European Heart Journal - Quality of Care and Clinical Outcomes (2023) **0**, 1–11
https://doi.org/10.1093/ehjqcco/qcad025

ORIGINAL ARTICLE

Predicted clinical and economic burden associated with reduction in access to acute coronary interventional care during the COVID-19 lockdown in two European countries

Mattia Lunardi [1,2], Mamas A. Mamas [3], Josepa Mauri [4,5], Carmen Medina Molina [6], Oriol Rodriguez-Leor [5], Simon Eggington [7], Jan B. Pietzsch [8], Natalie L. Papo [7], Silke Walleser-Autiero [7], Andreas Baumbach [9], Francesco Maisano [10], Flavio L. Ribichini [2], Darren Mylotte [11], Emanuele Barbato [12], Jan J. Piek [13], William Wijns [1,*] and Christoph K. Naber [14], On behalf of the We CARE Initiative

[1]The Lambe Institute for Translational Medicine, Smart Sensors Laboratory and Curam, University of Galway, Ireland; [2]Division of Cardiology, University Hospital of Verona, Verona, Italy; [3]Keele Cardiovascular Research, Keele University, Stoke on Trent, UK; [4]Gerència de Processos Integrats de Salut. Àrea Assistencial. Servei Català de la Salut. Generalitat de Catalunya, Barcelona, Spain; [5]Institut del Cor, Hospital Universiari Germans Trias i Pujol, Badalona, Spain; [6]Registry of Myocardial Infarction, Catalan Health Service, Catalunyia, Barcelona, Spain; [7]Health Economics, Policy and Reimbursement, Medtronic International Trading Sarl, Tolochenaz, Switzerland; [8]Wing Tech Inc., Menlo Park, CA, USA; [9]Centre for Cardiovascular Medicine and Devices, William Harvey Research Institute, Queen Mary University of London and Barts Heart Centre, London, UK; [10]Valve Center OSR, Cardiac Surgery IRCCS San Raffaele Hospital, Vita Salute University UniSR, Milano, Italy; [11]Galway University Hospital, SAOLTA Healthcare Group and University of Galway, Galway, Ireland; [12]Department of Clinical and Molecular Medicine, Sapienza University of Rome, Via di Grottarossa, Roma, Italy; [13]Department of Clinical and Experimental Cardiology, Heart Center, Amsterdam UMC, Amsterdam Cardiovascular Sciences, University of Amsterdam, Meibergdreef, Amsterdam, the Netherlands; and [14]Department of Internal Medicine I, Cardiology and Intensive Care, Klinikum Wilhelmshaven, Wilhelmshaven, Germany

Received 10 February 2023; revised 13 April 2023; accepted 11 May 2023;

Aims

As a consequence of untimely or missed revascularization of ST-elevation myocardial infarction (STEMI) patients during the COVID-19 pandemic, many patients died at home or survived with serious sequelae, resulting in potential long-term worse prognosis and related health-economic implications.

This analysis sought to predict long-term health outcomes [survival and quality-adjusted life-years (QALYs)] and cost of reduced treatment of STEMIs occurring during the first COVID-19 lockdown.

Methods and results

Using a Markov decision-analytic model, we incorporated probability of hospitalization, timeliness of PCI, and projected long-term survival and cost (including societal costs) of mortality and morbidity, for STEMI occurring during the first UK and Spanish lockdowns, comparing them with expected pre-lockdown outcomes for an equivalent patient group.

STEMI patients during the first UK lockdown were predicted to lose an average of 1.55 life-years and 1.17 QALYs compared with patients presenting with a STEMI pre-pandemic. Based on an annual STEMI incidence of 49 332 cases, the total additional lifetime costs calculated at the population level were £36.6 million (€41.3 million), mainly driven by costs of work absenteeism. Similarly in Spain, STEMI patients during the lockdown were expected to survive 2.03 years less than pre-pandemic patients, with a corresponding reduction in projected QALYs (−1.63). At the population level, reduced PCI access would lead to additional costs of €88.6 million.

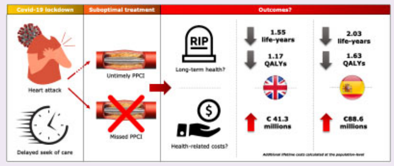
Conclusion

The effect of a 1-month lockdown on STEMI treatment led to a reduction in survival and QALYs compared to the pre-pandemic era. Moreover, in working-age patients, untimely revascularization led to adverse prognosis, affecting societal productivity and therefore considerably increasing societal costs.

* Corresponding author. Tel: +353 (0)91-495 178; Email: wwijns@europcr.com

Graphical Abstract

Lockdown leads to suboptimal treatment which translates into poor outcomes and increased societal costs.



Keywords COVID-19 • health economy • Quality of life • Myocardial infarction

Introduction

The COVID-19 pandemic had a dramatic impact on healthcare systems globally. Despite efforts to maintain systems of cardiovascular care during the pandemic, multiple factors—such as movement restrictions, bed shortages, restructure of services for management of COVID-19 illness, staff illness, and patient fears—contributed to reduced access to care and consequently adverse cardiovascular outcomes.[1] In particular, hospital admissions for ST-elevation myocardial infarction (STEMI) were reduced by more than 20%, with more than a 50% reduction in some areas[1–3] during the first pandemic wave.[4] This phenomenon, first documented in surveys of healthcare workers' perceptions, was subsequently confirmed by national registries comparing STEMI management during the pandemic to matched historical cohorts.[5–10]

This trend could not be explained by a temporary reduction in STEMI cases, which was postulated to occur due to less ischaemic trigger exposure during periods of lockdown (i.e. less pollution, reduced physical activity, and less risk factor exposure).[11] Indeed, data reporting increased cardiovascular death rates at home in the USA (from 35/day in 2013–17 to 200/day during the pandemic),[12] and increased rates of delayed STEMI presentations, as well as longer ischaemic times (from symptom onset to first-medical-contact),[6,7] suggest that STEMI incidence did not decrease, but rather, patients with ischaemic symptoms did not have access to, or did not seek, hospital care. As a consequence of untimely or missed coronary artery revascularization, significant numbers of patients died at home or survived with important sequelae. This hypothesis is further supported by reports documenting lower left ventricular ejection fraction at admission among STEMI patients during the pandemic vs. historical controls[13,14] and a significant rise in major cardiovascular complications (e.g. cardiogenic shock, life-threatening arrhythmias, cardiac rupture/ventricular septal defect, severe functional mitral regurgitation).[9,15–18]

Individuals who survive an acute myocardial infarction (AMI) with residual left ventricular dysfunction are more likely to develop heart failure, which impacts quality of life and prognosis.[19] Beyond patient outcomes, inadequate STEMI treatment has potential long-term health-economic and societal implications due to the required increased care and lost productivity.

The present analysis sought to estimate the long-term clinical and socio-economic implications of reductions in STEMI treatment during the COVID-19 pandemic based on data from the UK and Spanish healthcare systems.

