

Davillas, Apostolos; Pudney, Stephen

Working Paper

Biomarkers, disability and health care demand

GLO Discussion Paper, No. 517

Provided in Cooperation with:

Global Labor Organization (GLO)

Suggested Citation: Davillas, Apostolos; Pudney, Stephen (2020) : Biomarkers, disability and health care demand, GLO Discussion Paper, No. 517, Global Labor Organization (GLO), Essen

This Version is available at:

<https://hdl.handle.net/10419/215798>

Standard-Nutzungsbedingungen:

Die Dokumente auf EconStor dürfen zu eigenen wissenschaftlichen Zwecken und zum Privatgebrauch gespeichert und kopiert werden.

Sie dürfen die Dokumente nicht für öffentliche oder kommerzielle Zwecke vervielfältigen, öffentlich ausstellen, öffentlich zugänglich machen, vertreiben oder anderweitig nutzen.

Sofern die Verfasser die Dokumente unter Open-Content-Lizenzen (insbesondere CC-Lizenzen) zur Verfügung gestellt haben sollten, gelten abweichend von diesen Nutzungsbedingungen die in der dort genannten Lizenz gewährten Nutzungsrechte.

Terms of use:

Documents in EconStor may be saved and copied for your personal and scholarly purposes.

You are not to copy documents for public or commercial purposes, to exhibit the documents publicly, to make them publicly available on the internet, or to distribute or otherwise use the documents in public.

If the documents have been made available under an Open Content Licence (especially Creative Commons Licences), you may exercise further usage rights as specified in the indicated licence.

Biomarkers, disability and health care demand

Apostolos Davillas

Health Economics Group, University of East Anglia

Stephen Pudney

School of Health and Related Research, University of Sheffield

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 health affects future health service utilisation very strongly, via functional disability as a mediating outcome. Our model reveals that observed income inequality in the access to health care, is driven by the fact that higher-income people tend to make greater use of healthcare treatment, for any given health and disability status. This leads to a slight rise in utilisation with income, despite the lower average need for treatment shown by the negative income gradients for both baseline health and disability outcomes. 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; Healthcare Demand; Biomarkers; Disability

JEL codes: C3, C8, I10, I18

Contact: Steve Pudney, ScHARR, University of Sheffield, 30 Regent Street, S1 4DA, UK; tel. +44(0)114 222 9187; email: steve.pudney@sheffield.ac.uk

Understanding Society is an initiative funded by the Economic and Social Research Council and various Government Departments, with scientific leadership by the Institute for Social and Economic Research, University of Essex, and survey delivery by NatCen Social Research and Kantar Public. The research data are distributed by the UK Data Service. Participants gave informed consent for their blood to be taken for future scientific analysis. Biomarker collection was approved by the National Research Ethics Service (10/H0604/2). The funders, data creators and UK Data Service have no responsibility for the contents of this paper. We are grateful to the Economic and Social Research Council for financial support for this research via project "How can biomarkers and genetics improve our understanding of society and health?" (award no. ES/M008592/1), Understanding Society award no. (ES/K005146/1) and the MiSoC research centre (award no. ES/L009153/1). We are grateful to members of the project teams for many helpful comments. Any remaining errors are our sole responsibility.

1 Introduction

Disability prevalence in the UK is well above the European Union average. Almost one in five people in the UK during 2015/16 were found to experience some type of disability, indicating that there are around 13.3 million disabled individuals in the UK (DWP, 2017; Jones, 2016). There is also evidence of an increasing birth-cohort trend in functional difficulties for the older and low socio-economic status (SES) individuals in the UK, suggesting that future disability prevalence rates may not decrease unless there is implementation of successful interventions (Morciano et al., 2015a). Beyond its importance from the public health perspective, disability is linked to wider social and economic consequences. First, people with disabilities and their families tend to suffer from large impairments in several economic outcomes that include earnings, income and consumption (Meyer and Mok, 2019). Given that disability is prevalent across all age groups, its social and economic ramifications are not limited to older individuals. For example, it has been shown that disability for working-age people is associated with adverse labour market outcomes (Kidd et al., 2000; Jones, 2016). Second, unlike many illnesses and health conditions that can be cured or effectively managed, disability often implies long-lasting impairments that may prevent individuals from living an independent life on a long-term basis (WHO, 2011a). This indicates that individuals may be impaired in many aspects of their economic and social life for a long rather than a short period of time. Additionally, disability matters for social policy. The total public cost of disability support in Organisation for Economic Cooperation and Development (OECD) countries is around 10% of total public social expenditure, with some countries spending as much as 25% of their public social expenditure (WHO, 2011a).

