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Trajectories of the healthy ageing phenotype among middle-aged and older Britons, 2004–2013

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ABSTRACT

Objectives: Since the ageing population demands a response to ensure older people remain healthy and active, we studied the dynamics of a recently proposed healthy ageing phenotype. We drew the phenotype's trajectories and tested whether their levels and rates of change are influenced by health behaviours, comorbidities and socioeconomic positions earlier in the life course.

Design and outcomes: The English Longitudinal Ageing Study, a prospective, nationally representative sample of people aged ≥50 years, measured a set of eight biomarkers which make up the outcome of the healthy ageing phenotype three times over nearly a decade (N_{2004} = 5009, N_{2008} = 5301, N_{2013} = 4455). A cluster of health behaviours, comorbidities and socioeconomic positions were also measured repeatedly. We assessed the phenotype's distribution non-parametrically, then fitted linear mixed models to phenotypic change and further examined time interactions with gender and socioeconomic position. We ran additional analyses to test robustness.

Results: Women had a wider distribution of the healthy ageing phenotype than men had. The phenotype declined annually by −0.242 (95% confidence interval [CI]: −0.352, −0.131). However, there was considerable heterogeneity in the levels and rates of phenotypic change. Women started at higher levels, then declined more steeply by −0.293 (CI: −0.403, −0.183) annually, leading to crossover in the trajectories. Smoking and physical activity assessed on the Allied Dunbar scale were strongly associated with the trajectories.

Conclusion: Though marked by secular decline, the trajectories of the healthy ageing phenotype showed distinct socioeconomic gradients. The trajectories were also susceptible to variations in health behaviours, strengthening the case for serial interventions to attain healthy and active ageing.

1. Introduction

Recently, foundations of healthy ageing based on biomarkers have been proposed on both sides of the Atlantic [1–3]. Seemingly independent, these proposals nonetheless show considerable overlap and are driven by the same principles of deriving a phenotypic index which captures broad organ systems, while at the same time remaining pragmatically driven by available data in ageing studies. The healthy ageing phenotype, in particular, is sensitive to changes in multiple dimensions that people experience as they age [4], and it captures these by building the phenotype on measures including psychological wellbeing, social wellbeing, physical capability, cognitive function, and physiological and metabolic health [3]. We study one dimension of the phenotype, namely physiological and metabolic health.

Limited work has been done so far on the healthy ageing *phenotype* [3] or the healthy ageing *index* [2]. In the Cardiovascular Health Study, people with higher index scores had significantly lower mortality [1]. With adjustment for demographics, health behaviours and comorbidities, the index significantly predicts death during follow up; and it has been found to be heritable [2].

No empirical study has implemented the healthy ageing phenotype, let alone examined its distribution in the various groups in the population. Such an omission can prove a hindrance to an effective monitoring of and response to the population ageing challenge, for instance to reduce social gradients in health in later life [5]. Thus our first aim is to provide the distribution of the healthy ageing phenotype in the different groups in the population while taking up the suggestion in the proposal to broaden the basis of the phenotype. Next we aim to draw trajectories of phenotypic change from

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2004 to 2013 in the British population aged ≥ 50 years using an ongoing, nationally representative ageing study. Most importantly we weigh the contributions of early life course social determinants (including occupation and education) [5–9] and of contemporaneous comorbidities and health behaviours (smoking, drinking and physical activity) [5,10] on the levels and rates of change of the healthy ageing phenotype.

We test a number of hypotheses. First, given the well-known social gradients in health, we hypothesise that the phenotype levels will differ along socioeconomic positions throughout the life course, from earlier (education attainment) through more recent (occupation) to contemporaneous (wealth levels) positions. Second, even after accounting for social gradients in the average levels of trajectories in later life there will still be differences in the rates of change according to socioeconomic positions.

2. Methods

The English Longitudinal Study of Ageing (ELSA) is the main resource for a nationally-representative ageing study of the English older population. The first wave was in 2002 and subsequent waves follow biennially. Repeated biomarker information is available from the even numbered waves (2004, 2008 and 2012/2013) when nurses visited the participants. The data are freely available from the UK Data Archive (www.data-archive.ac.uk) as study number 5050. More details of the study are given elsewhere [11–13].