Methods

Model overview

A decision-analytic model was developed to project survival, quality of life, and cost outcomes for STEMI patients, comparing patients with STEMI occurring before and during the first wave of COVID-19 infections and performing separate analyses for the UK and Spain. In particular, the analysis focused on these outcomes at the peak of the first wave when reduced hospitalization rates were observed. Data on STEMI admissions from both time periods were supplemented with published evidence on STEMI incidence in each country [using published evidence from the UK and internal data provided by the AMI Catalan network registry (Codi IAM), the Minimum Basic Data Set from Catalonia, and the Spanish Society of Cardiology (SSC)].[7] Short-term and long-term survival projections were made according to patient age, hospitalization status, and time to treatment, using country-specific life tables and studies reporting survival outcomes for STEMI patients. Cost analysis focused on initial hospitalization and treatment, follow-up treatment, management of heart failure, plus—in line with recommendations for assessment of societal implications—an extended analysis considering productivity loss in patients unable to return to work. A lifetime horizon was used, with costs, life-years, and quality-adjusted life-years (QALYs) calculated for each group based on monthly cycles in the analysis model.

Model structure

The analysis model simulated expected outcomes for a STEMI cohort prior to the first wave of COVID-19 infections ('pre-pandemic group') and compared them with an equivalent STEMI cohort during the first wave ('pandemic group'). For the UK analysis, the analysis was performed based on the month following the first national lockdown, which began on 23 March 2020; for Spain, cases peaked slightly earlier (lockdown began on 14 March 2020), and the analysis therefore studied the month of March 2020. Separate short-term and long-term elements of the model were created and populated with data pertaining to these periods. The short-term component of the model calculated outcomes up to 30 days post-STEMI in each group (with outcomes differing according to probability and timing of hospitalization and treatment modality used). Patients surviving this period then entered the long-term model, which predicted survival outcomes over a lifetime horizon. The majority of hospitalized patients were assumed to receive either percutaneous coronary intervention (PCI) or non-thrombolytic management, with improved outcomes for those admitted sooner. In this regard, data from each country were used to determine the treatment split for hospitalized patients.[7,20] Non-hospitalized patients were assumed to initially receive no treatment, though the model accounted for subsequent follow-on PCI at a later time frame in a proportion of these. Smaller infarcts, such as inferior, will most likely be treated medically upon late presentation. The short-term model structure is shown in *Figure 1*, with the initial split denoting hospitalized and non-hospitalized patients.

The long-term component of the model then projected survival (and quality-adjusted survival) based on the level of short-term care received and resulting heart failure incidence, with elevated mortality risk for untreated patients. Patient age and gender were also covariates in the long-term survival model. To capture the societal effect of STEMI on employment, separate cohorts were simulated for working-age and retired individuals.

Costs and outcomes were discounted at 3.5% per year for the UK and at 3% per year for Spain, in line with current recommendations for

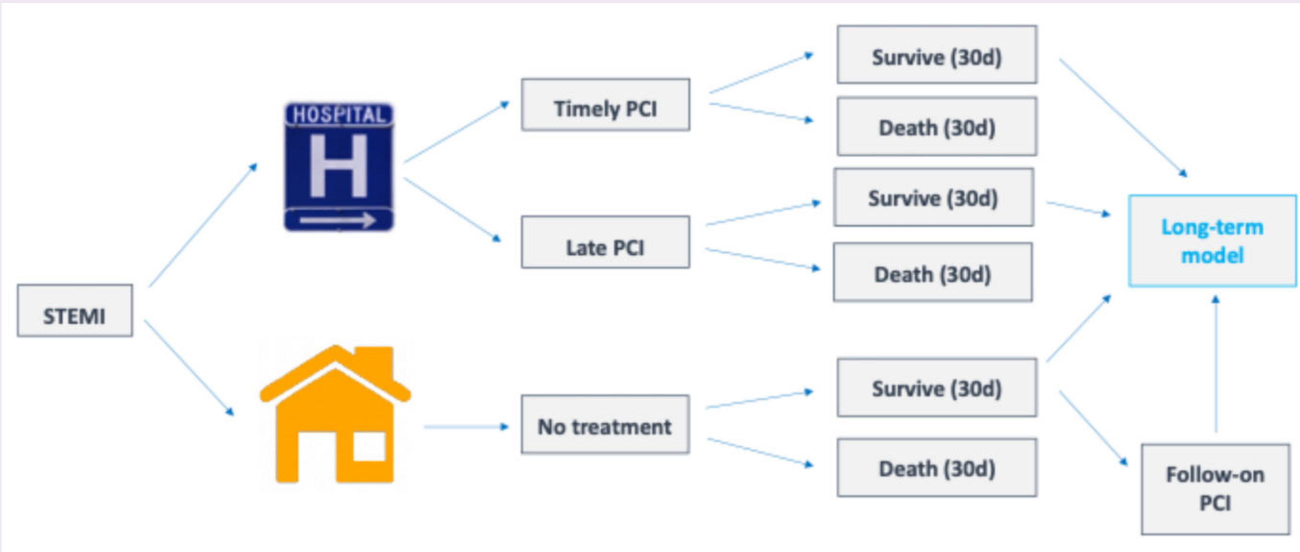


Figure 1 Overview of short-term model (up to 30 days post-STEMI). Timely PCI = PCI within 2 h of symptom onset; late PCI = PCI more than 2 h after symptom onset; and 30d = 30 days.

economic evaluations in each country.[21,22] Results were calculated on a per-patient basis and also scaled up to a national level. The model was developed in Microsoft Excel. *Table 1* shows a description of the key parameter groups used in the model, together with a brief explanation of their use and the underlying source data. A more detailed table of input values is given in Supplementary material online, *Table S1*.

STEMI incidence, admission, and patient demographic data

Incidence of hospitalized AMI cases in the UK was based on an estimate of 249 cases per 100 000 (based on data focusing on a population aged 35 years and over),[23] of which 40.5% were STEMI, and the assumption that 77.4% of cases are hospitalized.[24,25] These figures were combined with UK population data to give an estimated STEMI incidence of 49 332 cases per year in the UK. The age distribution of admitted patients was used together with the gender split to determine demographics of STEMI patients. Based on data from the same study,[24] and assuming a retirement age of 66 years, the mean ages of working-age admissions and retired admissions were 54 years and 77.4 years, respectively. In Spain, AMI incidence among the over-25s was 424 cases per 100 000 person-years (males) and 231 cases per 100 000 person-years (females), of which 45.63% were STEMI,[26] giving an annual STEMI incidence of 52 923 cases. Applying a retirement age of 66 years to the SSC and Catalonia data yielded a mean age of 54.4 years (working-age cases) and 76.1 years (retired admissions).

Baseline hospitalization rates for STEMI patients were set at 77.4% and 73.7% for the UK and Spain, respectively.[25,26] These rates were applied to STEMIs occurring in the pre-pandemic cohort. The reduction of PCI procedures for STEMI patients during the first UK lockdown was subsequently derived from a study by Kwok *et al.*, which reported a 43% reduction in PCI procedures for STEMI in April 2020 compared with the monthly average from 2017 to 2019.[6] This reduction was applied to the pre-pandemic hospitalization rate, for an estimated hospitalization rate of 44.12% of all STEMIs during the pandemic. In Spain, a 22.7% reduction in STEMI admissions was observed when comparing March 2020 vs. March 2019, giving an estimated hospitalization rate of 57% in the pandemic group. Hospitalized patients were divided into those receiving PCI and those receiving conservative management. Rates of PCI amongst hospitalized patients in the UK were 81.1 (pre-COVID) and 78.8% (during COVID),[20] compared with 87.7 (pre-COVID) and 87.8% (during COVID) in Spain.[7] As the available data did not provide a breakdown of the proportion of patients receiving 'timely' PCI—within 2 h of symptom onset—and 'late' PCI, the analysis assumed an equal split between the two. Data from the SSC showed that late admissions rose from 33.4% in March 2019 to 43.3% in March 2020—these data were used in the Spanish analysis.

