













# The collateral damage of COVID-19 to cardiovascular services: a meta-analysis

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Listen to the audio abstract of this contribution.

## Abstract

### Aims

The effect of the COVID-19 pandemic on care and outcomes across non-COVID-19 cardiovascular (CV) diseases is unknown. A systematic review and meta-analysis was performed to quantify the effect and investigate for variation by CV disease, geographic region, country income classification and the time course of the pandemic.

### Methods and results

From January 2019 to December 2021, Medline and Embase databases were searched for observational studies comparing a pandemic and pre-pandemic period with relation to CV disease hospitalisations, diagnostic and interventional procedures, outpatient consultations, and mortality. Observational data were synthesised by incidence rate ratios (IRR) and risk ratios (RR) for binary outcomes and weighted mean differences for continuous outcomes with 95% confidence intervals. The study was registered with PROSPERO (CRD42021265930). A total of 158 studies, covering 49 countries and 6 continents, were used for quantitative synthesis. Most studies (80%) reported information for high-income countries (HICs). Across all CV disease and geographies there were fewer hospitalisations, diagnostic and interventional procedures, and outpatient consultations during the pandemic. By meta-regression, in low-middle income countries (LMICs) compared to HICs the decline in ST-segment elevation myocardial infarction (STEMI) hospitalisations (RR 0.79, 95% confidence interval [CI] 0.66–0.94) and revascularisation (RR 0.73, 95% CI 0.62–0.87) was more severe. In LMICs, but not HICs, in-hospital mortality increased for STEMI (RR 1.22, 95% CI 1.10–1.37) and heart failure (RR 1.08, 95% CI 1.04–1.12). The magnitude of decline in hospitalisations for CV diseases did not differ between the first and second wave.

### Conclusions

There was substantial global collateral CV damage during the COVID-19 pandemic with disparity in severity by country income classification.

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## Structured Graphical Abstract

### Key Question

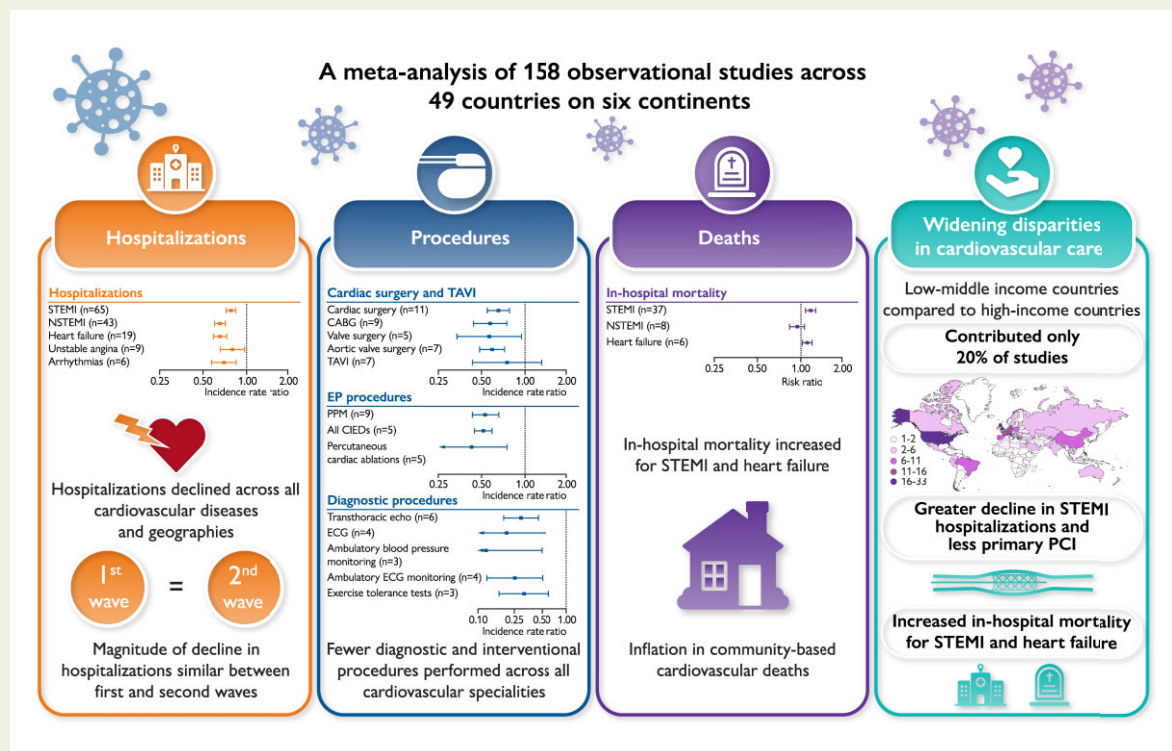
Has the covid pandemic had a detrimental effect on care and outcomes from non-COVID-19 cardiovascular diseases, and was there variation in the effect across cardiovascular diseases, geographical regions, country income classification, and the time-course of the pandemic?

