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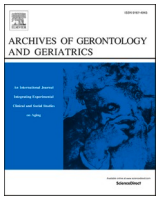

Impact of quality of life in developing cardiovascular disease later in life: Graphical chain model of the English Longitudinal Study of Ageing (ELSA)

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ABSTRACT

Introduction: The aim of this paper is to demonstrate how graphical chain models can be used to model how cardiovascular disease affected quality of life in later life over the course of 17 years of data.
Methods: Waves 1-9 of the English Longitudinal Study of Ageing was used to investigate how quality of life changed over each wave using the CASP-19 questionnaire, and whether having experienced a cardiovascular event had an effect on quality of life.
Results: A total of 12,099 participants were included in the study. Participants had a mean age of 64.2 years, the majority of which were over 50 years old. Older people are more likely to have cardiac events. A one-unit rise in CES-D 8-item score was related with a 14% increased risk of CVD at Wave 1. Those with an O-level, A-level, or degree (or equivalent) had lower CVD risks than those with no education. Women had half the CVD risk of men. Living alone reduced the risk of a CVD-event by 15%. Moderate and vigorous exercise lowered cardiac event risk compared to no exercise. Current or ex-smokers have a 30% higher risk of CVD than non-smokers. Cardiovascular event was significantly associated with quality of life at waves 1 and 2 only.
Discussion: Events related to cardiovascular disease only affected quality of life in later life up to 4 years. Factors such as age, depression, perceived position on social ladder, and high levels of physical activity affected quality of life throughout the majority of waves.

1. Introduction

The World Health Organisation (WHO) defines quality of life (QoL) as "an individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (The World Health Organization quality of life assessment (WHOQOL) 1995). This is especially important when considering quality of life in later life, as many older adults who become afflicted with chronic disease prefer quality of life to longevity (Rejeski & Mihalko, 2001).

Factors associated with health-related quality of life (HRQoL) in older adults include number of chronic illnesses, depression (Klompstra et al., 2019), physical activity (Baernholdt et al., 2012, Daengthern et al., 2020), gender (Alcañiz & Solé-Auró, 2018), and social engagement (Morgan et al., 1991). Various validated measures that quantify QoL exist, however the most common QoL measures are not old-age specific. One review of studies measuring HRQoL in older patients groups (Hickey et al., 2005) found that of the 37 studies reviewed, all 28 different HRQoL measures were not specific to just patients in old age (around 60 years plus). This allows comparison between age groups but items in these questionnaires tend to be phrased mostly in relation to physical function, which may discriminate against the aged population.

Cardiovascular diseases (CVD) are the leading cause of death around the world, amounting to almost 18 million deaths in 2019 ((WHO) WHO, 2021). They are various conditions that affect the heart or blood vessels including angina, chest pain caused by restricted blood flow to the heart, myocardial infarction, where blood flow to the heart is suddenly blocked, congestive heart failure, when the heart does not pump blood as well as it should, and stroke, when blood supple to part of the brain is cut-off.

CVD, and poorer outcomes as a result of CVD, mostly affects older people. One study found that the prevalence of CVD was less than 1% in people under the age of 50 years, 12.5% in people aged 60-69 years, 25.8% in people aged 70-79 years, and almost half (44.0%) in people

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aged 80 years or more (Hinton et al., 2018). In a similar vein, adults aged 65 years or more accounted for 82% of all deaths attributable to CVD in the USA in 2005 (Yazdanyar & Newman, 2009). A similar story is told in the UK between 1988 and 2011 (Bhatnagar et al., 2016) where patients in the two highest age groups, 65-74 years and 75 years or more, had the highest prevalence of CVD, and the percentage increased from 1988 to 2011. With respect to how CVD related to HRQoL, an increased number of CVD is generally associated with poorer HRQoL (Djärv et al., 2012), including fatigue, edema, and sleeping difficulties (Komalasari & Nurjanah, 2019).

To the best of our knowledge, no other study has investigated how experiencing a cardiovascular (CV) event associates with quality of life in later life over 17 years of follow-up with regular data collection around every two years. Therefore, the aim of the study was to investigate how quality of life among the adult population was related to experiencing a cardiovascular-related event later in life.

2. Methods

2.1. Data source

Data were drawn from the English Longitudinal Study of Ageing (ELSA) project, which collects data from people aged over 50 years to understand various aspects of ageing in England (Banks et al., 2021). The sample has been refreshed at waves 3, 4, 6, 7, and 9 so that it remains representative of the UK over fifty population. Data collection began in 2002 (wave 1) and has completed nine total waves of data collection, taken two years apart. Fieldwork for wave ten started in October 2021 and is due to be completed by July 2023. Inclusion criteria for wave 1 of ELSA included participants who fit the age eligibility criteria of a given ELSA cohort (50 years or older), participated in the sample-origin Health Survey for England (HSE) survey, and participated in the first wave of ELSA when invited to join the study. Participants were invited to subsequent waves to refresh the sample if they were participants of HSE and were aged from 50 years. Participants of HSE are chosen at random to ensure a truly representative picture of people living in private households in England.

2.2. Quality of life in later life

The CASP-19 questionnaire was administered from wave 1 and collected at every subsequent wave as part of the ELSA study. Participants are asked a series of 19 questions to assess the quality of life in individuals in early old age in four domains: control, autonomy, self-realisation, and pleasure. Responses on based on a 4-point Likert scale: 0=never, 1=not often, 2=sometimes, and 3=often. Negatively perceived questions are reverse scored. For example, item C1 “my age prevents me from doing the things I would like to do” is reverse scored. All responses are summed, yielding a score with range 0 to 57, where higher scores indicate high levels of satisfaction of quality of life. This was a continuous outcome and was modelled using a linear regression model.

2.3. Analytic framework

The analytic framework is shown in Fig. 1 and is displayed as a graphical chain model with three blocks. Block 1 contains the key baseline characteristics which are used as covariates in analyses for blocks 2 and 3 (denoted by the large arrow). Block 2 contains one variable: whether the participant has had a CVD event up to wave 1, which will be used as a covariate for block 3 analyses. Block 3 contains the CASP-19 total score outcomes from wave 1 up to wave 9. Further details are presented in subsequent sections.