Short-term data and outcomes

Mortality within 30 days of STEMI amongst patients receiving timely PCI was set at 3.5% using data from the lockdown period in the UK. Data from the SSC indicated 30-day mortality rates of 5.1 (March 2019) and 6.9% (March 2020) for PCI-treated patients. Those receiving 'late' PCI were assigned a higher mortality rate using data from a study reporting a hazard ratio of 1.1 per hour of delay in receiving PCI.[27] Outcomes for untreated patients were estimated by calculating a relative risk of survival in patients receiving medical management vs. those with revascularization, leading to a 30-day mortality rate of 24.9%.[28]

No specific data were available about the incidence of heart failure in untreated STEMI, so this was derived from a study comparing heart failure incidence amongst STEMI patients treated predominantly with PCI vs. predominantly with thrombolysis, although the latter likely underestimates the real occurrence of heart failure in the absence of any kind of revascularization. The study reported an incidence of 28% for PCI-treated patients vs. 50% for non-PCI-treated patients.[29]

Follow-on PCI

Evidence suggests that STEMI patients who do not immediately present to the hospital (and thus considered 'untreated' in the model) may subsequently undergo PCI. To capture this, the model used data from a randomized controlled trial reporting the rate of mechanical revascularization up to 3 years post-STEMI amongst patients initially treated with fibrinolytic therapy. Rates of revascularization were calculated for each 12-month period (up to 3 years) as follows: 38.9% (year one); 7.1% (year two); and 1.7% (year three).[30]

Table 1 Summary of parameters and sources

Parameter group	Model component	Use in model	Source—UK	Source—Spain
STEMI incidence	Annual incidence of AMI	To calculate national-level results from patient-level results	Asaria et al. (2017)[23]	Degano et al. (2013)[26]
	Proportion of AMI that is STEMI	To calculate national-level results specific to STEMI	Gale (2017)[24]	Degano et al. (2013)[26]
Hospitalization rates with STEMI	Probability of hospitalization (pre-pandemic)	Provides baseline probability of hospitalization under normal circumstances	Smolina et al. (2012)[25]	Degano et al. (2013)[26]
	Percent reduction in STEMI admissions during COVID lockdown	Used to calculate probability of hospitalization during lockdown	Kwok et al. (2020)[6]	Spanish Society of Cardiology (2019–2020)[a]
Patient demographics	Mean age of STEMI patients	Used to calculate mortality over time and estimate societal costs	Gale (2017)[24]	Spanish Society of Cardiology (2019–2020)[a]
PCI use	Proportion of admitted patients receiving PCI	To model any differences pre-pandemic and during lockdown. Remainder of non-admitted patients assumed to receive medical therapy	Wu et al. (2021)[20]	Rodriguez-Leor et al. (2020)[7]
	Probability of follow-on PCI among initially non-admitted patients	To account for delayed PCI (late presentation)	Busk et al. (2008)[30]	Busk et al. (2008)[30]
Mortality	30-day mortality with PCI	To model short-term STEMI outcomes	Kwok et al. (2020)[6]	Spanish Society of Cardiology (2019–2020)[a]
	Relative risk of 30-day mortality (non-PCI patients)	Applied to PCI rate to estimate mortality risk for non-PCI patients	Kochar et al. (2018)[28]	Kochar et al. (2018)[28]
	Long-term population-level mortality rates	Baseline mortality risks by age and sex	ONS (2018–2020)[31]	Instituto Nacional de Estadistica (2020)[32]
	Relative risk of mortality for PCI patients vs. general population	To calculate higher mortality rate (vs. general population) for STEMI patients	Brogan et al. (2019)[33]	Brogan et al. (2019)[33]
	Relative risk of mortality (non-PCI patients vs. PCI-treated patients)	To calculate higher risk of death for untreated patients	Kochar et al. (2018)[28]	Kochar et al. (2018)[28]
	Hazard ratio of mortality (late PCI vs. timely PCI)	To apply higher mortality for patients treated later with PCI	Terkelson et al. (2010)[27]	Terkelson et al. (2010)[27]
Quality of life	Age-specific general population utilities	Baseline utilities for all patients in model	Kind et al. (1999)[34]	Janssen and Szende (2014)[35]
	Disutilities for STEMI (by age)	Used to adjust baseline utilities for effect of STEMI	Schweikert et al. (2009)[36]	Schweikert et al. (2009)[36]
	Utility with heart failure	Applied to patients with heart failure	Berg et al. (2015)[37]	Berg et al. (2015)[37]
Unit costs	PCI procedure	To apply cost of PCI for admitted patients receiving PCI	NHS England (2021–22)[b]	Spanish DRG database[c]
	STEMI admission without PCI	Apply cost of admission for STEMI without PCI	NHS England, (2021–22)[b]	Spanish DRG database[c]
	Heart failure management	Applied to STEMI patients developing heart failure	Danese et al. (2016)[38]	Escobar et al. (2020)[d]

[a]Data from Spanish Society of Cardiology. Personal communication with Dr Oriol Rodriguez-Leor.
[b]NHS England Tariffs 2021–22.
[c]Spanish DRG database, 2022.
[d]Escobar C *et al.* *BMC Health Serv Res*, 2020;20:964.

Table 2 Mean costs, life-years and QALYs for pre-pandemic and pandemic groups—UK

	Undiscounted results			Discounted results		
Metric	Pre-pandemic	Pandemic	Difference	Pre-pandemic	Pandemic	Difference
Costs (NHS + societal)	£89 601	£98 498	£8897	£70 244	£77 516	£7272
Costs (NHS only)	£25 317	£25 531	£214	£18 064	£18 189	£125
Life-years	14.54	12.99	−1.55	9.74	8.79	−0.95
QALYs	10.67	9.50	−1.17	7.17	6.45	−0.72

NHS, National Health Service; QALYs, quality-adjusted life-years.

Long-term data and outcomes

Long-term outcomes for patients surviving to 30 days post-STEMI were modelled using a combination of general population life tables (matched for the gender split and mean age of patients in the model), (ONS 2018–2020; Instituto Nacional de Estadistica 2020)[31,32] data on relative mortality risk post-STEMI, and according to treatment received. The survival of patients treated with timely PCI was then calculated by applying relative survival estimates (vs. the general population mortality rates) from a recent study that stratified post-PCI survival by age category.[33] For patients with late PCI, a further hazard ratio of 1.1 was applied to the risk amongst early-PCI patients.[27] Survival of untreated patients was projected by applying a hazard ratio of 1.56 to the early-PCI mortality risk. This survival profile was also applied to patients who were initially untreated but subsequently received follow-on PCI.[28]

Quality of life data

To allow the calculation of QALYs for the 'pre-pandemic' and 'pandemic' groups, age-specific utilities were applied (ranging from 0.94 among patients under 25 years of age to 0.73 for patients over 75 years in the UK, with slightly higher figures for Spain).[34,35] Age-specific utility decrements (ranging from −0.06 to −0.007) were then applied to reflect lower quality of life amongst STEMI survivors than in the general population.[36] For patients with heart failure, a lower utility value of 0.69 was used.[37] In each case, the utility weights applied were based on underlying data collected via the EuroQol 5-Dimension questionnaire.