Disability therefore imposes direct social costs on society of maintaining reasonable standards of living for those with disability and their families, as well as indirect costs that include productivity losses, deterioration of human capital and non-economic costs such as the potential for social isolation of the disabled individuals (Meyer and Mok, 2019; WHO, 2011a). Given the high costs of disability for both the individuals themselves and society, a crucial question for policymakers is whether gains in longevity will be accompanied by a smaller increase in disability-free life expectancy and, hence, a rise in disability prevalence and demand for health services (Crimmins et al., 2004; Martin et al., 2010). Recent evidence suggests that the number of older people with disabilities is projected to increase by 25% by

2025 in the UK, with a quarter of the projected life expectancy at the age of 65 and above involving disability (Guzman-Castillo et al., 2017); this highlights the need for an effective disability prevention strategy.

Such a strategy requires a better understanding of the processes that lead to disability, allowing the development of screening and intervention programs that can be used to tackle disability more efficiently. It is particularly important to identify the profile of those individuals in the apparently healthy population, who have an elevated risk of becoming disabled, and to estimate the expected future impact on the utilisation of health services that their disability will bring.

In this paper, we build on and expand existing research on the predictive role of biomarkers for progression into disability (Davillas and Pudney, 2020) to understand the complex interaction between baseline health, disability progression and their effects on subsequent health services utilisation. We use wave 2 data from the nationally representative UK Household Longitudinal Study (UKHLS, also known as *Understanding Society*) to identify a set of individuals with no history of disability or severe chronic health conditions at baseline; and then to observe their disability and healthcare service utilisation five years later (UKHLS wave 7). For this sample group, we develop a predictive structural equation model to explore the predictive power of baseline biological health and other personal characteristics, on disability outcomes and health service utilisation five years on. The UKHLS allows us to use a proxy for baseline biological health based on objective blood-based and nurse collected biomarkers.

We make a number of new contributions to the literature. First, we focus specifically on the set of individuals who, from the perspective of the healthcare system, appear to be healthy in that they have no observed history of disability at baseline and have not being diagnosed with any serious chronic health condition. Existing research on disability and health services utilisation is often based on non-representative data from patients with specific health conditions or from older individuals and mostly determines cross-sectional associations (for example, Fried et al., 2001; Hansen et al., 2002; McColl et al., 2011, Spillman, 2004). Our focus on future disability and demand for healthcare services from the apparently healthy population opens the possibility of detailed targeting of health interventions within a large population group not already prioritised by the healthcare system, with the prospect of significant public cost savings.

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. This methodological approach overcomes the arbitrariness of approaches that are based on composite biological measures constructed as single biomarkers or arbitrary indexes of biomarkers. Our analysis allows us to develop an index for biomarkers that incorporates all available sample information and combines them optimally in a way that takes account of predictive power for disability and service utilisation outcomes five years after baseline. This distinguishes it from methods like component analysis that construct an index based only on internal correlations (for example, Nesson and Robinson, 2019). 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, 2020; 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. Previous research has also shown the presence of considerable random response error in the survey measurement of disability (Morciano et al., 2015b). As with baseline health, our modelling approach allows for a latent disability component that deals with both the multiplicity of indicators capturing different facets of disability, and the measurement “noise” inherent in each indicator.