2.4. Outcome variable

In the GCM framework, these are presented in block 3. The covariates used for the CASP-19 model were the baseline characteristics in block 1, and the CVD-event variable in block 2 of the framework. From wave 2 onwards, the CASP-19 score of the previous wave was also added to the model to assess how QoL score for one wave affects QoL score of the next wave.

2.5. Explanatory variables

Explanatory variables in block 1 were chosen based on the following.

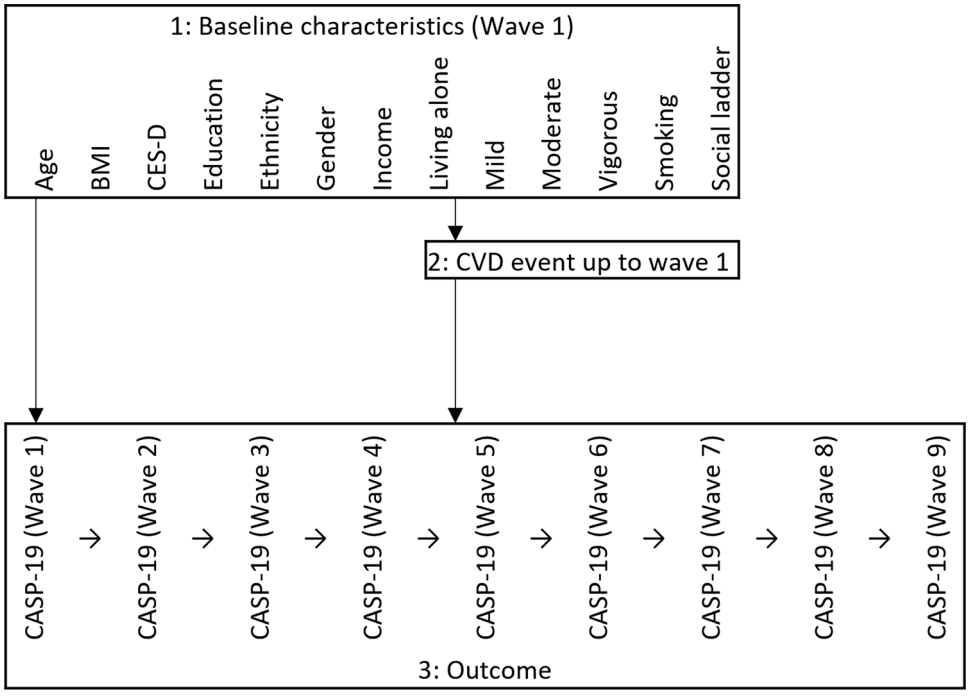

Fig. 1. Graphical chain model of the longitudinal relationship between CASP-19 score and key characteristics.

Ethnicity (whites vs non-white) was the main variable of interest for this analysis. The remaining variables were chosen on the basis that they have been shown in the literature to be associated with CASP-19 score (Howel, 2012). Age (years) and CES-D 8-item score (scored from 0 to 8 where higher scores signify higher levels of depression) were continuous variables, the remaining were categorical. Highest education qualification was grouped into no qualification, foreign/other, NVQ1/CSE, NVQ2/O-level, NVQ3/A-level, higher education below degree, and NVQ4-5/degree level. Gender was grouped into male vs female. Income was asked in the ELSA project as "About how much did your income from work amount to in the last year?", which was then categorised into quintiles. Participants were asked to describe other members of their households (such as partners or children), which was then used to create a single binary variable if a participant lives alone or not. Physical activity was grouped into never, 1-3 times a month, once a week, or more than once a week for three levels of activity: mild, moderate, and vigorous. Perceived position on social ladder (0-100 scale, 100=highest perceived social status) was divided into five groups (0-20, 21-40, 41-60, 61-80, 81-100). Smoking status was divided into never smoked, ex-smoker, and current smoker.

BMI is calculated using height and weight. In the ELSA project, these were collected in every even wave of ELSA, so not in wave 1. Therefore, BMI was calculated using wave 0 height and weight as a proxy for wave 1. Using the NHS ranges (NHS), BMI was categorised into underweight (BMI<18.5); normal (18.5≤BMI<25); overweight (25≤BMI<30); obese (BMI≥30).

Block 2 of the framework contained one binary variable: "Has the participant of the ELSA study had a CVD event up to wave 1?" This question is not explicitly asked in the ELSA study at any wave. Instead, participants are asked about the age at which they were diagnosed with ten different conditions, four of which are cardiovascular conditions: angina, myocardial infarction, congestive heart failure, and stroke. These were combined into a binary 'yes' and 'no' variable and modelled using a logistic regression model with the baseline characteristics in block 1 of the GCM framework included as covariates.

2.6. Statistical analysis

Details on graphical chain models can be found in a paper by Berrington et al. (2008). Briefly, graphical models provide a means of representing the dependency structure between a set of variables, especially useful for visualising the structure when there is a large number of variables being controlled for Ihler et al. (2007). The main components of a typical graphical model are:

- Nodes in the graphical model represent each variable of interest, including predictor and outcome variables.
- Edges (or lines) in the graphical model represent the association between the pair of variables.
- Conditional independence is key in graphical models. In this paper, two variables v_1 and v_2 are conditionally independent of each other if v_1 is independent of v_2 given the remaining variables in the graphical model, and this is represented by a missing edge between v_1 and v_2.

Chains graphs are useful when there are a set of variables that are ordered, either naturally or to some a priori underlying concept (Borgoni et al., 2012, Lauritzen & Richardson, 2002). Variables are partitioned into 'blocks' which are then ordered to create the chain where variables in one block are potential predictors of variables in all subsequent blocks.

A generalised linear model with identity link was fitted to the nine CASP-19 models separately, and a GLM with log-link was fitted to the CVD-event outcome. Covariates were selected for each model using the 'stepwise' command in Stata, which uses automated backward elimination (Henderson & Denison, 1989) to build a final model, so as to not rule out any covariates in advanced and ensure a parsimonious model. Only predictors whose p-value was less than 0.05 was included in the final model for each outcome, either by the F-test for continuous predictors, or by the likelihood ratio test for categorical predictors. The inclusion of all two-way interaction between significant covariates were considered. As the CASP-19 outcome is of primary interest, the association structure of block one was not modelled.