Cost data (National Health Service perspective)

The cost analysis was performed from a National Health Service (NHS) perspective and supplemented with a societal perspective (described below). The NHS perspective covered two elements of care: the cost of PCI procedures and the cost of heart failure management. Other post-STEMI management costs were excluded to simplify the analysis and avoid making assumptions regarding long-term care. The cost per PCI procedure was based on a weighted average of payment tariffs, giving a cost of £2837, which was applied to all patients undergoing PCI (covering timely, late, and follow-on PCI); for STEMI admissions without PCI, the tariff applied was £2671. In Spain, with data from the Economic Division of Assistance Services and Catalan Health Service, a diagnosis-related group (DRG) tariff of €8780 was applied for the PCI procedure, while the cost of a STEMI admission without PCI was €4087. Costs of heart failure were modelled as £6086 in year one and £3882 in all subsequent years, based on a UK study of the costs of cardiovascular events.[38] Heart failure costs in Spain were estimated at €3815 (year one) and €2930 (each subsequent year). Unit costs were adjusted to 2021 prices where necessary (Supplementary material online, *Table S1*).

Cost data (societal perspective)

As previously described, the model separated retired patients from those of working age, with the societal cost calculations based around projections for the latter group. Data on the age distribution of UK STEMI admissions were used to determine the mean age of working-age admissions (54.7 years),[24] and were combined with government employment rate data (including the proportion of part-time workers),[39] probability of returning to work,[40,41] mean return-to-work time post-STEMI, and median salary data from the UK and Spain.[41,42] These elements were used alongside the survival projections for the working-age cohort in both the 'pre-pandemic' and 'pandemic' groups to calculate the costs of work absenteeism.

Supplementary material online, *Table S1* provides a full list of model parameters and sources.

Model results for the UK

Patients with STEMI during the first month of the pandemic were predicted to lose an average of 1.55 life-years compared with someone having a STEMI pre-pandemic, with a corresponding reduction in projected QALYs over a lifetime horizon (1.17 QALYs). Costs from an NHS perspective were predicted to be similar in each group (+£214 during the pandemic), but higher for the 'pandemic' group when a broader societal perspective (including all work absenteeism costs plus all payer-borne costs) was adopted, where a difference of almost £9000 per patient was predicted (*Table 2*).

Based on an annual STEMI incidence of 49 332 cases in the UK, the reduced access to PCI during the first month of the UK lockdown would lead to a loss of 6367 life-years (or 3924 life-years when discounted) over a lifetime for patients having a STEMI during that period. Total additional lifetime costs calculated at the population level were £36.6 million (£29.9 million when discounted), with a loss of 4794 QALYs (2976 when discounted) over the lifetime of the patients.

In both groups, the majority of the cost comes from work absenteeism (+£8684 in the pandemic group) and from hospitalizations related to heart failure (+£774), while PCI costs are a relatively small proportion (*Table 3*).

Figure 2 shows the predicted survival of patients in the pre-pandemic and pandemic groups over the time horizon of the model. Also shown is the expected survival amongst the general population of an equivalent age and gender mix. The sharp decrease in survival in year one reflects the initial mortality of STEMI patients. Long-term survival is therefore lower than would be expected in the general population.

Table 4 shows the results of the one-way sensitivity analyses that were undertaken to identify key parameters in the UK model. For each scenario, the discounted mean societal costs, life-years, and QALYs are shown. For the scenarios involving the rate of timely PCI

Table 3 Cost breakdown per patient—UK

	Undiscounted cost			Discounted cost		
Cost component	Pre-pandemic	Pandemic	Difference	Pre-pandemic	Pandemic	Difference
Timely PCI	£865	£512	−£353	£865	£512	−£353
Late PCI	£865	£512	−£353	£865	£512	−£353
Follow-on PCI	£251	£621	£370	£246	£608	£362
Non-PCI admissions	£438	£214	−£224	£438	£214	−£224
HF hospitalizations	£22 897	£23 671	£774	£15 649	£16 342	£693
Work absenteeism	£64 284	£72 967	£8684	£52 180	£59 327	£7147
Total (NHS + societal)	£89 601	£98 498	£8897	£70 244	£77 516	£7272
Total (NHS only)	£25 317	£25 531	£214	£18 064	£18 189	£125

Timely: within 2 h of symptom onset; Late: more than 2 h after symptom onset; Follow-on: late PCI for initially untreated patients. HF, heart failure.

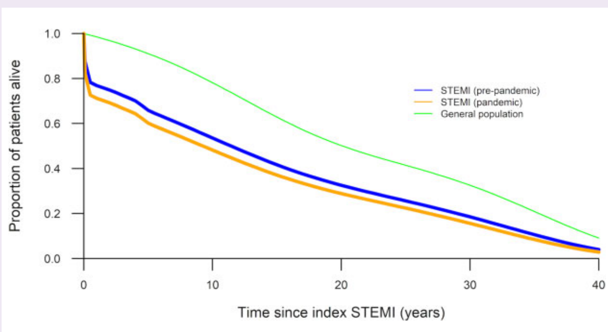


Figure 2 Projected survival for STEMI patients (pre-pandemic, during pandemic, and general population)—UK.

and the long-term hazard ratio for mortality for non-hospitalized patients, the results showed minimal change from the base-case scenario. Applying a higher rate of hospitalization and a lower risk of 30-day mortality in the 'pandemic' group, however, reduced the difference between the groups in terms of life-years and QALYs by around 50% in each case, suggesting that they are key inputs to the analysis.

Model results for Spain

The summary results for Spain are shown in *Table 5*, covering both perspectives and discounting scenarios. Spanish patients with STEMI during the first month of the first wave of the pandemic were predicted to lose an average of 2.03 life-years compared with someone having a STEMI pre-pandemic, with a corresponding reduction in projected QALYs over a lifetime horizon. Costs were similar from a payer perspective but higher in the 'pandemic' group when a societal perspective was adopted (mean additional costs of €20 069 per STEMI patient during the COVID era). Scaling these per-patient results up to a national picture, based on an annual incidence of 52 954 STEMI cases in Spain, reduced PCI access during March 2020 would lead to a loss of 8951 life-years (6018 when discounted) over a lifetime horizon for patients having a STEMI during that time. Estimated additional lifetime costs (including work absenteeism) would be €88.6 million (€75.5 million when discounted), with a loss of 7215 QALYs (4874 when discounted) over the lifetime of the patients.

Looking at the cost breakdown, under the payer perspective, heart failure hospitalizations were the main driver of total costs (€14,608 vs. €12 501; pre- and post-pandemic), while work absenteeism represented the majority of the cost when a societal perspective was used (€81 062 vs. €104 286; pre- vs. post-pandemic) (*Table 6*).

Figure 3 shows the predicted survival of patients in the pre-pandemic and pandemic groups over the time horizon of the Spanish model, together with the expected survival amongst the general population.

