UNIVERSITY OF LEEDS

This is a repository copy of *Quality of life trajectories in survivors of acute myocardial infarction: a national longitudinal study*.

White Rose Research Online URL for this paper:
http://eprints.whiterose.ac.uk/152571/

Version: Accepted Version

Article:
Munyombwe, T orcid.org/0000-0002-1307-6691, Hall, M orcid.org/0000-0003-1246-2627, Dondo, TB et al. (6 more authors) (2020) Quality of life trajectories in survivors of acute myocardial infarction: a national longitudinal study. Heart, 106 (1). pp. 33-39. ISSN 1355-6037

https://doi.org/10.1136/heartjnl-2019-315510

© Author(s) (or their employer(s)) 2019. No commercial re-use. See rights and permissions. Published by BMJ. This manuscript version is made available under the CC BY-NC 4.0 license https://creativecommons.org/licenses/by-nc/4.0/

Reuse
This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) licence. This licence only allows you to download this work and share it with others as long as you credit the authors, but you can't change the article in any way or use it commercially. More information and the full terms of the licence here: https://creativecommons.org/licenses/

Takedown
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

White Rose university consortium
Universities of Leeds, Sheffield & York

eprints@whiterose.ac.uk
https://eprints.whiterose.ac.uk/

Title: Quality of life trajectories in survivors of acute myocardial infarction: A national longitudinal study

Authors: Munyombwe T PhD[1]; Hall M PhD[1]; Dondo TB PhD[1]; Alabas OA PhD[2]; Oliver G [3]; West RM DPhil CStat [4], Pujades-Rodriguez M PhD[4]; Hall AS, PhD FRCP[1]; Chris P. Gale CP, PhD FRCP[1]

Affiliations:

1 Leeds Institute of Cardiovascular and Metabolic Medicine/ Leeds Institute for Data analytics, University of Leeds, Leeds, United Kingdom

2 Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom

3 Patient representative, Lancashire, United Kingdom

4 Leeds Institute of Health Sciences, University of Leeds, Leeds, United Kingdom

Correspondence: Dr Theresa Munyombwe,
Clinical and Population Sciences Department,
Leeds Institute of Cardiovascular and Metabolic Medicine
Faculty of Medicine and Health, University of Leeds,
Leeds, LS2 9JT
United Kingdom
Email: T.munyombwe@leeds.ac.uk
Tel: 0044 (0)113 343 0214

Twitter @cpgale3

Word count 2999

Abstract

Aim: To define trajectories of perceived health related quality of life (HRQoL) among survivors of acute myocardial infarction (AMI), and identify factors associated with trajectories.

Methods

Data on HRQoL among 9566 survivors of AMI were collected from 77 National Health Service hospitals in England between 1st November, 2011 and 24th June, 2015. Longitudinal HRQoL was collected using the EuroQol 5 dimension questionnaire measured at hospitalisation, 1, 6 and 12 months post-AMI. Trajectories of perceived HRQoL post MI were determined using multilevel regression analysis and latent class growth analysis (LCGA).

Results

One or more percieved health problems in mobility, self-care, usual activities, pain/discomfort and anxiety/depression was reported by 69.1% (6607/ 9566) at hospitalisation, and 59.7% (3011/5047) at 12 months. Reduced HRQoL was associated with women (-4.07[95% CI, -4.88 to -3.25]), diabetes (-2.87[-3.87 to -1.88]), Previous AMI(-1.60[-2.72 to -0.48]), previous angina (-1.72[-2.77 to -0.67]), chronic renal failure (-2.96[-5.08 to -0.84]),(-3,10[-5.72 to -0.49]), chronic obstructive pulmonary disease (-3.89[-5.07 to -2.72]) and cerebrovascular disease (-2.60[-4.24 to -0.96]). LCGA identified three subgroups of HRQoL which we labelled: improvers (68.1%), non-improvers (22.1%), and dis-improvers (9.8%). Non-improvers and dis-improvers were more likely to be women, NSTEMI and have long-term health conditions, compared with improvers.

Conclusions: Quality of life improves for the majority of survivors of AMI, but is significantly worse and more likely to decline for women, NSTEMI, and those with long-

term health conditions. Assessing health related quality of life both in hospital and post-discharge may be important in determining which patients could benefit from tailored interventions.

Trial registration: ClinicalTrials.gov NCT01808027 and NCT01819103

Key words

EQ-5D, Growth modelling, Health-related quality-of-life, Outcomes research, myocardial infarction

What is already known about this subject

Health related quality of life is an important outcome following acute myocardial infarction (AMI). Previous studies have shown that changes in perceived HRQoL after AMI are associated with a range of clinical outcomes, including death, anxiety and depression, and medication compliance. Little is known about how and among whom perceived HRQoL changes after AMI.

What this study Adds

In this national longitudinal cohort of 9566 hospital survivors of AMI, we identified three subgroups of HRQoL trajectories: improvers (68.1%), non-improvers (22.1%), and dis-improvers (9.8%). Dis-improvers, whose HRQoL decreased between hospitalisation and 12 months, were more likely to be women, have non ST-elevation myocardial infarction and long-term health conditions.