Third, we capitalise on the availability of data on GP and outpatient consultations and the length of inpatient hospital stays collected alongside disability as an outcome five years after baseline. The pathways of progression from health impairments to functional disabilities and healthcare utilisation are not clear (Fried et al., 1991; WHO, 1980, 2011a). Given this complexity, we provide an econometric analysis on how baseline health can predict future disability, and the influence of disability (net of baseline health itself) on health service utilisation. Understanding the mediating role of disability in the mechanism through which impaired baseline health predicts future health service utilisation is important for characterising the profile of those at risk of generating high future public healthcare costs.

Finally, we are able to explore the influence on healthcare utilisation of demographic and SES characteristics measured at baseline and the pathways by which that influence works. We can distinguish three pathways – via the demographic and SES profile of baseline health; via the mediating disability outcome; and a direct effect of personal characteristics on utilisation, conditional on baseline health and concurrent disability. Disentangling these three pathways is potentially informative about the mechanisms underpinning observed demographic and SES gradients in health services utilisation. It is also important for policy purposes, since each pathway has different policy implications: public health interventions target the health pathway; disability prevention targets the disability path and policies to control healthcare access targets the direct path. Moreover, factor loadings from the structural equation model help us to identify the information required to make these interventions more effective, by identifying the particular biomarkers that are strongest predictors of future health service utilisation.

We have found that the predictive role of baseline biological health on service utilisation is almost entirely channelled through the mediating disability outcome, which has a large, positive and highly significant association with concurrent health care demand measured by GP, outpatient consultations and inpatient days. Baseline personal characteristics have a strong predictive effect, with older individuals generating higher healthcare demand five years later. Men have lower overall rates of service utilisation than otherwise similar women, due to their better baseline health, which is only partially offset by their higher rate of disability, conditional on baseline health. There are clear socio-economic gradients in healthcare utilisation with respect to income and education. The overall effect of baseline income is a direct positive effect: individuals from high-income households have a higher probability of service use conditional on their baseline biological health and disability outcome. This is consistent with existing evidence on inequalities in health service usage (Cookson et al., 2016; Devaux, 2015). The pattern for education is rather different: lower education has a modest predictive effect on future healthcare utilisation, channelled mainly via the educational gradient in baseline health rather than the uptake of services.

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

Measures of adiposity, grip strength, resting heart rate, blood pressure, and lung function were collected at UKHLS wave 2 during visits by trained nurses. We use the 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 sulphate (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, 2011b).

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, 2011c).

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.

2.3 Health care utilisation measures

Retrospective information on the number of GP consultations, attendance at a hospital or clinic as an outpatient or day patient (OP), and inpatient (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. Given the high skewness of the data on IP days, we grouped inpatient days¹ to construct an ordinal variable: 0, for no IP days; 1, for a single day²; 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.

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, constructed from the GP, OP and IP variables as a five-category ordinal variable coded as 0-4 in the following way³:

¹ For women who reported any inpatient 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 inpatient days. This affects only 0.5% of the sample.

² This category includes 79 cases (1.5% of the sample) who reported having been an inpatient in the preceding 12 months, but then reported 0 days in the follow-up question on the number of IP days.

³ 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 (2019). These cost data are used to construct the five-category composite health services utilisation measure that is described here.

0. No GP or OP consultations and no IP days (implying zero health care costs);
1. One to two GP consultations and zero inpatient 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).

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, 2019 and 2020, 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.

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:

$$B_j = L_j(\alpha_{0j} + \alpha_{1j}h + \varepsilon_j), \quad j = 1 \dots J \quad (1)$$

where ε_j is a classical normally distributed random measurement error and $L_j(.)$ is a link function reflecting the nature of indicator j .⁴ Baseline biological health is determined by the individual's personal characteristics and circumstances, described by a vector of covariates X :

$$h = X\beta + u \quad (2)$$

where $u \sim N(0,1)$ 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:

$$d = \gamma_1 h + X\gamma_2 + v \quad (3)$$

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) $D_1 \dots D_K$:

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

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 :

⁴ 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.

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

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

We estimate two alternative variants of this latent variable model. One uses our single composite ordinal measure of healthcare utilisation (LV Model 1).⁵ 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 1.