To test for outliers, standardised residuals were assessed using histograms and quantile-quantile plots, and the Shapiro-Wilks test to test for normality. Observations whose residuals were more than three standard deviations outside the mean were removed from the analysis (Grubbs, 1969).

Main analyses were unweighted. Variables that can be used for weighting in each wave of the ELSA project were available in the datasets. In waves 1 and 2, weights were calculated for core sample members only (the original sample that was selected from the three years of HSE: 1998, 1999, and 2001). For waves 3 to 9, weights were defined for the subset of cases who had taken part in all waves. Additional weight variables were created for waves 8 and 9, defined as the subset of cases who had taken part in all waves since wave 4. These weights were considered in sensitivity analyses and were used to account for missing data.

The significance level was set at the 5% level and all analysis were performed in StataSE 17 (StataCorp, 2021). The modelling procedure was performed ten times. To control for type I error, the Bonferroni method (Etymologia: Bonferroni correction 2015, Armstrong, 2014) was used, setting the significance level to 0.5%.

3. Results

3.1. Baseline characteristics

The number of participants included in the study at each wave is presented in Fig. 2. Dropouts at each wave were between 2.1 and 26.5% with the highest study attrition occurring between waves 1 and 2. After which, dropouts remained steady at around 12-14% except between waves 4 and 5 where dropouts only amounted to 2.1% of participants.

Baseline characteristics and outcomes of Wave 1 participants of the ELSA project are presented in Table 1. A total of 12,099 participants were included in the study. These were the participants with a valid CVD-event variable. Participants had a mean age of 64.2 years (SD = 11.1), the vast majority of which were over 50 years old. Mean BMI was 25.6 km/m^2, which is categorised as overweight, and this is reflected in the respective BMI groups where the overweight and obese categories combined represented 70% of the sample. The vast majority of participants where white (97%) and there were slightly more males in the sample. About one-quarter of the sample live alone, just over two-fifths of the sample have no qualifications, and the remaining have a fairly even split of O-level or higher qualifications. A third of the sample had never smoked and 18% still smoked at the time of asking at Wave 1. More participants partook in regular mild or moderate physical activity than vigorous physical activity, which may be expected considering the age of the sample. Of the 12,099 total in this sample, only 254 (2%) reported income, with a mean income around £8,700. Again, considering the age of the sample, many are past retirement age, so this seems reasonable. In this sample, 15.6% of participant has experienced a cardiac event as of Wave 1.

3.2. Quality of life in later life over 9 Waves

There were 9910 participants with a valid CASP-19 score at Wave 1 in this sample. Due to expected study attrition, only 3,116 ELSA participants had a CASP-19 score at Wave 9. The total CASP-19 score gradually decreased slightly from Wave 1 to Wave 9, from a mean of 42.6 to a mean score of 41.7, with a low of 40.9 in Wave 6.

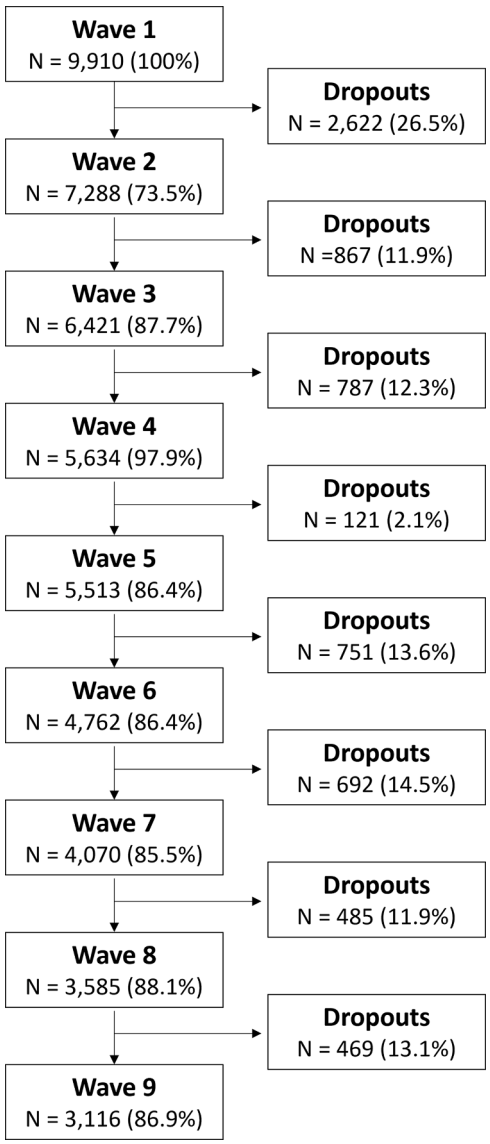

Fig. 2. Number of ELSA participants with valid CASP-19 score and the proportion of dropouts at each wave.

3.3. Model selection

The 'CVD-event' variable of block 2 was modelled first with the baseline characteristics in block 1 using backward elimination. The same procedure was used to model the CASP-19 scores in block 3 individually, including the CASP-19 score of the wave preceding the one being modelled. Results presented in the upcoming sections are based on all available cases and were unweighted.

3.4. Are cardiac events up to Wave 1 predicted by baseline characteristics?

First, whether the ELSA participant had experienced a CVD event up to Wave 1 or not was modelled, including only the baseline characteristic variables in the first block as predictors, the results of which are presented in Table 2. Older participants are more likely to have experienced a cardiac event than younger ones, increasing by 6% yearly, which is to be expected. There was no statistically significant difference between participants with normal and underweight participants, but participants with higher BMI had significantly higher odds of experiencing a CVD event. A one-unit increase in the CES-D 8-item score was

Table 1
Baseline characteristics of ELSA participants in Wave 1.

