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Heterogeneity in end of life health care expenditure trajectory profiles

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ABSTRACT

Treatment at the end of life forms a major component of aggregate health care expenditure. Expenditure, however, begins to increase several years before death and varies substantially across individuals. This paper investigates heterogeneity in expenditure profiles across a 36 month period preceding death using group-based trajectory models. A mixture of generalised linear models with four components fits the data best, and identifies decedents in to high cost late rise, medium-high cost late rise, medium-low cost, and low cost late rise expenditure profiles. Approximately 35% of the sample is allocated to the high cost late rise trajectory with average monthly expenditure of £493 36 months prior to death rising linearly for about 28 months before exponential growth to £4000 in the month preceding death. Health conditions at the beginning of the period increase the risk of being in a higher cost trajectory with cancer having the largest impact. The existence of concurrent morbidities substantially raises the probability of membership to the high-cost late rise profile group. A better understanding of the determinants of expenditure profiles in the run up to death contributes to informing policies aimed at mitigating costs while not compromising quality of care.

1. Introduction

Rising health care expenditures in many high income countries has raised concerns over the fiscal sustainability of health systems and their ability to meet population health care needs. Over the past 20 years or so, the average annual growth rate of public health spending in OECD countries has exceeded corresponding growth in GDP (OECD, 2015). The increasing share of expenditure relative to national income places pressure on systems to control expenditure growth, while ensuring the efficient use of resources. Supply-sides policies to promote greater sustainability of services without compromising quality of care include innovation in the configuration and management of health care provision, and the greater adoption of cost-effective technologies and medicines as they become available. It has long been recognised that health care spending near the end of life (EoL) represents a major component of aggregate medical expenditures. A multi-country study (French et al., 2017) estimated spending during the final 12 months of life being between 8.5% and 11.2% of total health care costs. For the English NHS, Aragon et al. (2016) found that expenditure summed across individuals within the final three years of life

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represented one-fifth of the national total inpatient expenditure. It is not surprising, therefore, that many policy makers across the world have advocated reductions in the cost of care during the final year of life as a means to alleviate pressures on health care budgets. For others, improving EoL care is a key driver for understanding differences in patient experiences (for example, for England see Health, 2008; England, 2014; Palliative and Partnership, 2015). However, focusing attention on the final year of life is likely to be too restrictive to fully understand how expenditures change in the run up to death. Studies have shown that health spending starts to increase several years before death (Seshamani and Gray, 2004b) and that the majority of patients in the highest expenditure groups are not in their final year of life (Aldridge and Kelley, 2015). The literature has identified three main determinants of health care spending: age, remaining lifetime, and morbidity. Because these factors interact in a dynamic and complex way, EoL spending over a longer period exhibits significant heterogeneity. In this paper, we aim to identifying distinctive trajectories (or profiles) of spending during the last three years of life and explore factors that account for their distinctiveness. This is informative of clinical areas where care delivery might be considered for further investigation to reduce costs without compromising quality.

We account for heterogeneity in expenditure profiles by applying a specific type of mixture growth model (Vermunt, 2007) developed by Nagin and colleagues (Nagin, 1999; 2005; Nagin and Odgers, 2010a; 2010b) known as group based trajectory models (GBTM). GBTMs assume that the population is composed of a mixture of distinct unobserved groups. A single response variable is measured across T occasions and the overall probability density of the T responses of an individual is a weighted average of group-specific densities where the group proportions serve as weights. Each group specific density is specified as a function of time with the parameters of time differing across latent groups. Accordingly, GBTM models between-class heterogeneity while individuals within a group are treated as homogeneous with respect to their trajectory over time.

It is well established that modelling health care costs is challenging. Distributions are non-negative and typically asymmetric and right-hand skewed, on occasion with long, thick tails, with some patients exhibiting extremely high costs (Jones et al., 2014; 2016). Furthermore, responses to covariates are likely to be nonlinear. These characteristics pose challenges to modelling expenditure profiles adopting the finite mixture modelling approach of GBTM. In this paper, we estimate GBTMs to model individual-level heterogeneity in EoL expenditure and characterise the emerging expenditure profiles into meaningful groups such as persistent users or late risers of health care use. We contribute to the literature in three important ways. First, the two studies we are aware of that model health expenditures using GBTMs (Davis et al., 2016; Hansen et al., 2020) both model trajectories as a mixture of normal distributions for log-transformed health care costs. We extend the GBTM approach by considering two flexible distributions (compared to the Gaussian) to fit better non-negative skewed health care data. More specifically, we apply finite mixtures of Generalised Linear Models (GLMs) and Lomax distributions. These distributions allow health care expenditures to be modelled directly without the need for a log (or other) transformation. Hence, results are obtained on the natural cost scale and do not require a re-transformation inherent in log transformed models (for example, see Duan, 1983). This allows us to categorise patients into distinct latent expenditure profile groups on the basis of observed health care use at the EoL. Second, in addition to modelling how individual characteristics such as demographic and health conditions determine group trajectory profile membership we explore the impact of various clinical events, for example, the subsequent occurrence of chronic kidney disease and/or cancer for patients suffering from diabetes, in dynamically altering the shape of expenditure trajectories. Finally, we explain the role of age, morbidity and TTD in the context of the identified expenditure profiles.

We find that a mixture of GLMs with four components fit the data best identifying decedents into expenditure profiles characterised as high-cost late rise, medium-high cost late rise, medium low cost, and low cost late rise. We identify risk factors associated with membership to a trajectory group by allowing for the probability of trajectory group membership to depend on morbidities and other patient characteristics measured at 36 months before death (i.e. prior to modelling the trajectory profiles). We demonstrate the role of time-varying covariates by analysing how morbidities occurring during the course of a trajectory impact on the shape of the trajectory. Patients with a cancer diagnosis during the 36 months are most likely to be categorised in the highest cost trajectory group. These findings on the shape of expenditure profiles and the characteristics that determine profile membership are essential to target the cost-effective use of resources, for defining optimal patient pathways, and the adoption of new technologies that lower the intensity of care needed, for example, for cancer patients. This patient group presents a high opportunity cost for EoL care, and where policies may be aimed to achieve substantive cost savings while preserving quality.

2. Health care expenditure in proximity to death

Early research identified population ageing as the main factor of rising health care spending (Heller et al., 1986). In a seminal study, Zweifel et al. (1999) using Swiss data found that the impact of age on health care costs diminishes once an individual's remaining lifetime (or time to death (TTD)) is taken into account. In the final two years of life, age was irrelevant in determining health care expenditures. The hypothesis that age is a red herring that acts as a proxy for TTD (known as the red herring hypothesis) is supported by a number of studies (Seshamani and Gray, 2004b; Zweifel et al., 2004; Seshamani and Gray, 2004a; Felder et al., 2010; Geue et al., 2014; Wong et al., 2011; Hazra et al., 2018). The rationale behind the red herring hypothesis is that the positive relationship between age and health care expenditure is observed because as individuals age they get closer to death and during the terminal years they receive more aggressive and expensive treatments. Therefore, closeness to death is more important than age in predicting health care costs.

The relative importance of age and TTD in determining health care costs is closely related to morbidity and disability. If the most serious morbidities and disabilities are experienced closer to death (rather than several years before) then TTD captures EoL morbidity and disability and is the main predictor of health care expenditures with ageing having a less relevant role (see for example, Howdon and Rice, 2018). In contrast, age might be a stronger predictor of health care costs incurred over a prolonged period of living with a given set of morbidities and disabilities. This may explain why the literature has, in general, found a more significant role for ageing in patients using long-term care (Werblow et al., 2007; Karlsson and Klohn, 2011; Colombier and Weber, 2011; Meijer et al., 2011).

Payne et al. (2007) discussed the complex dynamics between ageing, morbidity, and TTD in relation to the healthy ageing hypotheses which describe the relationship between life expectancy and morbidities. The compression of morbidity hypothesis (Fries, 1980) states that increases in life expectancy resulting from medical progress and improvements in lifestyle and socioeconomic conditions are accompanied by larger increases in the number of years lived in good or mild ill health. Therefore, the onset of chronic diseases and disability are compressed into an ever-decreasing proportion of an individual's life. The expansion of morbidity hypothesis (Olshansky et al., 1991), on the other hand, states that medical progress has limited impact on the incidence of disease but successfully improves the survival probabilities for a number of chronic diseases requiring life-long treatment. Therefore, if life expectancy increases, the years spent in ill health or disability also increase. Between the compression and expansion of morbidity lies the dynamic equilibrium hypothesis (Manton, 1982) stating that as life expectancy increases, the absolute number of years lived in good health or mild ill health increases by an amount equivalent to the increased life expectancy. These healthy ageing hypotheses have implications for the trajectories of health care costs. Since the compression of morbidity hypothesis predicts that the most serious morbidities are postponed towards EoL, it implies that cost trajectories have higher expenditures emerging closer to death. The expansion of morbidity hypothesis assumes that even when life expectancy increases, the onset of diseases continues to occur several years before death, and is therefore more suitable to explaining persistent and stable cost trajectories.

The above literature suggests that heterogeneity in health care expenditures arises because age, TTD, and morbidity vary (and interact differently) across patients and because different healthy ageing hypotheses are appropriate for different populations groups and care settings. While the literature has used a variety of approaches to estimating health care costs that account for the specific nature of expenditure data (for a summary of cost regressions see Jones et al. (2015) and Jones et al. (2016)), they have investigated only contemporaneous effects of patient characteristics on costs.

Modelling expenditure trajectories has been the focus of few studies. Two notable examples are Davis et al. (2016) who identified trajectories of health care expenditure among Medicare decedents in the last year of life and Hansen et al. (2020) who identified the most common health care trajectories over the last five years of life among older Danes. Both studies apply GBTM and assume that the population is composed of a mixture of distinct trajectory groups. Expenditures are specified on a log-transformed scale modelled through a mixture of normal distributions. Each trajectory is specified as a polynomial function of time and heterogeneity in expenditure trajectories is captured by differences in the parameters across polynomials.[1] We extend the GBTM approach as outlined above using linked primary (GP practice) and secondary (hospital) health care expenditures for a sample of English NHS patients within the final three years of life.

3. Data and empirical sample

We use primary care data from the Clinical Practice Research Datalink (CPRD) database linked at patient level to secondary care data from Hospital Episodes Statistics (HES) and mortality data from the Office of National Statistics (ONS). CPRD is a UK-based research service that collects fully coded and de-identified patient electronic health records from a network of GP practices.[2] Patients in CPRD are broadly representative of the English general population in terms of age, sex, ethnicity, and body mass index (Herrett et al., 2015; Campbell et al., 2013). CPRD includes records of clinical events in primary care such as medical diagnoses, referrals to specialists and secondary care settings, prescriptions, records of immunisations, diagnostic testing, and all other types of care administered as part of routine general practice. Clinical information in CPRD is captured as Read codes (Booth, 1994) - a hierarchical clinical data coding system used in primary care in the UK that classifies diseases, patient characteristics, procedures, and tests (Chisholm, 1990). Read codes are recorded by practice staff (doctors, nurses, administrative staff etc.) as part of routine data entry.

The linked HES data provide detailed information about the patient's demographic characteristics, medical conditions, and type of care received in inpatient, outpatient and A&E settings. Medical diagnoses in HES are captured using International Classification of Disease (ICD-10) codes.

Our study population consists of 48,073 patients who met the following criteria: i) their records met an acceptable standard based on recording of registration, clinical events, and demographic details, ii) they were registered at English practices that are eligible for linkage with HES inpatient, HES outpatient, HES A&E, and ONS datasets, iii) they died at age 60 or over between 01/01/2012 and 31/12/2014, iv) on the follow-up start date (36 months before death) patients were already registered with a practice that was up-to-standard (considered to have continuous high quality data fit for use in research), v) on the follow-up end date (death date) patients were still registered with the practice and data were still

[1] The focus of GBTM analysis is on between-class heterogeneity. Individuals within each latent class are assumed to start at the same value and exhibit the same general pattern of response over time.

[2] Specifically we use data from CPRD GOLD.

collected for this practice, and vi) there was information on the Index of Multiple Deprivation for the Lower Level Super Output Area of the patient's area of residence.

We followed individuals who died between 2012 and 2014 for a period from 36 months before death to death. We observe patients monthly costs for primary care activities (consultations, diagnostic tests, prescriptions) and secondary care activities (inpatient stays, outpatient appointments, and A&E visits). We also observe their demographic, socioeconomic, and clinical characteristics both 36 months before death and over their trajectory to death.

3.1. Variables

3.1.1. Expenditure data

We generated costs per patient within primary and hospital care based on patients use of health services beginning 36 months before death. We identified three types of primary care activity from CPRD data: consultations, drugs prescribed, and diagnostic tests. Linked HES data were used to identify episodes of inpatient, outpatient, and A&E activity. The methodology we used to cost health care activities is detailed in the appendix. A similar approach has been used elsewhere (Ride et al., 2020).