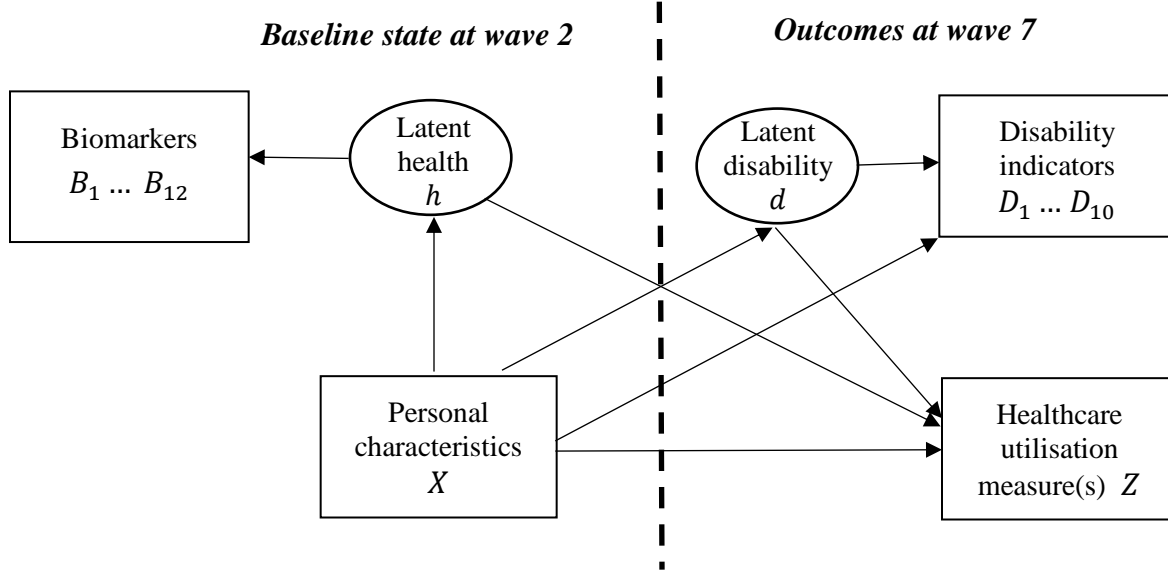


Figure 1. Path diagram for latent variable health-disability-healthcare utilisation model.

4 Results

We first discuss estimates relating to the determinants of baseline biological health h . Table 1 presents the estimated coefficients from model I (the version with a single composite

⁵ In the single-measure model ($M=1$), the two random terms are combined into a single residual error $\omega_m^* = (\lambda_{4m}\zeta + w_m)$, renormalised to have unit variance.

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 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 1. Determinants of latent baseline health h .

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

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

Table 2 presents estimates of the equations for the latent disability outcome d and the service utilisation outcomes (equations (3) and (5) above). For disability (first column in Models I and II, Table 2), 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 gender and income. Men are found to have a significantly higher risk of disability than women after controlling for baseline health and other characteristics. The gender estimates for h and d are intriguing: women tend to have worse biological baseline health than men (Table 1) but this health disadvantage translates into subsequent disability at a much slower rate. This may be for social rather than biological reasons, linked to the self-assessed nature of the disability indicators: women may on average feel less constrained by physical impairments than men if their capability expectations are lower. We also find that individuals with higher

income at baseline are significantly less likely to progress to disability by the five-year horizon (Table 2).