How might this impact on clinical practice

The characteristics of survivors of AMI associated with poor HRQoL identified in this study may be used to design targeted interventions to improve HRQoL in patients following AMI.

Introduction

Health related quality of life (HRQoL) after acute myocardial infarction (AMI) is an important clinical outcome.[1-3] It allows definition of health outcomes from a patient's perspective[2] and, therefore, offers the potential to collect patient-centred ill-health, which may be used as an additional endpoint in the evaluation of care.[4] Many patients consider the quality of additional life years gained just as important as the length of life [5] and the goal of contemporary therapies, therefore, should be not only to extend life expectancy, but also ensure a high quality long-term health state. Consequently, HRQoL is increasingly being used as an outcome measure in clinical trials evaluating both the impact of disease burden and the effectiveness of cardiovascular interventions.[2 6] However, patient reported outcome measures (PROMs) are poorly reported in literature despite being collected.[7] Despite HRQoL being recognised as an important clinical outcome after cardiovascular disease, little is known about how and among whom perceived health–related quality of life changes after AMI.

Participants of randomised studies are often a selected group of patients and their results may not be generalisable to the wider AMI population. Equally, 'real world' studies of AMI HRQoL have, to date, been limited by small sample sizes,[8 9] use of cross sectional designs,[9] [10] poor generalisability as there are focused on specific groups of patients and/or those who benefit from specific cardiovascular interventions.[1] There is often variability in HRQoL between individuals and across time hence longitudinal designs are useful for understanding the variability of HRQoL trajectories and the factors associated with these trajectories. The paucity of longitudinal HRQoL data for patients with AMI[11] limits the comprehensive evaluation of the burden of AMI, as well its appraisal as a potential study endpoint. The Evaluation of the Methods and Management of Acute Coronary Events (EMMACE)-3 and 4[12] national longitudinal cohort studies collected data concerning AMI, co-morbidities,

treatments, clinical outcomes and HRQoL for patients with AMI in 77 hospitals in England between 2011 and 2015. Thus, EMMACE represents an opportunity to study specific HRQoL trajectories of recovery following AMI and factors associated with these trajectories. We therefore aimed to address the gap in the knowledge base by firstly investigating how HRQoL among survivors of AMI vary over time, and secondly to identify factors associated with perceived poor health state.

Methods

Setting and design

The study was based on the analysis of data from the EMMACE-3 and 4, a longitudinal national cohort study described elsewhere.[12] Eligible patients included all adults aged 18 years and over hospitalised with AMI (ST-elevation myocardial infarction, STEMI or non-STEMI, NSTEMI) who were admitted to 77 National Health Service hospitals in England between 1st November, 2011 and 24th June, 2015 with an acute coronary syndrome. Records for consenting patients were linked to the United Kingdom (UK) national heart attack register (Myocardial Ischaemia National Audit Project, MINAP)[13] to gather data about their past medical history, type of AMI, and hospital treatments.

Assessment of Health related quality of life

The primary outcome was self-reported EQ-5D-3L.[14] This contains two subscales, a descriptive system (EQ-5D) and a visual analogue scale (EQ-VAS). EQ-5D comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each domain has three levels (3L), no problems, some problems, extreme problems. The EQ-

5D-3L dimensions data may be summarised as a single index score ranging from -0.5 to 1, with scores less than 0 indicating states 'worse than death', 0 indicating no quality of life, or 'death', and 1 indicating full health and therefore no problems in any domain. A difference in a score of 7 for VAS and 0.05 for EQ-5D is regarded as clinically important.[15] The index score was standardised to the UK population.[14] The EQ-VAS score ranges from 0 to 100 with 0 denoting the worst imaginable health state and 100 the best imaginable health state. The validity of EQ-5D questionnaire in patients after AMI is established.[16] EQ5D data was collected at the time of enrolment and at 1, 6 and 12 month following hospitalisation.

Statistical Analyses

Baseline characteristics for categorical data were described using frequencies and proportions. Normally distributed continuous data were described using means and standard deviations (SD), and data with a skewed distribution described using medians and interquartile ranges (IQR). Baseline differences between STEMI and NSTEMI were evaluated using Student's t test for continuous data and the Chi-squared test for categorical variables.

In order to analyse trajectories of HRQoL we used two approaches. Firstly multi-level models[17] were fitted to determine trajectories of EQ-VAS scores, and the extent to which baseline patient characteristics were associated with these trajectories, over 12 months by nesting multiple time measurements (baseline, 1, 6 and 12 months) within individuals within hospitals. Secondly to have a deeper insight into recovery patterns, latent class growth analyses (LCGA)[18] was used to determine subgroups of EQ-5D index scores with different courses of change (trajectories) of HRQoL over time. There is significant heterogeneity in HRQoL trajectories as shown in eFigure2 hence LCGA was used to capture this heterogeneity. LCGA are increasingly being used in the analysis of patient reported outcomes.[3 19]

The multi-level models adjusted for the following patient level factors: AMI phenotype (STEMI vs. NSTEMI), sex, age (<80, ≥80 years), smoking status (never vs. current or ex-smoker), ethnicity (white vs. other), previous angina, diabetes, hypertension, heart failure, peripheral vascular disease (PVD), cerebrovascular disease, chronic renal failure, chronic obstructive pulmonary disease (COPD), percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) surgery, discharge medication and cardiac rehabilitation. In addition, interactions of all covariates with the linear component of the time effect were fitted to ascertain which factors were associated with changes in health state. Finally, we conducted a stratified analyses by AMI phenotype to determine unique risk factor profiles for each phenotype.