Variable	Total N	Mean or N	SD or %
Age (years)			
Mean (SD)	12,099	64.2	11.1
Under 50 years	12,080	577	4.8%
50 to 59 years		4,275	35.4%
60 to 69 years		3,413	28.3%
70 to 89 years		3,719	30.8%
90+ years		96	0.8%
Body Mass Index (kg/m^2)			
Mean (SD)	10,710	25.6	4.6
Underweight	10,710	79	0.7%
Healthy		3,154	29.5%
Overweight		4,762	44.5%
Obese		2,715	25.4%
CES-D total score			
Mean (SD)	11,612	1.6	2.0
Highest educational qualification			
No qualification	12,064	5,008	41.5%
Foreign/other		1,015	8.4%
NVQ1/CSE grade equivalent		582	4.8%
NVQ2/GCE O level equivalent		1,974	16.4%
NVQ3/GCE A level equivalent		764	6.3%
Higher education below degree		1,333	11.1%
NVQ4/NVQ5/Degree or equivalent		1,388	11.5%
Ethnicity			
Non-white	12,017	11,658	97.0%
White		359	3.0%
Gender			
Female	12,099	5,335	44.1%
Male		6,764	55.9%
Income (£)			
Mean	254	8694.86	10145.28
Quintile 1 (£0 - £1,300)	254	51	20.1%
Quintile 2 (£1,301 - £3,500)		52	20.5%
Quintile 3 (£3,501 – £7,000)		50	19.7%
Quintile 4 (£7,001 - £15,000)		53	20.9%
Quintile 5 (£15,001 – Highest)		48	18.9%
Is participant living alone?			
No	12,099	9,250	76.5%
Yes		2,849	23.6%
Physical activity			
Mild	11,905		
More than once a week		8,667	72.8%
Once a week		1,367	11.5%
One to three times a month		458	3.9%
Hardly ever or never		1,413	11.9%
Moderate	11,903		
More than once a week		6,780	57.0%
Once a week		1,924	16.2%
One to three times a month		807	6.8%
Hardly ever or never		2,392	20.1%
Vigorous	11,905		
More than once a week		2,145	18.0%
Once a week		1,157	9.7%
One to three times a month		1,122	9.4%
Hardly ever or never		7,481	62.8%
Perceived position on social ladder			
Mean	10,598	57.4	17.6
0-20	10,598	453	4.3%
21-40		1,842	17.4%
41-60		4,664	44.0%
61-80		3,171	29.9%
81-100		468	4.4%
Smoking status			
Never	11,908	4,285	36.0%
Ex-smoker		5,461	45.9%
Current smoker		2,162	18.2%
Had a CVD-event up to			
Wave 1	12,099	1,891	15.6%
CASP-19 total score			
Wave 1	9,910	42.6	8.7
Wave 2	7,288	42.8	8.7
Wave 3	6,421	41.2	8.6
Wave 4	5,634	41.0	8.7
Wave 5	5,513	41.0	8.9

(*continued on next page*)

Table 1 (*continued*)

Variable	Total N	Mean or N	SD or %
Wave 6	4,762	40.9	8.7
Wave 7	4,070	41.9	8.6
Wave 8	3,585	41.6	8.6
Wave 9	3,116	41.7	8.6

Table 2
Parameter estimates from the logistic regression model of the CVD-event at wave 1 (2004-2005) outcome.

		Estimate	SE
Constant		0.006**	0.001
Age	Per one-year increase	1.06**	0.003
BMI	Normal	*Ref*	*Ref*
	Underweight	1.32	0.42
	Overweight	1.30**	0.10
	Obese	1.44**	0.12
CES-D total	Per one-unit increase	1.14**	0.02
Highest educational qualification	None	*Ref*	*Ref*
	Foreign/other	0.90	0.10
	NVQ1/CSE grade equivalent	0.88	0.12
	NVQ2/GCE O level equivalent	0.73**	0.07
	NVQ3/GCE A level equivalent	0.75*	0.11
	Higher education below degree	0.90	0.09
	NVQ4/NVQ5/Degree or equivalent	0.76*	0.09
Gender	Male	*Ref*	*Ref*
	Female	0.52**	0.03
Is the participant living alone?	No	*Ref*	*Ref*
	Yes	0.85*	0.06
Moderate physical activity	Never	*Ref*	*Ref*
	1-3 times a month	0.63**	0.08
	Once a week	0.61**	0.06
	More than once a week	0.53**	0.04
Vigorous physical activity	Never	*Ref*	*Ref*
	1-3 times a month	0.71**	0.08
	Once a week	0.70**	0.09
	More than once a week	0.74**	0.07
Smoking status	Never	*Ref*	*Ref*
	Ex	1.33**	0.09
	Current	1.27*	0.12

* Significant at the 5% level.
** significant at the 0.5% level.
Pseudo R^2=0.13; N=10,373.

associated with 14% increased odds of having had a CVD event at Wave 1. Those with O-level, A-level, or degree (or equivalent) qualifications had statistically significantly reduced odds of a CVD event compared to those with no qualification. Women were almost half as likely to have a CVD event compared to men. Those living alone had 15% lower odds of a CVD-event compared to those who were living with at least one other person. Moderate and vigorous intensity physical activity was found to statistically significantly reduced odds of a cardiac event, compared to not doing any exercise of this intensity. Being a current or ex-smoker increased the odds of a CVD event compared to people who had never smoked by around 30%. The remaining variables in block 1 were not found to be statistically associated with having a CVD event by Wave 1.

The pseudo-R^2 of 0.13 suggests that the baseline characteristics only account for 13% of the overall variation in this outcome, thus a substantial amount of heterogeneity still exists after controlling for these variables.

3.5. Is quality of life in later life associated with experiencing a cardiac event?

After first modelling CVD-event up to Wave 1, nine analyses were undertaken where the CASP-19 total score was modelled using the baseline characteristics and CVD-event variables as predictors. Additionally, since CASP-19 score from the previous Wave was added as a predictor, change in CASP-19 score was actually being modelled. Results from the analyses are presented in Table 3 (Waves 1-5), Table 4 (Waves 6-9), and Table 5 (interaction terms), including terms that were statistically significant at 5% and 0.5%.

