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Biomarkers, disability and health care demand

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Abstract: Using longitudinal data from a representative UK panel, we focus on a group of apparently healthy individuals with no history of disability or major chronic health condition at baseline. A latent variable structural equation model is used to analyse the predictive role of latent baseline biological health, indicated by a rich set of biomarkers, and other personal characteristics, in determining the individual's disability state and health service utilisation five years later. We find that baseline biological health affects future health service utilisation very strongly, via progression to functional disability channel. We also find systematic income gradients in future disability risks, with those of higher income experiencing a lower progress to disability. Our model reveals that observed pro-rich inequity in health care utilisation, is driven by the fact that higher-income people tend to make greater use of health care treatment, for any given biological health and disability status; this is despite the lower average need for treatment shown by the negative association of income with both baseline ill biological health and disability progression risk. Factor loadings for latent baseline health show that a broader set of blood-based biomarkers, rather than the current focus mainly on blood pressure, cholesterol and adiposity, may need to be considered for public health screening programs.

Keywords: Health Services; Health care Demand; Biomarkers; Disability

JEL codes: C3, C8, I10, I18

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1. Introduction

Health care costs have risen substantially over time in all OECD countries and are projected to continue rising faster than the rate of economic growth (OECD, 2015). In the United Kingdom (UK), about 10% of GDP is spent on the National Health Service (NHS), in line with the OECD average. Public health spending accounts for more than four-fifths of this spending. The proportion of the UK public spending allocated to the NHS has risen steadily since the establishment of the NHS in 1948 and had more than doubled by 2013/14 (Charlesworth and Bloor, 2018). As a result, almost 20% of UK government spending goes to the NHS (OECD, 2015).

In addition to technological innovation and rising expectations as factors increasing health care demand, population ageing and associated disability put further pressure on health care demand (Brilleman et al., 2014, Carreras et al., 2018, De Meijer et al., 2011, Howdon and Rice, 2018). For example, in the UK, the number of disabled people aged over 65 is projected to increase by 25% from 2015 to 2025, with a quarter of post-65 projected life expectancy involving disability (Guzman-Castillo et al., 2017). These projections imply large future rises in health service utilisation and associated costs. In this setting, it is important for policymakers to be able to identify population groups that are of higher risk for increasing health care demand, to establish priorities for resource planning and preventive policy.

Much recent research explores individual-level determinants of the demand for health care services and consequent costs with a particular focus on the role of ageing and time-to-death (e.g., Brilleman et al., 2014, Carreras et al., 2018, De Meijer et al., 201, Howdon and Rice, 2018; Zweifel et al., 1999). It has been shown that simple age-health expenditure curves may not yield an accurate picture of current and future health care expenditures, highlighting the importance of accounting for individuals' morbidity and disability status. Many existing studies (Brilleman et al., 2014, Carreras et al., 2018, Howdon and Rice, 2018) reveal contemporaneous associations between the morbidity profile of the population and health care demand and costs, but do not aim to identify pre-symptomatic individuals at risk of future high rates of health service utilisation. The majority of these studies use data accumulated from the health care system, relating to selected patient groups or older people, without adequate coverage of people with latent health conditions not yet at the stage of diagnosis. Most also have limited information on the range of

confounding personal and socioeconomic characteristics. Associations between impaired health, disability and intensive health services utilisation are often explored separately (e.g., Davillas and Pudney, 2020a, 2020b; Crimmins et al., 2004; Fried et al., 2001; Martin et al., 2010; McColl et al., 2011; Spillman, 2004), and studies exploring the full interplay between baseline health impairments and subsequent functional disability and increased demand for health care are much more limited. Joint prediction of future health service utilisation and disability is potentially important for forward-looking policies, particularly if we take a broad view covering needs for both medical treatment and social care.[1]

In this paper, we build on existing research on the predictive role of biomarkers for progression into disability (Davillas and Pudney, 2020b) to examine jointly the predictive power of baseline biological health for both disability and health care utilisation outcomes in the future. We use data from wave 2 of the nationally representative UK Household Longitudinal Study (UKHLS, also known as Understanding Society) to measure baseline ill health and wave 7, five years on, to observe subsequent disability and health service utilisation for the same individuals. For the analysis, we develop and implement a structural equation model of the service utilisation and functional disability outcomes, conditional on health and demographic and socioeconomic status at baseline. Analysis of the demand for health care using structural models is not new and we build on a long tradition of modelling health as a latent variable that is not directly measurable (Van de Ven and Van Der Gaag, 1982; Wagstaff, 1986).[2] We are able to exploit the advances in social science datasets made since those pioneering studies, capitalising on the availability of longitudinal data and more objectively measured health indicators (biomarkers).

We make a number of new contributions to the literature. First, although it has been shown that biological ill-health at baseline increases the risk of future disability (e.g., Davillas and Pudney, 2020b), less is known about the interrelationship of disability and health service utilisation at that future time. We use data on consultations at general practitioners (GP) and outpatient or day clinics (OP) and the length of inpatient (IP) hospital stays collected alongside disability as outcomes five years after baseline. Analysis of disability and service utilisation as joint outcomes

[1] It should be borne in mind that improvements in service provision utilisation and containment of costs depend on the effectiveness of practical interventions targeting those at risk. Our aim here is to use econometric analysis to identify the profile of those risks; the design, effectiveness or implementation of specific interventions is beyond the score of this paper.

[2] These models are sometimes called MIMIC (multiple indicator, multiple cause) models, being a variant of the linear independent structural relationships (LISREL) model of Jöreskog and Goldberger (1975).

reveals the important role of disability as a factor in the growth of treatment costs and suggests the possibility of large economic benefits if it is possible to design effective public health and social policy interventions that can prevent or slow the progression to functional disability. Of course, such interventions, if feasible, would have important impacts in the reduction of human suffering as well as public resource costs. The evidence presented in this paper is in line with with recent UK policy agendas that see disability as a largely preventable public health priority (Department of Health and Social Care, 2019).

Second, we develop a latent variable structural equation approach in which we allow for the possibility that our biomarker measures are noisy markers of an individual's biological health at baseline, rather than direct observations on the relevant biological concept. Part of the existing literature uses composite measures that combine a number of biological measures (biomarkers): either by summing dichotomous variables indicating values below or above predetermined cut-points for each of these biomarkers; or by transforming them into comparable measures (z-scores) which are summed to produce a composite measure; or by constructing principal components of the set of biomarker (for example, Nesson and Robinson, 2019; Seeman et al., 2004). These methods have various disadvantages: the use of arbitrarily determined biomarker thresholds; lack of weighting of the different biomarkers; and reliance purely on internal correlations. None of them deals explicitly with the problem of random measurement error ('noise') inherent in the laboratory and field measurement processes. We instead develop a latent index for baseline biological health that incorporates all available sample information and combines the selected biomarkers optimally in way that takes account of the predictive power of each biomarker for disability and service utilisation outcomes five years after baseline. This advantage of our methodology, together with the availability of a large set of biomarkers (spanning adiposity, grip strength, blood pressure, heart rate, lung functioning, inflammation, stress hormones, cholesterol levels, blood sugar, kidney function, liver function and anaemia) gives us an unusually full picture of individuals' baseline health states. Although biomarkers are the most objective health indicators available in social science surveys, they are still subject to measurement error (Davillas and Pudney, 2020b; Zang et al., 2015), and our method deals with measurement error to avoid the attenuation bias that would otherwise affect the estimated impact of biomarkers on the outcomes of interest. We use a similar multi-indicator latent disability approach to exploit the range of survey indicators measuring different facets of disability and to

deal with random response error in the survey measurement of disability found in previous research (Morciano et al., 2015b).