For each individual we allocated expenditure to each of the 36 months of the observation period as follows. For inpatient hospital activity we used the inpatient episode start and end date to determine the interval of care. Where the entire interval belonged to a specific month, episode expenditures were allocated to that month. Where the interval of care extended over two or more months, episode expenditures were apportioned uniformly into months (i.e. based on the proportion of total episode days in each month). For A&E, outpatient, and primary care, we allocated expenditures to the appropriate month based on the date of the activity (e.g. A&E arrival date, outpatient appointment date, GP consultation date, diagnostic test date and prescription date). Finally, for each decedent we aggregated their primary and secondary health care expenditures in each of the 36 months prior to their death, effectively obtaining a panel dataset.

3.1.2. Covariates

The set of control variables includes age at death, gender, ethnicity, small area deprivation profile based on patients residence, region, and twelve morbidities: asthma, cancer, cardiac heart disease, congestive heart failure, chronic kidney disease, COPD, cerebrovascular disease, dementia, diabetes, hypertension, hypothyroidism, and peripheral artery disease.

For ethnicity and morbidities we used information from both CPRD[3] and HES data while for all other variables information was obtained from CPRD. All variables were measured at the follow-up start date (36 months before death). Morbidities were also measured over the entire trajectory path of the patient.

4. Empirical models estimation approach

We set out below the group based trajectory model. Let $Y_i = (y_{i1}, y_{i2}, \ldots, y_{iT})$ denote the longitudinal sequence of health care expenditures on individual $i \quad (i = 1, \ldots, N)$ over T months. The observed responses, $Y_1, Y_2, \ldots, Y_N$, are assumed to come from J distinct groups with density functions, $f^1, f^2, \ldots, f^J$, in proportions, $\pi_1, \pi_2, \ldots, \pi_J$. That is, the unconditional probability of observing individual $i's$ longitudinal sequence of health care costs, Y_i, is:

$$f(Y_i) = \sum_{j=1}^{J} \pi_j f^j(Y_i), \tag{1}$$

where $f^j(Y_i)$ is the probability of Y_i given membership in group j, and π_j is the probability of a randomly chosen individual belonging to group j.

The model relies on the conditional independence assumption, which states that for each individual within a given trajectory group the distribution of expenditures in a given period is independent of the expenditures in prior periods:[4]

$$f^j(Y_i) = \prod_{t=1}^{T} f^j(y_{it}). \tag{2}$$

[3] The Read codes used to identify morbidities are obtained from the Cambridge Clinical Codes (www.phpc.cam.ac.uk/pcu/research/research-groups/crmh/cprd cam/codelists/v11) except from hypothyroidism which was obtained from the University of Manchester clinical codes repository (clinical-codes.rss.man.ac.uk)

[4] Time dependency has been incorporated into other growth mixture models (Vermunt, 2007) by including random effects in each group's trajectory specification and therefore allowing for serial correlation arising from the time invariant error component. However, we do not pursue this approach since the addition of random effects within a group-based model would allow for more within group variability in individual-level trajectories at the expense of clearly discerning trajectory groups, resulting in fewer distinct trajectories from which to infer trajectory profiles. In part, the objective of GBTM, is to minimise within-group variability in order to identify groups of individuals who follow approximately the same developmental trajectory (Nagin and Odgers, 2010a).

The probabilities of group membership, $\pi_1, \pi_2, \ldots, \pi_J$, are parameterised as follows:

$$\pi_j = \frac{\exp\left(\theta_j\right)}{1 + \sum_{j=2}^{J} \exp\left(\theta_j\right)}, \tag{3}$$

for $j = 2, \ldots, J$, and where $\pi_1 = 1 - \sum_{j=2}^{J} \pi_j$. θ_j are parameters that can take any value.

Combining Eq. (1)–(3), the likelihood for the entire sample of N individuals is,

$$L = \prod_{i=1}^{N} \left\{ \frac{1}{1 + \sum_{i=1}^{T} \exp(\theta_j)} \prod_{t=1}^{T} f^1(y_{it}) + \frac{\exp(\theta_2)}{1 + \sum_{i=1}^{T} \exp(\theta_j)} \prod_{t=1}^{T} f^2(y_{it}) + \ldots + \frac{\exp(\theta_J)}{1 + \sum_{i=1}^{T} \exp(\theta_j)} \prod_{t=1}^{T} f^J(y_{it}) \right\}. \tag{4}$$

The parameters defining the trajectories and the probabilities of group membership are estimated jointly via maximum likelihood.

4.1. Normal, GLM and lomax distributions

In the simplest form of the model, the trajectory distributions, $f^1, f^2, \ldots, f^J$, in Eq. (4) are specified as Normal distributions, such that,

$$f^j(y_{it}) = \frac{1}{\sigma_j} \varphi\left(\frac{y_{it} - X_{it}\beta_j}{\sigma_j} \right) \tag{5}$$

where $X_{it} = [1 \quad t \quad t^2 \quad \ldots \quad t^{\varrho}]$ is a vector of time polynomials, and $\beta_j = [\beta_{j0} \quad \beta_{j1} \quad \ldots \quad \beta_{\varrho}]'$ is a conformable vector of parameters to be estimated, and σ_j is the standard deviation.

It is well established however, that health care expenditure data is complex and presents challenge to empirical research (for example, see Deb et al., 2017). In particular, distributions of expenditures are very often non-negative, heteroscedastic, positively skewed and leptokurtic, which has led to an expanding array of alternative parametric and non-parametric approaches to estimation that provide potentially superior methods for handling heavy-tailed and non-normal distributions (Jones et al., 2014; 2015; 2016).[5]

A normal distribution fails to account for skewness typically observed in expenditure data (particularly apparent in hospital costs due to infrequent heavy users of care). Log transformations, and to a lesser extent a square-root transformation, have been used to achieve greater symmetry in the distribution (Jones, 2015). However, these produce predictions on a transformed scale which typically is unhelpful for interpretation. Accordingly, predictions are retransformed to their natural expenditure scale, but this requires the application of a smearing adjustment that often requires some knowledge of the form (as a function of covariates) of heteroscedasticity in the errors (see Duan, 1983). A more appealing approach is to use methods that estimate on the natural cost scale that explicitly model the variance as a function of covariates, and that can also incorporate an appropriate link function. Generalised linear models (GLM) offer such an approach, where a link function relates the index of covariates to the conditional mean of the outcome, and the distribution function describes the variance and a function of the conditional mean. We consider a GLM with a log-link function and a gamma distribution, with probability density function given by:

$$f^j(y_{it}) = \frac{1}{\Gamma\left(a_j\right)\left[\frac{1}{a_j}\exp\left(X_{it}\beta_j\right)\right]^{a_j}} y_{it}^{(a_j-1)} \exp\left(-\frac{y_{it}}{\frac{1}{a_j}\exp\left(X_{it}\beta_j\right)} \right), \tag{6}$$

where $\frac{1}{a_j}\exp\left(X_{it}\beta_j\right)$ is a scale parameter, a is a shape parameter, and $\Gamma(.)$ is the gamma function.

We also consider a Lomax distribution (Lomax, 1954). This is a two-parameter distributed nested within the more flexible four-parameter generalised beta of the second kind (GB2). The GB2 distribution offers flexibility in modelling health care costs as its three shape parameters (one scale parameter) allow greater precision in modelling higher moments of the distribution via skewness and kurtosis (see Kleiber and Kotz, 2003). This is however, at the expense of increased computational burden, and particularly where a more parsimonious nested distribution may provide a better fit to the data. The Lomax distribution has been used in a number of applications to model heavy-tailed data, including income and wealth (Atkinson and Harrison, 1978), firm size data (Corbellini et al., 2010), reliability and life testing (Harris, 1968). Importantly, for health care cost data, the support of the distribution begins at zero.[6] The Lomax probability density function is defined

[5] Also see Basu et al. (2004, 2006), Buntin and Zaslavsky (2004), Deb and Burgess (2003), Hill and Miller (2010) Manning et al. (2005) for comparisons of alternative regression-based approaches to estimating healthcare costs.

[6] For our application this is not an issue since for all individuals and months we observe positive costs. This is not surprising given we focus on expenditure at the end of life. However, for more general modelling of expenditure profiles, zero costs may be incurred over specific time intervals.

as follows:

$$f^j(y_{it}) = \frac{q_j / \exp\left(X_{it}\beta_j\right)}{\left(1 + \frac{y_{it}}{\exp\left(X_{it}\beta_j\right)}\right)^{(1+q_j)}}, \tag{7}$$

where q_j is a shape parameter, and $\exp\left(X_{it}\beta_j\right)$ is a scale parameter.

Maximum likelihood is used for estimation. For the GLM specification, starting values are obtained from GLM models estimated on four subgroups of equal size. The subgroups are created by categorising the standard deviation of individual costs over time by its quantiles.

4.2. Identification of trajectories

To calculate the probability that an individual with a given profile belongs to a specific trajectory group we derive the posterior probability of group membership. This quantity is different from the probability of group membership, π_j, that measures the proportion of the population that belongs to group, j, or equivalently the probability that a random individual belongs to trajectory, j. Applying the Bayes rule, the posterior probability of group membership is:

$$P(j|Y_i) = \frac{P(Y_i|j)\pi_j}{\sum_{j=1}^{J} P(Y_i|j)\pi_j},$$

where the probabilities of group membership, π_j, and probabilities of observing costs, Y_i, for individuals who are members of group j, $P(Y_i|j)$, are calculated using the estimated parameters, $\hat{\theta}_j$ and $\hat{\beta}_j$, respectively.

We assign each individual to the trajectory group for which the individual's posterior probability is largest. We then construct the profiles of individuals in each identified trajectory group by producing summary statistics of individual-level demographic and clinical characteristics for each group.

4.3. Including covariates

We extended the base model by adding covariates in two ways.

4.3.1. Group membership

First, we include individual-level characteristics to estimate their impact in determining membership to a trajectory group. In contrast to creating individual profiles after the trajectories are formed (in the post-estimation phase), the relationship of individual-level characteristics to trajectory group membership is estimated jointly with the trajectories. The advantage of explicitly modelling the effects of covariates is that it allows us to quantify the relationship between the individual characteristics and the probability of group membership and avoid reliance on statistical tests for cross-group differences that assume no classification error in group identification.

Since trajectory groups describe costs over a long period, individual characteristics that are added to the model as possible predictors of group membership are measured at the first observation period of the trajectories (36 months before death).

To include covariates, $Z_i = [Z_{1i}, \ldots, Z_{Li}]$, of trajectory group membership, Eq. (3) of the base model is modified to a multinomial logit model:

$$\pi_j(Z_i) = \frac{\exp\left(Z_i\theta_j\right)}{1 + \sum_{j=2}^{J} \exp\left(Z_i\theta_j\right)},$$

for $j = 2, \ldots, J$ and $\pi_1(Z_i) = 1 - \sum_{j=2}^{J} \pi_j(Z_i)$. Note that here, the coefficients, θ_j, estimate the influence of risks factors on the probability of membership in the jth trajectory group relative to membership in the comparison group. We adopt different scenarios involving various levels of the predictor variables, Z_i, to assess their overall impact on group membership.

4.3.2. Trajectory profiles

Second, we allow for conditions that are diagnosed during the course of a trajectory to alter the trajectory itself. Equation (5) is modified to describe the trajectory distributions as functions of both time polynomials and time varying morbidities, M_{it}, such that,

$$f^j(y_{it}) = \frac{1}{\sigma_j}\varphi\left(\frac{y_{it} - W_{it}\delta_j}{\sigma_j}\right),$$

where $W_{it} = [1 \quad t \quad t^2 \quad \ldots \quad t^{\varrho} \quad M_{1,it} \quad \ldots \quad M_{K,it}]$, and δ_j is a conformably dimensioned vector of parameters, $\delta_j = [\beta_{j0} \quad \beta_{j1} \quad \beta_{j2} \quad \ldots \quad \beta_{j\varrho} \quad \gamma_{j1} \quad \ldots \quad \gamma_{jK}]'$.

The coefficients of the conditions are group specific so that the model allows for differential profile effects of conditions on each trajectory. Since in the base model, the shape of a trajectory does not depend on any clinical events, the time

Table 1
Trajectory groups estimates: Linear.

	HC-LR		MHC-LR		MLC		LC	
	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error
Constant	1.054***	(0.010)	0.582***	(0.004)	0.257***	(0.003)	0.079***	(0.001)
t	-0.121***	(0.001)	-0.075***	(0.001)	-0.024***	(0.000)	-0.004***	(0.000)
t^2	0.005***	(0.000)	0.003***	(0.000)	0.001***	(0.000)	0.000***	(0.000)
$log(\sigma)$	0.784***	(0.001)	0.048***	(0.002)	-0.886***	(0.005)	-2.345***	(0.004)
$logit(\pi)$	-0.288***	(0.012)			-0.860***	(0.014)	-1.278***	(0.016)

*$p < 0.1$, **$p < 0.05$, ***$p < 0.01$.

parameters capture the development path of the trajectory group members averaged over all clinical events (and other contingencies) that might cause variation about the trajectory. In contrast, in the extended model, the time parameters describe the trajectory if no clinical events occurred during the development path.

In the context of GBTM, model selection concerns decisions about the number of trajectory groups and the shape of each group's trajectory. Our choice set consists of specifications with two to five groups and first (linear) to third (cubic) order time polynomials. We adopt a two-stage selection procedure as outlined in Nagin (2005) that compares models on the basis of the Bayesian Information Criterion (BIC) and prioritises the choice of the number of groups over the shape of the groups. Model specifications with five trajectory groups failed to converge and BIC support models with four groups. Two sets of time polynomial specifications were favoured based on BIC: a) all groups defined in terms of quadratic time polynomials and b) two groups specified as quadratic and two as cubic time functions. For uniformity we chose the former set.