### Key Finding

Across all cardiovascular diseases and geographies there were fewer hospitalizations, diagnostic and interventional procedures, and outpatient consultations during the pandemic. In low-middle income countries the decline in hospitalizations and procedures was more severe and in-hospital mortality increased.

### Take Home Message

There was a substantial global collateral cardiovascular damage during the COVID-19 pandemic with disparity in severity by country income classification. There is limited information about cardiovascular health and care from low-middle income countries.



Major findings of the collateral damage of the COVID-19 pandemic on cardiovascular services. Abbreviations in text.

**Keywords** Cardiovascular • COVID-19 • Hospitalization • Mortality • Treatment

## Abbreviations

ACHD	adult congenital heart disease	ICD	implantable cardioverter defibrillator
ACS	acute coronary syndrome	IE	infective endocarditis
CABG	coronary artery bypass graft	IRR	incidence rate ratio
CIED	cardiac implantable electronic device	LMIC	low–middle income country
COVID-19	coronavirus disease 2019	NSTEMI	non-ST-elevation myocardial infarction
CV	cardiovascular	OHCA	out-of-hospital cardiac arrest
D2B	door-to-balloon time	PCI	percutaneous coronary intervention
ECG	electrocardiogram	PPCI	primary PCI
ESC	European Society of Cardiology	RR	risk ratio
HF	heart failure	S-FMC	symptom to first medical contact
HIC	high-income country	STEMI	ST-elevation myocardial infarction
		TAVI	transcatheter aortic valve implantation

VA	ventricular arrhythmia
WHO	World Health Organization
WMD	weighted mean difference

## Introduction

During the coronavirus disease 2019 (COVID-19) pandemic, reports described fewer hospitalizations, procedures, and consultations for non-COVID-19 cardiovascular (CV) diseases.<sup>1–3</sup> After a short period of ‘recovery’, the emergence and rapid spread of the Omicron variant triggered the re-introduction of ‘lockdown’ restrictions,<sup>4,5</sup> portending a future of preparing for and coping with waves of the contagion.

Previous systematic reviews of the impact of the COVID-19 pandemic on CV services have provided an incomplete overview. Some studies focused on hospitalizations,<sup>6,7</sup> others were restricted to specific conditions,<sup>8–16</sup> and one investigated only a specific outcome.<sup>17</sup> Only one report has considered the impact of the pandemic across different geographic territories, and was limited to one CV care pathway.<sup>9</sup> None has considered whether the effect of the pandemic on CV services has varied over time. A quantitative understanding of the global impact of the COVID-19 pandemic on the breadth of CV services and health of individuals with CV disease could facilitate better preparation for future waves.

We therefore provide a systematic review of the literature with a meta-analysis to quantify the effects of the pandemic on CV services in terms of access, treatment, and outcomes. We investigate the occurrence of variation across CV conditions, geographic region, country income classification, and the time course of the pandemic. Finally, we consider how to better manage CV services to minimize collateral CV damage.

## Methods

We searched the Medline and Embase databases through the Ovid platform from 1 January 2019 through 15 December 2021 (because the earliest case was diagnosed in Wuhan, China in November 2019) for studies that reported a comparison of hospitalizations, diagnostic and interventional procedures, outpatient and community consultations, and mortality. The full search strategy is available in [Supplementary material online, S1](#). We defined CV services as healthcare services provided by any CV practitioner (cardiologist, cardiac surgeon, cardiac physiologist, cardiac nurse, or trainee) relating to CV diseases specified in the *ESC Textbook of Cardiovascular Medicine*.<sup>18</sup> We excluded CV diseases where care would primarily be overseen by other medical and surgical specialities—venous thrombo-embolism and peripheral vascular diseases (including aortic, peripheral arterial, and cerebrovascular disease)—which have been summarized elsewhere.<sup>6,19</sup> This review was registered on PROSPERO (CRD42021265930) and informed by the PRISMA statement (see [Supplementary material online, Table S63](#)).<sup>20</sup> The risk of bias for each report for each outcome was assessed using the ROBINS-I tool.<sup>21</sup> Reports with critical risk of bias were excluded.