Third, the paper contributes to the literature on horizontal equity in health service utilisation, using an approach different to the concentration indices typically employed in that literature. In most existing empirical work, horizontal inequity is measured as the degree to which individuals' own socio-economic status is associated with health services utilisation after accounting for differences in health care need (Cookson et al., 2016; Van Doorslaer et al., 2004; Van Doorslaer et al., 2006); typically, need-related differences in health care utilisation are proxied using self-reported general health, morbidity and disability measures in addition to demographic indicators. Instead, we use a latent biological health component based on large set of objectively measured biomarkers, and a disability component reflecting different facets of disability. Thus, unlike most existing studies we can explore the association between socioeconomic status measures and health services utilisation, allowing for health and disability latent components which are arguably more firmly based.

Our results are striking: we have found that the predictive role of baseline biological health on service utilisation is almost entirely channelled through disability progression, which has a large, positive and highly significant association with concurrent health care demand measured by GP, OP consultations and IP days. This underlines the potential importance of policy designed to delay or prevent progression to disability. Baseline personal characterises have a strong influence on baseline biological health. We also found systematic SES gradients in future disability risk, which is lower for those with higher baseline income among individuals with no reported disability history. For GP consultations, OP consultations and IP days, health care utilisation is found to favour those on higher incomes, after conditioning on baseline biological health, particularly for GP and OP consultations.

Importantly, we find that the appropriate predictive concept of baseline biological health loads more heavily on lung functioning, grip strength, anaemia status, stress-related hormones and liver functioning and to lesser extent on indicators that are the current focus of the public health screening programs, such as blood pressure, cholesterol and adiposity. As indicators of disability, physical difficulties with lifting/carrying, mobility, personal care, co-ordination and manual

dexterity are found to be much more strongly associated with utilisation of health services than are indicators of sensory and cognitive difficulties.

The rest of the paper is organised as follows. Section 2 introduces the data and Section 3 our empirical methodology. Section 4 presents the results of the study and the final section summarises and concludes.

2. Data

Understanding Society, also known as the UK Household Longitudinal Study (UKHLS), is a longitudinal, nationally representative survey of the UK household population, based on a two-stage stratified random sample of the household population. As part of wave 2 (2010-2011), nurse-measured and blood-based biomarkers were collected for adults resident in Great Britain (*i.e.* excluding Northern Ireland). Measures of disability and health service utilisation were collected at wave 7 (2015-16). After excluding individuals who provided no biomarker information or had missing data on any of the covariates or who were non-respondent at wave 7, the potential sample was a maximum of 10,625 individuals.

We further restricted the analysis to individuals who reported no disability at waves 1 and 2 and no history of major chronic health conditions (congestive heart failure, coronary heart disease, heart attack or myocardial infarction, stroke, cancer or malignancy, diabetes, high blood pressure and chronic bronchitis). This allows us to explore progression to disability following respondents of apparently good health, who were not currently prioritised by the health service. The resulting working sample contains a maximum of 5,286 individuals.

2.1 Nurse-collected and blood-based biomarkers at baseline

We use most of the large set of nurse-collected and blood-based biomarkers collected by the UKHLS. We follow the recent literature that explores (separately) the predictive role of a set of biomarkers on disability (Davillas and Pudney, 2020b) and health services utilisation (Davillas and Pudney, 2020a). Descriptive statistics for the raw biomarker variables are presented in Table 1. For the purpose of econometric modelling, the quantitative biomarkers were standardised to give the impacts of latent health on observed indicators in standard deviation units.

Measures of adiposity, grip strength, resting heart rate, blood pressure, and lung function were collected at wave 2 during visits by trained nurses. We use waist-to-height ratio (WHR),

calculated as waist circumference (in cm) over standing height (in cm), to measure adiposity. For grip strength, we use the highest reading from three repeated measurements (using a hand dynamometer) for the dominant hand. Pulse rate, which is often considered as a cardiovascular fitness measure, is used as a continuous variable in our analysis. We use a dummy variable to define hypertension, indicating cases where there is excess blood pressure (SBP > 140 or DBP > 90) and/or current use of antihypertensive medications (Johnston et al., 2009). Lung function is measured using the total amount of air forcibly blown out after a full inspiration (forced vital capacity; FVC). Higher FVC values indicate better lung functioning (Gray et al., 2013).

A set of blood-based biomarkers is also collected as part of the UKHLS wave 2 nurse visits. Our set of blood-based biomarkers covers inflammation, steroid hormones, total cholesterol, blood sugar, kidney function, liver function, and anaemia status. C-reactive protein (CRP) is our inflammatory biomarker; CRP rises as part of the immune response to infection and captures systemic inflammation. Following existing literature (Davillas and Pudney, 2017; Pearson et al., 2003), we exclude CRP values over 10 mg/L because such values generally reflect response to current transient infection rather than chronic processes. Dihydroepiandrosterone suphate (DHEAS) is a steroid hormone and one of the primary mechanisms through which psychosocial stressors may affect health (Vie et al., 2014). Low levels of DHEAS are associated with cardiovascular risk and all-cause mortality (Ohlsson et al., 2010). We use total cholesterol as our "fat in the blood" biomarker, with higher levels are associated with elevated risk of cardiovascular disease (e.g., Verschuren et al., 1995). Glycated haemoglobin (HbA1c) is our blood sugar biomarker, being a diagnostic test for diabetes (WHO, 2011a). The estimated glomerular filtration rate (eGFR), calculated based on the serum creatinine concentration (Benzeval et al., 2014), is our measure of kidney functioning. Higher eGFR levels indicate better kidney function (Levey et al., 2009). Liver functioning is measured by albumin, with lower levels suggesting impaired liver function (Benzeval et al., 2014). Anaemia status is proxied by low levels of haemoglobin (Hgb), an iron-containing protein responsible for carrying oxygen throughout the body (WHO, 2011b).

2.2 Disability measures

Our disability measures are collected at UKHLS wave 7, on average five years after collection of the baseline biomarker data. UKHLS wave 7 asks a detailed set of disability questions, giving us

the rare opportunity to cover the multidimensional nature of disability. Specifically, respondents were asked if they had any long-standing physical or mental impairment. Following a positive response, they were asked to indicate all specific functional difficulties they experience with everyday activities, from a standard list. We constructed ten binary indicators for disability or impairment with the following life domains: mobility (moving around at home and walking); lifting, carrying or moving objects; manual dexterity (using hands to carry out everyday tasks); continence (bladder and bowel control); hearing problems (apart from using a standard hearing aid); sight problems (apart from wearing standard glasses); memory or ability to concentrate, learn or understand; physical co-ordination (e.g., balance); difficulties with own personal care; and, any other health problem or disability. Descriptive statistics for the disability measures used in our analysis are also presented in Table 1.