Table 7 shows the results of the one-way sensitivity analysis, in which key parameters were varied. Thus, if a lower proportion of patients were to receive timely PCI during the pandemic period, then there would be a larger loss of life-years and higher average costs per patient. Conversely, reducing the relative risk of 30-day mortality for untreated patients (compared with PCI-treated patients) would reduce incremental costs and life-years lost.

Discussion

This study analysed the predicted long-term health and socio-economic consequences of reduced STEMI treatment during the first COVID-19 lockdown using an analytical framework that combined short-term registry data with a projection of subsequent patient survival and cost. As a result, patients presenting with STEMI during lockdown periods are expected to lose, on average, 1.55–2.03 life-years and 1.17–1.63 QALYs over a lifetime, compared to historical controls. On a patient level, while the reduced timely treatment is not predicted to impact significantly health-related costs, it increases societal costs considerably, in particular when considered at a population level. The more pronounced loss of life predicted for Spanish patients can be attributed to a higher rate of 30-day mortality amongst patients treated with PCI during the COVID era in Spain (compared with those in the UK). This elevated PCI mortality rate leads to even higher mortality amongst non-PCI-treated patients when the relative risk is applied, and thus a greater difference between PCI-treated and untreated patients in Spain than in the UK. Similarly, a greater QALY loss was predicted for Spanish patients vs. their UK counterparts, partly because of the aforementioned difference in short-term mortality (and therefore life expectancy) but also because of the higher population utility weights across all age groups in Spain.

The treatment of STEMI was adversely impacted during the early phase of the COVID-19 pandemic, resulting in long-term worsening of prognosis and associated secondary economic implications. We found that STEMI patients who did not seek care or did not receive appropriate timely coronary revascularization have a reduced life expectancy and quality of life. These adverse outcomes can be directly linked to the mechanical damage and rhythm disturbances induced by

Table 4 One-way sensitivity analysis (mean discounted results)—UK

Scenario	Pre-pandemic group			Pandemic group			Difference		
	Costs	Life-years	QALYs	Costs	Life-years	QALYs	Costs	Life-years	QALYs
Base-case	£70 244	9.74	7.17	£77 516	8.79	6.45	£7272	−0.95	−0.72
Elevated hospitalization rate during pandemic (61% vs. 44%)	£70 244	9.74	7.17	£73 698	9.29	6.83	£3454	−0.45	−0.34
Lower % of patients receiving timely PCI during pandemic (30% vs. 50%)	£70 244	9.74	7.17	£77 684	8.74	6.42	£7440	−1.00	−0.76
Lower HR for long-term mortality in non-hospitalized patients (1.493 vs. 1.563)	£70 203	9.80	7.22	£77 472	8.89	6.52	£7269	−0.92	−0.70
Lower relative risk of 30-day mortality for non-hospitalized patients (3 vs. 7.1)	£65 512	10.30	7.58	£70 354	9.70	7.11	£4842	−0.60	−0.47

HR, hazard ratio; QALYs, quality-adjusted life-years. Costs from societal perspective.

myocardial necrosis (e.g. reduced left ventricular function, mitral regurgitation, and life-threatening arrhythmias), which may lead to heart failure, arrhythmia, etc.[9,43,44] Heart failure, although initially treatable with medical therapy/cardiac resynchronization therapy/physical rehabilitation, ultimately yields chronic limiting symptoms (e.g. dyspnea), impacting routine activities and quality of life. In addition, in the pandemic scenario, patients with heart failure may have not received the optimal treatment because of limited community heart failure services offered, cancellation of routine hospital appointments for elective investigations such as echocardiography, and a backlog of other non-COVID activities responsible for additional delays. Such patients, who already have reduced life expectancy,[45] cope with these symptoms by avoiding trigger activities and finally enter a vicious circle leading to sedentary and frailty, well known to impact survival and ability to return to work.[46,47]

These predictions are corroborated by a recent health-economic analysis across four European regions performed by ‘Stent For Life’ initiative.[48] The study assessed the health and socio-economic impact deriving from the enhancement of timely access to primary PCI (pPCI) for STEMI patients in regions where the STEMI care was not considered guideline-directed. The model demonstrated that the implementation of timely pPCI pathways leads to a reduction in absolute mortality rate varying between 3.1 and 10.1%. Similarly, proper STEMI treatment reduced *indirect societal costs* due to productivity losses by 2.5 to 6.9%, with net societal costs reduction in all model regions by 2–4%.[48]

In the current analysis, indirect societal costs were found to be the main component of economic differences between the pandemic and pre-pandemic periods. In fact, costs related to health care resources *(direct costs)* were comparable between pandemic and pre-pandemic groups. This was somewhat unexpected, considering that the estimated heart failure (HF) incidence in patients not receiving pPCI (50%) was almost double that of patients timely revascularized (28%), potentially increasing the cost related to additional hospitalizations or outpatient management. However, the reduction in pPCI numbers and associated costs may have balanced the higher costs for HF therapies, resulting in net similar direct costs between pandemic and pre-pandemic patients.

Nevertheless, the societal costs due to work absenteeism, due to missed revascularization in the working-age cohort, were higher in the pandemic group (£8684/patient in the UK; €23 224/patient in Spain). This highlights the larger proportion of patients unable to return to work because of delayed or untreated STEMI. Of note, when scaling up to the incidence of STEMI across the UK and Spanish populations during the first month of lockdown, the impact at a population level of these cost differences was much greater and amounted to £36.6 million and €88.6 million in the UK and Spain, respectively (undiscounted). The interpretation of these data is of paramount importance for national authorities: a reduction in the STEMI admission rate during only 1 month of lockdown is associated with a considerable increase of lifetime economic costs. These extra costs may increase exponentially when considering prolonged/new lockdown periods. Indeed, a similar drop in admissions was observed also during the second wave of COVID-19, suggesting an even higher clinical and economic consequence if the entire pandemic period is considered.[49]

The study findings suggest that the key drivers of survival and economic differences during the pandemic were the reduction in admission rate and the rate of timely PCI, implying that the absolute absence of treatment within the proper timeframe is the major determinant of poor clinical outcomes and related costs.

Similar to the cardiovascular field, other conditions such as cancer and stroke have also been affected during the pandemic. There was a large increase in cancelled oncologic care in 2020, with resulting

Table 5 Mean costs, life-years, and QALYs for pre-pandemic and pandemic groups—Spain

	Undiscounted results			Discounted results		
Metric	Pre-pandemic	Pandemic	Difference	Pre-pandemic	Pandemic	Difference
Costs (payer + societal)	€102 504	€122 573	€20 069	€85 814	€102 929	€17 114
Costs (payer only)	€21 442	€18 287	−€3155	€17 077	€14 588	−€2490
Life-years	14.64	12.61	−2.03	10.17	8.81	−1.36
QALYs	11.58	9.95	−1.63	8.07	6.97	−1.10

QALYs, quality-adjusted life-years.