The Latent Class Growth Analysis (LCGA) estimated models for up to 6 latent trajectories, with the best class solution selected based on Bayesian Information Criterion (BIC), Akaike Information Criterion (AIC), entropy and clinical interpretability of the emerging classes.

Missing data

Multiple imputation[20] by chained equations was used to produce 10 imputed data sets to minimise potential bias caused by missing data (eMethods and eTables 1-4). A sensitivity analysis was conducted comparing estimates from data with no imputations (etable 7a) and imputed data analysis (Table 2). LCGA models were estimated using a full information maximum likelihood method (FIML).[21] All statistical tests were 2 sided and statistical significance was considered at $p < 0.05$. Statistical analyses were conducted using Stata (IC) version 15, R studio software, and Mplus version 8.

Patient involvement

Whilst no patients were involved in setting the research question or the study design, we have involved a patient in the interpretation of the research findings, critical review of the manuscript and its dissemination.

Results

Study sample

From 16,780 acute coronary syndrome hospitalisations of consented patients across 77 hospitals in England between 2010 to 2015, we excluded 4,250 which were not AMI, 2,964 non-index hospitalisations (re-admissions) leaving an analytical cohort of 9,566 patients (n=3908 STEMI, n=5658 NSTEMI) (eFigure 1 in the supplement) for whom the EQ-5D-3L questionnaire response rates were 97.5% (9332/9566), 74.7% (6679/8945), 63.9% (5572/8719) and 62.7% (5047/8043) at hospitalisation, 1 month, 6 months and 12 months respectively. Sixty nine patients (0.7%) died in hospital. Missing data levels were low for baseline patient demographic characteristics, being <5% except for IMD (55.0%), BMI (35.3%) and ethnicity (9.3%) (Table 1). The mean age for the analytical cohort was 64.1 (SD 11.9) years; 25.1% women, mean body mass index (BMI) 28.7 (6.04) kg/m^2, median IMD 18.5 (IQR 10.9 to 31.8). Long-term health conditions were common, including hypertension (42.6%), angina (18.7%), diabetes (17.9%) and COPD (12.2%) and high rates of current or ex-smokers (65.3%). Typically, NSTEMI more frequently had a history of angina, hypertension, peripheral vascular disease, cerebrovascular disease, chronic renal failure, diabetes, heart failure, previous AMI, previous PCI, and CABG surgery.

Table 1: Patient baseline characteristics, stratified by STEMI and NSTEMI

Variables	**STEMI n=3908**	**NSTEMI n=5658**	**P value**	**All AMI N=9566**	**N. (%) missing**
Female, n. (%)	890 (22.8)	1507 (26.6)	<0.001	2397 (25.1)	15 (0.2)
Age, mean (SD), yr.	61.5 (11.5)	65.9 (11.9)	<0.001	64.1 (11.9)	19 (0.2)
White ethnicity, n. (%)	3337 (85.4)	4799 (84.8)	0.512	8136 (85.1)	887 (9.3)
IMD, median (IQR)	19.1 (11.0-34.1)	18.0 (10.9-30.4)	0.04	18.5 (10.9-31.8)	5260 (54.9)
BMI, mean(SD), kg/ m^2	28.2 (6.4)	29.1 (5.8)	<0.001	28.7 (6.0)	3374 (35.3)
Previous angina, n. (%)	343 (8.8)	1449 (25.6)	<0.001	1792 (18.7)	427 (4.5)
Diabetes, n. (%)	474 (12.1)	1240 (21.9)	<0.001	1714 (17.9)	330 (3.5)
Hypertension, n. (%)	1370 (35.1)	2708 (47.9)	<0.001	4078 (42.6)	420 (4.4)
Heart failure, n. (%)	24 (0.6)	188 (3.3)	<0.001	212 (2.2)	436 (4.6)
Peripheral vascular disease, n. (%)	76 (1.9)	241 (4.3)	<0.001	317 (3.3)	435 (4.6)
Cerebrovascular disease, n. (%)	116 (2.9)	312 (5.5)	<0.001	428 (4.5)	431 (4.5)
Chronical renal failure, n. (%)	43 (1.1)	246 (4.3)	<0.001	289 (3.02)	431 (4.5)
COPD, n. (%)	391 (10.0)	775 (13.7)	<0.001	1166 (12.2)	429 (4.5)
Smoker and ex-smoker, n. (%)	2631 (67.3)	3617 (63.9)	<0.001	6248 (65.3)	263 (2.8)
CABG surgery, n. (%)	104 (2.7)	539 (9.5)	<0.001	643 (6.7)	454 (4.8)
Previous PCI, n. (%)	201 (5.1)	698 (12.3)	<0.001	899 (9.4)	462 (4.8)
Previous AMI, n. (%)	322 (8.2)	1200 (21.2)	<0.001	1522 (15.9)	427 (4.5)
Cardiac rehabilitation, n. (%)	3623(96.2)	4886(86.3)	<0.001	8509(88.9)	306(3.2)
Discharge medications					
Beta-blocker, n (%)	3408(87.2)	4184(73.9)	<0.001	7592(79.4)	36(0.38)
ACE inhibitor, n. (%)	3437(87.9)	4172(73.7)	<0.001	7609(79.5)	61(0.64)