Table 1. Summary statistics: biomarkers and disability indicators

	Mean	St. Dev.
Biomarkers		
Grip strength (in kg)	35.52	11.32
Waist to height ratio	0.538	0.077
Hypertension†	0.153	0.358
Pulse rate (beats per minute)	68.34	10.05
FVC (L)	4.065	1.030
Total cholesterol (mmol/L)	5.489	1.097
CRP (mg/L)	1.735	1.837
HbA1c (mmol/mol)	35.20	4.643
DHEAS (µmol/L)	5.125	3.174
eGFR	95.06	17.31
HGB (g/l)	137.06	13.81
Albumin (g/L)	47.30	2.767
Disability indicators		
Mobility†	0.030	0.170
Lifting, carrying/ moving objectives†	0.032	0.175
Manual dexterity†	0.010	0.100
Continence†	0.007	0.086
Hearing†	0.007	0.081
Sight†	0.006	0.076
Memory/ability to concentrate/understand†	0.012	0.110
Physical co-ordination†	0.008	0.090
Own personal care†	0.005	0.071
Other disability†	0.023	0.149

† Binary variables

2.3 Health care utilisation measures

Retrospective information on the number of GP consultations, attendance at a hospital or clinic as an OP, and IP days in the preceding 12 months were also collected at UKHLS wave 7. The numbers of GP and OP consultations were collected as five-category ordinal variables: 0, 1-2, 3-5, 6-10, more than 10 consultations. Figure 1 shows the distribution of the number of GP and OP consultations in the preceding 12 months. Given the high skewness of the data on IP days, we grouped IP days[3] to construct an ordinal variable: 0, for no IP days; 1, for a single day[4]; 2, for more than one and up to three days; 3, for more than three and up to six days; and 4 for more than six days. Figure 1 also presents the relevant distribution for our IP variable (panel C).

We implemented two variants of the statistical model. One uses the three health care utilisation variables (GP, OP and IP) as separate ordinal outcome variables. The other uses a single utilisation variable (Figure 1, Panel D), constructed from the GP, OP and IP variables as a five-category ordinal variable coded as 0-4 in the following way[5]:

0. No GP or OP consultations and no IP days (implying zero health care costs);

1. One to two GP consultations and zero IP and OP days (equivalent to health care cost in the range of £66 to £132);

2. Three to five GP consultations and zero OP consultations and IP days; or zero to two GP consultations, one OP consultation and zero IP days (equivalent to health care cost ranging between £198 and £330);

3. Six to ten GP consultations and zero OP consultations and IP days; or three to five GP consultations and one OP consultation and no IP days; or zero to two GP consultations and either two OP consultations or one IP day (equivalent to health care cost between £361 and £868);

4. Any other utilisation outcome (equivalent to health care costs exceeding £868).

[3] For women who reported any IP days for childbirth during this period, we subtract 1.5 days (the average length of stay after childbirth in the UK; Campbell et al., 2016) from their reports on the total number of IP days. This affects only 0.5% of the sample.

[4] This category includes 79 cases (1.5% of the sample) who reported having been an IP in the preceding 12 months, but then reported 0 days in the follow-up question on the number of IP days.

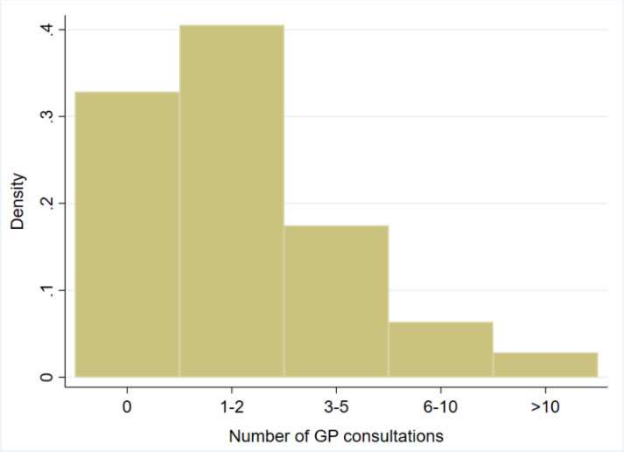
[5] Data on the average unit cost of GP consultations (roughly £66 per consultation) and the weighted average unit cost of OP consultations (£163 per consultation) and IP days (£542 per day) are extracted from Davillas and Pudney (2020a). These cost data are used to construct the five-category composite health services utilisation measure that is described here.

This variable should be viewed as a composite measure grouping individuals' health care utilisation in the preceding 12 months to create similar health care costs (in bands) rather than a description of service utilisation patterns. Beyond the practical advantages of a single composite measure, this measure acknowledges the fact that an episode of treatment often involves a combination of GP consultations and hospital care, particularly for heavy users of health care services, since GPs are typically (but not necessarily) the gatekeepers to hospital care.[6] Using the UKHLS data, it is not possible to analyse sequential patterns of utilisation, distinguishing GP-initiated hospital episodes from other episode types. Respondents may report an annual utilisation count that represents multiple conditions and treatment episodes, and the 12-month reporting period may capture only part of the sequence of consultations generating a treatment episode.

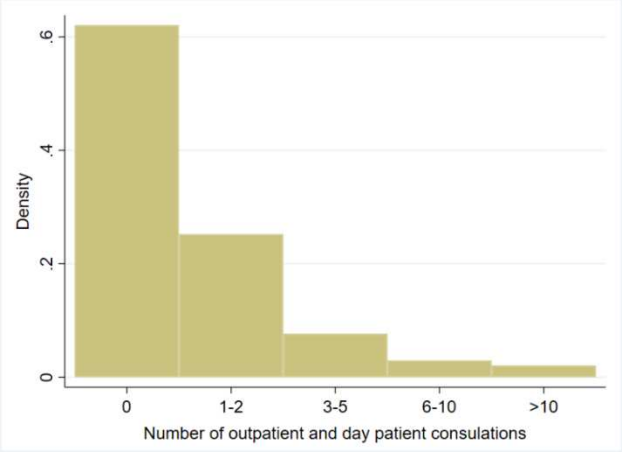
[6] The composite measure allows (in categories 2-4) the possibility of zero GP consultations with a number of OP and IP days. Note that the gatekeeper role of GPs is not completely sharp in practice: OP or IP cases may result from GP consultations outside the 12-month recall period, and emergency cases may be admitted to hospital without GP involvement. About 14% of UKHLS respondents reported zero GP consultations with at least one OP consultation within the same 12-month recall period; almost 10% reported zero GP consultations but at least one IP day.

Figure 1. Distribution of the numbers of GP consultations, OP consultations, IP days and our composite utilisation measure.