Table 6 Cost breakdown per patient—Spain

	Undiscounted cost			Discounted cost		
Cost component	Pre-pandemic	Pandemic	Difference	Pre-pandemic	Pandemic	Difference
Timely PCI	€3779	€2491	−€1289	€3779	€2491	−€1289
Late PCI	€1895	€1902	€7	€1895	€1902	€7
Follow-on PCI	€789	€1110	€320	€776	€1091	€315
Non-PCI admissions	€370	€284	−€86	€370	−€284	−€86
HF hospitalizations	€14 608	€12 501	−€2107	€10 256	€8820	−€1436
Work absenteeism	€81 062	€104 286	€23 224	€68 737	€88 341	€19 604
Total (payer + societal)	€102 504	€122 573	€20 069	€85 814	€102 929	€17 144
Total (payer only)	€21 442	€18 287	−€3155	€17 077	€14 588	−€2490

Timely: within 2 h of symptom onset; Late: more than 2 h after symptom onset; Follow-on: late PCI for initially untreated patients. HF, heart failure.

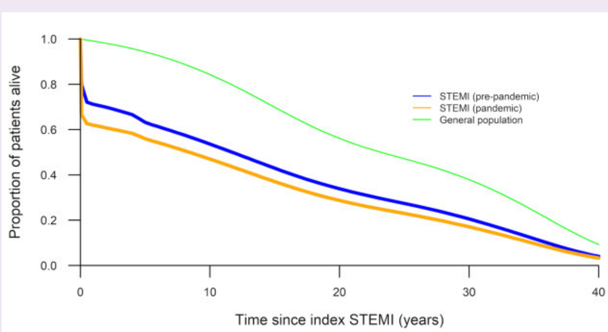


Figure 3 Projected survival for STEMI patients (pre-pandemic, during pandemic, and general population)—Spain.

implications for delayed diagnosis and treatment. These delays could be expected to lead to more advanced disease, complicating morbidities, and ultimately worse long-term outcomes.[50]

Eventually, the implications of the current analysis should be considered at two levels. Firstly, governments need to develop and implement strategies for future responses to health crises (such as COVID-19) in order to maintain equivalent quality of care for other life-threatening conditions. Secondly, public awareness campaigns need to communicate to prospective patients the benefits of seeking timely care, even during pandemic or other disruptive events.

Limitations

The study findings are subject to several limitations. First, the projected outcomes are specific to significant reduction observed during the first lockdown period of the COVID-19 pandemic. However, a similar reduction in admissions was also observed during the second wave, suggesting that the projections, directionally, also apply to subsequent waves of COVID-19.[49] Second, the analysis model focused on specific aspects of STEMI care (e.g. long-term impact of heart failure, survival), while other areas of cost were not included (e.g. physical rehabilitation programmes). This might potentially underestimate the total cost effects. Third, only limited data are available on outcomes for untreated STEMI patients, and the model, therefore, applied data from studies in which patients received thrombolysis to make projections about short- and long-term outcomes. The effect of this may have been to overestimate survival for untreated patients. Similarly, the baseline probability of hospitalization for STEMI (pre-COVID) was taken from a Spanish study whose results may be less generalizable to other countries. However, other studies have reported a similar hospitalization rate for STEMI in different regions.[25,49] [3] Finally, the prediction of cost effects at a population level did not consider other variables such as season and geographical variability of STEMI incidence.

STEMI admissions data were taken from analyses conducted in the UK and Spain, covering both the pre-pandemic period and the national lockdown period. In both cases, data were collected from hospitals routinely providing PCI care for STEMI patients and were thus considered representative of patients managed more broadly in each country (e.g. the UK analysis was based on data from 44 hospitals across England). Thus, the estimates of the change in STEMI

Table 7 One-way sensitivity analysis (mean discounted results)—Spain

Scenario	Pre-pandemic group			Pandemic group			Difference		
	Costs	Life-years	QALYs	Costs	Life-years	QALYs	Costs	Life-years	QALYs
Base-case	€85 814	10.17	8.07	€102 929	8.81	6.97	€17 114	−1.36	−1.10
Elevated hospitalization rate during pandemic (65% vs. 57%)	€85 814	10.17	8.07	€100 727	9.18	7.28	€14 912	−0.99	−0.80
Lower % of hospitalized patients receiving timely PCI during pandemic (30% vs. 56%)	€85 814	10.17	8.07	€106 034	8.30	6.56	€20 220	−1.88	−1.51
Lower HR for long-term mortality in non-hospitalized patients (1.493 vs. 1.563)	€85 761	10.22	8.11	€102 872	8.86	7.01	€17 111	−1.36	−1.10
Lower relative risk of 30-day mortality for non-hospitalized patients (3 vs. 7.1)	€78 609	11.01	8.72	€90 349	10.51	8.28	€11 740	−0.50	−0.44

HR, hazard ratio; QALYs, quality-adjusted life-years. Costs from societal perspective.

activity before and during the pandemic were considered suitable for estimating national-level patterns. Estimating the proportion of STEMI patients not hospitalized pre-pandemic is problematic due to potential missing data; however, we have used the best-available data to inform these parameters to allow per-patient national-level results to be presented.

Conclusion

Direct or indirect restrictions to treatment of life-threatening conditions have important negative effects in the short- and long-term, for either patients' health and well-being, or the entire society.

Even during natural or health catastrophes, emergency services remain a priority to maintain.

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

Author contributions

All co-authors are part of the We Care Initiative.

Francesc Güell-Viaplana, Gerència de Processos Integrats de Salut, Servei Català de la Salut

Lorena Bernàldez Arjana, Divisió d'Anàlisi de la Demanda, Servei Català de la Salut

Rosa Vidal Álvarez, Divisió Econòmica de Serveis Assistencials, Servei Català de la Salut

Aida Ribera Solé, PhD, Head of Cardiovascular Outcomes Research and Epidemiology Unit, and Cardiology Department, Hospital Universitari Vall d'Hebron, Institut de Recerca Vall d'Hebron

Funding

This work is supported by a Science Foundation Ireland Research Professorship Award to W.W. (15/RP/2765) and a Science Foundation Infrastructure Research Grant supporting M.L.

S.E., N.L.P., and S.W.A. are employees of Medtronic, who provided financial support to the WeCare.

Wing Tech Inc. (J.B.P.) provided consulting services to Medtronic.

Conflict of interest: S.E., N.L.P., and S.W.A. are employed by Medtronic. A.B. receives consulting fees from MicroPort, Pi-Cardia, Faraday, and Jenavalve; he receives payment or honoraria for lectures from MicroPort and AstraZeneca. D.M. receives a research grant from Medtronic; consulting fees and honoraria for lectures from Medtronic, Boston Scientific and MicroPort. E.B. receives speaker's and consulting fees from BSCI, Abbott Vascular, and Insight Lifetech. F.M. receives grants and/or research institutional support from Abbott, Medtronic, Edwards Lifesciences, Biotronik, Boston Scientific Corporation, NVT, Terumo, and Venus; he receives consulting fees and honoraria from Abbott, Medtronic, Edwards Lifesciences, Xeltis, Cardiovalve, Occlufit, Simulands, Mtex, Venus, and Squadra. He receives stock options from Cardiogard, Cardiovalve, Magenta, SwissVortex, Transseptal Solutions, 4Tech, and Perifect. F.R. receives honoraria for lectures from Edwards, Medtronic, and Boston Scientific. J.B.P., as an employee of Wing Tech Inc., provided consulting services to Medtronic to support the present manuscript preparation. J.B.P. receives consulting fees from Philips and participates on data safety monitoring board of the DSMB Ultracolor trial. O.R.L. receives grants from Shockwave and Philips and consulting fees from Medtronic. W.W. receives institutional research grant and honoraria (Steering Committee) for the Target AC trial from MicroPort; he received the Gruentzig Award of the Swiss Cardiac Society 2022; he received travel grants from organizers for attending and/or lecturing at PCR courses and other medical congresses; he participates on data safety monitoring board of the MultiStars trial (DSMB member); he is a Senior Advisor of Corrib Core Laboratory, University of Galway; he is a Senior Advisor of Rede Optimus Research; and Co-founder Argonauts, an innovation facilitator. Other authors have nothing to declare.