Variables	STEMI n=3908	NSTEMI n=5658	P value	All AMI N=9566	N. (%) missing
Statin, n. (%)	3553(90.9)	4587(81.1)	<0.001	8140(85.1)	39(0.41)
Aspirin, n. (%)	3583(91.7)	4564(80.7)	<0.001	8147(85.2)	34(0.36)

Note: IMD indicates Index of Multiple Deprivation; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; AMI, Acute Myocardial Infarction; COPD, chronic obstructive pulmonary disease; BMI, body mass index; STEMI, ST-elevation myocardial infarction; NSTEMI, non ST-elevation myocardial infarction.

Patterns of Health related quality of life over time

During hospitalisation, 69.1% (6607/9566) reported ≥ 1 problem on EQ-5D dimensions which increased to 73.9% (4935/6679) at 30 days, decreased to 62.6% (3491/5572) at 6 months, and 59.7% (3011/5047) at 12 months. The most frequent problems (some problems or extreme problems) reported at baseline were for activities (50.1%), followed by mobility (37.6%), pain (35.5%), anxiety (35.4%), self-care (14.4%) and at 12 months were pain (41.8%) followed by activities (38.8%), mobility (36.7%), anxiety (28.6%), and self-care (13.6%) (Figure 1, eTable 5). Activities and anxiety improve over time, while mobility and self-care are static. Pain is increased at 1 month and then declines slightly (Figure 1). Compared with STEMI, the proportion of NSTEMI reporting ≥ 1 problem was higher during hospitalisation (71.2% vs. 65.9 %), at 30 days (75.7% vs. 71.2%), 6 months (65.1% vs. 58.9%) and 12 months (62.8% vs. 54.8%).

On average, health status scores improved between hospitalisation and 12 months (EQ-VAS score: 63.3 [sd 20.8] vs.73.9 [sd 18.5]; EQ-5D-3L score: (0.72 [0.3] vs. 0.78 [0.3]. At 12 months, health status was worse for those with than without NSTEMI (mean [sd] EQ-VAS score 72.6 [19.1] vs.76.1 [17.5]), diabetes (68.2 [19.9] vs.75.0 [18.0]), heart failure (EQ-VAS 61.6 [18.7] vs.74.2[18.5]), chronic renal failure (62.7 [18.6] vs.74.3[18.4]). It was also worse for women (70.8 [19.1] vs. 74.9 [18.3]), and for people aged >80 years (66.9 [18.5] vs. 74.7

[18.4]). Similarly, EQ-5D-3L scores were worse at 12 months for patients with than without NSTEMI (0.77 [0.27] vs. 0.81 [0.25]), diabetes (0.69 [0.30] vs. 0.80 [0.25]), heart failure (0.62 [0.28] vs. 0.79 [0.26]), chronic renal failure (0.60 [0.32] vs. 0.79 [0.25]), for women (0.73 [0.30] vs. 0.80 [0.25], for those aged >80 years (0.70 [0.26] vs. 0.79 [0.26]) and for those with no referral for cardiac rehabilitation (0.71 [0.27] vs. 0.79 [0.26]). At 30 days EQ-5D-3L scores were worse for patients with CABG surgery compared to PCI (0.68 [0.22] vs. 0.77 [0.25]) but the scores were similar at 6 months (0.79 [0.23] vs. 0.79 [0.27]) and slightly better for CABG surgery at 12 months (0.83[0.21] vs. 0.80 [0.26]). (At all-time points, NSTEMI had lower HRQoL scores compared with STEMI (Figure 2a and b, eTable 6 in the supplement).

Factors associated with health related quality of life trajectories

On average, the multilevel modelling analyses found that each month following AMI was associated with an increase in patients's EQ-VAS score of 2.16 (95% CI, 2.00 to 2.33) (Table 2). Adjusted analysis showed that factors associated with lower health states were female sex (-4.07[95% CI, -4.88 to -3.25]), ex or current smoking (-0.92[-1.74 to -0.09]), diabetes (-2.87[-3.87 to -1.88)], Previous AMI(-1.60[-2.72 to -0.48)], previous angina (-1.72[-2.77 to -0.67]), chronic renal failure (-2.96[-5.08 to -0.84]), heart failure(-3,10[-5.72 to -0.49]), PVD (-2.66[-4.69 to -0.63]), COPD (-3.89[-5.07 to -2.72]) and cerebrovascular disease (-2.60[-4.24 to -0.96]), previous CABG surgery (-2.56[-4.13 to -1.00]). There was no evidence of a significant association between referral for cardiac rehabilitation or discharge medications with HRQoL. Statistically significant interactions with time were observed for age, cerebrovascular disease, COPD, previous angina, ex or current smoking status, and previous PCI.

The stratified analyses by STEMI and NSTEMI showed similar associations with the

exception of previous angina, CABG surgery, and chronic renal failure, which were only statistically significant for NSTEMI and cerebrovascular disease which was significant in STEMI patients.