5. Results

5.1. Descriptive statistics

The sample consists of 48,084 patients from 321 practices. This constitutes a sufficiently large sample to identify and analyse expenditure trajectory groups consisting of groups as small as about 1% of the full sample (about 500 individuals). All patients were followed from 36 months before death to death. A breakdown of the number of patients by explanatory variable is provided in Table A.1.

All patients incurred drug costs throughout the 36-month period (see Fig. A.1). The percentage of patients having outpatient and test expenditures declined during the last month before death. In contrast, there was a dramatic increase in the percentage of patients with inpatient costs (from 33% to 63%) and A&E costs (19% to 46%) in the last month before death. The percentage of patients with primary care costs also increased sharply during the last two months before death from 62% to 74%.

Inpatient costs (£146) and drug costs (£57) contribute most of the patient's total cost of care (£270) 36 months before death but in the last month of life inpatient costs (£3203) account for the majority of total costs (£3634) (see Figs. A.2 and A.3). In general, inpatient, A&E, tests, and primary care costs appear to increase more rapidly at around 8 months before death while outpatient costs take off from 36 months before death exhibiting a relatively more linear trend. Drug costs appear to be the most stable over time increasing by less than three times over the study period. In contrast, inpatient costs increased by 22 times and A&E costs by 18 times.

Average costs by morbidity and broken down by setting of care are shown in Fig. A.4. Costs are calculated at the first month of the follow-up period, i.e. 36 months before death and conditions ordered from the highest (Cancer, £432) to the lowest (Dementia, £243) average cost. The most frequent condition is hypertension with 30,127 patients having the condition incurring monthly costs of £303 on average. However, these expenditures are for people recorded as having hypertension and all the other conditions that they suffer. The cost is not for treating hypertension alone. For all conditions, inpatient and drug costs account for the largest proportion of average costs. Average costs varied little over age bands (see Fig. A.5) due to our sample consisting of individuals aged 60 years or over who are approaching the end of life.

5.2. Trajectory estimates

Tables 1, 2, and 3 present estimates for the linear, GLM and Lomax specifications containing time polynomials only (i.e without covariates). For all models we identify four distinct trajectory groups.

For each model, we calculate the posterior probabilities of group membership and apply the maximum posterior probability assignment rule to allocate each individual to a trajectory group. The groups identified by the three models do not consist of the same individuals but there are similarities in their trajectories.

All time coefficients are significant. The negative linear and positive quadratic terms imply that all trajectories follow an upward-facing parabola. The probabilities of group membership for the GLM model (derived from the estimated logit parameter) are 0.36 for the first group (HC-LR), 0.34 for the second group (MHC-LR), 0.10 for the third group (MLC) and 0.20 for the final group (LC-LR). Group labels are defined below. Therefore, an individual is more likely to be randomly

Table 2
Trajectory groups estimates: GLM .

	HC-LR		MHC-LR		MLC		LC-LR	
	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error
Constant	-0.527***	(0.007)	-1.220***	(0.008)	-2.150***	(0.009)	-2.716***	(0.011)
t	-0.009***	(0.001)	-0.107***	(0.001)	-0.059***	(0.001)	-0.176***	(0.001)
t^2	0.001***	(0.000)	0.004***	(0.000)	0.002***	(0.000)	0.008***	(0.000)
α	0.445***	(0.001)	0.752***	(0.003)	1.412***	(0.007)	0.520***	(0.001)
$logit(\pi)$			-0.065***	(0.013)	-1.313***	(0.018)	-0.592***	(0.014)

$^{*}p < 0.1$, $^{**}p < 0.05$, $^{***}p < 0.01$.

Table 3
Trajectory groups estimates: Lomax.

Lomax	HC-LR		MHC-LR		MLC-LR		LC-LR	
	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error
Constant	-0.622***	(0.012)	-1.236***	(0.010)	-2.913***	(0.012)	-4.784***	(0.015)
t	-0.008***	(0.001)	-0.058***	(0.001)	-0.073***	(0.001)	-0.098***	(0.002)
t^2	0.001***	(0.000)	0.003***	(0.000)	0.003***	(0.000)	0.004***	(0.000)
$log(q)$	0.548***	(0.005)	0.628***	(0.004)	0.216***	(0.005)	-0.140***	(0.005)
$logit(\pi)$			0.639***	(0.016)	0.410***	(0.016)	-0.657***	(0.021)

$^{*}p < 0.1$, $^{**}p < 0.05$, $^{***}p < 0.01$.

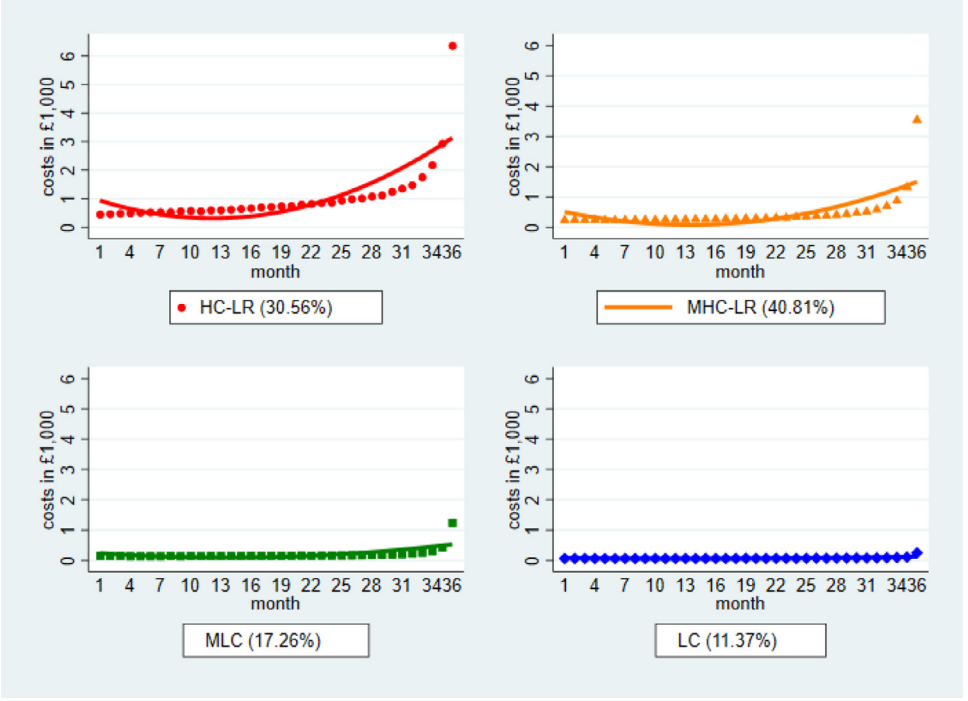

Fig. 1. Trajectory plots Linear.

assigned to the HC-LR group. In contrast, the linear and Lomax models suggest that an individual is more likely to be randomly assigned to the MHC-LR groups (with probability 0.41 and 0.39 respectively).

The average (over the members of each group) monthly costs are plotted for each group over the course of the sample period, and presented in Figs. 1, 2, and 3. We characterise a group as high (HC), medium-high (MHC), medium-low (MLC) or low cost (LC) based on the average costs 36 months before death. At the beginning of the sample period, monthly costs range between £458 and £624 for the high cost groups, £220-£268 for the medium-high cost groups, £93-£155 for the medium-low cost groups, and £40-£63 for the low cost groups. We further characterise groups that exhibit an exponential increase in costs towards the end of life as 'late rise' (LR) groups. Six patterns of cost trajectories emerge across the three

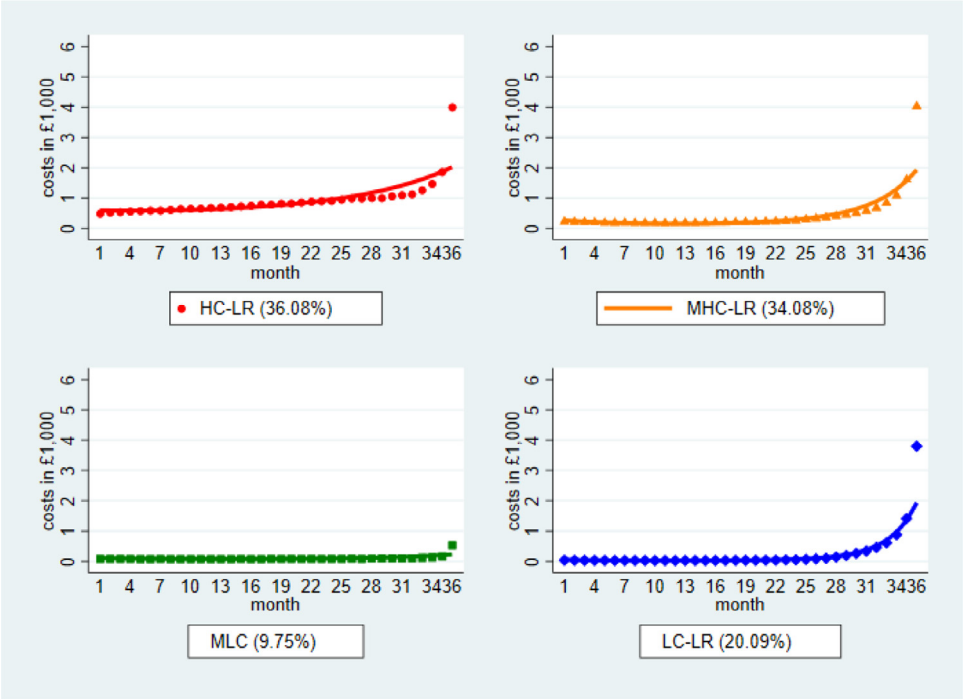

Fig. 2. Trajectory plots GLM.

models: high cost with late rise (HC-LR), medium-high cost with late rise (MHC-LR), medium-low cost with late rise (MLC-LR), medium-low cost (MLC), low cost with late rise (LC-LR), and low cost (LC).

The linear model identifies trajectory groups exhibiting the HC-LR, MHC-LR, MLC, and LC patterns. The average cost over the entire period is £1049 for the HC-LR group, £454 for the MHC-LR group, £207 for MLC group, and £72 for the LC group (see Table A.2). Individuals in the LC group exhibit low costs throughout the 36-month period with costs exceeding significantly the group average only in the final month prior to death (£246). Costs for individuals in the MLC group are relatively stable around £150 in the first two years. From the beginning of the third year, they start increasing gradually exceeding the group's average six months before death (£213) and doubling it one month before death (£426). Although costs jump to £1249 in the last month, overall cost increase is gradual for this group.

Individuals in the HC-LR group have significantly higher costs than those in the other three groups throughout the sample period. Costs for this group increase almost linearly for two and a half years from £458 in the first month to £1126 in month 29. After this point they take off exponentially to reach £2940 one month before death and £6363 in the last month. The MHC-LR group stands between the MLC and HC-LR groups. Individuals in this group have lower costs than those in the HC-LR group (and higher than those in the MLC group) but their trajectory mirrors the trajectory of the HC-LR group. Costs increase steadily for two and a half years until they exceed the group average in month 30 (£471), thereafter they increase steeply reaching £1321 one month before death and £3542 in the last month. An important observation is that the trajectories of the three groups do not intersect. Throughout the 36-month period, average costs for the HC-LR group are higher than average costs for the MHC-LR group which are in turn higher than average costs for the MLC and LC groups.

Like the linear model, the GLM identifies groups that exhibit late rise patterns for the two higher cost groups. The HC-LR and MHC-LR trajectories are very similar across the two models with average monthly costs across the entire period around £1000 for the HC-LR group and around £450 for the MHC-LR group. However, the trajectories of the lowest cost groups identified by the linear and GLM differ significantly. In the linear LC group, average costs remain relatively stable at below £100 until the last month while average costs in the GLM LC-LR group start from £40 but they exponentially increase during the third year, and exceed £3000 in the last month (see Table A.3). This late rise component explains the difference in average monthly costs across the entire period (£72 for the linear vs £255 for the GLM). In both the linear and GLM medium-low cost groups, average costs increase during the last 3 months but this change is not as dramatic as in the high cost groups and therefore these groups are not considered late risers. However, the two groups differ in that average costs are consistently higher in the linear MLC group.

