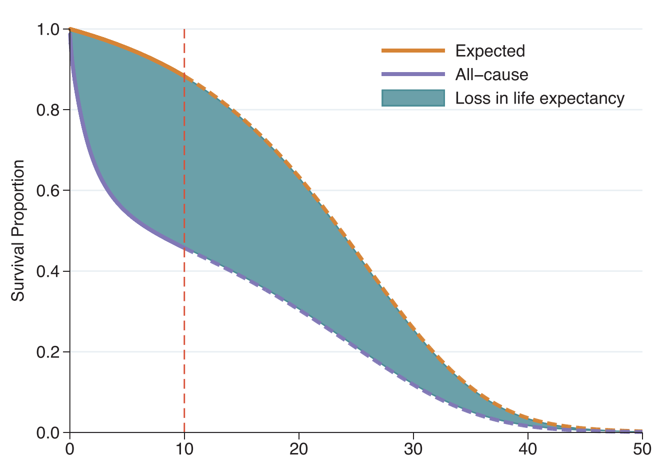


**Fig. 1.** Example of how loss in life expectancy calculated using estimates for a 60-year-old female colon cancer patient. The red dashed line shows a typical follow-up period that may be available in a population-based setting, beyond this point extrapolation techniques are required (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

higher accumulation of excess mortality for that cancer site. The pattern over age is of interest for ovarian cancer; with a lower loss at younger ages (< 50) driven by the significantly better prognosis for these patients. The loss in life expectancy measure can be usefully presented both at an individual and population level to report the impact in two separate ways. The overall total life years lost for those diagnosed in 2013 with colon cancer is predicted to be just under 70,000 life years across the roughly 10,000 females diagnosed (Table 1). As a comparison, the total life years lost for those diagnosed with breast cancer in 2013 in England is in excess of 215,000 life years, with this value driven by the much higher incidence (˜41,000 cases in 2013), given that the loss by individual on average is lower for breast cancer (Fig. 2(b)).

## 4. Example 2 – conditional measures of life expectancy

A large component of the excess mortality for many cancer types is concentrated shortly after diagnosis. Therefore, it can also be of interest to calculate conditional measures in order to understand the impact of cancer for those that survive for a given time period beyond their initial diagnosis. Fig. 3 shows the distribution of age at death for female lung (Fig. 3(a)), ovarian (Fig. 3(b)), colon (Fig. 3(c)) and breast cancer (Fig. 3(d)) patients diagnosed at age 60, together with the distribution of age at death for females aged 60 in general. The topmost plots shows the estimates from diagnosis. It is clear that the impact of cancer is typically greatest in the short-term with over 15% of patients dying within a year for both ovarian and colon cancer, and around 60% of patients dying in the first year for those diagnosed with lung cancer. This has a large impact on the average loss in life expectancy, which reflects the separation of the means of the two distributions, resulting here in a loss of over 10 years on average for colon cancer, more than 15 years for ovarian cancer and a nearly 22 years for lung cancer. In the case of breast cancer (Fig. 3(d)), the impact of cancer on mortality is more modest; there is a noticeably shift in the distribution at death but less of a harsh peak shortly after diagnosis. The bottom two plots of each subfigure show the same estimates for patients who have survived for 1 and 5 years post diagnosis respectively, showing conditional survival measures. Surviving for 5 years following diagnosis, makes the death distributions for those with and without a cancer diagnosis very similar for colon cancer, with the conditional loss in life years being around 2 years; if these plots were to overlay then a point of statistical cure would be said to have been reached [20–22]. These conditional estimates are useful to portray an updated impact of cancer on mortality for those patients who have survived for a given period after diagnosis, but are still evaluated over the remaining lifetime horizon. The effect of ovarian cancer on mortality is sustained for longer (see Fig. 3(b)), which results in a still considerable loss of 6 years on average for those patients who have already survived 5 years following the initial diagnosis [23]. It is also well known that breast cancer has a modest but long-term effect on excess mortality for many years following diagnosis [24], which can be seen to be persistent in Fig. 3(d).