We undertook quantitative syntheses of cohort studies that compared the COVID-19 pandemic period and a pre-pandemic period (all definitions in [Supplementary material online, S1](#)). A meta-analysis was performed to synthesize observational data for binary and continuous outcomes. Incidence rate ratios (IRRs, a comparison of incidence rates during each period) and risk ratios (RRs, a ratio of the probability of an

event occurring in the intervention compared with the probability of the event occurring in the control, where each event is independent) were used for binary outcomes and counts data; weighted mean differences (WMDs) were used for continuous outcomes measured with the same scale. The DerSimonian and Laird random effects models were fitted in all analyses because of the variation amongst studies in population, intervention, comparator, timing, and setting.<sup>22</sup> Funnel plots and Egger’s test were used to assess publication bias.<sup>23</sup> Heterogeneity scores were measured by the  $I^2$  statistic and Cochran’s Q test, with 40% or  $P < 0.10$ , respectively, indicative of substantial heterogeneity.<sup>24</sup> Where quantitative synthesis could not be undertaken, we have provided a narrative synthesis.

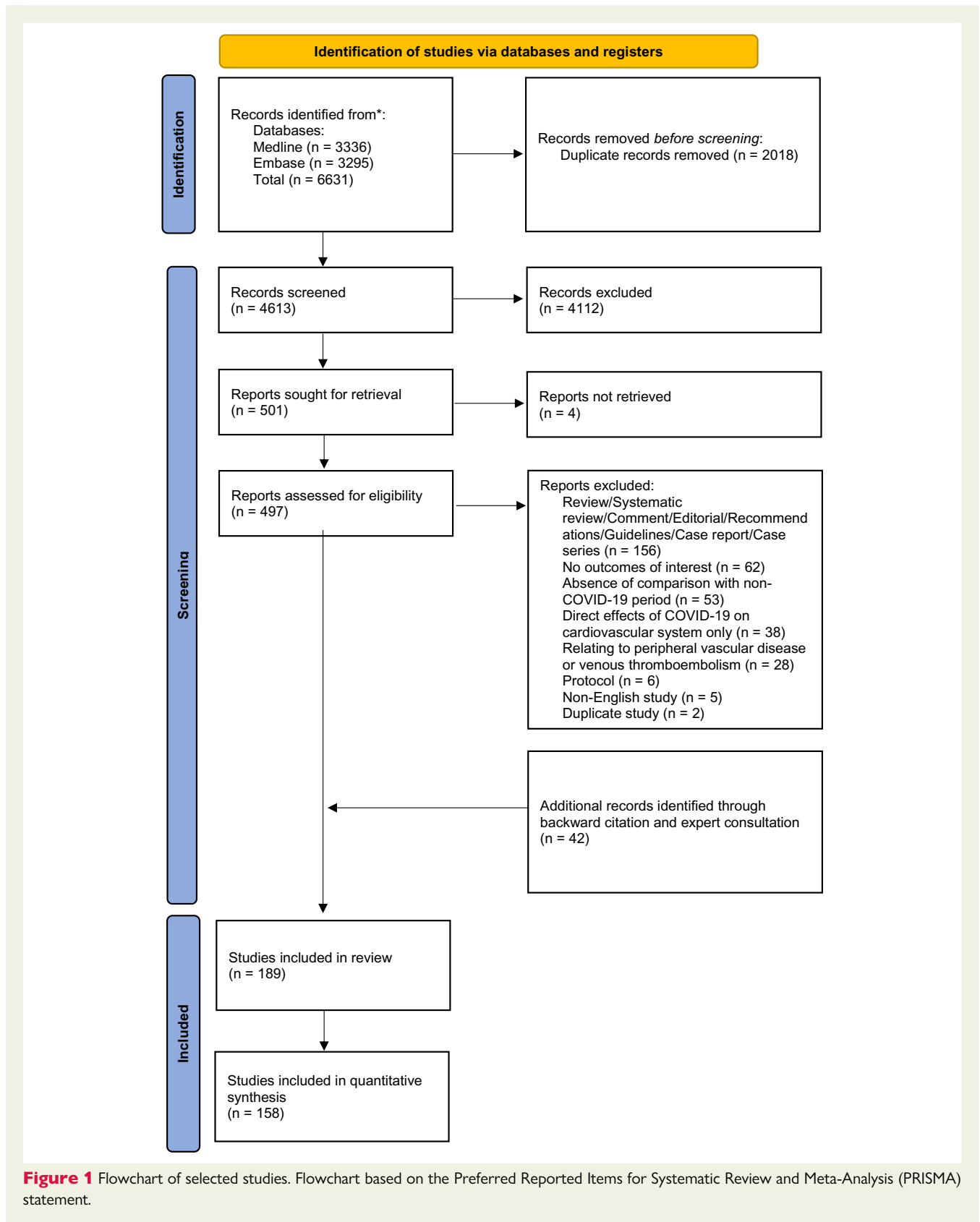
To explore for differences in effect of the pandemic across geographic boundaries, country wealth, and time course, we performed meta-regression by geographic region, country-level income, and wave of pandemic covered by each report. Geographic regions were defined as Europe, North America, and other countries, and country-level income as high income (HIC) vs. low–middle income (LMIC) using the World Bank classification of income.<sup>25</sup> We also investigated for sources of heterogeneity by meta-regression of a range of study characteristics: sample size, data source, duration of study period during the pandemic, presence or absence of matched comparator periods, study definition of pandemic period, and whether or not patients with co-existent COVID-19 diagnosis were included. Detailed methods are available in [Supplementary material online, S2](#).