Table 2. 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	-0.152*** (0.046)	-0.054 (0.037)	-0.146*** (0.046)	-0.114*** (0.038)	0.005 (0.067)	-0.086 (0.062)
d		0.646*** (0.048)		0.604*** (0.044)	1.107*** (0.144)	0.475*** (0.061)
Male	0.622** (0.258)	0.110 (0.206)	0.576** (0.260)	0.389 (0.221)	-0.179 (0.376)	0.345 (0.349)
Age	-0.025 (0.068)	-0.057 (0.053)	-0.004 (0.068)	-0.169*** (0.056)	0.087 (0.100)	-0.144 (0.092)
Ln income	-0.199*** (0.054)	0.190*** (0.043)	-0.188*** (0.055)	0.148*** (0.044)	0.332*** (0.088)	0.119* (0.070)
Degree	-0.147 (0.108)	0.105 (0.090)	-0.147 (0.107)	0.007 (0.095)	0.389** (0.167)	0.099 (0.158)
A-level	-0.030 (0.115)	0.054 (0.096)	-0.028 (0.116)	-0.073 (0.101)	0.342* (0.178)	0.165 (0.168)
O-level	-0.028 (0.102)	0.029 (0.087)	-0.027 (0.101)	-0.074 (0.091)	0.249 (0.160)	0.087 (0.154)
Single	-0.071 (0.091)	0.067 (0.070)	-0.059 (0.091)	0.042 (0.073)	0.083 (0.132)	0.041 (0.117)
Divorced	0.107 (0.095)	-0.155* (0.088)	0.099 (0.096)	-0.092 (0.084)	-0.322** (0.155)	-0.045 (0.133)
Widowed	0.043 (0.152)	-0.033 (0.122)	0.037 (0.149)	-0.025 (0.126)	-0.120 (0.222)	0.061 (0.197)
Urban	-0.028 (0.070)	0.084 (0.054)	-0.019 (0.069)	0.054 (0.055)	0.144 (0.103)	0.190** (0.094)

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

Table 2 also presents the estimated coefficients in the equation(s) (5) which determine 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.

As might be expected, we find 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 healthcare.

Controlling for health and disability, there remains a strong positive income gradient in health service utilisation. 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 generally consistent with most findings in the existing research literature on equity in health care utilisation that, conditional on health care needs, inequalities in health care utilisation and quality favours those of higher SES (Cookson *et al.*, 2016; Devaux, 2015; Labeit and Peinemann, 2017; Terraneo, 2015).

4.1 Pathway analysis on the role of the baseline demographics and SES.

Assessing the overall influence of personal baseline characteristics on health services utilisation is complex and needs to consider pathway analysis based on the structure of our LV model. Specifically, our LV model implies that the influence of personal characteristics on the utilisation of healthcare services operates via three paths, shown schematically in Figure 1: the first indirectly via latent health, the second indirectly via disability, and the third directly. The total influence of baseline characteristics on the utilisation outcome is the combination of all paths. Distinguishing these three paths is informative about the processes at work and each of these pathways may be relevant to different policies. Public health policies target health and, thus, operate via the health path; treatments that prevent ill-

health developing into functional disability target the disability path; and policies to control access to services exploit the direct path.

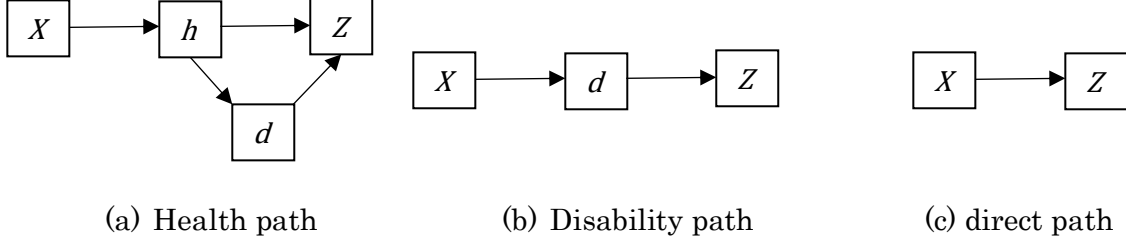


Figure 2. Paths linking personal baseline characteristics X to healthcare utilisation outcome Z , directly and indirectly via latent biological health and/or disability.