## 5. Example 3 – proportional measures of life expectancy

We can calculate proportional, rather than the absolute loss in life expectancy, in order to report a metric that is more comparable across age, and is also a useful further metric for reporting [6,14]. Fig. 4 shows the average proportion of life years lost for female cancer patients across the four cancer sites; the average number of years of life lost as a proportion of the average life years without cancer. It is clear that across the majority of the age range, female colon cancer patients lose around 40% of their expected remaining life years due to a cancer diagnosis, and that this estimate is very consistent across age at diagnosis aside from those diagnosed at and older than 80. If a single summary impact across age is desired to understand the magnitude of a cancer diagnosis on life expectancy, then a proportional measure is typically better suited. The estimate for lung cancer for females is closer to 85%,

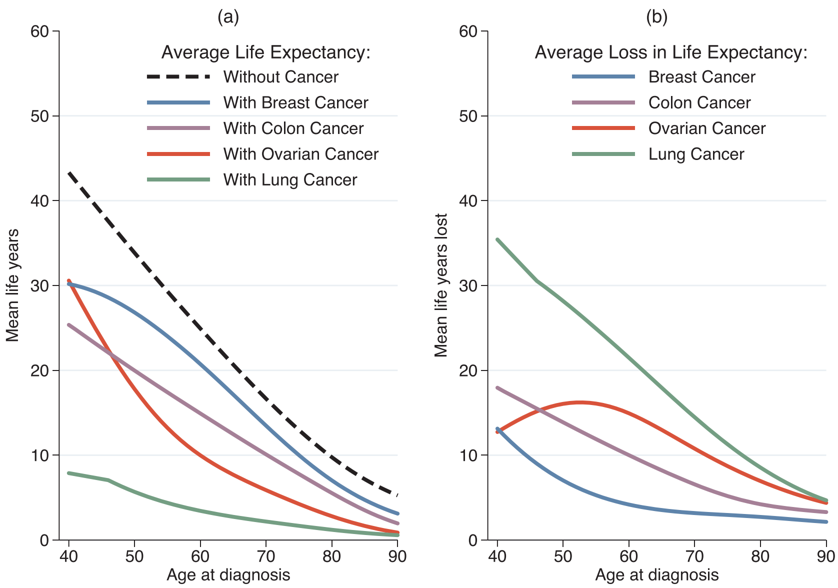


**Fig. 2.** (a) Average years of life remaining with and without cancer across age at diagnosis for female colon, ovarian, lung and breast cancer patients. (b) The loss in life expectancy for the same range of cancer sites. The lines in Fig. 2(b) give the difference between the dashed line for those without cancer and the respective line for each cancer site in Fig. 2(a), and is an overall summary measure of the impact of cancer for each age.

**Table 1**
Estimated total life years lost for female colon, lung, ovarian and breast cancer patients diagnosed in 2013.

| | Age-group (years) | Cohort size in 2013 (females) | Total life years lost |
|---|---|---|---|
| **Colon Cancer** | **< 45** | 444 | 8,986 |
| | **45-54** | 623 | 8,556 |
| | **55-64** | 1,498 | 14,992 |
| | **65-74** | 2,536 | 16,883 |
| | **75+** | 4,562 | 18,689 |
| | **Total** | 9,663 | 68,106 |
| **Breast Cancer** | **< 45** | 4,080 | 57,042 |
| | **45-54** | 9,242 | 67,414 |
| | **55-64** | 9,117 | 39,092 |
| | **65-74** | 9,386 | 30,698 |
| | **75+** | 8,744 | 23,119 |
| | **Total** | 40,599 | 217,364 |
| **Lung Cancer** | **< 45** | 170 | 6,308 |
| | **45-54** | 862 | 23,856 |
| | **55-64** | 2,843 | 60,384 |
| | **65-74** | 5,244 | 77,674 |
| | **75+** | 6,675 | 54,133 |
| | **Total** | 15,794 | 222,355 |
| **Ovarian Cancer** | **< 45** | 685 | 7,353 |
| | **45-54** | 889 | 14,123 |
| | **55-64** | 1,199 | 17,760 |
| | **65-74** | 1,436 | 15,944 |
| | **75+** | 1,436 | 9,706 |
| | **Total** | 5,645 | 64,887 |

showing again the higher impact of a diagnosis of a typically more lethal disease.