For CASP-19 score at Wave 1, a one-unit increase in CES-D total, signifying higher levels of depression, decreased quality of life score by 2. Non-white participants had a lower score compared to Whites, as did male participants compared to females. Higher levels of regular moderate or vigorous physical activity increase quality of life score compared to those who did not to exercise at this intensity. CASP-19 score increased as perceived position on social ladder group increased. There was no significant difference between participants who never smoked and who were ex-smokers, but current smokers had a decreased QoL score. Participants who had experienced a CVD-event as of Wave 1 had a decreased QoL score by 1.57 compared to those who did not. The effect of CES-D total was found to interact with gender and vigorous physical activity.

From Wave 2 onwards, age plays a statistically significant role in QoL scores, where an increase in age is associated with a lower QoL score by 0.07 to 0.11, depending on Wave. CES-D total also played a significant role in QoL score, where higher levels of depression decreased QoL score, except at Wave 4, where a one-unit increase in depression score increased QoL score. This was not a statistically significant result alone, but due to the interaction between CES-D score and both BMI and QoL score, it was included in the model. CASP-19 from the previous Wave was statistically significant at all Waves, where a one-unit increase in CASP-19 score from the previous Wave was associated with an increased CASP-19 score at the current Wave by around 0.7. Similarly, to Wave 1, the higher the perceived position on social ladder in Waves 2 to 8, the higher the QoL score.

Variables that were not significant at every Wave but were statistically significant at individual Waves, other than age, CES-D, and previous CASP-19 score were physical activity (regular moderate and vigorous physical activity increases QoL), higher perceived position on social ladder increased QoL, smoking decreased QoL, higher education qualifications increased QoL compared to no qualifications, and females were associated with higher levels of QoL.

The following variables were not statistically significant predictors of CASP-19 score at any wave, after adjusting for all the aforementioned variables: income quintile, and whether the participant was living alone or not.

3.6. Sensitivity analyses

Outlying residual accounted for 0.6-1.2% of observations in the sample across of all the ELSA waves, defined as residuals outside of ±3 SDs from the mean. Additionally, outlying residuals accounted for 4.6-5.6% of residuals outside of ±1.96 SDs from the mean, which is consistent with what is expected under normality assumptions (that 95% of observations are ≤1.96 SDs from the mean). Inspection of the respective scatterplots, QQ plots, and statistically via the Shapiro-Wilks test also concluded that there were a few outliers but no major violations of the normality assumption in this sample. When the outliers were removed from the analysis, there was no evidence of an absence of normality, nor were there any significant changes to results when modelling the full sample.

Similarly, when using the weights that were available in the ELSA project database, results were consistent with the unweighted analysis. This included the weight variables for waves 8 and 9 which were defined for (i) cases who had taken part in all waves, and (ii) cases who had taken part in all waves since wave 4.

Table 3
Parameter estimates of the linear regression of CASP-19 score of Waves 1-5.

		Results for the following waves (years)									
		Wave 1 2002-2003		Wave 2 2004-2005		Wave 3 2006-2007		Wave 4 2008-2009		Wave 5 2010-2011	
		Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
Constant		35.86	0.43	16.49	1.48	15.72	0.82	14.42	0.98	11.64	0.95
Age	Per one-year increase			-0.08**	0.02	-0.07**	0.01	-0.08**	0.01	-0.07**	0.01
BMI	Normal			Ref	Ref			Ref	Ref		
	Underweight			0.02	1.02			2.17	1.44		
	Overweight			0.07	0.17			0.17	0.22		
	Obese			-0.51*	0.20			-0.44	0.27		
CES-D total score	Per one-unit increase	-2.11**	0.06	-0.41**	0.05	-0.53**	0.05	0.27	0.20	-0.38**	0.05
Highest educational qualification	None									Ref	Ref
	Foreign/other									0.86**	0.31
	NVQ1/CSE grade equivalent									0.45	0.42
	NVQ2/GCE O level equivalent									0.41	0.24
	NVQ3/GCE A level equivalent									0.27	0.33
	Higher education below degree									0.26	0.26
	NVQ4/NVQ5/Degree or equivalent									0.04	0.27
Ethnicity	White	Ref	Ref								
	Non-white	-0.97*	0.48								
Gender	ref=Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref		
	Female	1.44**	0.17	0.63**	0.15	0.36*	0.16	0.29	0.16		
Mild physical activity	Never										
	1-3 times a month										
	Once a week										
	More than once a week										
Moderate physical activity	Never	Ref	Ref	Ref	Ref					Ref	Ref
	1-3 times a month	1.68**	0.31	-4.61*	2.27					0.18	0.40
	Once a week	2.37**	0.24	-0.16	1.79					0.29	0.32
	More than once a week	3.01**	0.20	-3.75*	1.44					0.66*	0.27
Vigorous physical activity	Never	Ref	Ref	Ref	Ref			Ref	Ref		
	1-3 times a month	0.31	0.28	1.62	1.38			0.59*	0.26		
	Once a week	0.96**	0.28	-0.65	1.54			0.24	0.25		
	More than once a week	1.27**	0.22	3.68*	1.15			0.47*	0.20		
Position on social ladder	0-20	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
	21-40	3.13**	0.39	0.92	0.48	0.49	0.49	0.73	0.53	1.97**	0.54
	41-60	6.51**	0.37	1.54**	0.47	1.77**	0.48	0.87	0.51	2.35**	0.52
	61-80	8.41**	0.38	2.07**	0.48	2.71**	0.49	1.64**	0.52	2.68**	0.53
	81-100	10.52**	0.48	3.22**	0.58	3.91**	0.58	1.45*	0.61	3.84**	0.62
Smoking status	Never	Ref	Ref					Ref	Ref		
	Ex	-0.02	0.15					-0.07	0.17		
	Current	-0.41*	0.20					-0.84**	0.24		
Had CVD event up to wave 1?	No	Ref	Ref	Ref	Ref						
	Yes	-1.57**	0.20	-0.82**	0.24						
CASP-19 total score from previous wave	Per one-unit increase	NA	NA	0.68**	0.01	0.66**	0.01	0.75**	0.01	0.76**	0.01

* Significant at the 5% level.
** significant at the 0.5% level.
Constant: $p<0.0001$ for all Waves

3.7. The graphical chain model

The results of the 10 models, nine linear and one logistic, are summarised in two graphical chain models, Fig. 3 represents the overall GCM, Fig. 4 represents the interaction terms. Terms with no lines (edges) between them are independent of each other after adjusting for all the other variables. CASP-19 score from Wave 3 onwards is independent of CVD-event up to Wave 1. CASP-19 is independent of ethnicity group at all Waves except Wave 1 and Wave 6.