Table 2: Results from multi-level modelling of EQ-VAS scores (regression coefficients, 95% confidence intervals), stratified according to AMI phenotype.

Variable	All AMI	STEMI	NSTEMI
Constant	61.63(54.29 to 68.98)	73.74(52.69 to 94.80)	60.42(52.29 to 68.55)
Time (month) †	2.16(1.99 to 2.33)***	2.43(2.16 to 2.69)***	1.98(1.77 to 2.19)***
Month squared	-0.11(-0.12 to -0.09)***	-0.12(-0.14 to -0.10)***	-0.09(-0.11 to -0.08)***
NSTEMI	-0.58(-1.35 to 0.19)	n/a	n/a
Age ≥80 years	0.62(-0.72 to 1.97)	-0.16(-2.64 to 2.31)	0.75 (-0.84 to 2.35)
Female	-4.07(-4.88 to -3.25)***	-4.12(-5.45 to -2.80)***	-3.98(-5.01 to -2.95)***
White ethnicity	0.48(-1.83 to 2.79)	0.44(-3.28 to 4.16)	0.48(-2.29 to 3.26)
Current or ex-smoker	-0.92(-1.74 to -0.09)*	-0.75(-2.13 to 0.63)	-0.97(-2.01 to 0.07)
Hypertension	-0.69(-1.41 to 0.03)	-0.25(-1.48 to 0.98)	-0.90(-1.82 to 0.02)
Diabetes	-2.87(-3.87 to -1.88)***	-2.74(-4.46 to -1.01)**	-2.97(-4.14 to -1.80)***
Previous AMI	-1.60(-2.72 to -0.48)**	-2.27(-4.54 to 0.002)	-1.32(-2.64 to 0.01)
Previous angina	-1.72(-2.77 to -0.67)***	-1.33(-3.41 to 0.76)	-1.95(-3.16 to -0.73)**
CRF	-2.96(-5.08 to -0.83***	-3.62(-8.95 to 1.70)	-2.83(-5.12 to -0.53)*
Heart failure	-3.10(-5.72 to -0.49)*	-4.85(-11.47 to 1.78)	-2.97(-5.82 to -0.12)*
PVD	-2.66(-4.69 to -0.63)**	-2.87(-7.33 to 1.58)	-2.65(-4.86 to -0.44)*
COPD	-3.90(-5.07 to -2.72)***	-4.21-6.02 to -2.40)***	-3.71(-5.23 to -2.19)***
Cerebrovascular disease	-2.60(-4.24 to -0.96)**	-4.30(-7.64 to -0.95)**	-1.92(-3.92 to 0.07)
Previous PCI	-1.10(-2.57 to 0.37)	-2.44(-5.28 to 0.40)	-0.71(-2.46 to 1.04)
Previous CABG surgery	-2.56(-4.13 to -1.00)**	-2.66(-6.17 to 0.85)	-2.38(-4.18 to -0.58)**
Cardiac rehabilitation	0.69(-2.11 to 3.50)	-0.11(-5.93 to 5.71)	1.15(-1.88 to 4.18)
Discharged on beta-blocker	0.74(-2.56 to 4.04)	4.21(-1.95 to 10.38)	-0.80(-4.87 to 3.27)
Discharged on ACE inhibitor	1.18(-1.84 to 4.21)	-1.77(-7.09 to 3.54)	2.11(-1.26 to 5.48)

Variable	All AMI	STEMI	NSTEMI
Discharged on statin	2.86(-1.63 to 7.35)	0.37(-10.74 to 11.49)	3.37(-1.67 to 8.41)
Discharged on aspirin	1.73 (-3.06 to 6.52)	-7.69(-25.22 to 9.83)	2.25(-2.87 to 7.38)
Age*time	-0.53(-0.70 to -0.35)***	-0.59(-0.86 to -0.32)***	-0.48(-0.67 to -0.29)***
Previous angina*time	-0.10(-0.18 to -0.01)*	-0.16(-0.33 to 0.004)	-0.06(-0.16 to 0.04)
Cerebrovascular disease*time	0.16(0.05 to 0.26)**	0.13(-0.06 to 0.31)	0.16(0.03 to 0.29)**
COPD*time	-0.14(-0.22 to 0.05)**	-0.15(-0.31 to -0.002)*	-0.14(-0.25 to -0.02)**
Ex or current smoker*time	-0.16(-0.27 to -0.05)**	-0.19(-0.35 to -0.03)*	-0.16(-0.30 to -0.02)*
Previous PCI*time	-0.14(-0.28 to 0.01)*	-0.08(-0.32 to 0.17)	-0.16(-0.29 to -0.02)*
Previous CABG surgery* Time	-0.08(-0.23 to 0.07)	0.03(-0.25 to 0.31)	-0.13(-0.29 to 0.03)
Variance (Hospital)	1.29 (0.84 to 1.98)	1.06 (0.35 to 3.23)	1.34 (0.78 to 2.29)
Variance (Cons)	12.41 (12.02 to 12.81)	12.32 (11.74 to 12.92)	12.42 (11.95 to 12.92)
Variance (month)	0.74 (0.66 to 0.82)	0.68 (0.55 to 0.83)	0.77 (0.68 to 0.87)
Covariance (month, cons)	-0.21(-0.30 to -0.11)	-0.26 (-0.38 to -0.13)	-0.18 (-0.28 to -0.08)
Variance (resid)	13.71(13.50 to 13.93)	13.39 (13.04 to 13.74)	13.92 (13.68 to 14.16)