The groups identified by the Lomax model follow similar trajectories with those of the GLM groups for the HC-LR, MHC-LR, and LC-LR groups. The average costs across the entire period are also comparable for these groups across the linear and Lomax models. However, the medium-low cost group for the Lomax model has a late rise component that distinguishes it

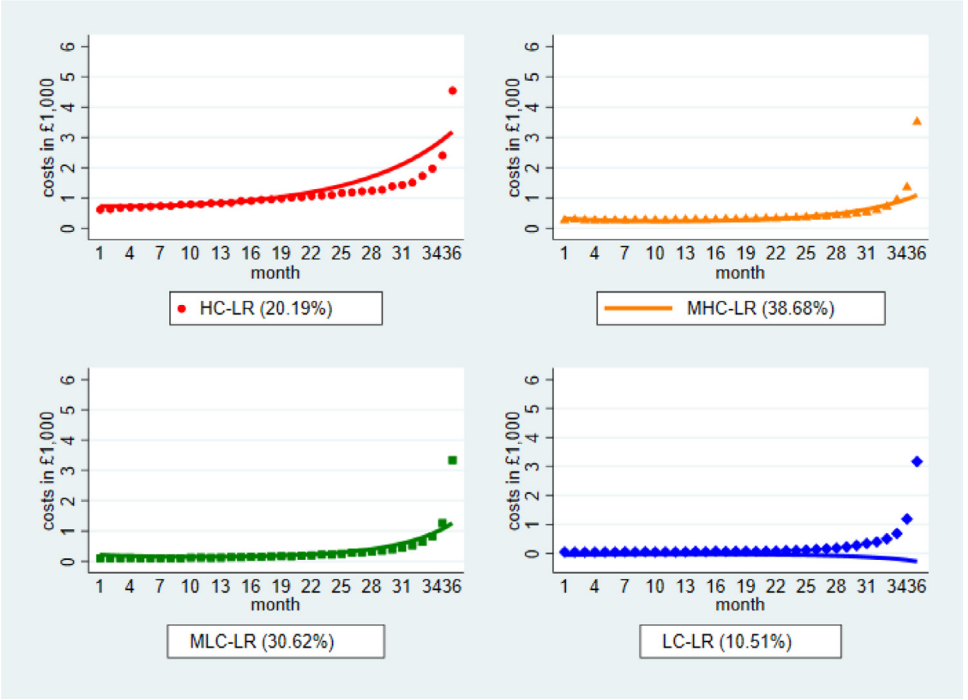

Fig. 3. Trajectory plots Lomax.

Table 4
Overlap of trajectory groups identified by the linear and GLM models.

Linear/GLM	HC-LR	MHC-LR	MLC	LC-LR
HC-LR	10,170 (21.2%)	2978 (6.2%)	0 (0.0%)	1546 (3.2%)
MHC-LR	6780 (14.1%)	8814 (18.3%)	14 (0.0%)	4016 (8.4%)
MLC	397 (0.8%)	4532 (9.4%)	1300 (2.7%)	2069 (4.3%)
LC	1 (0.0%)	65 (0.1%)	3374 (7.0%)	2028 (4.2%)

from the linear and GLM models. Average costs across the entire period are also significantly higher for the Lomax MLC-LR (£350) compared with then linear and GLM MLC groups (see Table A.4).

The sizes of the groups vary significantly across models with Lomax identifying the smallest HC-LR group (20.19%) and the largest medium-low cost group (30.16%). For the GLM model, the HC-LR group consists of 17,348 individuals (36.08%), the MHC-LR group consists of 16,389 individuals (34.08%), and the MLC and LC-LR groups consist of 4688 (9.75%) and 9659 (20.09%) individuals respectively.

Table 4 shows the degree to which the trajectory groups (ordered from high to low costs) identified by the linear and GLM models overlap. Trajectory groups of the same order may reflect similarities in the trajectory patterns (e.g. HC-LR groups) or just similarities in the initial costs (e.g.linear LC-LR group and GLM LC group). Therefore, the overlap between the various groups is only indicative of the degree of agreement in classifying patients across models. About 47% of individuals are identified to groups of the same order by the linear and GLM models. About 59% of patients assigned to the HC-LR group by the GLM model are also assigned to the linear HC-LR group.

5.3. Model selection and diagnostics

To compare the models in terms of quality of predictions, we use three metrics that are commonly used to assess models in the health care expenditure literature (Andersen et al., 2000; Austin et al., 2003; Duan, 1983; Hill and Miller, 2010; Jones et al., 2016). The mean prediction error (MPE), the root mean square error (RMSE), and the mean absolute prediction error

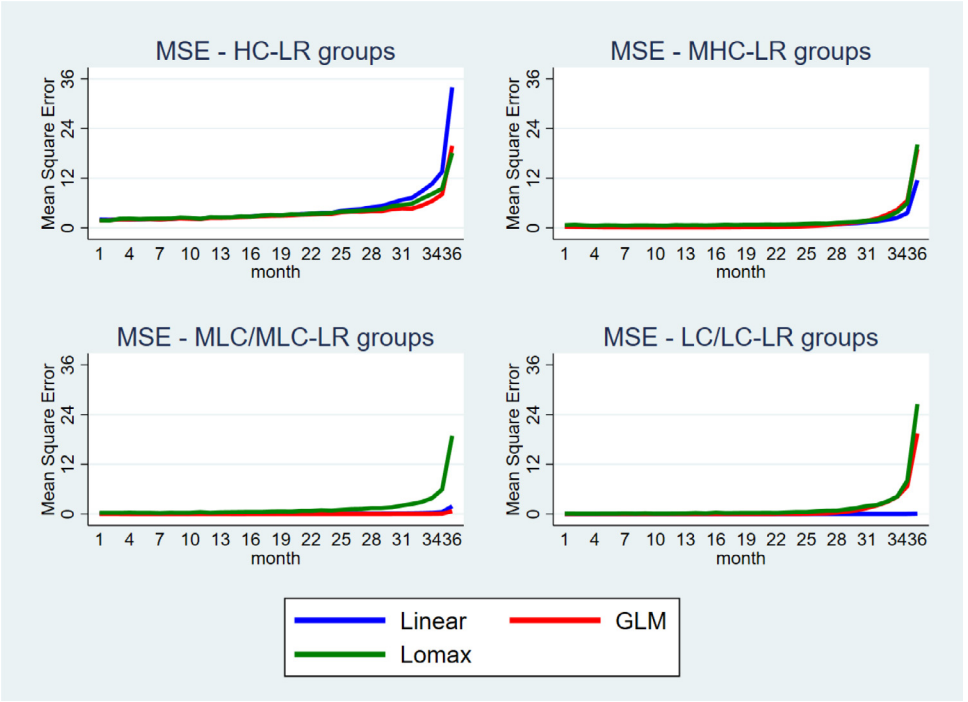

Fig. 4. Mean Square Error.

(MAPE):

$$MPE = \sum_{j=1}^{J}\sum_{i\in j}\sum_{t=1}^{T}\left(y_{it} - \hat{y}_t^j\right)/NT,$$

$$RMSE = \sqrt{\sum_{j=1}^{J}\sum_{i\in j}\sum_{t=1}^{T}\left(y_{it} - \hat{y}_t^j\right)^2}/NT,$$

$$MAPE = \sum_{j=1}^{J}\sum_{i\in j}\sum_{t=1}^{T}\left|y_{it} - \hat{y}_t^j\right|/NT,$$

where $\hat{y}_t^j$ denotes either the mean or median predicted cost for a patient at time t in trajectory group j (calculated using the estimated coefficients for group j). Allocation to group j is based on the maximum posterior probability of membership across the J groups.[7] y_{it} is the corresponding observed cost.

MPE assesses the overall bias. In Figs. 1, 2, and 3, MPE at each month is the difference between the solid and dotted lines (also see A.6 in the appendix). It is clear that the GLM results in significantly lower bias for the first three groups compared to the linear model. The drawback of MPE is that very low bias might be observed in models with low predictive precision when large positive errors are offset by large negative errors.

RMSE and MAPE are measures of predictive accuracy. RMSE promotes unbiased forecasts but penalises more heavily larger errors and therefore it is more sensitive to outliers. The RMSE favours the linear model (1.395) over the GLM (1.409) and the Lomax (1.442) while the MAPE favours the GLM model (0.623) over the Lomax (0.625) and linear (0.644). As the overall RMSE and MAPE do not provide overwhelming support for one of the models, we explore the performance of the models by calculating the mean square error (MSE) and MAPE for each trajectory group and each month. Results are summarised in Figs. 4 and 5 and Table 5. Note that here we count months from the start of our observation period for each individual. Accordingly, month 1 represents the observation at 36 months prior to death, and month 36 is the month of death.

[7] Note, there are alternative ways to define *MPE*, *RMSE*, and *MAPE*. For example, by forming predictions, $\hat{y}_{it}$, based on a weighted average across the J groups at time t, with weights determined by the posterior probability of group $J(j = 1, \ldots, J)$ membership. That is, $\hat{y}_{it} = \sum_{j=1}^{J} P(j|y_{it})\hat{y}_t^j$. Due to the models being able to discriminate between group membership for a given individual, in practice this alternative method of calculating the three metrics leads to negligible differences.

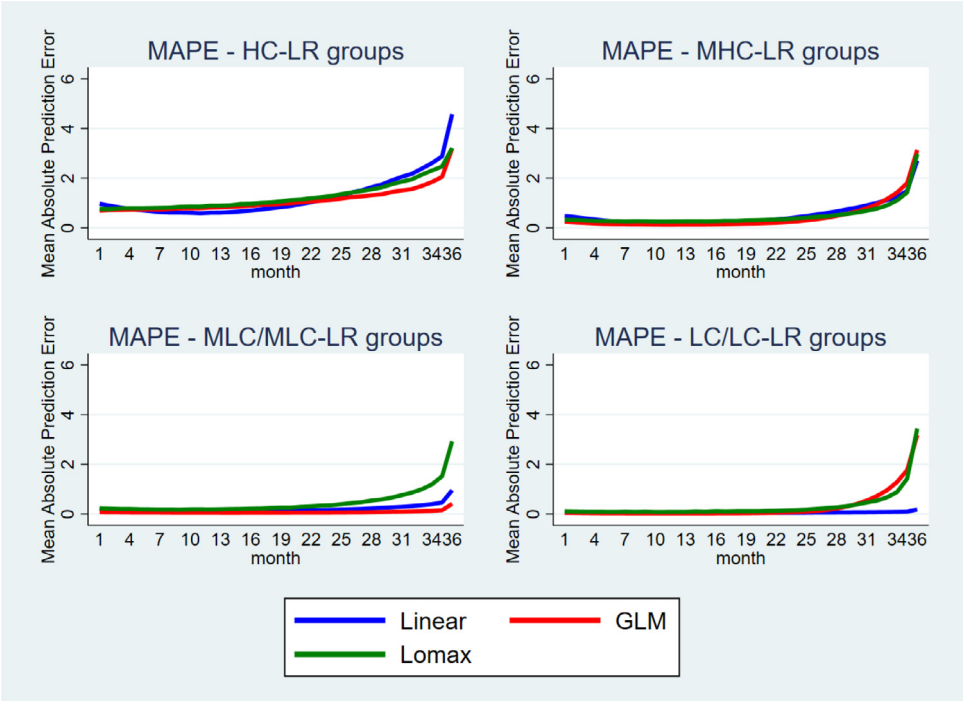

Fig. 5. Mean Absolute Prediction Error.

Table 5
Model comparison: MSE and MAPE.

	MSE			MAPE		
	Linear	GLM	Lomax	Linear	GLM	Lomax
Average in						
HC-LR	4.798	3.700	3.996	1.249	1.119	1.272
MHC-LR	1.099	1.264	1.661	0.538	0.447	0.500
MLC/MLC-LR	0.169	0.033	1.523	0.208	0.077	0.464
LC/LC-LR	0.009	1.083	1.560	0.060	0.294	0.317
Overall	1.945	1.986	2.079	0.644	0.623	0.625

The overall MSE (MAPE) for each model is calculated by adding up the group MSE (MAPE) averages-across-time using group sizes as weights. The square root of the overall MSE is the RMSE.

For the HC-LR groups, the GLM performs significantly better than the linear model in terms of both MSE and MAPE from the beginning of the third year onwards. As a result, the average (across months) MSE and MAPE are larger for the linear model (4.798, 1.249) compared to the GLM (3.700, 1.119). For the MHC-LR groups, the GLM performs better in terms of MSE until month 28. Thereafter, the linear model performs significantly better. As a result, the average MSE across months favours the linear (1.099) over the GLM (1.264) and Lomax (1.661). In terms of MAPE, the GLM is dominant over a longer time period, and it is only in month 33 that the linear performs better. This is reflected in the average across months which favors the GLM (0.447) over the Lomax (0.500) and the linear (0.538). The GLM is a clear winner of the MLC groups as both MSE and MAPE are lower over the entire period while the linear model claims the LC groups as both MSE and MAPE increase exponentially in the last 6 months for the GLM and Lomax models.

To shed more light on model performance, skewness calculated for each trajectory group and each month is presented in Fig. 6. The HC-LR groups identified by the GLM and the linear model exhibit comparable levels of skewness. On the other hand, the LC-LR group identified by the GLM exhibits much higher skewness compared to the LC group identified by the linear model. It appears that the predictive accuracy of the models is a combination of how they slice the data to determine group membership (which affects skewness within groups) and their ability to fit skewed costs. Because the GLM fits skewed data better it outperforms the linear model except where differences in skewness are considerably large. This is the case in the LC-LR/LC groups. The GLM tries to fit a much more skewed LC-LR group - if it was applied to the LC group generated by the linear model it would dominate.