2.1. Dependent variable: healthy ageing phenotype

The healthy ageing phenotype was constructed following its definition [3] with an extension to take up a suggestion to broaden its base. These biomarkers as originally proposed include: (*a*) arterial blood pressure as a measure of cardiovascular function, (*b*) fasting glucose and glycated haemoglobin (HbA1C) as markers of glucose homeostasis, (*c*) forced expiratory volume in 1 s as a marker of lung function, (*d*) waist circumference as a marker of adiposity and (*e*) plasma concentrations of HDL cholesterol and triglycerides as markers of lipid metabolism. To this list, another group (*f*) consisting only of serum concentration of high sensitivity C-reactive protein was added. The original definition shared some indicators with the healthy ageing index [2]. The six groups (*a*–*f*), or eight biomarkers, were collected repeatedly and are representative of an array of organ systems.

2.2. Collection and assay

Biomarkers data were collected by trained nurses. Systolic blood pressure was measured using a standardised method. Three readings were collected at one-minute intervals using the Omron HEM-907 equipment; the highest reading was used. It was ensured that the room temperature was between 15 °C and 25 °C. Glucose was analysed using the Tosoh Analyzer HLC-723G8. Lung function tests were done using a hand-held Vitalograph spirometer. Three consecutive readings were taken, and the maximum was recorded. Concentrations of HDL cholesterol and triglycerides were measured using Roche Modular Analyzer. High sensitivity C-reactive protein concentration was determined using Roche Modular P. These biomarkers have been described in a number of official ELSA technical reports [14–16].

We followed the earlier construction [2] by using tertiles or clinical cut-offs (coding 0, 1 and 2 accordingly) of each of the eight biomarkers, then added the codes to give a score which ranges from 0 to 16. The clinical cut-offs for fasting glucose are 6.1 and 7.0 mmol/l (National Institute for Health and Care Excellence; www.nice.org.uk/guidance/ph38/chapter/glossary, accessed 10 August 2015). The cut-offs for waist circumference they are 80 and 88 cm (women) and 94 and 102 cm (men); and for systolic blood pressure they are 130 and 140 mmHg [17]. Being treated for certain diseases coded the related biomarkers to the unhealthiest tertile; as in the instance of receiving treatment for diabetes and its glucose code or receiving treatment for hypertension and its systolic blood pressure code. But we departed from the precedent by reversing the coding to give higher scores for healthier phenotypes.

2.3. Covariates

For this first empirical examination of the trajectories, we included an extensive set of covariates. Demographic covariates include gender and age. Since age is capped at 90 in ELSA, information from respondents aged 50–89 was used. Like other health functions, healthy ageing phenotype is also shaped by social determinants of health. These include threefold social class (managerial, intermediate and routine-manual as reference), wealth tertiles (top, middle and bottom as reference), education (some college and high school or less as reference), marital status (married/cohabiting and other as reference).

Based on positive medical history (self-report of 'has been diagnosed by professionals'), a set of indicators about comorbidities were included, covering cardiovascular diseases of angina, arrythmia, high blood pressure, congestive heart failure, myocardial infarct and heart murmur; chronic obstructive pulmonary disease; diabetes; stroke; arthritis; osteoporosis and cancer. In addition, depression score (Center for Epidemiologic Studies Depression) is included and entered as a continuous variable. Behavioural risk factors known to be important in other studies include smoking (current smoker versus not current smoker as reference), drinking (days in a week having a drink) and physical activity on the Allied Dunbar scale [18] entered as a continuous variable.

Participants with incomplete information on any of the variables were excluded from the analysis, giving an analytic sample of 14,765 observations. Following the "Strengthening the Reporting of Observational Studies in Epidemiology" or STROBE guide [19], a flowchart summarising the included sample is given as a supplement. Differences between those included and excluded were tested using *t*-test (continuous variables) or χ^2 test (categorical variables). At baseline, compared to those excluded, the analytic sample is younger (65 versus 68 year, $p < 0.001$), has fewer women (54% versus 57%; $p = 0.016$), is on average wealthier (£63,310 versus £49,674, $p = 0.001$) and has healthier ageing phenotype (7.2 versus 5.4, $p < 0.001$).

2.4. Statistical analysis

Since the healthy ageing phenotype distribution was found to be symmetrical and near-normally distributed (see Fig. 1 later), a linear mixed model with random intercepts was fitted to estimate trajectories of change. The random intercepts capture all within individual variations that did not change during study period, including genetic variation. In the baseline model all main effects are included, comprising gender, age, marital status, comorbidities, socioeconomic positions and health behaviours. In the interactions models, in addition to the main effects, interactions between age (in years) with gender, with wealth, with occupation and with education were included separately. Together there were four interactions models. The best model is chosen based on Bayesian Information Criterion [20], picking one with the smallest statistic as the best. All analyses were done in Stata 14 (StataCorp LP, College Station, Texas).