Data availability

The data underlying this article are available in the article and in its online supplementary material.

Appendix

About We CARE

Today an initiative of the not-for-profit organization We Care Alliance, We CARE was born in the aftermath of the first COVID-19 lockdown, under the aegis of PCR and Stent-Save a Life!, with the mission to help all stakeholders in the CVD field restore and sustainably deliver effective and timely cardiac care—including rebuilding patients' confidence in the healthcare systems—through knowledge, education, and training.

Mobilizing a large network of interventional cardiologists and healthcare professionals around the world, We CARE has taken on an active role to investigate and raise awareness on the deleterious effects of delayed CVD treatment on patients' outcomes during and after COVID-19.

Drawing lessons from the pandemic, We CARE is strongly advocating the need for more resilient healthcare systems in case of new eventual cross-border crises. The initiative recently applied for European funding with a project aiming at developing a resilience assessment tool and a set of recommendations for the maintenance of essential critical care that cannot be disrupted in any situation, hence ensuring the continuity of CVD care in the future.

References

1. Mayol J, Artucio C, Batista I, Puentes A, Villegas J, Quizpe R *et al.* An international survey in Latin America on the practice of interventional cardiology during the COVID-19 pandemic, with a particular focus on myocardial infarction. *Neth Heart J* 2020;**28**:424–430.
2. Cataldo P, Verdugo FJ, Bonta C, Dauvergne C, García A, Méndez M *et al.* Consequences of COVID-19 pandemic on myocardial infarction reperfusion therapy and prognosis. *Rev Med Chil* 2021;**149**:672–681.
3. Hauguel-Moreau M, Pillière R, Prati G, Beaune S, Loeb T, Lannou S *et al.* Impact of Coronavirus Disease 2019 outbreak on acute coronary syndrome admissions: four weeks to reverse the trend. *J Thromb Thrombolysis* 2021;**51**:31–32.
4. Roffi M, Capodanno D, Windecker S, Baumbach A, Dudek D. Impact of the COVID-19 pandemic on interventional cardiology practice: results of the EAPCI survey. *EuroIntervention* 2020;**16**:247–250.
5. Pessoa-Amorim G, Camm CF, Gajendragadkar P, De Maria GL, Arsac C, Laroche C *et al.* Admission of patients with STEMI since the outbreak of the COVID-19 pandemic: a survey by the European Society of Cardiology. *Eur Heart J Qual Care Clin Outcomes* 2020;**6**:210–216.
6. Kwok CS, Gale CP, Kinnaird T, Curzen N, Ludman P, Kontopantelis E *et al.* Impact of COVID-19 on percutaneous coronary intervention for ST-elevation myocardial infarction. *Heart* 2020;**106**:1805–1811.
7. Rodriguez-Leor O, Cid-Álvarez B, de Prado AP, Rossello X, Ojeda S, Serrador A *et al.* [Impact of COVID-19 on ST-segment elevation myocardial infarction care. The Spanish experience]. *Rev Esp Cardiol* 2020;**73**:994–1002.
8. Hannan EL, Wu Y, Cozzens K, Friedrich M, Tamis-Holland J, Jacobs AK *et al.* Percutaneous coronary intervention for ST-elevation myocardial infarction before and during COVID in New York. *Am J Cardiol* 2021;**142**:25–34.
9. De Rosa S, Spaccarotella C, Basso C, Calabrò MP, Curcio A, Filardi PP *et al.* Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era. *Eur Heart J* 2020;**41**:2083–2088.
10. Mafham MM, Spata E, Goldacre R, Gair D, Curnow P, Bray M *et al.* COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. *Lancet* 2020;**396**:381–389.
11. Claeys MJ, Argacha JF, Collart P, Carlier M, Van Caenegem O, Sinnaeve PR *et al.* Impact of COVID-19-related public containment measures on the ST elevation myocardial infarction epidemic in Belgium: a nationwide, serial, cross-sectional study. *Acta Cardiol* 2021;**76**:863–869.
12. Wadhera RK, Shen C, Gondi S, Chen S, Kazi DS, Yeh RW. Cardiovascular deaths during the COVID-19 pandemic in the United States. *J Am Coll Cardiol* 2021;**77**:159–169.
13. Cammalleri V, Muscoli S, Benedetto D, Stifano G, Macrini M, Di Landro A *et al.* Who has seen patients with ST-segment-elevation myocardial infarction? First results from Italian real-world coronavirus disease 2019. *J Am Heart Assoc* 2020;**9**:e017126.
14. Haddad K, Potter BJ, Matteau A, Gobeil F, Mansour S. Implications of COVID-19 on time-sensitive STEMI care: a report from a North American epicenter. *Cardiovasc Revasc Med* 2021;**30**:33–37.
15. Kitahara S, Fujino M, Honda S, Asaumi Y, Kataoka Y, Otsuka F *et al.* COVID-19 pandemic is associated with mechanical complications in patients with ST-elevation myocardial infarction. *Open Heart* 2021;**8**:e001497.
16. Leng WX, Yang JG, Li XD, Jiang WY, Gao LJ, Wu Y *et al.* Impact of the shift to a fibrinolysis-first strategy on care and outcomes of patients with ST-segment-elevation myocardial infarction during the COVID-19 pandemic-the experience from the largest cardiovascular-specific centre in China. *Int J Cardiol* 2021;**329**:260–265.
17. Bryndza MA, Litwinowicz R, Bartuś S, Nosal M, Godlewski J, Orzechowska A *et al.* Incidence of mechanical complications following myocardial infarction during the first two months of the COVID-19 pandemic in the Southern Poland region: a multicenter study. *Kardiol Pol* 2021;**79**:66–68.
18. Lin TW, Tsai MT, Wu HY, Roan JN, Luo CY. Mechanical complications of acute myocardial infarction during the COVID-19 pandemic. *Acta Cardiol Sin* 2021;**37**:114–116.
19. Gerber Y, Weston SA, Enriquez-Sarano M, Berardi C, Chamberlain AM, Manemann SM *et al.* Mortality associated with heart failure after myocardial infarction: a contemporary community perspective. *Circ Heart Fail* 2016;**9**:e002460.
20. Wu J, Mamas M, Rashid M, Weston C, Hains J, Luescher T *et al.* Patient response, treatments, and mortality for acute myocardial infarction during the COVID-19 pandemic. *Eur Heart J Qual Care Clin Outcomes* 2021;**7**:238–246.
21. Moss AJ, Williams MC, Newby DE, Nicol ED. The updated NICE Guidelines: cardiac CT as the first-line test for coronary artery disease. *Curr Cardiovasc Imaging Rep* 2017;**10**:15.
22. López-Bastida J, Oliva J, Antoñanzas F, García-Altés A, Gisbert R, Mar J *et al.* Spanish recommendations on economic evaluation of health technologies. *Eur J Health Econ* 2010;**11**:513–520.
23. Asaria P, Elliott P, Douglass M, Obermeyer Z, Soljak M, Majeed A *et al.* Acute myocardial infarction hospital admissions and deaths in England: a national follow-back and follow-forward record-linkage study. *Lancet Public Health* 2017;**2**:e191–e201.
24. Gale CP. Acute coronary syndrome in adults: scope of the problem in the UK. *Br J Cardiol*, 2017;**24**:S3–S9.
25. Smolina K, Wright FL, Rayner M, Goldacre MJ. Incidence and 30-day case fatality for acute myocardial infarction in England in 2010: national-linked database study. *Eur J Public Health* 2012;**22**:848–853.
26. Dégano IR, Elosua R, Marrugat J. Epidemiology of acute coronary syndromes in Spain: estimation of the number of cases and trends from 2005 to 2049. *Rev Esp Cardiol* 2013;**66**:472–481.
27. Terkelsen CJ, Sørensen JT, Maeng M, Jensen LO, Tilsted HH, Trautner S *et al.* System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. *JAMA* 2010;**304**:763–771.
28. Kochar A, Chen AY, Sharma PP, Pagidipati NJ, Fonarow GC, Cowper PA *et al.* Long-term mortality of older patients with acute myocardial infarction treated in US clinical practice. *J Am Heart Assoc* 2018;**7**:e007230.
29. Desta L, Jernberg T, Löfman I, Hofman-Bang C, Hagerman I, Spaak J *et al.* Incidence, temporal trends, and prognostic impact of heart failure complicating acute myocardial infarction. The SWEDEHEART Registry (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies): a study of 199,851 patients admitted with index acute myocardial infarctions, 1996 to 2008. *JACC Heart Fail* 2015;**3**:234–242.
30. Busk M, Maeng M, Rasmussen K, Kelbaek H, Thayssen P, Abildgaard U *et al.* The Danish multicentre randomized study of fibrinolytic therapy vs. primary angioplasty in acute myocardial infarction (the DANAMI-2 trial): outcome after 3 years follow-up. *Eur Heart J* 2008;**29**:1259–1266.
31. Office for National Statistics, 2021. UK life tables 2018–2020. www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/nationallifetablesunitedkingdomreferencetables (30 September 2021).
32. Instituto Nacional de Estadística, 2021. Spanish life tables 2020. www.ine.es/dyngs/INEbase/en/operacion.htm?c=Estadistica_C&cid=1254736177004&menu=ultiDatos&idp=1254735573002 (30 September 2021).
33. Brogan RA, Alabas O, Almudarra S, Hall M, Dondo TB, Mamas MA *et al.* Relative survival and excess mortality following primary percutaneous coronary intervention for ST-elevation myocardial infarction. *Eur Heart J Acute Cardiovasc Care* 2019;**8**:68–77.
34. Kind P HG, Macran S. UK population norms for EQ-5D. Discussion Paper No. 172, Centre for Health Economics, University of York, 1999.