## Results

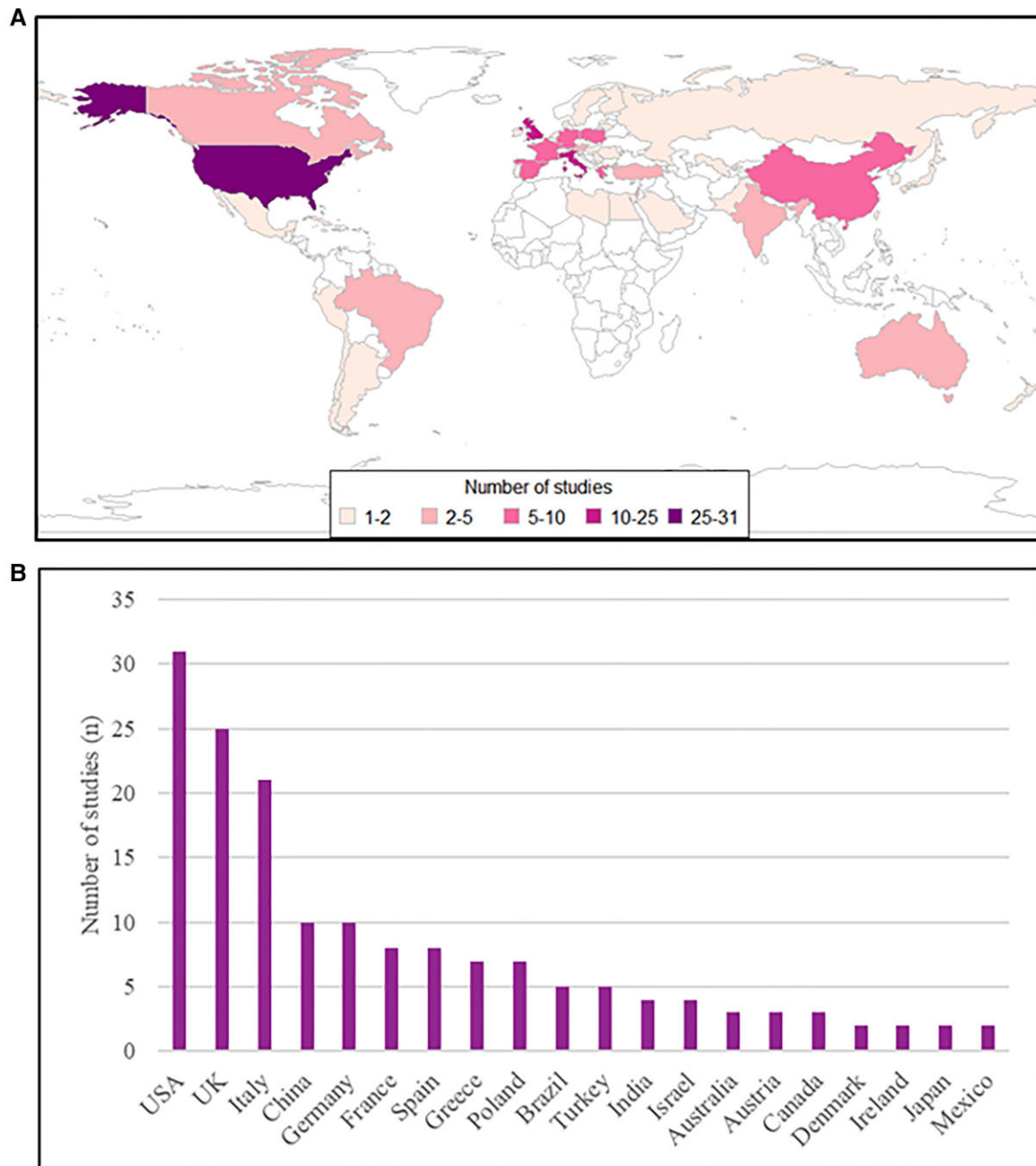
We identified 4613 unique records, reviewed 497 full-text reports, and included 189 studies, 158 of which were used in quantitative synthesis ([Supplementary material online, S4 Tables S38–S61](#)). [Figure 1](#) shows the PRISMA flow diagram. In total, 49 countries were covered across six continents. There was geographic and economic disparity in the number of available studies; the majority were from Europe ( $n = 111$ , 59%; of which the UK  $n = 25$ , 13%, and Italy  $n = 21$ , 11%) and North America ( $n = 34$ , 18%) ([Figure 2](#)). Most studies provided information exclusively relating to HICs ( $n = 151$ , 80%). Over half of studies described acute coronary syndromes (ACS) ( $n = 96$ , 51%), followed by heart failure (HF) ( $n = 16$ , 8%) and arrhythmias ( $n = 15$ , 8%). The vast majority of studies reported data from the first wave of the pandemic ( $n = 152$ , 80%). A minority of studies ( $n = 19$ , 10%) excluded patients diagnosed with concurrent SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection. We classified 26% of studies across all outcomes as being at severe risk of bias, with 57% at moderate risk of bias ([Figure 3](#); [Supplementary