Note: IMD indicates Index of Multiple Deprivation; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; AMI, acute myocardial infarction,;COPD, chronic obstructive pulmonary disease; STEMI, ST-elevation myocardial infarction; NSTEMI, non ST-elevation myocardial infarction; CRF, chronic renal failure,; PVD, peripheral vascular disease,; cons: constant, n/a not applicable; †Time consists of 4 time points measured at baseline, 1 month, 6 months and 12 months. *p<0.05, ** p<0.01, *** p<0.001; ns: not significant

Subgroups of health related quality of life trajectories

Based on the goodness of fit statistics, the 5-class solution provided the best model fit for the LCGA of EQ-5D index scores (etable 8a in supplement) but the 3 class solution was preferred based on clinical interpretability. The three identified distinct HRQoL trajectories were: improvers (68.1%), non-improvers (22.1%), and dis-improvers (9.8%) (Figure 2c and d). The classes were named based on the class average EQ-5D-3L scores at baseline, 1, 6 and 12 month. Improvers' HRQoL increased between hospitalisation and 12 months (VAS score:

67.24 [sd 19.37] vs. 81.44 [sd 13.04]; EQ-5D-3L score: (0.83 [0.2] vs. 0.92 [0.11]), compared with declining HRQoL in dis-improvers (VAS score: 51.0 [sd 21.3] vs.47.85 [sd 19.16]; EQ-5D-3L score: (0.31[0.34] vs. 0.13 [0.23]). The EQ-5D-3L and EQ-VAS scores for non-improvers remained stable over time.

Age, gender, previous angina, previous AMI, and diabetes were significant predictors of class membership (Table 3). Compared with the improvers, non-improvers and dis-improvers were more likely to be older age (62.6 vs. 68.5 and 64.5), women (19.4% vs. 37.6% and 35.2%), have NSTEMI (55.8% vs. 69.9% and 65.8%), previous angina (12.8% vs. 34.5% and 31.7%), diabetes (12.6% vs. 28.4% and 34.2%), previous AMI (11.1% vs. 28.2% and 28.3%), previous CABG surgery (4.43% vs 13.3% and 11.2%), and previous PCI (7.0% vs. 15.8% and 15.6%) (Figure 3, etable 9). Compared with improvers, non-improvers and dis-improvers were less likely to be referred for cardiac rehabilitation (92.1% vs. 88.3% and 87.65). The rates of PCI revascularisation were slightly higher for improvers compared to dis-improvers and non-improvers (38.2% vs. 34.8% and 31.3%) and were lower for CABG surgery for dis-improvers (dis-improvers (2.56%); non improvers (4.41%) and improvers 4.04%).

Table 3: Predictors of class membership, reference class 3(Improvers)

	Class 1(Dis improvers)	**Class 2(Non improvers)**
Variable	**OR(95% CI)**	**OR(95% CI)**
Age	0.99(0.98, 1.00)ns	1.01(1.01, 1.02)***
Men	0.39(0.33, 0.47)***	0.45(0.38, 0.52)***
Previous angina	2.07(1.66, 2.69)***	2.01(1.67, 2.43)***
Previous AMI	2.15(1.72,2.69)***	1.75(1.43, 2.15)***
Diabetes	2.85(2.35, 3.47)***	1.89(1.56, 2.28)***

Note: AMI, Acute Myocardial Infarction.
*p<0.05, ** p<0.01, *** p<0.001; ns: not significant

Discussion

This nationwide longitudinal study specifically set out to investigate how HRQoL, as measured using EuroQol EQ-5D-3L, changes over time following AMI. Among 9566 respondents surveyed over four time points up to 12 months, we found that over two thirds reported one or more problem affecting their HRQoL at baseline and 30 days after MI. Whilst in general HRQoL improved in the year following AMI, for a third of patients it failed to improve or declined, and was worse than that of the UK general population (VAS: 82.8; EQ5D:0.86), [22] average differences with the UK general population were greater than the minimum clinically important difference for EQ-5D-3L (0.05) and EQ-VAS (7 points)[15]. Following AMI, women, NSTEMI and those with long-term health conditions were less likely to report an improvement in their HRQoL.

HRQoL is a critical measure of both disease burden and the effectiveness of treatment interventions.[2 3 6] It is not surprising then that the importance of measures of patient reported health status has been increasingly recognised in randomised controlled trials.[6] Such studies collect HRQoL data not only for the purposes of health economic evaluations, but because of the realisation that health longevity is highly relevant to those who experience ill health.