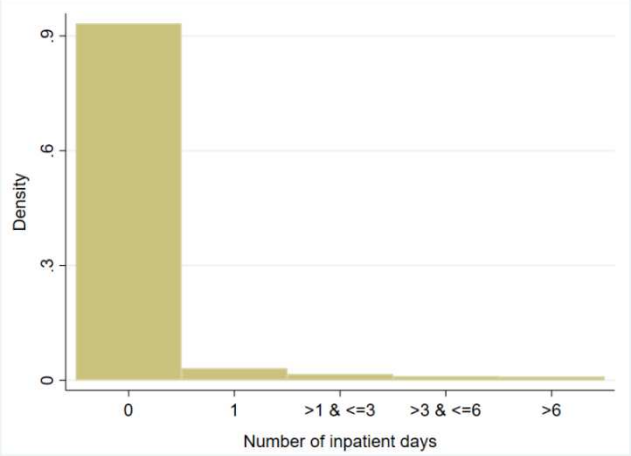
Panel A: GP consultations



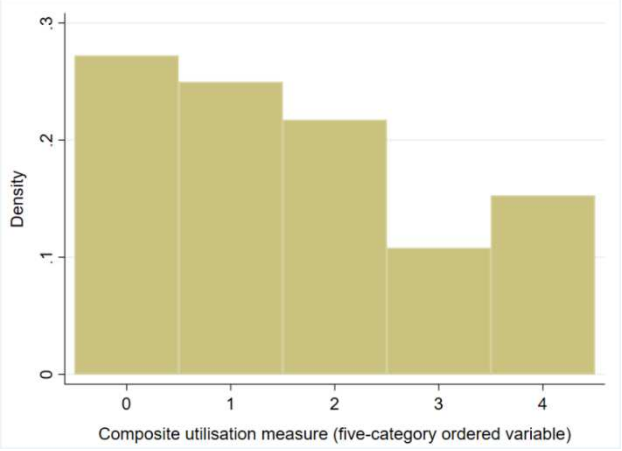
Panel B: OP consultations



Panel C: IP days



Composite health care utilisation measure



2.4 Covariates

The explanatory covariates used in our analysis are demographic and socioeconomic characteristics that have been shown in previous research to affect disability and utilisation of health care services either directly or indirectly (for example, Davillas and Pudney, 2020a,b, van Doorslaer and Jones, 2004 and Morciano et al., 2015a). These variables were collected at baseline as part of the UKHLS wave 2 main survey, along with our biomarker measures.

We use two indicators of SES: educational attainment and household income. Education is measured as a 4-level categorisation: degree, A-level or equivalent, O-level or equivalent and no/basic qualification (reference category). Household income data is available as a derived variable in UKHLS but, to avoid spurious correlation arising from the fact that disability creates eligibility for disability benefits, any receipts of disability benefit are excluded from our household income measure (Morciano et al., 2015a). The resulting income measure is then equivalised using the modified OECD equivalence scale to account for the household composition, and log-transformed to allow for the concavity of the health-income associations and to moderate the skewness of the income distribution. Marital status is captured as four categories: married (reference category), single, divorced and widowed. Age (or polynomials of age, where statistically significant), and a gender dummy are also included in our analysis. We allow for location effects through a dummy variable indicating residence in an urban area. Descriptive statistics of all covariates used in our analysis are presented in Table 2.

Table 2. Summary statistics: covariates

	Mean	**St. Dev.**
Male†	0.420	0.494
Age (years)	45.41	15.09
Ln income	7.409	0.593
Degree†	0.437	0.496
A-level/equivalent†	0.199	0.400
O-level/equivalent†	0.287	0.453
Basic/no qualification†	0.078	0.268
Married†	0.725	0.447
Single†	0.162	0.369
Divorced†	0.081	0.273
Widowed†	0.031	0.175
Urban†	0.762	0.426
Rural†	0.238	0.426

† Dummy variables

3. Latent variable (LV) models

We observe a set of biomarkers denoted $B_1 \dots B_J$ (section 2.1) which act as indicators of latent biological health h at baseline via linear measurement equations:

$$B_j = L_j\left(\alpha_{0j} + \alpha_{1j}h + \varepsilon_j\right), \qquad j = 1 \dots J \tag{1}$$

where ε_j is a classical normally distributed random measurement error and $L_j(.)$ is a link function reflecting the nature of indicator j.[7] Baseline biological health is determined by the individual's personal characteristics and circumstances, described by a vector of covariates X:

$$h = X\beta + u \tag{2}$$

where $u \sim N(0,1)$ is a represents any unobservable factors that are independent of X. The unit variance for u is a normalisation that fixes the scale of h. Biological health at baseline, together with characteristics X, determines (latent) functional disability d, which is observed five years later:

$$d = \gamma_1 h + X\gamma_2 + v \tag{3}$$

where $v \sim N(0,1)$ represents any further unobservable determinants of disability. There is no loss of generality in assuming that u and v are distributed independently. The realised disability outcome is indicated by a set of observed binary indicators capturing a number of functional difficulties (section 2.2) $D_1 \dots D_K$:

$$D_k = \begin{cases} 1 & \text{if } \delta_{0k} + \delta_{1k}d + \eta_k > 0 \\ 0 & \text{otherwise} \end{cases}, \qquad k = 1 \dots K \tag{4}$$

We also observe one or more ordinal measures of health service utilisation five years after baseline (section 2.3), $Z_1 \dots Z_M$, which are driven by biological health and functional disability and also influenced by personal characteristics X:

$$Z_m = r \quad \text{if} \quad C_{m(r-1)} < \lambda_{1m}h + \lambda_{2m}d + X\lambda_{3m} + \lambda_{4m}\zeta + w_m \leq C_{mr} \tag{5}$$

where $r = 0 \dots 4$ are the five levels of each utilisation indicator and the C_{mr} are threshold parameters specific to the mth type of health care service. $\zeta \sim N(0,1)$ is an unobservable representing personal willingness or reluctance to use health care services and $\omega_m \sim N(0,1)$ represents any further unobservable determinants specific to use of the mth service. All parameters of the model (1)-(5) are estimated jointly by maximum likelihood.

[7] All but one of the biomarkers are continuous variables, for which $L_j(y) \equiv y$. The other is a binary indicator of hypertension, for which $L_j(y) \equiv 1$ if $y > 0$ and $L_j(y) \equiv 0$ otherwise.

We estimate two alternative variants of this latent variable model. One uses our single composite ordinal measure of health care utilisation (LV Model 1).[8] The other uses the GP, OP and IP measures separately (LV Model 2), with the factor ζ accounting for the correlation between them. The structure of the model is summarised graphically in Figure 2.

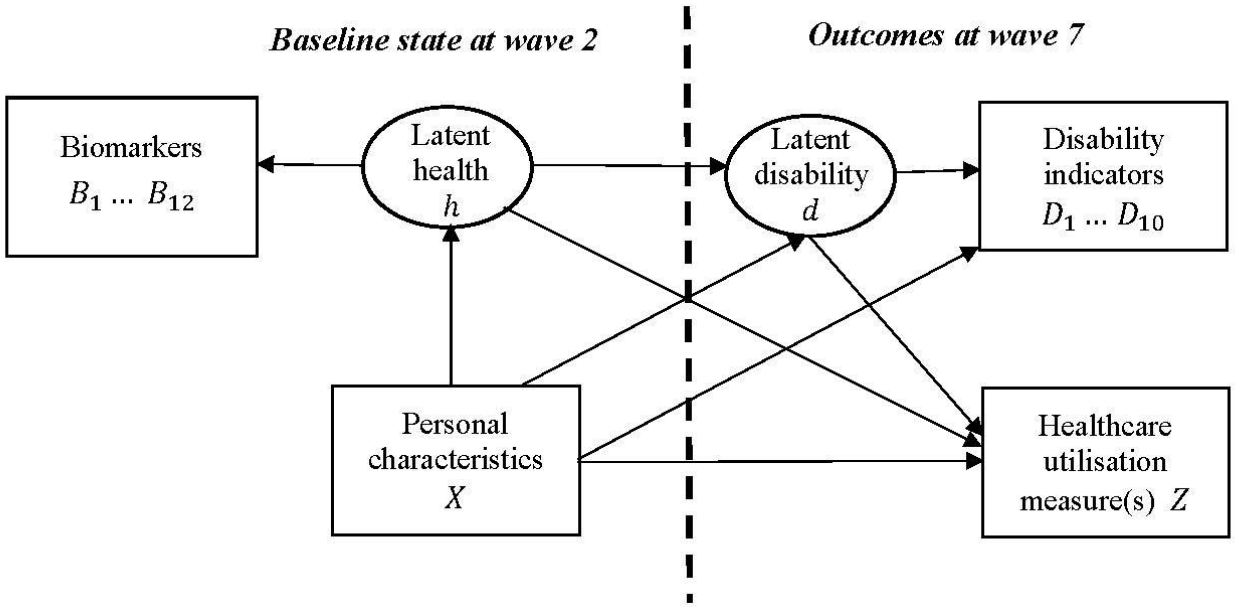


Figure 2. Path diagram for latent variable health-disability-health care utilisation model.