material online, S3 Tables S1–S37](#)). Confounding was the most common source of elevated risk of bias (26% severe, 56% moderate). Studies reporting mortality outcomes were the most likely to be classified as being at severe risk of bias (51%), partly due to incomplete reporting of concurrent SARS-CoV-2 infection. Egger’s test did not identify any significant publication bias ([Supplementary material online, S6 Figures S19–S22](#); all  $P$ -values were non-significant).

### Acute cardiovascular disease hospitalizations

Hospitalizations declined across the breadth of CV disease during the pandemic. Hospitalization rates for each subtype of ACS declined; ST-elevation myocardial infarction (STEMI) [IRR 0.78, 95% confidence interval (CI) 0.72–0.85,  $I^2 = 97.4\%$ ], non-STEMI (NSTEMI) (IRR 0.66,



95% CI 0.60–0.72,  $I^2 = 98.3\%$ ), and unstable angina (IRR 0.80, 95% CI 0.66–0.98,  $I^2 = 85.8\%$ ) (Figure 4; Supplementary material online, S1–S3). Hospitalizations for HF declined during the pandemic (IRR 0.66, 95% CI 0.59–0.73,  $I^2 = 99.9\%$ ) (Supplementary material online, Figure S4), reflective of a decline in admissions with both decompensated chronic HF and *de novo* presentations.<sup>26</sup>