4. Discussion

4.1. Main result

In this subsample of the ELSA project, ethnicity was associated with CASP-19 at Wave 1 and Wave 6 (data for which was collected ten years after Wave 1) where Non-whites had lower QoL at Wave 1 compared to Whites. After adjusted for other confounders, ethnicity had no effect on CASP-19 score throughout the majority of the Waves in the ELSA project. Interestingly, and perhaps counter-intuitively, Non-white participants were associated with a 9.6-unit increase in CASP-19 score at Wave 6 compared to Whites (significant at 5% level, not at 0.5% level).

Depression, as calculated using the CES-D 8-item questionnaire, was associated with all outcomes except QoL at Wave 4, parallel to (GHDP et al., 2015) where depression was significantly negatively associated with all domains of the SF-36 questionnaire. Perceived position on social ladder was associated with QoL at all Waves except Wave 9.

Results coincided, in part, with a study by Ludt et al (Ludt et al., 2011) where female participants and increases in age were negatively correlated with QoL using the EQ-5D utility score, and physical activity was positively correlated with QoL. We found like other studies that regular exercise at higher intensities were associated with improved mental aspects of health-related quality of life (Ballin et al., 2019, Lee, Hung, Lin, & Chiang, 2019, Banegas et al., 2007).

Income quintile was not a significant predictor at any wave. As mean age was 64.2 years, many of the participants were above UK retirement age (currently 66 years), so this may explain the huge amount of missing data regarding income. If more income data were present, it may have been a significant predictor of QoL, *as was the case in one study by Zagorski et al. (2014), where subjective financial QoL was negatively*

Table 4
Parameter estimates of the linear regression of CASP-19 score of Waves 6-9.

		Results for the following waves (years)							
		Wave 6 2012-2013		Wave 7 2014-2015		Wave 8 2016-2017		Wave 9 2018-2019	
		Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
Constant		12.92	1.17	13.70	2.42	16.56	1.27	15.64	1.47
Age	Per one-year increase	-0.08**	0.01	-0.10**	0.02	-0.11**	0.01	-0.11**	0.01
BMI	Normal					Ref	Ref	Ref	Ref
	Underweight					0.33	1.38	-0.52	1.50
	Overweight					-0.49*	0.23	1.13	1.04
	Obese					-0.73*	0.27	-1.28	1.08
CES-D total score	Per one-unit increase	-0.38**	0.05	-0.28**	0.05	-0.36**	0.06	-0.38**	0.17
Highest educational qualification	None								
	Foreign/other								
	NVQ1/CSE grade equivalent								
	NVQ2/GCE O level equivalent								
	NVQ3/GCE A level equivalent								
	Higher education below degree								
	NVQ4/NVQ5/Degree or equivalent								
Ethnicity	White	Ref	Ref						
	Non-white	9.62*	3.69						
Gender	ref=Male	Ref	Ref						
	Female	3.07**	1.06						
Mild physical activity	Never							Ref	Ref
	1-3 times a month							0.42	1.37
	Once a week							-0.75	1.01
	More than once a week							-0.80	0.86
Moderate physical activity	Never							Ref	Ref
	1-3 times a month							0.07	0.76
	Once a week							0.07	0.63
	More than once a week							0.99	0.57
Vigorous physical activity	Never	Ref	Ref	Ref	Ref				
	1-3 times a month	0.48	0.27	5.67	2.14				
	Once a week	0.56*	0.26	-0.41	2.07				
	More than once a week	0.40*	0.20	-2.75	1.66				
Position on social ladder	0-20	Ref	Ref	Ref	Ref	Ref	Ref		
	21-40	1.08	0.93	0.34	2.47	0.96	0.75		
	41-60	2.45*	0.90	4.67*	2.35	1.86*	0.73		
	61-80	3.01**	0.90	2.95	2.41	2.56**	0.74		
	81-100	3.61**	1.00	10.19**	3.44	3.51**	0.82		
Smoking status	Never					Ref	Ref		
	Ex					-0.01	0.21		
	Current					-1.02**	0.31		
Had CVD event up to wave 1?	No								
	Yes								
CASP-19 total score from previous wave	Per one-unit increase	0.73**	0.01	0.79	0.07	0.72**	0.01	0.78**	0.01

* Significant at the 5% level.
** significant at the 0.5% level.
Constant: $p<0.0001$ for all Waves

corrected with overall QoL. Conversely, another study conducted in the Netherlands (Drukker et al., 2004) found that income inequality at neighbourhood level was not associated with QoL, and a meta-analysis (Ngamaba et al., 2018) of studies that investigated the association between income inequality and subjective well-being found that the overall association between income and well-being to be almost zero. This is something to consider in future studies.

4.2. Strengths and limitations

An advantage of using a graphical chain model to model longitudinal panel data is that it allows the understanding of complicated frameworks through more simpler models, often modelled a priori or follow a natural ordering. The GCM approach allowed the use of a variable, in this case CVD-event, as both an outcome and then a predictor for another outcome. GCMs deal with dropouts over the course of the data by utilising all available data at each timepoint, as opposed to removing observations who may have QoL scores missing at some Waves but present at others if a GCM was not used. Weighted and outlying analyses were performed to assess how sensitive the results were to account for non-response or outlying data. Moreover, data from the ELSA project has been collected for over 17 years of follow-up (between Waves 1-9), increasing confidence in the temporal ordering of the predictors before the outcome of QoL.