4. Results

We first discuss estimates relating to the determinants of baseline biological health h. Table 3 presents the estimated coefficients from model I (the version with a single composite utilisation measure), and model II (with separate equations for GP, OP and IP services). The health coefficients are practically identical in the two models.

The latent baseline health h is normalised to reflect good, rather than ill, health. Controlling for demographic and socioeconomic influences, men experience better health, on average, than women. As expected, health deteriorates with baseline age at an accelerating rate (since both age

[8] In the single-measure model (M=1), the two random terms are combined into a single residual error $\omega_m^* = (\lambda_{4m}\zeta + \omega_m)$, renormalised to have unit variance.

and age squared have highly significant negative coefficients). There is also a strong SES gradient in latent baseline health, consistent with previous evidence for self-reported health measures and biomarkers (Carrieri and Jones, 2017; Deaton and Paxson, 1998; Jones and Wildman, 2008). Higher income is associated with better health, and those with a degree, A-level or O-level qualifications experience on average better biological health at baseline compared to those with no or basic educational qualifications (reference category).

There is some weak evidence of poorer baseline health among those who were single rather than married/cohabitating, confirming the protective effect of marriage on health (Rendall et al., 2011). There is also a strong health disadvantage for people resident in urban areas, which is consistent with a range of environmental health threats such as air pollution (Shah et al., 2013) and lack of green space (Twohig-Bennett and Jones, 2018).

Table 3. Determinants of latent baseline health *h (good health)*

Covariate	Model I	Model II
Male	5.467***	5.467***
	(0.265)	(0.264)
Age	-1.185***	-1.186***
	(0.075)	(0.074)
Age squared	-0.356***	-0.357***
	(0.031)	(0.031)
Ln income	0.294***	0.294***
	(0.051)	(0.051)
Degree	0.434***	0.434***
	(0.113)	(0.113)
A-level	0.474***	0.475***
	(0.120)	(0.120)
O-level	0.327***	0.328***
	(0.111)	(0.111)
Single	-0.169*	-0.168*
	(0.091)	(0.091)
Divorced	0.034	0.034
	(0.093)	(0.093)
Widowed	0.014	0.014
	(0.152)	(0.152)
Urban	-0.410***	-0.410***
	(0.063)	(0.062)

Standard errors in parentheses; statistical significance: * = 10%, ** = 5%, *** = 1%

Table 4 presents estimates of the equations for the latent disability outcome *d* and the service utilisation outcome (equations (3) and (5) above). For disability (first column in Models I and II, Table 4), good biological health, *h*, at baseline has a highly significant influence in restraining disability progression to the five-year horizon. The effect is robust and similar in both variants of the model.

After controlling for baseline biological health *h*, few other personal characteristics are found to have a significant influence on the disability outcome. The exceptions are income and gender. We find that individuals with higher income at baseline are significantly less likely to progress to disability by the five-year horizon. The gender estimates for *h* and *d* are intriguing: men are found to have a significantly higher risk of disability than women after controlling for baseline health and other characteristics (Table 4). However, women tend to have worse biological baseline health than men (Table 3) but this health disadvantage translates into subsequent disability at a much slower rate (Table 4). These findings accord with results from studies based on self-reported health measures, that women on average have poorer health than men across most age and SES groups (Case and Deaton, 2005; van Kippersluis et al., 2010). A combination of more rapid physical deterioration of individuals in low-paying jobs and the lower labour force participation of women may provide an explanation for the slower disability progression among women; this extends the existing evidence on health deterioration to disability progression (Case and Deaton, 2005).[9]

[9] A formal test of this hypothesis would require construction of detailed employment histories and would require econometric modelling of the four-way interaction between labour force participation, biological health, disability progression, and health care demand. This is a challenging opportunity for further research.

Table 4. Determinants of disability and service utilisation outcomes.

	Model I		Model II			
	Latent disability	**Composite utilisation measure**	**Latent disability**	**GP utilisation**	**OP utilisation**	**IP utilisation**
h (good health)	-0.152***	-0.054	-0.146***	-0.114***	0.005	-0.086
	(0.046)	(0.037)	(0.046)	(0.038)	(0.067)	(0.062)
d		0.646***		0.604***	1.107***	0.475***
		(0.048)		(0.044)	(0.144)	(0.061)
Male	0.622**	0.110	0.576**	0.389	-0.179	0.345
	(0.258)	(0.206)	(0.260)	(0.221)	(0.376)	(0.349)
Age	-0.025	-0.057	-0.004	-0.169***	0.087	-0.144
	(0.068)	(0.053)	(0.068)	(0.056)	(0.100)	(0.092)
Ln income	-0.199***	0.190***	-0.188***	0.148***	0.332***	0.119*
	(0.054)	(0.043)	(0.055)	(0.044)	(0.088)	(0.070)
Degree	-0.147	0.105	-0.147	0.007	0.389**	0.099
	(0.108)	(0.090)	(0.107)	(0.095)	(0.167)	(0.158)
A-level	-0.030	0.054	-0.028	-0.073	0.342*	0.165
	(0.115)	(0.096)	(0.116)	(0.101)	(0.178)	(0.168)
O-level	-0.028	0.029	-0.027	-0.074	0.249	0.087
	(0.102)	(0.087)	(0.101)	(0.091)	(0.160)	(0.154)
Single	-0.071	0.067	-0.059	0.042	0.083	0.041
	(0.091)	(0.070)	(0.091)	(0.073)	(0.132)	(0.117)
Divorced	0.107	-0.155*	0.099	-0.092	-0.322**	-0.045
	(0.095)	(0.088)	(0.096)	(0.084)	(0.155)	(0.133)
Widowed	0.043	-0.033	0.037	-0.025	-0.120	0.061
	(0.152)	(0.122)	(0.149)	(0.126)	(0.222)	(0.197)
Urban	-0.028	0.084	-0.019	0.054	0.144	0.190**
	(0.070)	(0.054)	(0.069)	(0.055)	(0.103)	(0.094)

Standard errors in parentheses; statistical significance: * = 10%, ** = 5%, *** = 1%

Table 4 also presents the estimated coefficients in the equation(s) (5) for the utilisation of health services. Overall, we find that the impact of the latent health state at baseline (*h*) on service utilisation is almost entirely channelled through disability *d*, which has a large positive and highly significant coefficient in every case, while the direct effect of *h* is generally insignificant. The one exception to this is in model II, where good biological health at baseline (*h*) has a highly significant negative effect on GP consultations, in addition to its indirect effect via disability.