## 6. Example 4 – understanding the impact of socioeconomic differences in excess mortality

Understanding the impact of socioeconomic (and other population subgroup) differences in excess mortality is also often of interest when analysing population-based registry data. Typically differences in relative survival or the number of deaths avoided by removing inequalities are given as metrics to show the magnitude and impact of these differences. The solid lines in Fig. 5 show the expected and all-cause survival curves for a 60-year old female colon cancer patient in the most deprived group. The area difference between these curves gives a total average loss in life expectancy of around 10.6 years. The dashed line, and shaded area represent the loss in life expectancy should the most deprived patients obtain the relative survival of the least deprived patients, whilst maintaining their own expected survival experience. This reduces the life expectancy loss to 8.7 years on average, resulting in a gain in life expectancy of almost 2 years on average for patients diagnosed at 60. It is also possible to calculate the total values of life years gained by removing the inequalities in cancer patient survival by multiplying these averages by a typical cohort size of patients to appreciate the population gain in life years. Across all ages for female colon cancer, 4000 life years would be gained for a typical cohort size in 2013 by removing deprivation inequalities that persist in excess mortality across deprivation quintiles in England, which would reduce the total life years lost overall for female colon cancer from approximately 68,000, which is reported in Table 1 to approximately 64,000.

## 7. Discussion

The average loss in life expectancy offers a single summary measure of cancer impact that appropriately distils information on the overall impact of the accumulated excess mortality from diagnosis onwards. Of course, the impact of cancer is not simply a reduced life expectancy, but routinely collected population-based cancer registry data typically lacks details on the impact on quality of life and other information post-diagnosis. The average life expectancy with and without cancer provides survival information in a more tangible form than reporting relative survival proportions at given points following diagnosis. Furthermore, these measures can also be used in the setting of understanding population group inequalities; offering again a more tangible metric for the reporting of the effect of inequalities at both the individual and population level.

There are a number of caveats to consider for these life expectancy measures; firstly, they are highly age-dependent and therefore it can be useful to report separately by age. It is possible to circumvent this to an extent by reporting proportional measures of cancer impact or providing the average life expectancy loss across age if a single summary is desired for reporting purposes. Secondly, as an overall average across the lifespan, the measures do not allow the appreciation of when cancer mortality will have the most impact. The use of conditional measures can overcome this issue and gives updated prognosis to patients that have survived for a given time period following diagnosis who would like an updated understanding of the impact of their cancer. Finally, this approach relies on being able to extrapolate the all-cause survival function for all patients until it reaches zero. This may be more challenging for certain disease types which may have extremely long-term