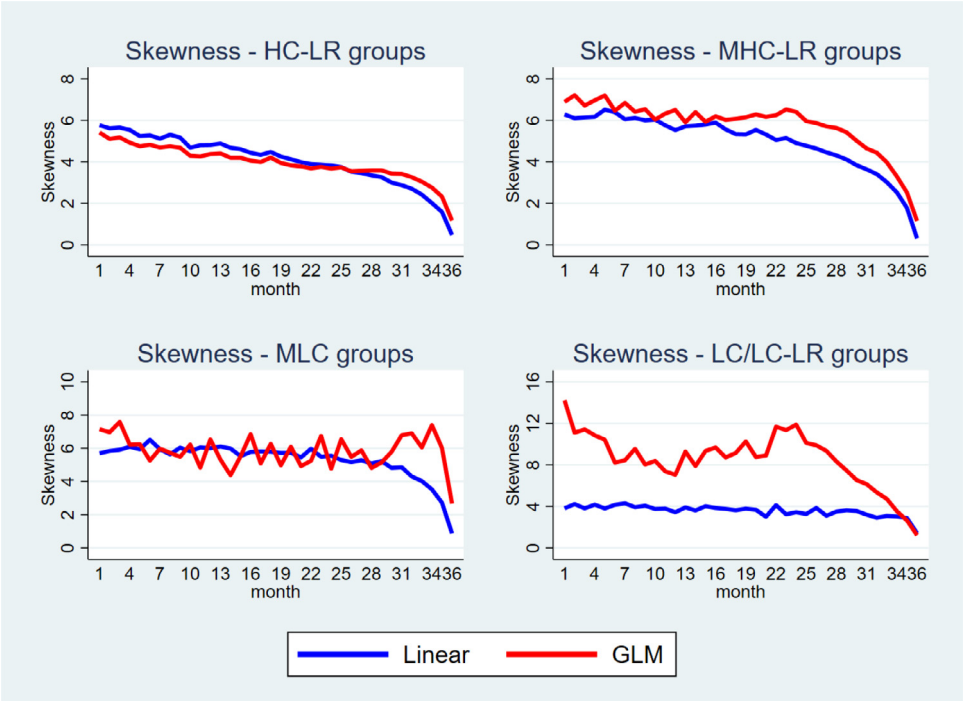

Fig. 6. Skewness.

Differences in skewness can also explain why the GLM performs better in the MHC-LR group until the quarters close to death (the part of the EoL trajectory where differences in skewness are relatively small) while the linear dominates in the months nearer to death.

Across these criteria, our preferred specification is the GLM; it is more flexible (it deals better with skewness), and performs better in the HC-LR category. The only group where the linear model outperforms the GLM is the LC groups. However, this group is of less concern for our analysis since it contains patients for whom cost savings are less likely to be gained.

The capacity of the GLM to accurately identify trajectory groups is assessed in three ways. First, the proportion of the sample that is assigned to a group on the basis of the largest posterior probability is within two decimal places to the estimated probability of group membership (HCLR: 0.36; MHC-LR: 0.34; MLC: 0.10; LC-LR: 0.20). Second, we calculate the average posterior probability (APP) of membership in each group for those individuals who were assigned to the group based on the maximum posterior probability assignment rule. APP approaching 1 implies that all individuals in the group are assigned to the group with certainty. We find APP close to 1 for all groups (HC-LR: 0.98; MHC-LR: 0.96; MLC: 0.97; LC-LR: 0.98). Third, we calculate the odds of correctly classifying individuals into group j on the basis of the maximum posterior probabilities over the odds of correctly classifying individuals into group j based on random assignment as follows:

$$OOC_j = \frac{APP_j/\left(1-APP_j\right)}{\pi_j/\left(1-\pi_j\right)} \tag{8}$$

If the maximum probability assignment rule has no predictive capacity beyond random chance then $OCC_j = 1$. Larger values of OCC_j indicate higher model accuracy with $OCC_j \to \infty$ when the maximum posterior probability rule assigns individuals into groups with certainty, that is, when $APP_j \to 1$. We found large OCC values for all groups (HC-LR: 69; MHC-LR: 43; MLC: 287; LC-LR: 165).

5.4. Understanding the role of relevant covariates

Table A.5 summarises the profiles of individuals in the four groups identified by the GLM. The prevalence of morbidities at the beginning of the three-year period is clearly associated with the relative position of the trajectories. For most morbidities, the percentage of individuals that have a record of the morbidity 36 months before death is the highest in the HC-LR group followed by the MHC-LR, MLC, and LC-LR groups. The incidence for asthma and COPD is particularly low among people in the LC-LR group compared to the other three groups. A remarkable exception is dementia which is recorded in 27.2% of individuals in the MLC group compared to only 6.3% of individuals in the HC-LR group. Deprivation and region are comparable across all groups. Interestingly, individuals in the HC-LR group are on average about 3–4 years younger than

Table 6
Estimates for trajectory group membership: GLM.

	MHC-LR		MLC		LC-LR	
	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error
Constant	-1.977***	(0.132)	-3.625***	(0.198)	0.808***	(0.141)
Age at death	0.023***	(0.001)	0.048***	(0.002)	0.010***	(0.001)
White	-0.106	(0.065)	-1.594***	(0.067)	-1.318***	(0.058)
Male	0.017	(0.024)	-0.324***	(0.038)	0.007	(0.029)
IMD						
Quint 1 (reference)						
Quint 2	-0.002	(0.035)	-0.005	(0.053)	0.037	(0.042)
Quint 3	-0.020	(0.036)	0.039	(0.054)	0.028	(0.043)
Quint 4	0.048	(0.037)	0.010	(0.058)	0.151***	(0.044)
Quint 5	0.011	(0.040)	0.061	(0.061)	0.104**	(0.048)
Morbidities						
Asthma	0.046	(0.033)	-0.207***	(0.055)	-0.842***	(0.054)
Cancer	-0.247***	(0.029)	-0.699***	(0.054)	-1.128***	(0.043)
CHD	-0.046*	(0.027)	-0.072*	(0.042)	-0.505***	(0.038)
CHF	-0.144***	(0.034)	-0.115**	(0.054)	-0.589***	(0.054)
CKD	-0.008	(0.026)	-0.313***	(0.041)	-0.244***	(0.035)
COPD	0.120***	(0.031)	-0.135**	(0.054)	-1.274***	(0.056)
Cerebrovascular dis	0.005	(0.030)	0.081*	(0.044)	-0.520***	(0.043)
Dementia	0.260***	(0.045)	1.428***	(0.049)	-0.147**	(0.057)
Diabetes	0.092***	(0.029)	-0.040	(0.047)	-0.895***	(0.045)
Hypertension	0.122***	(0.026)	-0.084**	(0.039)	-0.349***	(0.030)
Hypothyroidism	0.019	(0.037)	0.076	(0.054)	-0.475***	(0.053)
Peripheral artery dis	-0.131***	(0.037)	-0.183***	(0.064)	-0.468***	(0.059)
Region						
East (ref)						
East Midlands	-0.019	(0.142)	0.155	(0.217)	0.328**	(0.159)
London	-0.156***	(0.052)	-0.401***	(0.083)	-0.271***	(0.063)
North East	-0.083	(0.083)	-0.117	(0.134)	-0.079	(0.101)
North West	0.037	(0.048)	0.019	(0.075)	0.001	(0.058)
South East	0.161***	(0.044)	0.298***	(0.068)	0.201***	(0.052)
South West	0.044	(0.049)	0.244***	(0.074)	-0.017	(0.059)
West Midlands	0.049	(0.050)	0.073	(0.078)	0.050	(0.059)
Yorkshire Humber	-0.030	(0.085)	-0.058	(0.138)	0.028	(0.102)

Estimates capture the effect of a variable on the probability of an individual following each trajectory group relative to membership in the HC-LR group. Note that the interpretation of the estimates are in terms of predicted probabilities, not posterior probabilities that are calculated post-estimation. Estimations based on full sample of 1,731,024 observations (48,084 patients by 36 months). $^{*}p < 0.1$, $^{**}p < 0.05$, $^{***}p < 0.01$.

individuals in the other three groups (age at death is 80.8 for the HC-LR group, 82.7 for the MHC-LR group, 85.6 for the MLC group, and 80.7 for the LC-LR group). This is mainly driven by the low proportion of elderly over 90 years old in the HC-LR group. The individual profiles emerging form the groups identified by the linear and Lomax models are shown in the appendix in Tables A.6 and A.7.

Table 6 reports the estimates for the model with time invariant covariates. Each coefficient estimate measures how this variable influences the probability of membership in the particular trajectory group relative to membership in the HC-LR group. For all trajectory groups, most of the conditions recorded 36 months before death increase the risk for following the HC-LR trajectory. The risk increases the most relative to the LC-LR trajectory and the least relative to the MHC-LR trajectory. This is in line with the profiles shown in Table A.5. A higher proportion of individuals residing in London display a HC-LR trajectory compared to individuals living in the East. Being from an ethnic minority is associated with greater probability of being categorised into the MLC and LC-LR groups relative to the HC-LR and MHC-LR groups. Males are more likely to follow the HC-LR trajectory relative to the MLC and LC-LR trajectories. Older individuals are less likely to follow the HC-LR trajectory. Individuals from the most deprived quintile are less likely to belong to the HC-LR group. For comparison, group membership estimates for the linear and lomax models are presented in the appendix (Tables A.8 and A.9).

To assess the collective impact of morbidities on group membership we consider 13 scenarios involving various combinations of conditions for an 82 year old white male from an area in the South East region of England that falls into the third deprivation quintile. The first scenario assumes that individuals have none of the twelve conditions at the beginning of the three-year period; in scenarios 2–8 individuals have only one condition; in scenario 9 individuals have CHD, diabetes, and hypertension; in scenario 10 individuals have cancer, COPD, and CVD; in scenario 11, individuals have the six conditions in scenarios 9–10; scenario 12 assumes individuals have all conditions but dementia (eleven in total); and scenario 13 assumes individuals have all twelve conditions.

Table 7
Predicted probability of group membership under various scenarios.

Scenarios	HC-LR	MHC-LR	MLC	LC-LR
Randomly chosen individual	0.36	0.34	0.1	0.2
Individual with:				
1: No conditions	0.25	0.24	0.44	0.07
2: Cancer	0.40	0.31	0.23	0.05
3: CHD	0.31	0.29	0.33	0.08
4: COPD	0.35	0.39	0.17	0.08
5: CKD	0.28	0.27	0.39	0.06
6: Diabetes	0.33	0.35	0.24	0.09
7: Hypertension	0.28	0.31	0.34	0.07
8: Dementia	0.20	0.26	0.31	0.23
9: CHD, diabetes, hypertension	0.37	0.43	0.11	0.08
10: Cancer, COPD, CKD	0.48	0.41	0.06	0.04
11: CHD, diabetes, hypertension, cancer, COPD, CVD	0.47	0.48	0.01	0.03
12: All conditions but dementia	0.53	0.44	0.00	0.03
13: All conditions	0.44	0.47	0.00	0.09

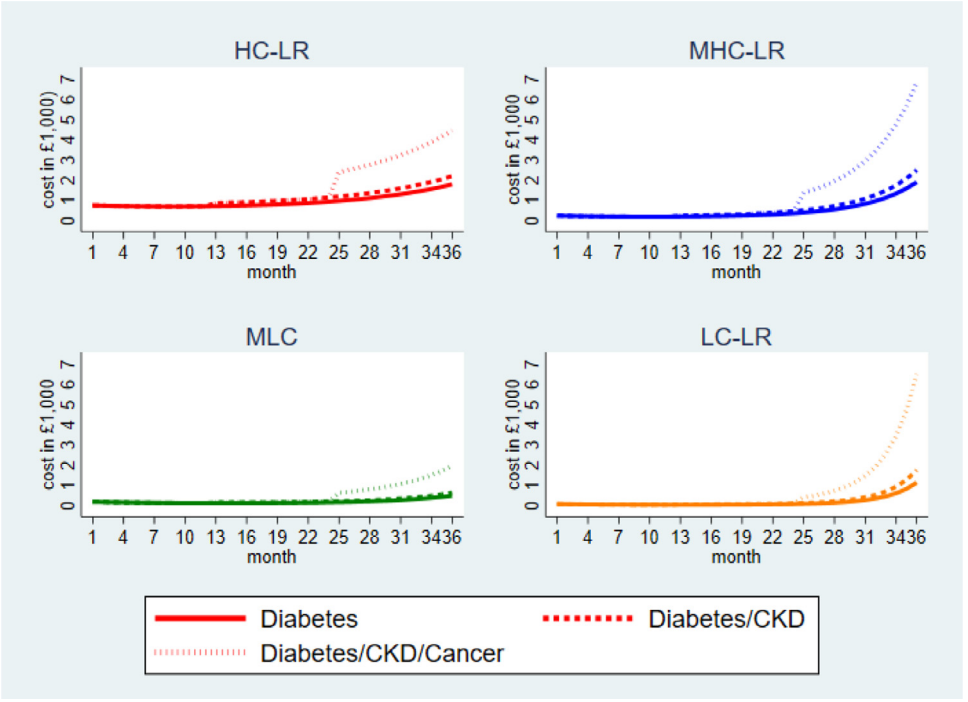

Fig. 7. Impact of time-varying morbidities on trajectories.