The ELSA project is observational in nature, so causation cannot be assumed, rather the analysis in this paper have shown correlation between certain background variables and the two outcomes, CV-event and CASP-19 score (at nine Waves of data). It is a certainty that other confounders have not been collected and thus controlled for in the analysis. However, future studies can address this by planning the study round the associations found in this paper with randomisation. The vast majority of ELSA project participants were White (97%). Although ethnicity was adjusted for, it is possible that analysis was underpowered, and this figure is not representative of the UK (Statistics OfN, 2018), questioning the generalisability of the results to the UK population from which the ELSA project data was collected. CVD-event was based on patient recall and a few participants could not recall the age that they experienced. Even though they were included as having had a CVD-event, it is still possible that not being able to recall a CVD-event may affect recall for other variables and introduce recall bias. Moreover, a study comparing three different quality of life in older life scales (Bowling, 2009) found that the CASP-19 scale had acceptable levels of reliability and validity on the British population sample that it was tested on, but not in the ethnically diverse population, thus

Table 5
Parameter estimates of the interaction terms for linear regression of CASP-19 score of Waves 1-9 where applicable.

	Estimate	SE
Wave 1		
Gender*CES-D total		
Female	0.16*	0.07
Vigorous physical activity*CES-D total		
One to three times a month	0.45**	0.13
Once a week	0.36*	0.14
More than once a week	0.15	0.10
Wave 2		
Moderate physical activity*Age		
One to three times a month	0.08*	0.04
Once a week	0.01	0.03
More than once a week	0.07**	0.02
Vigorous physical activity*CASP-19 score (Wave 1)		
One to three times a month	-0.03	0.03
Once a week	0.02	0.03
More than once a week	-0.07*	0.03
Wave 4		
BMI*CES-D total		
Underweight	-1.50*	0.65
Overweight	-0.23*	0.11
Obese	-0.22	0.12
CES-D total*CASP-19 score (Wave 3)	-0.01*	0.00
Wave 6		
Ethnicity*Perceived position on social ladder		
Non-white*(Quintile 1)	-10.38*	3.97
Non-white*(Quintile 2)	-12.00**	3.85
Non-white*(Quintile 3)	-12.50**	3.96
Non-white*(Quintile 4)	-10.20*	4.37
Gender*Perceived position on social ladder		
Female*(Quintile 1)	-1.99	1.15
Female*(Quintile 2)	-3.06**	1.09
Female*(Quintile 3)	-2.86*	1.09
Female*(Quintile 4)	-2.25	1.26
Wave 7		
Vigorous physical activity*Age		
One to three times a month	-0.09*	0.04
Once a week	0.01	0.03
More than once a week	0.06*	0.03
Perceived position on social ladder*CASP-19 score (Wave 6)		
Quintile 1	0.01	0.07
Quintile 2	-0.07	0.07
Quintile 3	-0.02	0.07
Quintile 4	-0.17*	0.09
Wave 9		
BMI*Mild physical performance		
Underweight*Hardly ever, or never	NA	NA
Underweight*One to three times a month	NA	NA
Underweight*Once a week,	11.77*	5.42
Underweight*More than once a week	NA	NA
Overweight*One to three times a month	-4.38*	1.69
Overweight*Once a week,	-1.21	1.27
Overweight*More than once a week	-1.34	1.07
Obese*One to three times a month	-0.20	1.95
Obese*Once a week,	0.43	1.41
Obese*More than once a week	0.42	1.12
Moderate physical activity*CES-D total		
One to three times a month	0.07	0.26
Once a week,	0.59*	0.24
More than once a week	0.16	0.19

*Significant at the 5% level.
**significant at the 0.5% level.

interpretation of CASP-19 scores should be careful when considering ethnic minority groups. Study attrition is a common issue with the longitudinal design and can result in mean estimates being increasingly biased as attrition rates increased (Gustavson et al., 2012). In this study, only 31.4% of participants had a valid CASP-19 score at wave 9 compared to that at wave 1. Weighted analyses were used to deal with attrition and explore how attrition may have affected results, and were consistent with unweighted analyses. With higher levels of study attrition, and generally in studies of this type, missing data becomes an issue and can lead to biased estimates and invalid conclusions (Kang, 2013). There are two primary reasons why attrition can bias estimates. To begin, attrition leads to a decrease in the size of the sample, and when the size of the sample gets too low, it puts the statistical power at risk. Second, there is the possibility of non-response bias being caused by attrition if it is not a random occurrence (which affects the validity of the study estimates).

4.3. Implications and future research

The findings in this paper highlight the importance of depression, physical activity, and other predictors, in predicting quality of life in later life over time, thus appropriate mental health and exercise support should be offered post-event. Results suggest that experiencing a CVD-event only affects patient-reported QoL for two Waves of the ELSA project, but not afterwards, after adjusting for baseline confounders.

Future studies should measure more types of CVD beyond the four reported in Wave 1 of the ELSA project and measure them consistently at every timepoint available. This will allow investigators to see how the longitudinal effects of experiencing a CVD event compared to using it as a baseline predictor in this paper. It may be difficult to ascertain whether or not a study participant experiences a cardiovascular event between waves but, this way, future studies can directly study the effects of experiencing a cardiac event on a person's short-term mental and physical health. A more representative sample of the UK, with respect to distributions of age, gender, ethnicity, and other important covariates will allow the results can be generalised to the overall UK population better.

4.4. Conclusion

In conclusion, results from this sample of the ELSA project suggest that experiencing a cardiovascular event affects quality of life in the ageing population only for first few years, and then plays a less important role in determining QoL. Possible explanations of this could be lifestyle changes adopted by participants after undergoing a CVD-event or due to treatment. Ethnicity, larger, plays no significant role in determining QoL, but this may be due to the uneven distribution of Whites and Non-whites in the ELSA project. Depression plays a critical role in QoL, as does regular physical activity. Nevertheless, despite the longitudinal nature of the sample, it is unreasonable to rule out the impact of unobserved variables on changes in quality of life in later life.

Ethics approval

Information on the ethnical approval received for each wave of the ELSA project can be found at https://www.elsa-project.ac.uk/ethical-approval and is listed below:

ELSA Wave 9 received ethical approval from the South Central – Berkshire Research Ethics Committee on 10th May 2018 (17/SC/0588).

ELSA Wave 8 received ethical approval from the South Central – Berkshire Research Ethics Committee on 23rd September 2015 (15/SC/0526).

ELSA Wave 7 received ethical approval from the NRES Committee South Central - Berkshire on 28th November 2013 (13/SC/0532).