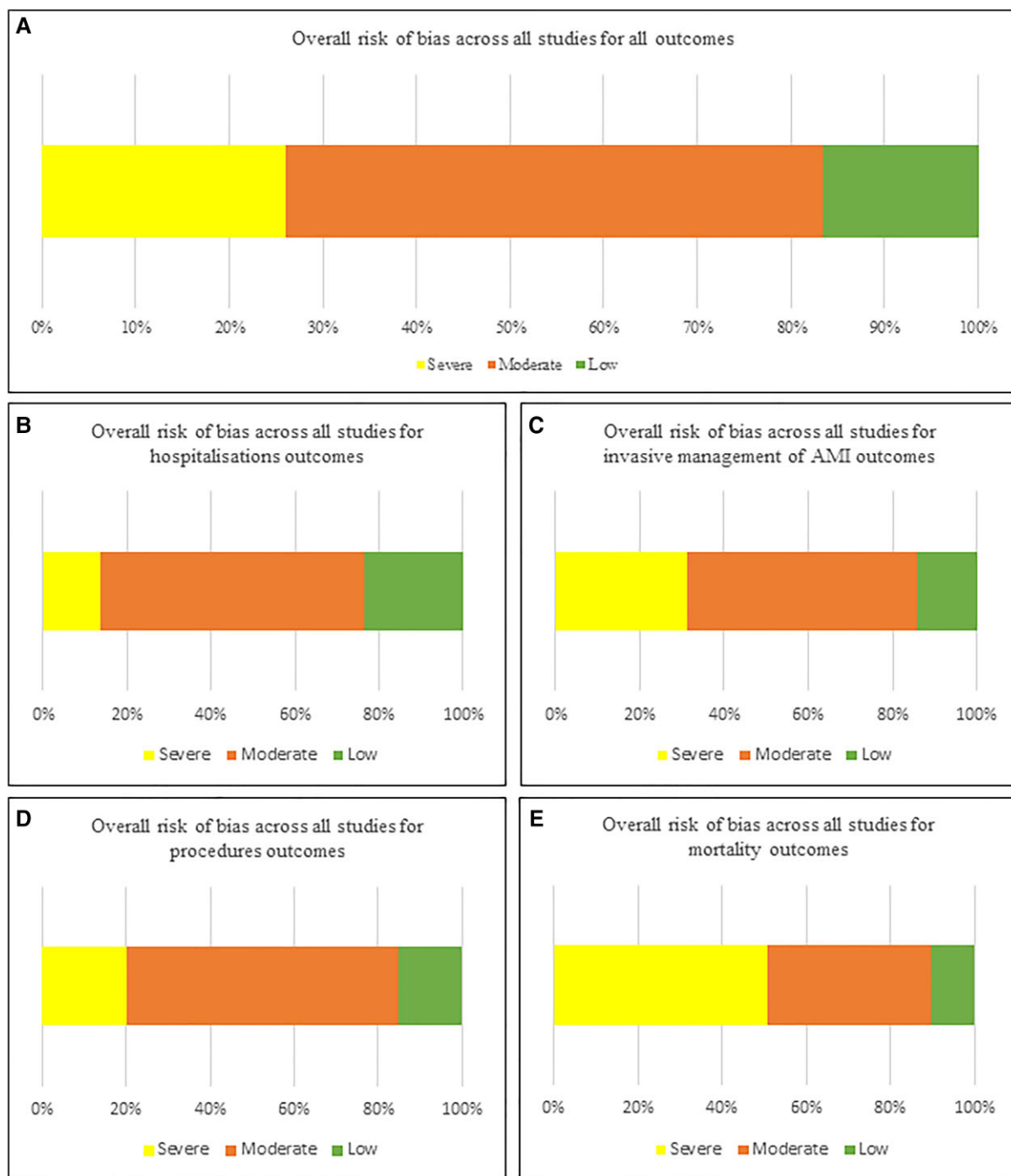
**Figure 2** The origin of included studies demonstrated on a global choropleth (A), and a chart including the number of studies per country for the 20 most commonly represented countries (B).

The total number of hospitalizations for arrhythmias also declined (IRR 0.70, 95% CI 0.57–0.85,  $I^2 = 95.2\%$ ) (Supplementary material online, Figure S5), an effect consistently reported for each of bradyarrhythmias,<sup>27–29</sup> atrial fibrillation/flutter,<sup>30–32</sup> and ventricular arrhythmias (VAs).<sup>28</sup> However, studies reporting arrhythmias detected by remote monitoring of cardiac implantable electronic devices (CIEDs) painted a different picture of arrhythmia incidence in the community in individuals with CV disease. Three studies reported increases in episodes of atrial fibrillation during the pandemic, which correlated with areas of high COVID-19 prevalence.<sup>33–35</sup> During the peak COVID-19 incidence in New York City, New Orleans,

and Boston, an increase in implantable cardioverter defibrillator (ICD) shock burden was observed,<sup>36</sup> whilst two large studies found a reduction in VA incidence amongst individuals with ICDs after major public health restrictions.<sup>37,38</sup>