To quantify the estimated association between the disability outcome *d* and health service utilisation for any individual, we can contrast his or her probability of a high utilisation burden conditional on the absence or presence of disability. Averaged across individuals, that contrast is

important for policy purposes, since it indicates the scale of potential cost savings that might arise from effective interventions designed to prevent or slow progression to disability. Table 5 gives calculations based on Model I, and shows the key role of disability. There is no unambiguous distinction between disability and non-disability, but if we define disability as a value of *d* above its median, then the mean probability of high health care costs (the top two utilisation categories) is calculated as 0.11 if progression to disability does not occur, but 0.41 if it does: a 260% increase. If we define disability as the top quartile of *d* and any lower level as non-disability, then the probabilities are 0.17 and 0.53: a 200% difference. These results underline the importance of considering health and disability policy together, since they show that preventing or delaying progression to disability is immensely valuable for control of health care costs and therefore an important policy objective quite apart from its benefit to the individuals concerned.

Table 5. The role of disability in generating high service utilisation rates (model I)

Threshold for definition of disability	Mean probability of high utilisation outcome[§] without disability	Mean probability of high utilisation outcome with disability
Median of *d* [†]	0.11	0.41
Top quartile of *d* [†]	0.17	0.53

[§] High utilisation defined as the composite utilisation indicator $Z = 3$ or 4. Conditional probabilities of the form $\Pr(Z>C|X, d<D)$ or $\Pr(Z>C|X, d>D)$ are computed exactly for each sampled individual using the bivariate normal distribution and then averaged over individuals, where C is the relevant threshold parameter for Z and D is the median or upper quartile point of d. [†] Median and quartile points of the distribution of d estimated by Monte Carlo simulation from the estimated equations (2) and (3).

Table 4 shows only limited direct demographic influences on health service utilisation, given that the models account for the effects of latent disability and baseline health, which both have strong demographic profiles. Age and gender have no significant effect, except again for a negative impact of age on GP consultations. It must be borne in mind that there are strong age influences on health *h* and disability *d*, so the overall effect of age on utilisation is in fact positive. Although older people tend to use GP services more than younger people, the estimates of model II imply that their GP utilisation rate is actually lower than would be expected, given their much poorer baseline health and disability outcomes. This is consistent with some existing evidence (Deb and

Trivedi, 1997; Oliver, 2009) that older people may face ageism in the delivery of primary health care services, or perceive less benefit in engaging with primary health care.

Controlling for health and disability, there remains a strong positive income gradient in health service utilisation (Table 4). This is so for the composite utilisation measure (Model I), and also (Model II) for the GP and OP consultation counts and less strongly for IP days. The education gradient is less clear, with a statistically significant effect only found for OP consultations. These results are consistent with existing evidence on inequity in health services utilisation literature which, particularly for the UK, does not find a pro-poor distribution of GP consultations (Cookson et al., 2016; Van Doorslaer et al., 2004; Van Doorslaer et al., 2006) after allowing for differences in need for health care by using self-assessed health and morbidity measures. There is some previous evidence of pro-rich inequity in OP consultations in the U.K., but this is not a universal finding and there is little evidence of income-related inequity for IP visits (Cookson et al., 2016; Van Doorslaer et al., 2004; Van Doorslaer et al., 2006). Our results show clearer pro-rich inequity in utilisation of all types of health service after adjusting for differences in health care need using latent biological health and disability components. As existing evidence is based on self-reported health measures (Cookson et al., 2016; Van Doorslaer et al., 2004; Van Doorslaer et al., 2006), our evidence may highlight the importance of more objective adjustment for health care needs in the context of inequity in health care.

4.1 Factor loadings for the baseline biological health and disability component.

The factor loadings for latent biological health at baseline (parameters α_{1j} in (1)) and the latent disability outcome (parameters δ_{1k} in (4)) are important, since they tell us the relative predictive powers of each biomarker and disability indicator. This may be valuable for policy purposes as a guide to the type of information that should be collected for monitoring and screening purposes. Estimated loadings are almost identical in models I and II, and all statistically significant loadings have the expected signs.

The left-hand panel of Table 6 shows the estimated loadings for latent health. Except for the binary hypertension measure, the biomarkers were standardised to give the impacts of latent health on observed indicators in standard deviation units. In these units, latent health loads most heavily on lung function (0.25), grip strength (0.25), haemoglobin (0.18), DHEAS (0.17) and liver function (0.14). Smaller, but still statistically significant, are the loadings on markers for

kidney function (0.07), blood sugar (HbA1c) (-0.05), inflammation (CRP) (-0.05), resting pulse rate (-0.04) and total cholesterol (-0.02). This pattern of estimated loadings differs quite substantially from the design of many current public health general screening programmes, which mostly rely heavily on blood pressure, cholesterol and body mass index. There are grounds here for widening the range of biomarkers used.

Loadings for latent disability are shown in the remainder of Table 6. The dominant indicators relate to physical difficulties with lifting/carrying, mobility, personal care, co-ordination and manual dexterity. Loadings for indicators of sensory and cognitive difficulties are statistically significant but less strongly linked with health service utilisation. It should be borne in mind that we are concerned here only with use of medical resources, not with the need for social care. In the UK system with its sharp distinction between medicine and social services, it is likely that many of the needs associated with sensory and cognitive impairment fall into the domain of social rather than medical care.

Table 6. Properties of model I: loadings for latent health (*h*) and disability (*d*).

(Good) Health latent component (*h*)			**Disability latent component (*d*)**		
Biomarker	**Model I**	**Model II**	**Disability indicator**	**Model I**	**Model II**
Grip strength	0.247*** (0.012)	0.247*** (0.012)	Mobility	2.195*** (0.270)	2.130*** (0.255)
Waist to height ratio	-0.008 (0.005)	-0.008 (0.006)	Lifting, carrying/ moving objectives	2.323*** (0.313)	2.301*** (0.309)
Hypertension	-0.012 (0.009)	-0.012 (0.009)	Manual dexterity	1.339*** (0.182)	1.344*** (0.179)
Pulse rate	-0.037*** (0.006)	-0.037*** (0.006)	Continence	0.680*** (0.089)	0.685*** (0.090)
FVC	0.252*** (0.012)	0.251*** (0.012)	Hearing	0.538*** (0.099)	0.529*** (0.098)
Total cholesterol	-0.022*** (0.007)	-0.022*** (0.007)	Sight	0.595*** (0.100)	0.612*** (0.100)
CRP	-0.046*** (0.006)	-0.046*** (0.006)	Memory/ability to concentrate/understand	0.840*** (0.103)	0.856*** (0.103)
HbA1c	-0.048*** (0.007)	-0.048*** (0.007)	Physical co-ordination	1.514*** (0.207)	1.484*** (0.200)
DHEAS	0.173*** (0.009)	0.173*** (0.009)	Own personal care	1.848*** (0.340)	1.851*** (0.350)
eGFR	0.068*** (0.007)	0.068*** (0.007)	Other disability	0.498*** (0.049)	0.493*** (0.050)
HGB	0.184*** (0.009)	0.184*** (0.009)			

Albumin	0.136*** (0.008)	0.136*** (0.008)	

Standard errors in parentheses; statistical significance: * = 10%, ** = 5%, *** = 1%

5. Conclusions

The aim of this paper is to explore and better understand the complex interaction between biological health, and subsequent disability and health service utilisation. Using longitudinal data from a representative UK panel, we focused on the group of apparently healthy individuals with no history of disability or major chronic health condition at baseline. For this sample group, a latent variable structural equation model was used to analyse the predictive role of latent baseline biological health, indicated by a rich set of biomarkers, and other personal characteristics, in determining the individual's disability state and health service utilisation five years later. We found evidence that sub-diagnostic biological health deficits at baseline have a large impact on future health service utilisation. That impact operates almost entirely via progression to disability: conditional on the realised disability state, baseline biological health has little direct impact on utilisation.