To distinguish the paths empirically, we first construct a hypothetical “standard” group of individuals who all have the same baseline characteristics X , but may differ in terms of the random factors (u , v and w) that affect respectively their baseline health state, disability and healthcare utilisation outcomes. The standard individual is someone who is married, female, aged 45, has median equivalised household income, is educated to A-level and live in a suburban or rural area. To summarise the outcome, we use the single combined measure of utilisation (model I) and focus on the probability of the highest level of use. Working from the reduced form for the equation system (1)-(5), and allowing for all the paths detailed in Figure 2, that probability is:

$$Pr(Z = 4|X) = 1 - \Phi\left(\frac{C_4 - X\beta(1 + \lambda_1 + \lambda_2\gamma_1) - X\gamma_2\lambda_2 - X\lambda_3}{\sqrt{1 + \lambda_2^2 + (\lambda_1 + \lambda_2\gamma_1)^2}}\right) \quad (6)$$

where $\Phi(\cdot)$ is the $N(0,1)$ distribution function. In expression (6), the three separate terms in X represent the three paths shown in Figure 2. To assess the influence of a particular characteristic on the probability of a high-utilisation outcome via a specific path, we vary that element of X only in the relevant term in (6) and observe the change in the probability. For instance, if we want to know the influence of income via the health path alone, we vary the assumed income level in the term $X\beta(1 + \lambda_1 + \lambda_2\gamma_1)$, but leave the terms $X\gamma_2\lambda_2$ and $X\lambda_3$ fixed at their values for median income. Figure 3 shows the results of varying income from the 5th to 95th percentile levels, via each path separately and also jointly to give the total income

effect. Note, however, that total effect is not identical to the average of the effects via the three separate paths, owing to the nonlinearity of the function $\Phi(\cdot)$.

We found that the total effect of income is a slight positive gradient, so that high income individuals make slightly higher use of healthcare services than others (Figure 3). This is due entirely to the direct path, conditional on baseline health and progression to disability, and is despite their lesser need for treatment – shown by the negative gradients via the health path and disability path. This supports some existing research findings, suggesting that inequalities in health care utilisation, conditional on health care need, favours those at higher SES (Cookson et al., 2016; Devaux, 2015; Labeit and Peinemann, 2017; Terraneo, 2015).

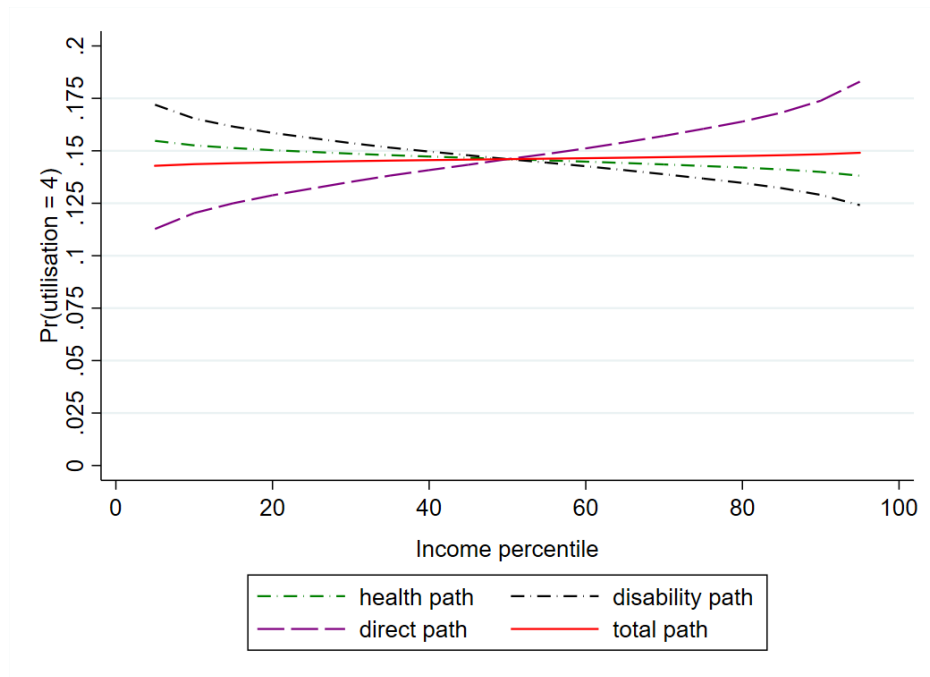


Figure 3. Properties of model I: Gradient along each path of income influence on the probability of the highest level of healthcare utilisation by a hypothetical standard individual (45-year old married woman with median household income, education to A-level, resident in suburban/rural district)

Figure 4 shows a very different picture for age. As we would expect, the model picks up a strong overall age gradient in utilisation, and this is entirely due to the health path – baseline health is substantially poorer for older people. The decline in the estimated probability of

high utilisation via the direct and disability paths is not statistically significant, since the age coefficients in the left-hand panel of Table 2 are grossly insignificant.