Results are presented in Table 7. Scenarios 1–7 show that all conditions except dementia increase the probability of membership to the HC-LR group. Cancer has the largest impact - even larger than CHD, diabetes and hypertension combined (scenario 9). Concurrent presence of morbidities results in more substantial changes in the probability of membership in the HC-LR group as shown in scenarios 10–11. When all morbidities but dementia are present (scenario 12), the shift in the probability of membership in the HC-LR group relative to the no-conditions scenario is dramatic, doubling from 0.25 to 0.53. Dementia is a notable exception to the pattern formed by other conditions. It is alone responsible for increasing the probability of following the LC-LR trajectory from 0.07 to 0.23. This is likely to be due to a large number of dementia patients reside in nursing homes and utilise fewer secondary care services. It has been reported that practices with higher proportions of nursing home patients have lower emergency admissions for dementia and elective admissions (Kasteridis et al., 2015).

The first row in Table 7 shows the estimated probabilities of group membership for a randomly chosen individual. The randomly chosen individual is an 82 year old white male with 2–3 morbidities from an area in South East that falls into the third deprivation quintile, i.e. an individual whose profile is closer to scenario 9. Indeed, the probabilities of group membership under scenario 9 are close to those in the first row of the table.

In addition to affecting the probability of group membership, morbidities may also alter the shape of the group's trajectory. To investigate this, we allow morbidities to enter the trajectory equations as time varying covariates. We assume that after a morbidity is diagnosed for first time, it remains present in all following periods. The estimates from a model that includes three time-varying morbidities: diabetes, CKD, and cancer are presented in A.10 in the appendix.

Figure 7 visualises the impact of the three morbidities. Each graph refers to one of the four trajectory groups. The lines represent three scenarios. In all three, patients are assumed to suffer from diabetes throughout the follow-up period. Under the first scenario (solid lines), they have no other condition. In the second scenario, they are diagnosed with CKD two years before death (dashed lines). In the third scenario, they are diagnosed with CKD two years before death and with cancer one year before death (dotted lines).

Predictions are carried out using the group-specific parameter estimates of the time-varying morbidities corresponding to the above scenarios. The trajectories are identical for all scenarios during the first year of the follow-up period. Focusing on the HC-LR group, those diagnosed with CKD 24 months before death experienced a cost increase (relative to those with no CKD diagnosis) at a rate of 1.23 each month. This translates to a relative increase of £158 at month 13 and £404 at month 36. Comparing the third with the second scenario, a cancer diagnosis at month 25 results in a relative increase in monthly cost at a rate of 2.04 (an increase of £1219 at month 25 and £2262 at month 36).

6. Conclusions

For many individuals, health care expenditure is far greater at the EoL than at any other point in their lifetime. This has often led to the characterisation of EoL expenditure being, in part, wasteful and offering an area where efficiencies may be sought while attempting to maintain quality of care. The literature that has estimated EoL expenditure has tended to treat all decedents equally and has averaged expenditure within specific time intervals in the run up to death to reveal an expenditure profile that is often characterised by a steady increase in expenditure across time followed by a steep rise in the months close to death. It is, however, not difficult to perceive that expenditure profiles at EoL will vary across individuals and that variation is linked to both the characteristics of the individual and the cause of death. For example, a young person who dies from a road traffic accident will not display a health care expenditure profile the same as an elderly individual with chronic conditions who dies after experiencing a remitting and recurrent cancer. Observed heterogeneity across individuals is, therefore, likely to lead to heterogeneity in expenditure profiles. For some individuals, expenditure growth may be fairly stable across the final months and years of life, for others expenditure increases gradually at the EoL, and for others still, there is the usual characterisation of a steep rise in the final months before death. Understanding the shape of expenditure profiles and the characteristics that determine profile membership is important to target the cost-effective use of resources. This might include consideration of optimal patient pathways, particularly for individuals with complex comorbidities; the adoption of new technologies which lower the intensity of care needed, for example, as a result of reducing emergency hospital readmission rates and innovations to the organisation and delivery of care, for example shifting care across settings from inpatient to outpatient, or hospital to primary care. These are likely to prove most effective at reducing the opportunity cost of EoL care, while preserving quality, when aimed at well defined patient groups known to be substantive drivers of overall health care costs.

We employed group based trajectory modeling to explore patterns of EoL expenditure for a diverse range of individuals across a three-year period prior to death. The method assumes that the population is composed of a mixture of distinct groups, each following a unique cost trajectory. That is, heterogeneity in expenditure profiles is modeled as between group heterogeneity. We extend the GBTMs literature by considering two flexible distributions (compared to the Gaussian) to fit better health care cost data: a GLM with log link and gamma distribution and a Lomax distribution. The predictive accuracy of a GBTM depends on how skewed the expenditures are in each trajectory group identified by the model and the model's ability to fit skewed costs. We conclude that the GLM model with log link and gamma error preforms better than the linear and Lomax specifications in terms of RMSE and MAPE.

Our estimates identified four distinct EoL trajectory groups. About 36% of the sample is allocated to the high cost with late rise group. Their monthly expenditures start from £493 36 months before death, increase linearly for about 28 months, and exponentially during the last 10 months of life exceeding £4000 at the month of death. Individuals allocated in the medium-high cost with late rise group (34% of the sample) and the low cost with late rise group (20% of the sample) incur lower costs but they exhibit similar expenditure patterns. For individuals in the medium-low cost group (9.75%), expenditures remain relatively stable over the 3-year period with only a small increase in expenditures during the last 3 months of life.[8]

Health conditions, which were recorded 36 months prior to death, increase the risk of an individual following a higher cost trajectory with cancer having the largest impact. Dementia is a notable exception to this pattern having a very large positive effect on the probability of an individual following a lower cost trajectory. A large number of these patients are in nursing homes and consequently utilise fewer secondary care services. Unfortunately, we lack reliable individual level

[8] Descriptive analysis of expenditures by group (determined on the basis of membership based on posterior probabilities) in each of the health care settings (inpatient, outpatient, A&E, GP visits, drugs and tests) exhibit similar profiles to total costs. Exceptions are outpatient costs where the HC-LR group appears to increase steadily across the duration of the 36 months leading to death, and drug costs for which all profile groups exhibit a late rise at the EoL and for which there is a greater demarcation between the LC-LR and MLC groups.

social care data to fully reflect all the expenditure for dementia patients. Concurrent presence of morbidities results in more substantial changes in the probability of membership in the HC-LR group. We also demonstrate that conditions such as cancer have a large impact on the shape of group trajectories.

Our results illustrate the complex dynamics between ageing, morbidity, and TTD and contribute to the discussion about their relative importance. The time variables in the specifications of trajectory groups capture TTD. As death approaches, expenditures increase for all groups but the effect of TTD varies significantly across groups as shown by the distinct trajectory shapes. Our results also suggest that the trajectory groups differ with regard to the morbidity profiles, which confirms that the importance of TTD in determining expenditures is closely related to morbidity.

Healthy ageing hypotheses play an important role in explaining heterogeneity in health care expenditures along with age, morbidity and time to death. The expansion of morbidities hypothesis states that medical progress and improvements in socioeconomic conditions increase survival probabilities but that the impact on the incidence and onset of chronic conditions is limited. As a result, extending life will result in more years lived in ill health, which is consistent with persistent cost trajectories. On the other hand, the compression of morbidities hypothesis assumes that medical progress increases life expectancy but at the same time, it postpones the onset of serious chronic conditions by a larger number of years. This is consistent with cost trajectories where high expenditures emerge close to death. At the population level, the trajectory of health expenditures depends on which healthy ageing hypothesis holds true. Over time and as life expectancy increases, the health cost trajectory of the population may remain unchanged (dynamic equilibrium), or change (compression or expansion of morbidities hypothesis). While this is not testable within our analytical framework, our results suggest that the population can be divided in group of patients whose cost trajectories resemble those that are consistent with the compression of morbidities hypothesis (for example, low cost late risers) and other groups whose cost trajectories are similar to those implied by the expansion of morbidities hypothesis (moderate low cost). Other profile groups are more nuanced in supporting one of the two hypotheses over the other. The relative proportions of individuals within profiles supportive of a compression or expansion of morbidity will have profound consequences for long-term projections of health care needs and associated expenditure growth.

In addition to age, TTD, morbidities, and demographics that are taken into account in our empirical model, non-demographic and non-health related drivers may also be significant determinants of health care expenditures. For instance, Laudicella et al. (2020) found that technological progress and changes in medical practice can explain about 60% of the increment in health care expenditure in Denmark over a period of roughly 10 years. However, we expect that their role should be weaker over the shorter period of 3 years. Unobserved characteristics such as physician beliefs and patient preferences could also explain membership to specific trajectories but likely negligible impact on the shape of trajectories. Conceptually, the predictors of trajectory group membership are time stable and do not carry information about the specific form of the trajectory over time.

The identification of distinct expenditure profiles at EoL raises the possibility of the better targeting of individuals (or their trajectory groups) that may be more amenable to efficiency gains. The majority of the decedents in our sample exhibit profiles that are best characterised by either high cost with late rise, or medium-high costs with late rise. Unsurprisingly, the occurrence of multiple comorbidities raises the risk of membership to these profile groups. Such patients are known to have greater contact with health services (Marengoni et al., 2011), and are increasingly relevant in explaining the rise in expenditure for admitted care services (Aragon and Rice, 2021).

A research focus on multimorbidity has gained much traction (Whitty et al., 2020). Related to this is a need to classify multiple comorbidity into useful clusters of conditions that are meaningful in terms of their health care resources implications. Our research strengthens claims that a productive avenue for research is to consider clusters of conditions defined not on population prevalence but on the costs they generate in care setting (Stokes et al., 2021).

When considering potential areas for expenditure savings, EoL care is an obvious target due to the additional costs this often entails. It is important, however, to recognise heterogeneity in EoL expenditure and how different requirements for care lead to different expenditure trajectories in the run-up to death. Identifying and understanding health care expenditure patterns in the years preceding death enables policy makers to develop better strategies to mitigate costs without compromising EoL care quality. For example, policies to achieve cost savings in the treatment of chronic conditions associated with persistent use of care, may free resources that can be used to support high quality terminal care (e.g palliative care) during the last few months of life. Such strategies will not only be ethically acceptable but will also represent an efficient use of resources.

Declaration of Competing Interest

The authors Panagiotis Kasteridis, Nigel Rice, and Rita Santos declare no competing interests.

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We use data from the Clinical Practice Research Datalink obtained under licnese from the UK Medicines and Healthcare products Regulatory Agency. The data is provided by patients and collected by the NHS as part of their care and support. The interpretation and conclusions contained in this study are those of the authors alone.

This project was undertaken on the Data Safe Haven, which is an ISO 27001 certified environment for handling sensitive data and is provided by the University of York. We are grateful for support by the York Data Safe Haven team and the research Computing team.

Appendix A

A1. Costing health care activity

A1.1. Primary care activity

For each individual we identified primary care activity since 36 months before death from CPRD data. We used Read codes to identify three types of primary care activity: consultations, drugs prescribed, and diagnostic tests.

Consultations We considered multiple consultations in a day for a patient to a single staff member as duplicates, but allowed for consultations to different staff members on the same day. We costed each consultation as the product of the consultation duration times the cost per minute of consultation.

The CPRD visit duration variable is based on the time that a patient's electronic record is open for use by a member of practice staff, and our use of this variable assumed that GPs and nurses would open the electronic file when they were about to see the patient and close it at the end of the consultation. We capped the maximum duration at 120 min, assuming that this reflected a file being left open but without ongoing patient care.

Table A.1
Descriptive statistics.

Variable	N patients	(%)
Age at death		
60–69 (ref)	6423	13
70–79	11,525	24
70–89	18,545	39
>=90	11,591	24
White	45,218	94
Male	22,757	47
IMD		
Quint 1 (ref)	9856	20
Quint 2	10,753	22
Quint 3	10,538	22
Quint 4	9016	19
Quint 5	7921	16
Morbidities		
Asthma	7149	15
Cancer	7907	16
CHD	13,258	28
CHF	6392	13
CKD	14,231	30
COPD	7946	17
Cerebrovascular dis	8696	18
Dementia	4447	9
Diabetes	8976	19
Hypertension	30,127	63
Hypothyroidism	5135	11
Peripheral artery dis	4717	10
Region*		
East (ref)	4243	9
East Midlands	360	1
London	5241	11
North East	1168	2
North West	8451	18
South East	13,990	29
South West	7187	15
West Midlands	6360	13
Yorkshire Humber	1084	2

The table shows the number and percentage of patients for each of the covariates. *Region denotes the Strategic Health Authority for practices within England

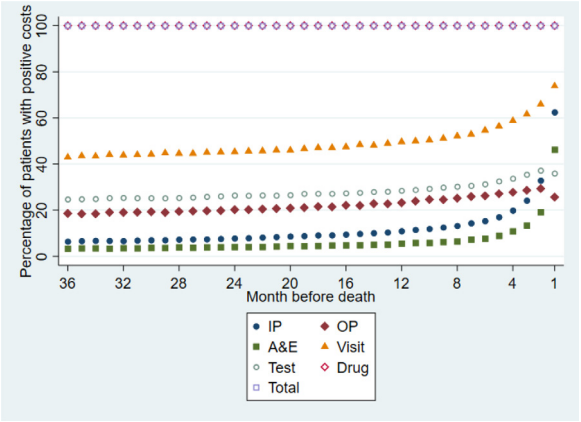

Fig. A.1. Percentage of patients with positive costs by month and setting The figure shows the percentage of patients with positive cost for each health care setting and each of the 36 months prior to death.