Baseline personal characterises have a strong influence on baseline biological health. We also found systematic SES gradients in future disability risks; disability risks five year ahead are lower for those with higher baseline income, among those individuals without any reported disability history. We see no evidence of accelerated progression to disability for older people (conditional on baseline biological health), nor of a direct tendency for older people to make greater demands on the health care system (conditional on baseline health and current disability state).

Our findings are also relevant to the equity in health care utilisation literature. We found that higher-income individuals extract treatment from the health care system more effectively, conditional on their health and disability status (*i.e.* adjusting for differential health care need). The corresponding results for educational attainment are less clear, limited to more OP visits, for those with higher education, after adjusting for health and disability-related need. Overall, our results show pro-rich inequity in all types of health services utilisation, which is most pronounced for GP and OP consultations. This contrasts with most of the existing literature using self-reported health to adjust for health care need, which reports little evidence of pro-poor

inequity in GP consultations and only weak evidence of pro-rich inequity for OP visits in the UK (Cookson et al., 2016; Van Doorslaer et al., 2004; Van Doorslaer et al., 2006; although see Bago d'Uva et al. 2009 for findings similar to ours on pro-rich inequity in access to specialist consultations, after accounting for unobserved health care needs. In the context of the universal publicly funded UK health care system, our results can be seen as a call for policies to secure more equal health care opportunity at the point of the health care delivery.

Our focus on the population who were apparently healthy at baseline and, therefore, not prioritised by the health care system, has policy implications for prevention strategies, with the possibility of significant potential public costs savings. Our results suggest that strategies focusing on disability progression, may be a fruitful approach to policy intended to control the demand for health services. A further important policy issue is the design of screening and monitoring programmes. The estimated factor loadings for the biomarkers in our structural equation model show that the predictive latent biological health measure loads most heavily on lung functioning, grip strength, anaemia status, stress-related hormones and liver functioning. The indicators, such as blood pressure, cholesterol and adiposity, that are the current focus of public health screening programs are less informative as predictors of disability and utilisation outcomes. For example, the NHS England Health Check program mainly offers quinquennial blood pressure, cholesterol tests and BMI measurements to those aged 40-74 (Robson et al., 2016). Our results highlight the importance of widening the range of health indicators considered by public health screening programs. This is increasingly feasible using dried blood spot sampling (drops of whole blood collected on filter paper from a finger prick), which offers a minimally invasive basis for carrying out a wide range of blood tests at low cost (Martial, 2016; Samuelsson, 2015).

References

Bago d'Uva, T. B., Jones, A. M., Van Doorslaer, E. (2009). Measurement of horizontal inequity in health care utilisation using European panel data. *Journal of Health Economics*, 28(2), 280-289.

Benzeval, M., Davillas, A., Kumari, M., Lynn, P. (2014). Understanding society: the UK Household Longitudinal Study Biomarker User Guide and Glossary. Institute for Social and Economic Research, University of Essex.

Brilleman, S. L., Gravelle, H., Hollinghurst, S., Purdy, S., Salisbury, C., Windmeijer, F. (2014). Keep it simple? Predicting primary health care costs with clinical morbidity measures. *Journal of Health Economics*, 35, 109-122.

Campbell, O. M., Cegolon, L., Macleod, D., Benova, L. (2016). Length of stay after childbirth in 92 countries and associated factors in 30 low-and middle-income countries: compilation of reported data and a cross-sectional analysis from nationally representative surveys. *PLoS Medicine*, 13(3):e1001972.

Carreras, M., Ibern, P., Inoriza, J. M. (2018). Ageing and health care expenditures: Exploring the role of individual health status. *Health Economics*, 27(5), 865-876.

Carrieri, V., Jones, A.M. (2017). The income–health relationship 'beyond the mean': New evidence from biomarkers. *Health Economics*, 26(7), 937-956.

Case, A., Deaton, A.S. (2005). Broken down by work and sex: How our health declines. In Analyses in the Economics of Aging (pp. 185-212). University of Chicago Press.

Charlesworth, A., Bloor., K. (2018). 70 years of NHS funding: how do we know how much is enough? *BMJ*, 361, p. k2373

Cookson, R., Propper, C., Asaria, M., Raine, R. (2016). Socio-economic inequalities in health care in England. *Fiscal Studies*, 37(3-4), 371-403.

Crimmins, E. M. (2004). Trends in the health of the elderly. *Annual Review of Public Health*, 25, 79-98.

Davillas, A., Pudney, S. E. (2017). Concordance of health states in couples: analysis of self-reported, nurse administered and blood-based biomarker data in the UK Understanding Society panel. *Journal of Health Economics*, 56:87–102.

Davillas, A., Pudney, S. (2020a). Using biomarkers to predict health care costs: Evidence from a UK household panel. *Journal of Health Economics*, 102356.

Davillas, A., Pudney, S. E. (2020b). Biomarkers as precursors of disability. *Economics and Human Biology*, 100814.

De Meijer, C., Koopmanschap, M., d'Uva, T. B., Van Doorslaer, E. (2011). Determinants of long-term care spending: age, time to death or disability?. *Journal of Health Economics*, 30(2), 425-438.

Deaton, A. S., Paxson, C. H. (1998). Aging and inequality in income and health. *American Economic Review*, 88(2), 248-253

Deb, P., Trivedi, P. K. (1997). Demand for medical care by the elderly: a finite mixture approach. *Journal of Applied Econometrics*, 12(3), 313-336.

Department of Health and Social Care. (2019). Advancing our health: prevention in the 2020s–consultation document.

Fried, T. R., Bradley, E. H., Williams, C. S., Tinetti, M. E. (2001). Functional disability and health care expenditures for older persons. *Archives of Internal Medicine*, 161(21), 2602-2607.

Gray, L. A., Leyland, A.H., Benzeval, M., Watt, G.C. (2013). Explaining the social patterning of lung function in adulthood at different ages: the roles of childhood precursors, health behaviours and environmental factors. *Journal of Epidemiology and Community Health*, 67(11):905–911.

Guzman-Castillo, M., Ahmadi-Abhari, S., Bandosz, P., Capewell, S., Steptoe, A., Singh-Manoux, A.,O'Flaherty, M. (2017). Forecasted trends in disability and life expectancy in England and Wales up to 2025: a modelling study. *The Lancet Public Health*, *2*(7), e307-e313.

Howdon, D., Rice, N. (2018). Health care expenditures, age, proximity to death and morbidity: Implications for an ageing population. *Journal of Health Economics*, 57, 60-74.