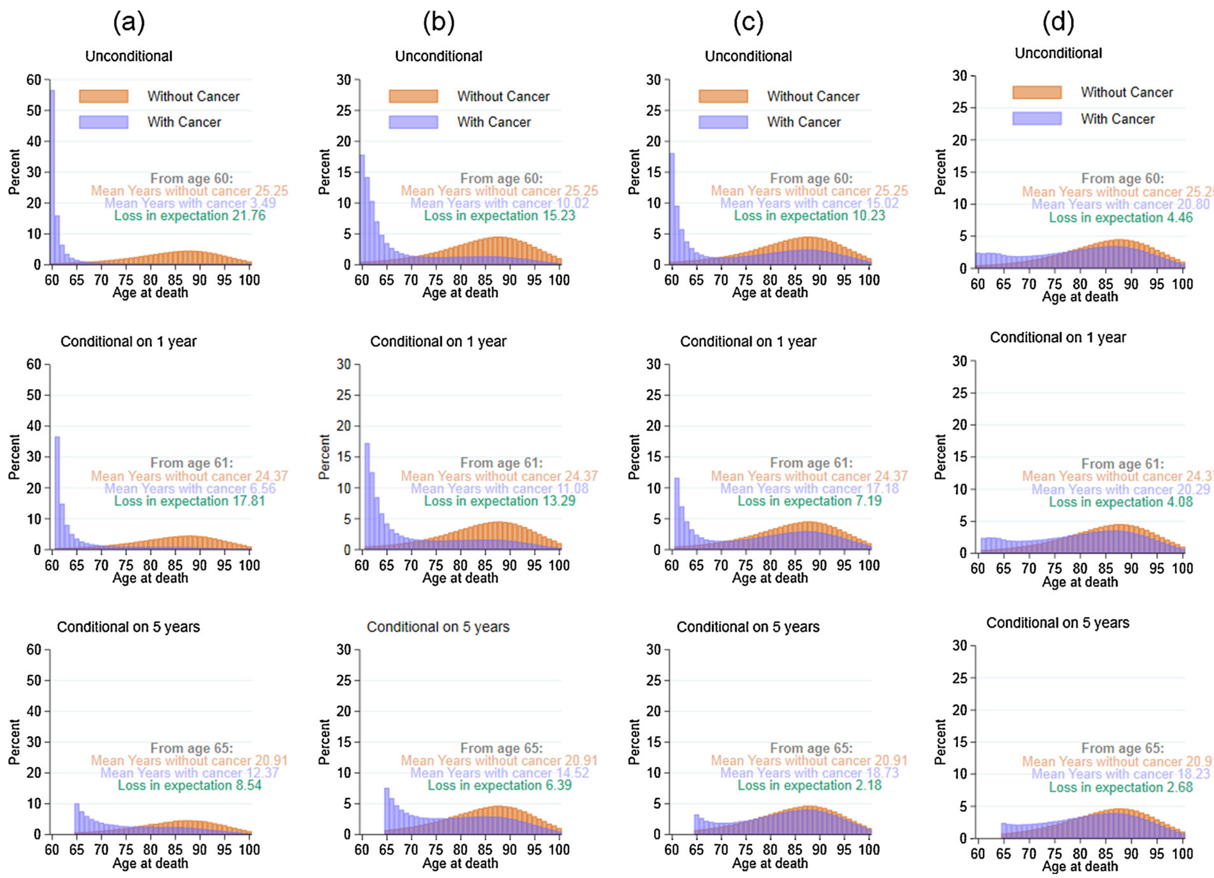


**Fig. 3.** Example of conditional distributions of age at death compared to estimates from general population mortality rates calculated using estimates for (a) a 60 year old lung cancer patient (b) a 60 year old female ovarian cancer patient (c) a 60 year old female colon cancer patient (d) a 60 year old female breast cancer patient. The topmost plot of each subfigure is unconditional, with the latter two plots being conditioned on 1 and 5 years post diagnosis respectively. Note the different y scale range for lung cancer.

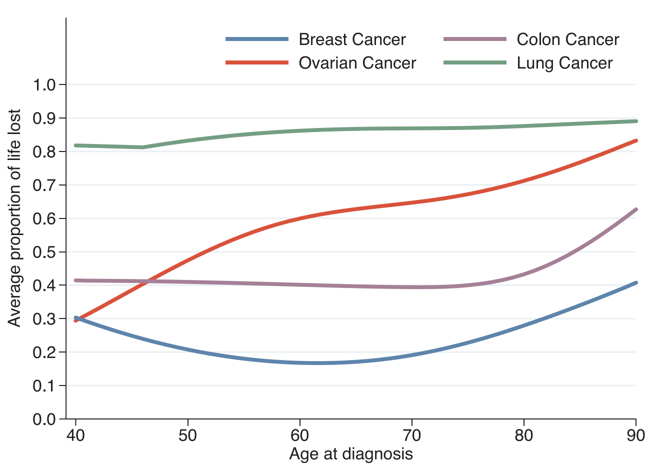


**Fig. 4.** average proportion of life lost across age at diagnosis for female colon cancer patients.

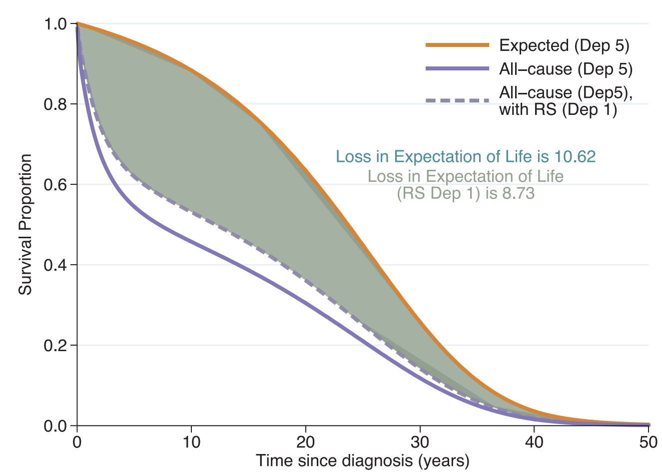


**Fig. 5.** Gains in life expectancy by removing inequalities in deprivation-specific relative survival (RS) for female colon cancer patients. The dashed line represents the all-cause survival for patients in the most deprived group (Dep 5) having taken the relative survival of the least deprived group (Dep 1).