35. Szende A, Janssen B Cabases J, eds. *Self-Reported Population Health: An International Perspective Based on EQ-5D*. Dordrecht: Springer; 2014.
36. Schweikert B, Hunger M, Meisinger C, König HH, Gapp O, Holle R. Quality of life several years after myocardial infarction: comparing the MONICA/KORA registry to the general population. *Eur Heart J* 2009;**30**:436–443.
37. Berg J, Lindgren P, Mejhert M, Edner M, Dahlström U, Kahan T. Determinants of utility based on the EuroQol five-dimensional questionnaire in patients with chronic heart failure and their change over time: results from the Swedish Heart Failure Registry. *Value Health* 2015;**18**:439–448.
38. Danese MD, Gleeson M, Kutikova L, Griffiths RI, Azough A, Khunti K *et al.* Estimating the economic burden of cardiovascular events in patients receiving lipid-modifying therapy in the UK. *BMJ Open* 2016;**6**:e011805.
39. OECD, 2021. Part-time employment rates. www.ine.es/dyngs/INEbase/en/operacion.htm?c=Estadistica_C&cid=1254736177004&menu=ultiDatos&idp=1254735573002. (30 September 2021).
40. Smith GR, O'Rourke DF. Return to work after a first myocardial infarction. A test of multiple hypotheses. *JAMA* 1988;**259**:1673–1677.
41. Isaaz K, Coudrot M, Sabry MH, Cerisier A, Lamaud M, Robin C *et al.* Return to work after acute ST-segment elevation myocardial infarction in the modern era of reperfusion by direct percutaneous coronary intervention. *Arch Cardiovasc Dis* 2010;**103**:310–316.
42. Office for National Statistics. Employee earnings in the UK: 2020. *Statistical Bulletin*.
43. Honda S, Asaumi Y, Yamane T, Nagai T, Miyagi T, Noguchi T *et al.* Trends in the clinical and pathological characteristics of cardiac rupture in patients with acute myocardial infarction over 35 years. *J Am Heart Assoc* 2014;**3**:e000984.
44. Pilato E, Pinna GB, Parisi V, Manzo R, Comentale G. Mechanical complications of myocardial infarction during COVID-19 pandemic: an Italian single-centre experience. *Heart Lung* 2020;**49**:779–782.
45. Arnold JMO, Liu P, Howlett J, Ignaszewski A, Leblanc M-H, Kaan A *et al.* Ten year survival by NYHA functional class in heart failure outpatients referred to specialized multidisciplinary heart failure clinics 1999 to 2011. *Eur Heart J* 2013;**34**:P1505.
46. Bachettini NP, Bielemann RM, Barbosa-Silva TG, Menezes AMB, Tomasi E, Gonzalez MC. Sarcopenia as a mortality predictor in community-dwelling older adults: a comparison of the diagnostic criteria of the European Working Group on Sarcopenia in Older People. *Eur J Clin Nutr* 2020;**74**:573–580.
47. Kalantar-Zadeh K, Rhee C, Sim JJ, Stenvinkel P, Anker SD, Kovesdy CP. Why cachexia kills: examining the causality of poor outcomes in wasting conditions. *J Cachexia Sarcopenia Muscle* 2013;**4**:89–94.
48. Wein B, Bashkireva A, Au-Yeung A, Yoculan A, Vinereanu D, Deleanu D *et al.* Systematic investment in the delivery of guideline-coherent therapy reduces mortality and overall costs in patients with ST-elevation myocardial infarction: results from the stent for life economic model for Romania, Portugal, Basque Country and Kemerovo region. *Eur Heart J Acute Cardiovasc Care* 2020;**9**:902–910.
49. Wu J, Mamas MA, de Belder MA, Deanfield JE, Gale CP. Second decline in admissions with heart failure and myocardial infarction during the COVID-19 pandemic. *J Am Coll Cardiol* 2021;**77**:1141–1143.
50. John N, Wang GM, Cioffi G, Waite K, Patil N, Kyasaram R *et al.* The negative impact of the COVID-19 pandemic on oncology care at an academic cancer referral center. *Oncology (Williston Park)* 2021;**35**:462–470.