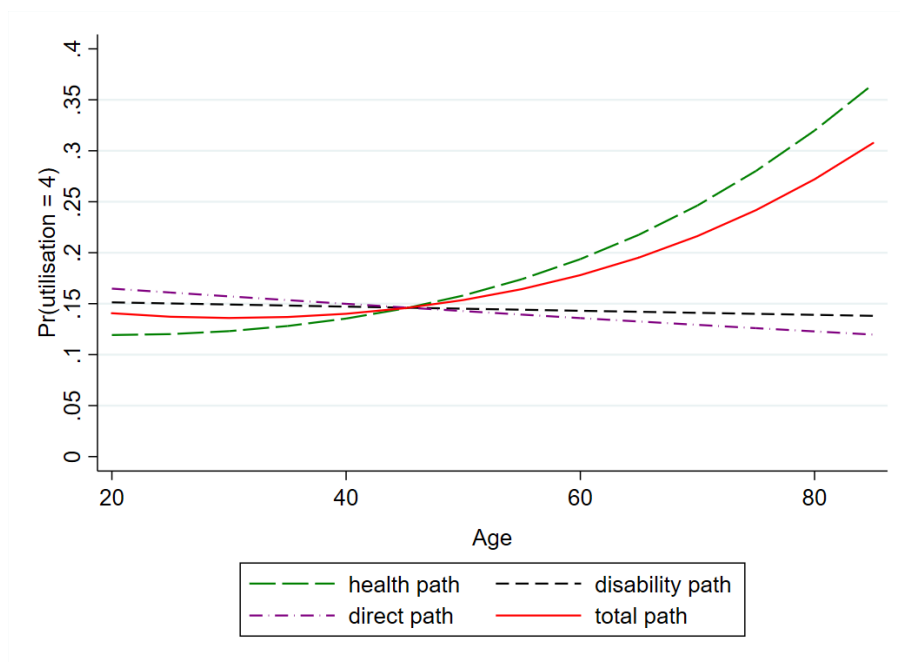


Figure 4. Properties of model I: Gradient along each path of age influence on the probability of the highest level of healthcare utilisation by a hypothetical standard individual (45-year old married woman with median household income, education to A-level, resident in suburban/rural district).

Table 3 shows the estimated effects (for model I) of variations in each of the discrete characteristics in X that have significant coefficients in Table 1 or 2. The standard individual used as a basis for these comparisons has a 15% probability of the highest level of healthcare utilisation. Gender has a significant role via both the health and disability paths, but a less pronounced direct effect on utilisation. The effects via health and disability have opposite signs; on average, men have significantly better biological health at baseline but, for any given baseline health state, they are at higher risk of functional disability. The health effect outweighs the disability effect so, overall, men are significantly less likely (by 5 percentage points) than otherwise similar women to be intensive users of health services. Education and location also have significant effects on the utilisation outcome, but only via their influence on baseline health. The lowest level of educational attainment and urban residence both have

a modest negative influence on health which raises the probability of intensive utilisation five years later by 1 and 3 percentage points, respectively.

Table 3. Properties of model I: Effects of changing characteristics of individual.

	Effect of change in characteristics...			
	via health path	via disability path	via direct path	via all paths
Standard individual [†] , probability of highest utilisation level	0.146	0.146	0.146	0.146
<i>Marginal effect of changing characteristics to...</i>				
...male	-0.106	+0.090	+0.022	-0.053
...no qualifications	+0.014	+0.004	-0.010	+0.007
...urban	+0.012	-0.003	+0.017	+0.026

[†] 45-year old married woman with median household income, education to A-level, resident in suburban/rural district. Effects via separate paths do not average to the effect via all paths combined, due to nonlinearity of the probability (6)

4.2 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 4 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 4. 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 4. Properties of model I: loadings for latent health (h) and disability (d).