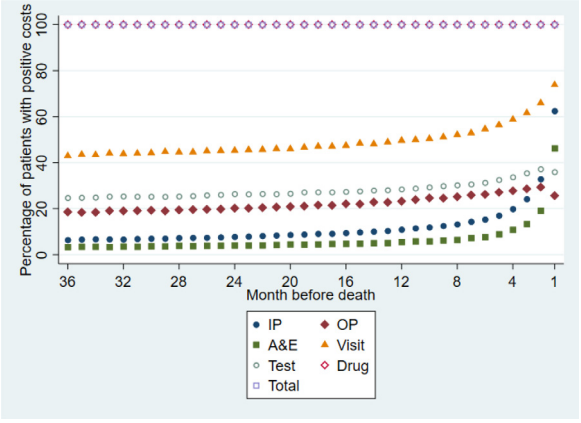

Fig. A.2. Average costs by month and setting: inpatient, drug and total The figure shows the average costs for each of the 36 months prior to death for inpatients, drug and total costs.

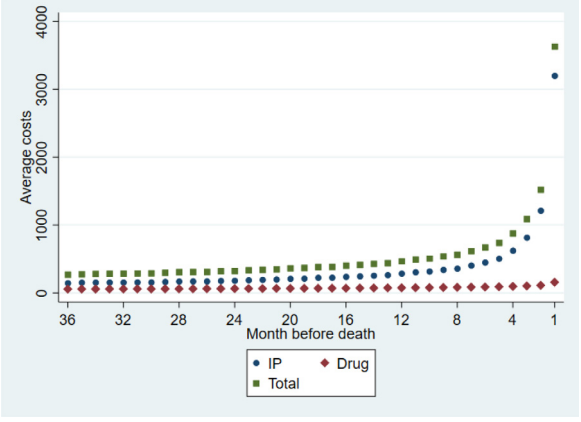

Fig. A.3. Average costs by month and setting: outpatient, A&E, GP visits and tests The figure shows the average costs for each of the 36 months prior to death for outpatients, A&E, GP visits and diagnostic tests.

Table A.2
Average monthly costs by trajectory group: Linear.

	Linear			
	HC-LR	MHC-LR	MLC	LC
N	14,694	19,624	8298	5468
Month				
1	458	235	155	63
2	474	248	148	61
3	490	244	149	61
4	497	247	145	62
5	519	235	145	59
6	531	235	142	60
7	533	235	144	61
8	540	243	150	61
9	571	249	141	60
10	584	241	150	60
11	573	254	145	60
12	603	255	150	61
13	611	259	151	61
14	627	267	147	60
15	652	266	150	62
16	673	270	157	61
17	706	279	156	63
18	721	278	156	64
19	747	295	156	65
20	756	295	161	64
21	802	298	164	63
22	824	313	160	65
23	864	314	166	65
24	870	335	167	64
25	944	348	172	67
26	995	371	178	71
27	1023	385	180	70
28	1088	407	188	72
29	1126	438	192	73
30	1252	471	204	76
31	1362	517	213	75
32	1481	585	235	80
33	1764	695	263	85
34	2188	877	313	92
35	2940	1321	426	106
36	6363	3542	1249	246
1 to 36	1049	454	207	72

The table shows the average monthly costs for each trajectory group. Individuals are classified into trajectory groups based on the highest posterior probability of group membership. Month 1 represents the beginning of the observation period for an individual, that is 36 months prior to death. Month 36 is the month of death.

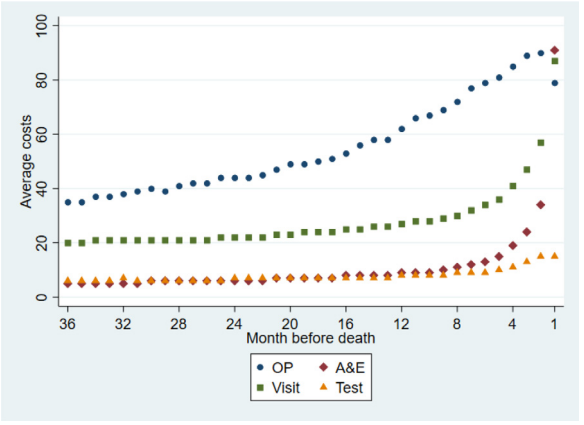

Fig. A.4. Average cost by setting across conditions The figure shows the average costs for each health care setting by diagnostic condition.

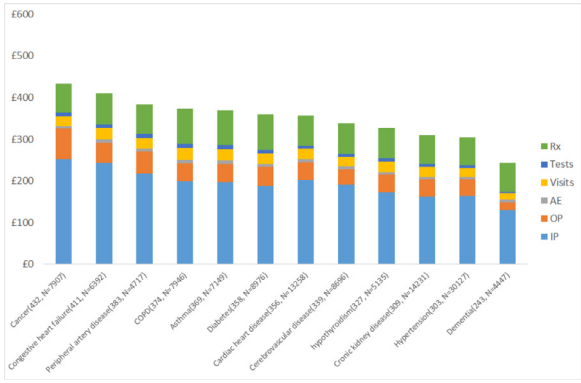

Fig. A.5. Costs by setting across age groups The figure shows the average costs for each health care setting by age group.

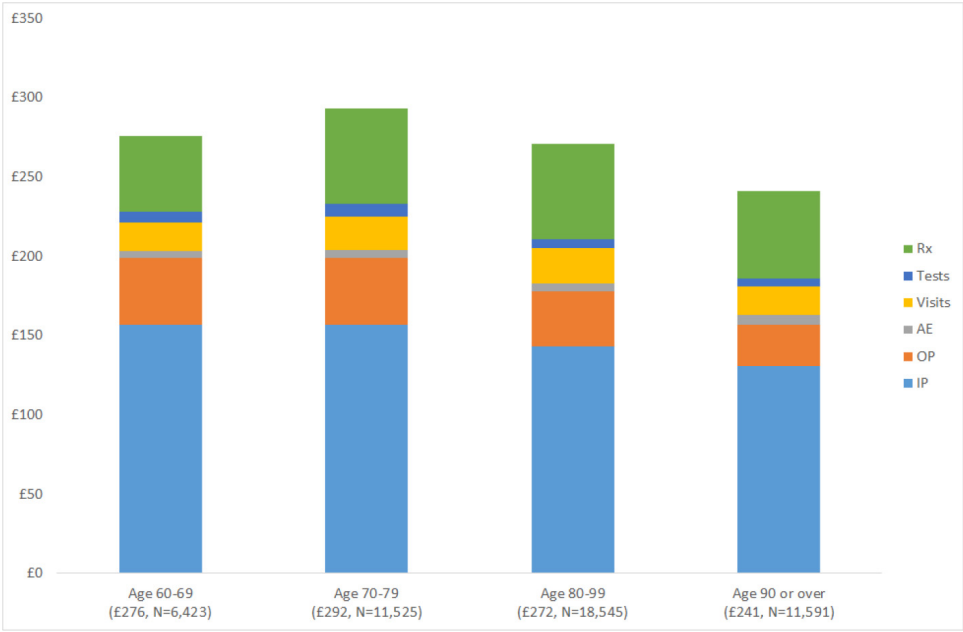

Fig. A.6. Mean Prediction Error.

Costs per minute of consultations conducted by doctors (e.g. salaried partner, senior partner, associate, locum) and by nurses (e.g. practice nurse, community nurse, midwife) were obtained from the Personal Social Services Research Unit (PSSRU) unit costs (Curtis, 2014).

The cost of £3.60 per minute of patient contact for GPs included travel and qualification costs but excluded direct care staff costs since we were separately accounting for these through counting nurse visits separately. The cost of £0.88 per minute of patient contact for practice nurses included qualification costs.

Tests Utilisation volume of each test was taken from Read terms recorded in the Test section of the CPRD dataset. These were classified into groups that corresponded to the NHS Reference Costs categories using the classification proposed in Ride et al. (2020). National average unit costs for diagnostic tests were taken from the NHS Reference Costs[9] (Health, 2014).

Prescriptions We costed all prescriptions included in the therapy section of the CPRD dataset. Prescription costs were taken from the Prescription Costs Analysis (PCA) published by NHS Digital.[10] PCA provides details of the net ingredient cost (NIC) of all prescriptions dispensed in the community in England listed by British National Formulary (BNF) therapeutic class (Committee, 2013). NIC is the price listed in the national Drug Tariff. It is the basic cost of the drug and does not include any contract prices or discounts, dispensing fees, or adjustment for income. We identified about 15 million drug prescriptions in CPRD for the population and period of interest. About 79% of them were matched with PCA cost files at subparagraph level (the most detailed hierarchy level). The remaining were matched at the most specific BNF level available: paragraph (9%), section (12%), chapter (0.1%).

A1.2. Hospital activity

Linked HES data were used to identify episodes of inpatient, outpatient, and A&E activity. These were costed via Healthcare Resource Groups (HRGs) and the Reference Cost Grouper software for the relevant financial year.

Inpatient activity (core, high cost, and long stay) All episodes of care were assigned to one of more than 2000 core HRGs based on the clinical and demographic information of the patient. In the grouping process, procedures (OPCS codes) are ranked based on severity (5 up to 40). HRG allocation is determined by the procedure with the highest hierarchy value. If no procedure codes with hierarchy value 5 or more is recorded, the HRG is determined by the diagnosis code (ICD-10 code) with the highest value.

Separate unbundled HRGs were assigned to episodes with high cost elements of treatment such as high cost procedures, chemotherapy, diagnostic imaging, and high cost drugs.

HRGs may contain episodes with much higher length of stay than the average episode in the group. To deal with these long-stay outliers an upper trimming point was calculated by adding 1.5 times the inter-quartile range to the third quartile. Any day exceeding the upper trim point is reimbursed at the excess bed days rate.

Costs of the core, unbundled and excess bed day activity were taken from the hospital reported Reference Costs (RC). All NHS hospitals report RCs for each HRG broken down by setting (eg. general surgery) and type of activity (day-case, elective, non-elective). As our research does not relate to the variation in costs across hospitals or settings, we aggregated RCs only by HRGs and type of activity. Unbundled costs were aggregated on the HRG level only.

A&E and outpatient activity A&E activity was grouped similarly to inpatient activity with the exception that the clinical information needed for grouping comes from treatment and investigation codes rather than procedure and diagnosis codes.

Costing HES outpatient activity differs in that RCs for non-procedural activity (outpatient activity for which no procedure is recorded) are separated into RCs for consultant led and non-consultant led activity. However, this separation of activity requires consultant codes, which were not available to us. Instead, we took a weighted average of consultant led and non-consultant led RCs for each known HRG, which we used to match to HES outpatient activity.

[9] Reference costs are the average unit costs to National Health Service trusts and NHS foundation trusts of providing defined services in a given financial year to NHS patients.

[10] https://digital.nhs.uk/data-and-information/publications/statistical/prescription-cost-analysis.

Table A.3
Average monthly costs by trajectory group: GLM.

	GLM			
	HC-LR	MHC-LR	MLC	LC-LR
N	17,348	16,389	4688	9659
Month				
1	493	220	93	40
2	527	212	91	35
3	543	206	91	34
4	565	192	89	34
5	581	181	88	31
6	594	178	87	29
7	594	181	89	31
8	617	176	87	30
9	644	178	86	29
10	654	174	86	29
11	660	172	86	29
12	683	176	88	29
13	693	178	87	30
14	716	176	85	30
15	733	181	89	30
16	754	186	88	31
17	786	191	88	32
18	790	198	91	34
19	822	206	89	36
20	828	209	90	38
21	861	220	89	39
22	886	227	91	43
23	906	243	89	49
24	916	261	91	52
25	957	294	91	66
26	994	321	97	84
27	993	355	94	102
28	1009	404	100	140
29	1005	449	101	192
30	1067	501	107	261
31	1101	576	109	340
32	1131	674	116	457
33	1266	839	125	612
34	1477	1080	137	879
35	1870	1606	174	1414
36	4006	4027	540	3801
1 to 36	937	440	109	255

The table shows the average monthly costs for each trajectory group. Individuals are classified into trajectory groups based on the highest posterior probability of group membership. Month 1 represents the beginning of the observation period for an individual, that is 36 months prior to death. Month 36 is the month of death.

Table A.4
Average monthly costs by trajectory group: Lomax.

	Lomax			
	HC-LR	MHC-LR	MLC-LR	LC-LR
N	9708	18,599	14,724	5053
Month				
1	624	268	115	46
2	639	283	116	42
3	684	270	115	40
4	703	263	121	42
5	713	265	115	44
6	728	266	115	42
7	743	261	113	52
8	745	275	117	45
9	790	277	114	55
10	804	267	128	45
11	807	266	130	48
12	840	279	126	48
13	843	282	133	50
14	856	284	141	66
15	908	278	144	55
16	915	285	154	74
17	954	301	156	63
18	965	294	170	71
19	992	310	181	72
20	1019	310	175	67
21	1035	320	201	76
22	1077	320	212	79
23	1089	330	233	92
24	1108	346	231	99
25	1174	362	258	113
26	1195	387	289	138
27	1230	390	303	160
28	1250	421	343	182
29	1277	446	362	218
30	1395	480	401	274
31	1439	530	461	339
32	1516	593	535	396
33	1737	714	646	503
34	1982	934	841	686
35	2412	1352	1268	1188
36	4554	3505	3350	3167
1 to 36	1160	473	350	244

The table shows the average monthly costs for each trajectory group. Individuals are classified into trajectory groups based on the highest posterior probability of group membership. Month 1 represents the beginning of the observation period for an individual, that is 36 months prior to death. Month 36 is the month of death.