Our results support previous findings of worse HRQoL at baseline, 1, 6 and 12 months after AMI compared with the general population,[2 23] and shows effects of a comparable magnitude to estimates amongst patients with chronic conditions such as cancer [24] pulmonary embolism.[25] Whereas limitations in self-care were infrequent, moderate or severe problems were frequently reported for usual activities, pain, anxiety, and mobility, both at baseline and at 12 months of follow up. We noted, as others have, that following AMI, HRQoL more frequently declines in women,[9 26] NSTEMI,[9] the elderly and people with co-morbidities.[9 27] Poor HRQoL in NSTEMI has been attributed to having more symptomatic disease and a

history of angina pectoris, [9] a finding replicated in our study.

Consistent with previous studies, we noted that HRQoL was better for patients recovering from PCI at 1 month, but this gap was reduced at 6 months and became significantly in favour of CABG at 12 months[28 29] and this improvement is attributed to greater angina relief in patients with CABG surgery compared to PCI.[29]

This research, which to our knowledge is the largest reported to date, provides novel findings. In particular, we identified three data-driven clusters of unique HRQoL trajectories – those with low HRQoL, which declined over time; those with high HRQoL, which improved; and those with moderate levels of HRQoL, which did not change significantly over the study period. Each unique class of HRQoL trajectory was associated with certain patient characteristics collected at baseline. Thus enabling the prediction of future health status as well as the early identification of a group of patients with AMI who may benefit from healthcare interventions to maintain and/or improve their HRQoL. For example, dis-improvers were typically women, NSTEMI, smokers or ex-smokers and patients who had diabetes, previous angina, and COPD. Such patients could be targeted for additional care and benefit from support services (e.g. tailored cardiac rehabilitation, enhanced interaction with health and social care professionals, or use of pharmacotherapies). The benefits of interventions for improving quality of life have been demonstrated in other diseases.[30] NSTEMI is synonymous with older age and multi-morbidity, and may explain our finding of co-morbidities and NSTEMI being associated with a declining HRQoL trajectory.

Strengths and weaknesses

The strengths of this research lie in its nationwide coverage which minimises selection bias and increases generalisability, the use of a longitudinal study design and group based trajectory modelling using LCGA methods.[3 18] Nonetheless there are limitations to our study.

Other growth mixture models were not explored, however the LCGA analysis used in this study produced clinically meaningful classes. We used a generic quality of life metric rather than a disease specific quality of life measure. However, the generic quality of life measure used in this study does capture dimensions that are impacted by AMI such as mobility, depression/anxiety and pain. Quality of life beyond 1 year was not considered and a UK cohort with limited racial diversity and universal healthcare access was used. The generalisability of our findings may be affected by selection bias because participants who were lost to follow up may be those with a greater disease burden or lower health related quality of life; however, we used multiple imputation to mitigate against the potential bias this may have caused. There is a possibility that HRQoL in MI survivors is affected by socioeconomic status, cardiac rehabilitation uptake, coronary anatomy, coronary artery disease burden, acuity of presentation, cardiogenic shock, cardiac arrest and other clinical factors, and therefore residual confounding remains.

Conclusions

This nationwide longitudinal study including over 9,000 survivors of hospitalised AMI found that whilst HRQoL improves for the majority, it is significantly worse and more likely to decline for women, NSTEMI, and people with long-term health conditions. Moreover, a data driven approach has enabled the identification of three distinct, but readily identifiable groups of patients who have significantly different trajectories of HRQoL, and who may be suitable for tailored interventions to improve and maintain their HRQoL following AMI.

Acknowledgements We gratefully acknowledge the contributions from all hospitals and healthcare professions and patients who participated in the EMMACE study.

Contributors: TM analysed the data and drafted the manuscript. CPG contributed to the design of the study, provided clinical expert advice in interpretation of the results, and was involved in manuscript writing. MH and OA were involved in design of the study, data management, and writing the manuscript. RW provided statistical advice, interpreted data, and was involved in manuscript writing. MP and TBD were involved in manuscript writing and interpretation of the results. GO was involved as a patient advisor in the interpretation of the research and the writing of the manuscript. AH contributed to the design of the study and manuscript writing. All authors made critical revisions and provided intellectual content to the manuscript, approved the final version to be published and agreed to be accountable for all aspects of the work. CPG and TM are the guarantors for this study.

"The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article (if accepted) to be published in HEART editions and any other BMJPGL products to exploit all subsidiary rights"

Funding: This research was funded by the National Institute for Health Research (NIHR/CS/009/004). CPG was funded by the National Institute for Health Research (NIHR/CS/009/004). TBD and MH were funded by the British Heart Foundation (PG/13/81/30474).

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf. The authors have no conflicts of interest.

Patient consent: Not required

Ethics approval: EMMACE-3 and 4 were given a favourable ethical opinion by the Leeds (West) and West Midlands Research Ethics committees (REC reference: 10/H131374 and 12/WM/0431) are registered on ClinicalTrials.gov (NCT01808027and NCT01819103), and were adopted onto the National Institute for Health Research Comprehensive Research Network portfolio (9102).