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 a disability pathway: conditional on the realised disability state, baseline biological health has little direct impact on utilisation.

Our analysis also allows us to understand better the source of the observed gradients of health service utilisation with respect to demographic characteristics and SES. In addition to their direct impact, we have distinguished two indirect paths for the influence of these personal characteristics on subsequent utilisation, one via their influence on baseline health, the other via their influence on the progression to disability over the 5-year observation window, conditional on baseline health. The most striking results relate to age and income.

Specifically, our analysis suggests that the observed positive association between age and health service utilisation is entirely attributable to the poorer baseline biological health of the older individuals. 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 healthcare system (conditional on baseline health and current disability state).

Our results are consistent with existing evidence on income inequalities in access to, or take-up of, healthcare (Cookson et al., 2016; Devaux, 2015), conditional on healthcare need. We found that this is driven by the direct path, with higher-income individuals extracting treatment from the healthcare system more effectively, conditional on their health and disability status. This leads to an overall slight positive income gradient in health service utilisation, despite the strong negative gradient in treatment needs; the latter is evidenced by the negative income gradients for both baseline health and disability outcomes. This

finding, in the context of the universal publicly funded UK healthcare system can be seen as a call for policies to secure more equal healthcare opportunity at the point of the healthcare delivery.

Our focus on the population who were apparently healthy at baseline and, therefore, not prioritised by the health care system, has potential policy implications for prevention strategies, with the possibility of significant potential public costs savings. Our results suggest that strategies focusing on disability progression as a mediating stage, 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

- 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.
- 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.
- Carrieri, V., Jones, A.M. (2017). The income–health relationship ‘beyond the mean’: New evidence from biomarkers. *Health Economics*, 26(7), 937-956.
- 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. E. (2019). Baseline health and public healthcare costs five years on: A predictive analysis using biomarker data in a prospective household panel. ISER Working Paper Series, No. 2019-01.
- Davillas, A., Pudney, S. E. (2020). Biomarkers as precursors of disability. *Economics and Human Biology*, 100814.
- 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.
- Devaux, M. (2015). Income-related inequalities and inequities in health care services utilisation in 18 selected OECD countries. *European Journal of Health Economics*, 16(1), 21-33.
- DWP, 2017. Family Resources Survey: financial year 2015/16. Department for Work and Pensions, DWP National Statistics. U.K.

- 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.
- Hansen, M. S., Fink, P., Frydenberg, M., and Oxhøj, M. L. (2002). Use of health services, mental illness, and self-rated disability and health in medical inpatients. *Psychosomatic Medicine*, 64(4), 668-675.
- 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.
- Jones, M., 2016. Disability and labor market outcomes. IZA World of Labor. doi: 10.15185/izawol.253
- Kidd, M. P., Sloane, P. J., Ferko, I. (2000). Disability and the labour market: an analysis of British males. *Journal of Health Economics*, 19(6), 961-981.
- Labeit, A. M., Peinemann, F. (2017). Determinants of a GP visit and cervical cancer screening examination in Great Britain. *PLOS One*, 12(4), e0174363.
- 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., Henriët, 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.
- Meyer, B.D., Mok, W.K. (2019). Disability, earnings, income and consumption. *Journal of Public Economics*, 171, 51-69.
- 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
- 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 healthcare 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.
- 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.
- Terraneo, M. (2015). Inequities in health care utilization by people aged 50+: evidence from 12 European countries. *Social Science and Medicine*, 126, 154-163.
- 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 Doorslaer, E.V., Jones, A.M. (2004). Income-related inequality in health and health care in the European Union. *Health Economics*, 13(7), 605-608.
- 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.
- WHO (1980). International Classification of Impairments, Disabilities, and Handicaps: A Manual of Classification Relating to the Consequences of Disease. World Health Organization, Geneva, Switzerland.
- WHO (2011a). World report on disability 2011. World Health Organization. Geneva, Switzerland.
- WHO (2011b). Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus. World Health Organisation. Geneva, Switzerland.
- WHO (2011c). 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.