Table A.5
Trajectory group profiles: GLM.

	HC-LR	MHC-LR	MLC	LC-LR
Age at death				
60–69 (ref)	0.151	0.097	0.075	0.193
70–79	0.270	0.234	0.167	0.231
70–89	0.377	0.424	0.375	0.340
>=90	0.202	0.245	0.384	0.236
White	0.967	0.965	0.880	0.879
Male	0.499	0.475	0.351	0.483
IMD				
Quint 1 (ref)	0.202	0.205	0.212	0.206
Quint 2	0.221	0.223	0.226	0.228
Quint 3	0.219	0.217	0.234	0.216
Quint 4	0.186	0.190	0.174	0.193
Quint 5	0.171	0.164	0.154	0.159
Morbidities				
Asthma	0.175	0.180	0.128	0.059
Cancer	0.214	0.174	0.106	0.087
CHD	0.315	0.309	0.270	0.152
CHF	0.158	0.149	0.138	0.059
CKD	0.317	0.334	0.281	0.201
COPD	0.198	0.206	0.134	0.053
Cerebrovascular dis	0.189	0.201	0.236	0.104
Dementia	0.063	0.088	0.272	0.066
Diabetes	0.213	0.221	0.178	0.085
Hypertension	0.648	0.681	0.632	0.492
Hypothyroidism	0.112	0.118	0.133	0.065
Peripheral artery dis	0.121	0.108	0.082	0.049
Region				
East (ref)	0.090	0.087	0.084	0.089
East Midlands	0.007	0.007	0.007	0.009
London	0.124	0.104	0.090	0.100
North East	0.027	0.024	0.020	0.022
North West	0.184	0.179	0.158	0.165
South East	0.265	0.295	0.321	0.318
South West	0.148	0.150	0.174	0.140
West Midlands	0.131	0.133	0.126	0.136
Yorkshire Humber	0.024	0.022	0.019	0.022

The table shows the prevalence of each of the individual characteristics across the four trajectory groups. For example, 49.9% of individuals in the HC-LR group are male, only 35.1% are male in the MLC group.

Table A.6
Trajectory group profiles: Linear.

	HC-LR	MHC-LR	MLC	LC
Age at death				
60–69 (ref)	0.171	0.113	0.111	0.142
70–79	0.297	0.224	0.213	0.182
70–89	0.373	0.406	0.392	0.338
>=90	0.158	0.257	0.285	0.339
White	0.965	0.965	0.947	0.776
Male	0.519	0.471	0.451	0.392
IMD				
Quint 1 (ref)	0.205	0.203	0.209	0.205
Quint 2	0.218	0.225	0.230	0.226
Quint 3	0.216	0.218	0.219	0.232
Quint 4	0.189	0.190	0.182	0.184
Quint 5	0.172	0.165	0.159	0.154
Morbidities				
Asthma	0.177	0.150	0.135	0.091
Cancer	0.207	0.164	0.141	0.085
CHD	0.311	0.275	0.261	0.206
CHF	0.153	0.134	0.118	0.100
CKD	0.313	0.307	0.287	0.222
COPD	0.195	0.174	0.146	0.084
Cerebrovascular dis	0.174	0.183	0.184	0.188
Dementia	0.039	0.081	0.121	0.234
Diabetes	0.222	0.183	0.168	0.133
Hypertension	0.653	0.634	0.611	0.552
Hypothyroidism	0.110	0.108	0.101	0.102
Peripheral artery dis	0.122	0.097	0.086	0.058
Region				
East (ref)	0.094	0.087	0.082	0.089
East Midlands	0.007	0.008	0.008	0.007
London	0.133	0.103	0.085	0.102
North East	0.025	0.026	0.021	0.021
North West	0.179	0.181	0.174	0.150
South East	0.248	0.298	0.331	0.322
South West	0.150	0.144	0.154	0.161
West Midlands	0.142	0.129	0.124	0.130
Yorkshire Humber	0.022	0.025	0.021	0.019

The table shows the prevalence of each of the individual characteristics across the four trajectory groups. For example, 51.9% of individuals in the HC-LR group are male, only 45.1% are male in the MLC group.

Table A.7
Trajectory group profiles: Lomax.

	HC-LR	MHC-LR	MLC-LR	LC-LR
Age at death				
60–69 (ref)	0.167	0.092	0.116	0.273
70–79	0.325	0.223	0.204	0.240
70–89	0.381	0.426	0.371	0.289
>=90	0.127	0.258	0.309	0.198
White	0.960	0.960	0.939	0.835
Male	0.520	0.465	0.437	0.520
IMD				
Quint 1 (ref)	0.206	0.205	0.207	0.198
Quint 2	0.215	0.218	0.232	0.235
Quint 3	0.213	0.222	0.222	0.213
Quint 4	0.185	0.187	0.189	0.188
Quint 5	0.180	0.168	0.150	0.166
Morbidities				
Asthma	0.236	0.183	0.086	0.037
Cancer	0.276	0.172	0.113	0.071
CHD	0.365	0.323	0.228	0.073
CHF	0.186	0.160	0.100	0.025
CKD	0.355	0.335	0.272	0.109
COPD	0.272	0.213	0.081	0.031
Cerebrovascular dis	0.199	0.218	0.164	0.058
Dementia	0.041	0.112	0.118	0.044
Diabetes	0.293	0.221	0.126	0.034
Hypertension	0.705	0.678	0.613	0.324
Hypothyroidism	0.132	0.127	0.092	0.029
Peripheral artery dis	0.145	0.113	0.074	0.025
Region				
East (ref)	0.091	0.088	0.086	0.094
East Midlands	0.008	0.007	0.008	0.007
London	0.141	0.103	0.094	0.114
North East	0.029	0.025	0.023	0.019
North West	0.191	0.183	0.165	0.152
South East	0.248	0.285	0.319	0.313
South West	0.143	0.157	0.150	0.135
West Midlands	0.126	0.132	0.133	0.142
Yorkshire Humber	0.024	0.022	0.021	0.025

The table shows the prevalence of each of the individual characteristics across the four trajectory groups. For example, 52% of individuals in the HC-LR group are male, only 43.7% are male in the MLC-LR group.

Table A.8
Estimates for trajectory group membership: Linear.

	HC-LR		MLC		LC	
	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error
Constant	2.241***	(0.126)	-0.744***	(0.149)	0.317*	(0.171)
Age at death	-0.034***	(0.001)	0.005***	(0.002)	0.008***	(0.002)
White	0.126**	(0.062)	-0.474***	(0.065)	-2.159***	(0.054)
Male	0.048**	(0.024)	-0.043	(0.028)	-0.201***	(0.035)
IMD						
Quint 1 (ref)						
Quint 2	-0.065*	(0.035)	0.004	(0.041)	0.006	(0.050)
Quint 3	-0.055	(0.035)	-0.001	(0.041)	0.081	(0.050)
Quint 4	-0.110***	(0.037)	-0.034	(0.044)	0.024	(0.053)
Quint 5	-0.097**	(0.039)	0.008	(0.047)	0.031	(0.057)
Morbidities						
Asthma	0.143***	(0.033)	-0.031	(0.042)	-0.293***	(0.057)
Cancer	0.287***	(0.029)	-0.154***	(0.038)	-0.607***	(0.055)
CHD	0.125***	(0.028)	-0.001	(0.033)	-0.094**	(0.042)
CHF	0.156***	(0.035)	-0.079*	(0.044)	-0.026	(0.056)
CKD	0.090***	(0.027)	-0.079**	(0.032)	-0.338***	(0.041)
COPD	0.005	(0.032)	-0.142***	(0.041)	-0.523***	(0.058)
Cerebrovascular dis	0.004	(0.031)	-0.005	(0.036)	0.039	(0.043)
Dementia	-0.588***	(0.053)	0.400***	(0.045)	1.214***	(0.045)
Diabetes	0.133***	(0.029)	-0.051	(0.037)	-0.277***	(0.048)
Hypertension	0.115***	(0.026)	-0.073**	(0.030)	-0.204***	(0.035)
Hypothyroidism	0.065*	(0.037)	-0.096**	(0.045)	-0.028	(0.054)
Peripheral artery dis	0.173***	(0.038)	-0.036	(0.049)	-0.174***	(0.067)
Region						
East (ref)						
East Midlands	-0.148	(0.135)	0.095	(0.160)	-0.005	(0.202)
London	0.209***	(0.050)	-0.160**	(0.065)	-0.195**	(0.076)
North East	-0.146*	(0.081)	-0.145	(0.102)	-0.036	(0.123)
North West	-0.128***	(0.047)	0.040	(0.057)	-0.077	(0.070)
South East	-0.269***	(0.044)	0.157***	(0.052)	0.126**	(0.062)
South West	0.004	(0.048)	0.134**	(0.058)	0.194***	(0.069)
West Midlands	0.017	(0.049)	0.017	(0.060)	0.053	(0.072)
Yorkshire Humber	-0.190**	(0.084)	-0.099	(0.103)	-0.092	(0.127)

The table shows the coefficients and standard errors for the effect covariates on trajectory group membership. All estimates are contrasted against the baseline group of MHC-LR. * denotes significance at 10% level, ** at the 5% level and *** at the 1% level.

Table A.9
Estimates for trajectory group membership: Lomax.

	HC-LR		MHC-LR		MLC-LR	
	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error
Constant	-0.574***	(0.199)	-3.468***	(0.180)	-3.111***	(0.177)
Age at death	-0.030***	(0.002)	0.021***	(0.002)	0.027***	(0.002)
White	1.541***	(0.078)	1.440***	(0.065)	0.986***	(0.059)
Male	-0.089**	(0.042)	-0.122***	(0.038)	-0.170***	(0.038)
IMD						
Quint 1 (ref)						
Quint 2	-0.225***	(0.061)	-0.195***	(0.056)	-0.095*	(0.055)
Quint 3	-0.208***	(0.063)	-0.092	(0.057)	-0.036	(0.057)
Quint 4	-0.333***	(0.065)	-0.180***	(0.059)	-0.050	(0.059)
Quint 5	-0.385***	(0.069)	-0.234***	(0.063)	-0.159**	(0.063)
Morbidities						
Asthma	1.566***	(0.087)	1.352***	(0.085)	0.736***	(0.088)
Cancer	1.993***	(0.066)	1.288***	(0.064)	0.673***	(0.067)
CHD	1.232***	(0.069)	1.104***	(0.066)	0.834***	(0.066)
CHF	1.274***	(0.112)	1.105***	(0.110)	0.820***	(0.111)
CKD	0.833***	(0.060)	0.627***	(0.057)	0.484***	(0.057)
COPD	2.307***	(0.094)	2.104***	(0.092)	1.060***	(0.096)
Cerebrovascular dis	1.033***	(0.075)	1.023***	(0.071)	0.709***	(0.072)
Dementia	0.285***	(0.099)	1.079***	(0.083)	1.014***	(0.082)
Diabetes	2.258***	(0.094)	1.973***	(0.092)	1.321***	(0.094)
Hypertension	1.172***	(0.045)	1.006***	(0.040)	0.858***	(0.040)
Hypothyroidism	1.546***	(0.103)	1.409***	(0.099)	1.057***	(0.100)
Peripheral artery dis	0.909***	(0.107)	0.756***	(0.104)	0.550***	(0.106)
Region						
East (ref)						
East Midlands	0.003	(0.243)	-0.059	(0.225)	0.279	(0.216)
London	0.383***	(0.088)	0.032	(0.082)	-0.056	(0.082)
North East	0.385**	(0.154)	0.281*	(0.145)	0.314**	(0.145)
North West	0.163*	(0.084)	0.185**	(0.077)	0.192**	(0.077)
South East	-0.196**	(0.076)	0.001	(0.069)	0.132*	(0.068)
South West	0.138	(0.086)	0.204***	(0.078)	0.164**	(0.077)
West Midlands	-0.044	(0.086)	0.022	(0.078)	0.072	(0.077)
Yorkshire Humber	-0.109	(0.146)	-0.123	(0.132)	-0.080	(0.131)

The table shows the coefficients and standard errors for the effect covariates on trajectory group membership. All estimates are contrasted against the baseline group of LC. * denotes significance at 10% level, ** at the 5% level and *** at the 1% level.

Table A.10
Estimates for time-varying morbidities.

	Diabetes		CKD		Cancer	
	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error
HC-LR	0.307***	(0.006)	0.205***	(0.005)	0.712***	(0.006)
MHC-LR	0.432***	(0.006)	0.273***	(0.005)	1.010***	(0.006)
MLC	0.476***	(0.008)	0.262***	(0.007)	1.152***	(0.008)
LC-LR	0.544***	(0.009)	0.437***	(0.007)	1.319***	(0.007)

The table shows the coefficients and standard errors for the effect of diabetes, chronic kidney disease and cancer when entered as time-varying covariates in the trajectory profiles.

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