excess mortality, or excess mortality that begins to increase again after a long time period; for instance due to long-term consequences of treatment. For cancer, this extrapolation approach has been shown to be robust for a number of cancer sites [7]. Restricted measures similar to those proposed here, not requiring extrapolation, have also been recommended in an RCT setting for comparison across treatment groups [25]. Another measure that is common for reporting the impact of a given disease on life expectancy is to calculate the person years of life lost due to a particular disease [16,26–28]. This measure is related to those discussed here, but is calculated from the perspective of mortality rates. The potential life years lost are evaluated for those that die in a set period, by comparing the age at death to a reference value corresponding to the typical age at death for the population, with those that die after this reference not contributing to the metric. The PYLL measure does not rely on extrapolation in the same way as the loss in expectation of life approach, but does have limitations in that this measure will contain a mix of patients diagnosed at different points in calendar time. The years of life lost measure may also rely on accurate cause of death information if the analysis sample is defined by using only those that die due to the disease. Furthermore, the fact that those that die after the cut-off value do not contribute to the measure also limits the generalisability of the estimates for diseases with good prognosis.

We believe that these under-used, and relatively easy to calculate, measures of overall impact can supplement reporting of cancer survival metrics and improve the comprehensibility compared to the metrics typically reported.

## Conflict of interest statement

None declared.

## Author contribution

All authors contributed to the study design and conception. MJR conducted the statistical analysis and the initial drafting of the manuscript. All others contributed to the critical review of the final manuscript.

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## Appendix A

We give outline code to estimate the life expectancy measure following fitting an stpm2 [29] model in Stata. A similar approach could be conducted using the R package rstpm2 [30] to fit the relative survival model, and then combining predictions with population lifetable projections, followed by applying numerical integration techniques to the estimated all-cause survival functions for each covariate pattern.

In the below, the popmort_England file contains a population mortality file stratified by individual age, sex, and calendar year, with values for the probability of dying (prob) within 1 year (i.e. between age and (age + 1)) and the corresponding mortality rate (rate).

```
**Define period window from 2007 until 2013, and set the data for **survival analysis; dx – diagnosis date (date format), dexit – date **of exit from study (date format), status – 1 = death, 0 = censored.
stset dexit, failure(status = = 1) enter(time mdy(1,1,2007)) exit (time mdy(12,31,2013)) origin(dx) id(patid) scale(365.24)
**Create attained age and attained calendar year variables for **merging purposes
gen age = min(int(agediag + _t),99)
gen year = year(dx + _t*365.25)
gen yeardiag = year(dx)
**Merge in background mortality rates at event time
merge m:1 sex year age using "popmort_England.dta", ///
keep(match master) keepusing(rate) nogen
**Create spline terms to model age flexibly and non-linearly
rcsgen agediag, df(3) gen(rcsa) orthog
**Fit an stpm2 excess mortality model, with age splines as only **covariate
stpm2 rcsa*, df(5) scale(h) tvc(rcsa*) dftvc(3) bhaz(rate)
**Only need to make predictions for a given calendar year and unique **covariate patterns
keep if yeardiag = = 2013
bys agediag: gen unique = = 1 if _n = = 1
**Estimate life expectancy measures using predict function. Here
**we merge with the same population mortality lifetable as above.
**tinf is the maximum follow-up for the integration in years.
predict ll if unique = = 1, lifelost mergeby(sex year age) ///
diagyear(yeardiag) attage(age) attyear(year)///
diagage(agediag) nodes(40) ///
tinf(80) using(popmort_England) ///
stub(surv) survprob(prob) maxyear(2016) ci
/*This command will create variables detailing the loss in life expectancy (ll), and the expected and observed mean survival in years (survexp, survobs). From this, it is possible to calculate the proportion and absolute measure of life expectancy given in Examples 1 and 3.
The tcond() option can be added to calculate conditional life expectancy measures as illustrated in Example 2.*/
```

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