Johnston, D.W., Propper, C., Shields, M.A. (2009). Comparing subjective and objective measures of health: Evidence from hypertension for the income/health gradient. *Journal of Health Economics*, 28(3):540–552.

Jones, A.M., Wildman, J. (2008). Health, income and relative deprivation: Evidence from the BHPS. *Journal of Health Economics*, 27(2), 308-324.

Jöreskog, K.G. and Goldberger, A.S. (1975). Estimation of a model with multiple indicators and multiple causes of a single latent variable. *Journal of the American Statistical Association*, 70(351a), 631-639.

Levey, A. S., Stevens, L. A., Schmid, C. H., Zhang, Y. L., Castro, A. F., Feldman, H. I., Kusek, J. W., Eggers, P., Van Lente, F., Greene, T., Coresh, J., Chronic Kidney Disease Epidemiology Collaboration (2009). A new equation to estimate glomerular filtration rate. *Annals of Internal Medicine*, 150(9):604–612.

Martial, L. C., Aarnoutse, R. E., Schreuder, M. F., Henriet, S. S., Brüggemann, R. J. M. and Joore, M. A. (2016). Cost evaluation of dried blood spot home sampling as compared to conventional sampling for therapeutic drug monitoring in children, *PloS One*, 11(12), e0167433.

Martin, L. G., Freedman, V. A., Schoeni, R. F., and Andreski, P. M. (2010). Trends in disability and related chronic conditions among people ages fifty to sixty-four. *Health affairs*, 29(4), 725-731.

McColl, M. A., Shortt, S., Gignac, M., and Lam, M. (2011). Disentangling the effects of disability and age on health service utilisation. *Disability and Rehabilitation*, 33(13-14), 1253-1261.

Morciano, M., Hancock, R. M., Pudney, S. (2015a). Birth-cohort trends in older-age functional disability and their relationship with socio-economic status: evidence from a pooling of repeated cross-sectional population-based studies for the UK. *Social Science and Medicine*, 136:1–9.

Morciano, M., Hancock, R., and Pudney, S. (2015b). Disability Costs and Equivalence Scales in the Older Population in Great Britain. *Review of Income and Wealth*, 61(3), 494-514.

Nesson, E. T., and Robinson, J. J. (2019). On the measurement of health and its effect on the measurement of health inequality. *Economics and Human Biology*, *35*, 207-221

OECD (2015). Fiscal sustainability of health systems: Bridging health and finance perspectives. Organisation for Economic Co-operation and Development, Paris, France.

Ohlsson, C., Labrie, F., Barrett-Connor, E., Karlsson, M.K., Ljunggren, O., Vandenput, L., Mellstrom, D., Tivesten, A. (2010). Low serum levels of dehydroepiandrosterone sulfate predict all-cause and cardiovascular mortality in elderly Swedish men. The Journal of *Clinical Endocrinology and Metabolism*, 95(9):4406–4414.

Oliver, D. (2009). Age based discrimination in health and social care services. *BMJ*, 339:b3400.

Pearson, T.A., Mensah, G.A., Alexander, R.W., Anderson, J.L., Cannon III R.O., Criqui, M., Fadl, Y.Y., Fortmann, S.P., Hong, Y., Myers, G.L., Rifai, N., Smith, S.C., Taubert, K.,

Tracy, R.P., Vinicor, F. (2003). Markers of inflammation and cardiovascular disease. Application to clinical and public health practice: a statement for health care professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation*, 107(3):499–511.

Rendall, M. S., Weden, M. M., Favreault, M. M., Waldron, H. (2011). The protective effect of marriage for survival: a review and update. *Demography*, 48(2), 481.

Robson, J., Dostal, I., Sheikh, A., Eldridge, S., Madurasinghe, V., Griffiths, C., ... & Hippisley-Cox, J. (2016). The NHS Health Check in England: an evaluation of the first 4 years. *BMJ open*, 6(1), e008840.

Samuelsson, L. B., Hall, M. H., McLean, S., Porter, J. H., Berkman, L. Marino, M., Sembajwe, G., McDade, T. W. and Buxton, O. M. (2015). ,Validation of biomarkers of CVD risk from dried blood spots in community-based research: Methodologies and study-specific serum equivalencies. *Biodemography and Social Biology*, 61(3), 285-297.

Seeman, T., Glei, D., Goldman, N., Weinstein, M., Singer, B., Lin, Y.H. (2004). Social relationships and allostatic load in Taiwanese elderly and near elderly. *Social Science & Medicine*, 59(11), 2245-2257.

Shah, A. S., Langrish, J. P., Nair, H., McAllister, D. A., Hunter, A. L., Donaldson, K., Newby, D.E., Mills, N. L. (2013). Global association of air pollution and heart failure: a systematic review and meta-analysis. *The Lancet*, *382*(9897), 1039-1048.

Spillman, B. C. (2004). Changes in elderly disability rates and the implications for health care utilization and cost. *The Milbank Quarterly*, 82(1), 157-194.

Twohig-Bennett, C., Jones, A. (2018). The health benefits of the great outdoors: A systematic review and meta-analysis of greenspace exposure and health outcomes. *Environmental Research*, 166, 628-637.

Van de Ven, W.P., Van Der Gaag, J. (1982). Health as an unobservable: a MIMIC-model of demand for health care. *Journal of Health Economics*, 1(2), 157-183.

Van Doorslaer, E., Koolman, X., Jones, A.M. (2004). Explaining income-related inequalities in doctor utilisation in Europe. Health economics, 13(7), 629-647.

Van Doorslaer, E., Masseria, C., Koolman, X. (2006). Inequalities in access to medical care by income in developed countries. *Canadian Medical Association Journal*, 174(2), 177-183.

Van Kippersluis, H., O'Donnell, O., Van Doorslaer, E., Van Ourti, T. (2010). Socioeconomic differences in health over the life cycle in an Egalitarian country. *Social Science & Medicine*, 70(3), 428-438.

Verschuren, W. M., Jacobs, D. R., Bloemberg, B. P., Kromhout, D., Menotti, A., Aravanis, C. and Karvonen, M. J. (1995). Serum total cholesterol and long-term coronary heart disease mortality in different cultures: Twenty-five-year follow-up of the seven countries study. *JAMA*, 274(2), 131-136.

Vie, T.L., Hufthammer, K.O., Holmen, T. L., Meland, E., Breidablik, H.J. (2014). Is self-rated health a stable and predictive factor for allostatic load in early adulthood? Findings from the Nord Trøndelag Health Study (HUNT). *Social Science and Medicine*, 117:1–9.

Wagstaff, A. (1986). The demand for health: some new empirical evidence. *Journal of Health Economics*, 5(3), 195-233.

WHO (2011a). Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus. World Health Organisation. Geneva, Switzerland.

WHO (2011b). Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. World Health Organization. Geneva, Switzerland.

Zang, Y., Liu, S., and Yuan, Y. (2015). Optimal marker-adaptive designs for targeted therapy based on imperfectly measured biomarkers. *Journal of the Royal Statistical Society: Series C (Applied Statistics)*, 64(4), 635-650.

Zweifel, P., Felder, S., Meiers, M. (1999). Ageing of population and health care expenditure: a red herring?. *Health Economics*, 8(6), 485-496.