References

1. Fairbairn TA, Meads DM, Mather AN, et al. Serial change in health-related quality of life over 1 year after transcatheter aortic valve implantation: predictors of health outcomes. Journal of the American College of Cardiology 2012;**59**(19):1672-80.
2. Yinko S, Pelletier R, Behlouli H, et al. Health-Related Quality of Life in Premature Acute Coronary Syndrome: Does Patient Sex or Gender Really Matter? Journal of the American Heart Association 2014;**3**(4).
3. Sajobi TT, Wang M, Awosoga O, et al. Trajectories of Health-Related Quality of Life in Coronary Artery Disease. Circulation: Cardiovascular Quality and Outcomes 2018;**11**(3):e003661.
4. Calvert M, Kyte D, Mercieca-Bebber R, et al. Guidelines for inclusion of patient-reported outcomes in clinical trial protocols: the SPIRIT-PRO extension. Jama 2018;**319**(5):483-94.
5. Thompson DR, Yu C-M. Quality of life in patients with coronary heart disease-I: assessment tools. Health and quality of life outcomes 2003;**1**(1):42.
6. Lewis E, Zile MR, Swedberg K, et al. Health-related Quality of Life Outcomes in Paradigm-hf. Circulation 2015;**132**(Suppl_3):A17912.
7. Calvert M, Kyte D, Price G, et al. Maximising the impact of patient reported outcome assessment for patients and society. BMJ 2019;**364**:k5267.
8. Staniūtė M, Brožaitienė J. Changes in health-related quality of life among patients with coronary artery disease: a 2-year follow-up. Medicina 2010;**46**(12):843-50.
9. Bahall M, Khan K. Quality of life of patients with first-time AMI: a descriptive study. Health and quality of life outcomes 2018;**16**(1):32.
10. Mollon L, Bhattacharjee S. Health related quality of life among myocardial infarction survivors in the United States: a propensity score matched analysis. Health and quality of life outcomes 2017;**15**(1):235.
11. Rometsch S, Greutmann M, Latal B, et al. Predictors of quality of life in young adults with congenital heart disease. European Heart Journal-Quality of Care and Clinical Outcomes 2018;**5**(2):161-68.
12. Alabas OA, West RM, Gillott RG, et al. Evaluation of the Methods and Management of Acute Coronary Events (EMMACE)-3: protocol for a longitudinal study. Bmj Open 2015;**5**(6).
13. Herrett E, Smeeth L, Walker L, et al. The myocardial ischaemia national audit project (MINAP). Heart 2010;**96**(16):1264-67.
14. Cheung K, Oemar M, Oppe M, et al. EQ-5D User Guide. Basic information on how to use EQ-5D. . March 2009.
15. Nolan CM, Longworth L, Lord J, et al. The EQ-5D-5L health status questionnaire in COPD: validity, responsiveness and minimum important difference. Thorax 2016:thoraxjnl-2015-207782.
16. Nowels D, McGloin J, Westfall JM, et al. Validation of the EQ-5D quality of life instrument in patients after myocardial infarction. Quality of life research 2005;**14**(1):95-105.
17. Goldstein H. *Multilevel statistical models*: John Wiley & Sons, 2011.
18. Jung T, Wickrama K. An introduction to latent class growth analysis and growth mixture modeling. Social and personality psychology compass 2008;**2**(1):302-17.
19. Klotsche J, Reese JP, Winter Y, et al. Trajectory classes of decline in health-related quality of life in Parkinson's disease: a pilot study. Value in Health 2011;**14**(2):329-38.
20. Rubin DB. *Multiple imputation for nonresponse in surveys*: John Wiley & Sons, 2004.
21. Collins L, Lanza S. Latent class and latent transition analysis. Hoboken: NJ: Wiley, 2010.
22. Janssen B, Szende A. Population norms for the EQ-5D. Self-reported population health: an international perspective based on EQ-5D: Springer, 2014:19-30.
23. De Smedt D, Clays E, Annemans L, et al. Health related quality of life in coronary patients and its association with their cardiovascular risk profile: Results from the EUROASPIRE III survey. International Journal of Cardiology 2013;**168**(2):898-903.

24. Downing A, Morris EJ, Richards M, et al. Health-related quality of life after colorectal cancer in England: a patient-reported outcomes study of individuals 12 to 36 months after diagnosis. Journal of Clinical Oncology 2015;**33**(6):616-24.
25. Tavoly M, Utne KK, Jelsness-Jørgensen L-P, et al. Health-related quality of life after pulmonary embolism: a cross-sectional study. BMJ open 2016;**6**(11):e013086.
26. Kang K, Gholizadeh L, Inglis SC, et al. Interventions that improve health-related quality of life in patients with myocardial infarction. Quality of Life Research 2016;**25**(11):2725-37.
27. N'Goran AA, Déruaz-Luyet A, Haller DM, et al. Comparing the self-perceived quality of life of multimorbid patients and the general population using the EQ-5D-3L. PloS one 2017;**12**(12):e0188499.
28. Cohen DJ, Van Hout B, Serruys PW, et al. Quality of life after PCI with drug-eluting stents or coronary-artery bypass surgery. New England Journal of Medicine 2011;**364**(11):1016-26.
29. Kulik A. Quality of life after coronary artery bypass graft surgery versus percutaneous coronary intervention: what do the trials tell us? Current opinion in cardiology 2017;**32**(6):707-14.
30. Duncan M, Moschopoulou E, Herrington E, et al. Review of systematic reviews of non-pharmacological interventions to improve quality of life in cancer survivors. BMJ open 2017;**7**(11):e015860.