ELSA Wave 6 received ethical approval from the NRES Committee South Central - Berkshire on 28th November 2012 (11/SC/0374).

ELSA Wave 5 received ethical approval from the Berkshire Research Ethics Committee on 21st December 2009 (09/H0505/124).

ELSA Wave 4 received ethical approval from the National Hospital for Neurology and Neurosurgery & Institute of Neurology Joint Research Ethics Committee on 12th October 2007 (07/H0716/48).

ELSA Wave 3 received ethical approval from the London Multi-Centre Research Ethics Committee on 27th October 2005 (05/MRE02/63).

ELSA Wave 2 received ethical approval from the London Multi-

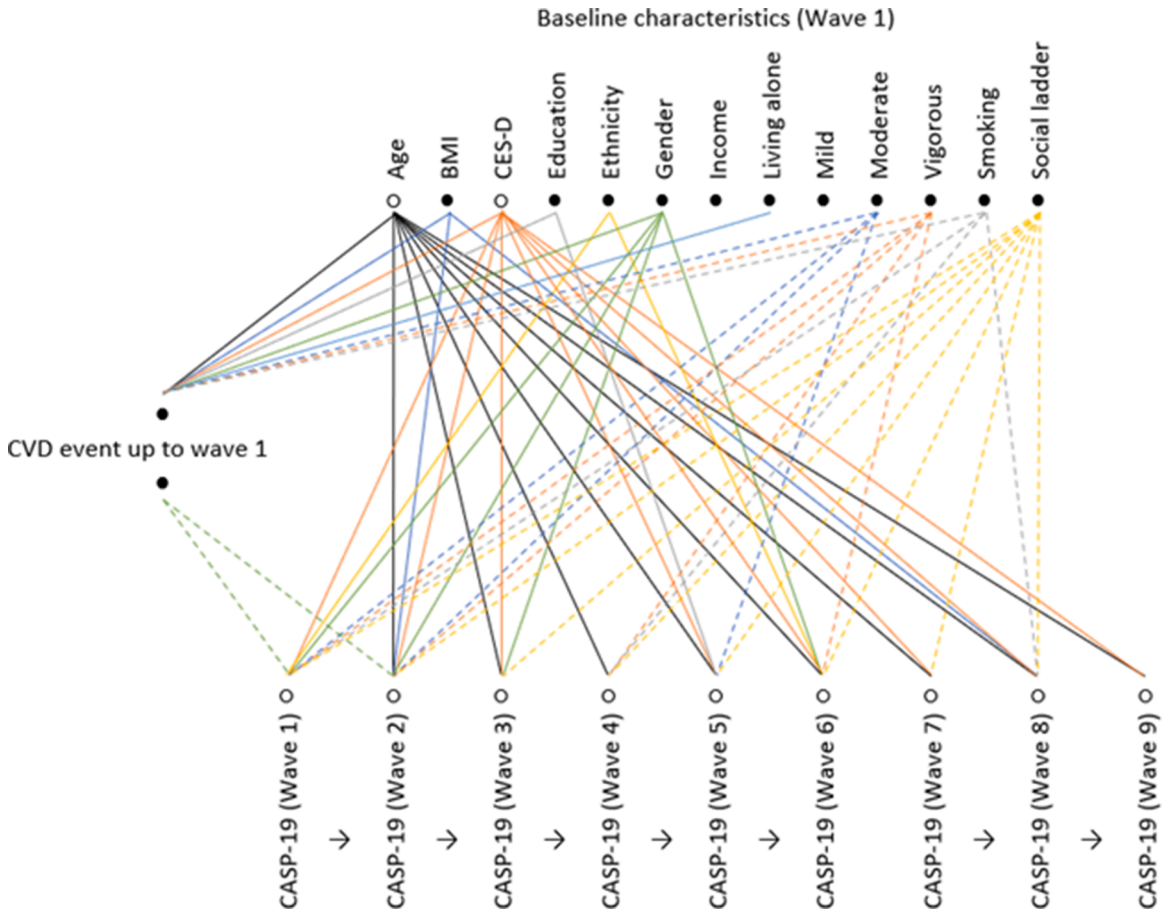

Fig. 3. Final graphical chain model without interactions (Abbreviations: BMI=Body Mass Index; CASP19 = Control, Autonomy, Self-Realisation and Pleasure 19-item; CESD = Centre for Epidemiological Studies-Depression; CVD=cardiovascular disease).

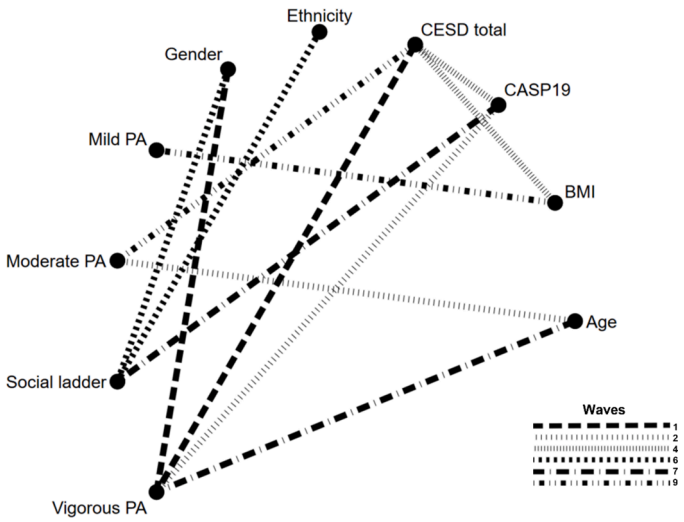

Fig. 4. Final graphical chain model interaction terms association structure (Abbreviations: BMI=Body Mass Index; CASP19 = Control, Autonomy, Self-Realisation and Pleasure 19-item; CESD = Centre for Epidemiological Studies-Depression; PA=Physical Activity).

Centre Research Ethics Committee on 12th August 2004 (MREC/04/2/006).

ELSA Wave 1 received ethical approval from the London Multi-Centre Research Ethics Committee on 7th February 2002 (MREC/01/2/91).

CRediT authorship contribution statement

Mubarak Patel: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Project administration. **Olalekan Uthman:** Validation, Supervision, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

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