On meta-regression, we found that the decline in hospitalizations for CV disease was consistent across different geographical regions (Supplementary material online, Table S62). However, there was a greater decline in STEMI hospitalizations during the pandemic in LMICs (RR = 0.79, 95% CI 0.66–0.94). Notably, between the first and second wave, we found no difference in decline of hospitalizations for STEMI, NSTEMI, and HF. However, studies that reported



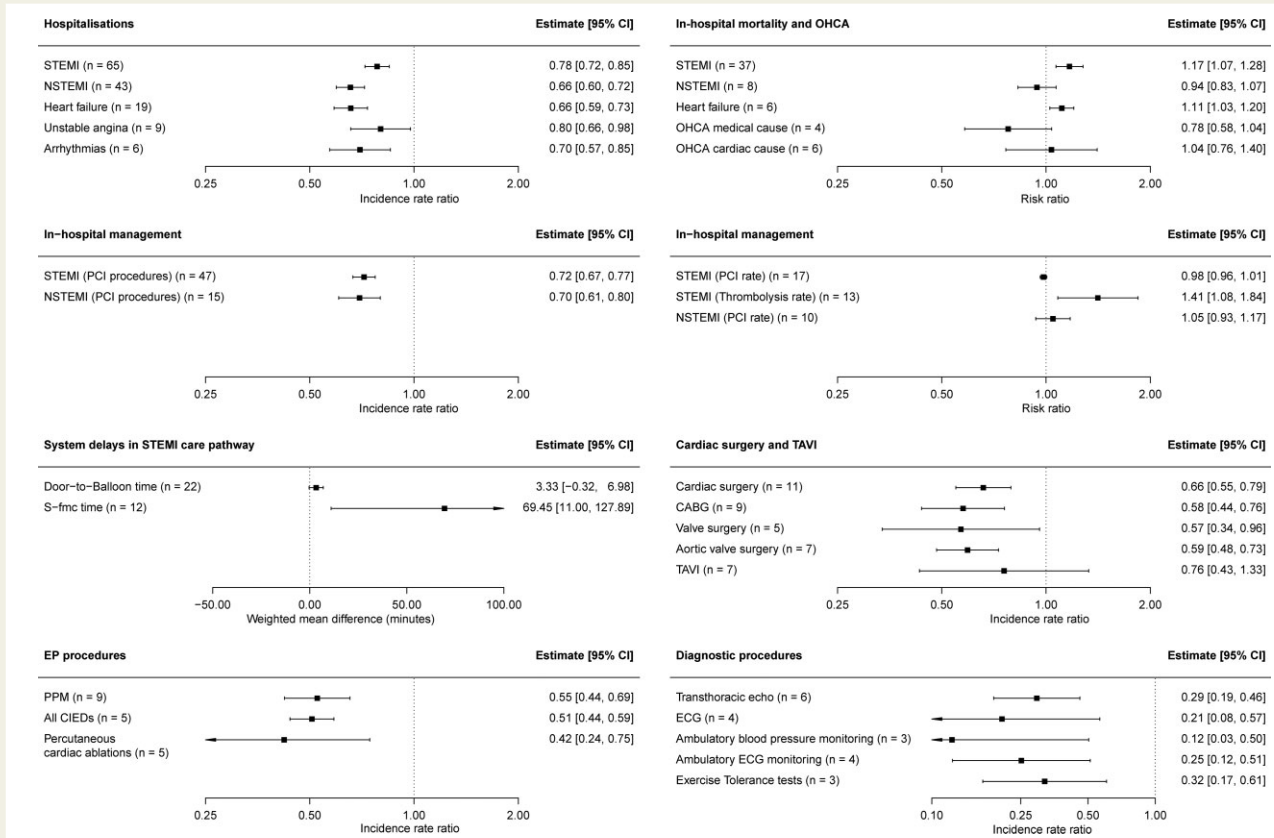


**Figure 3** Summary of overall risk of bias scores assessed using the ROBINS-I tool for all studies across all outcomes (A) and subdivided by categories of outcomes (B–E). AMI, acute myocardial infarction.

data pertaining to a longer time span during the pandemic demonstrated a less extreme effect size for decline in hospitalizations for STEMI and NSTEMI compared with studies that reported a shorter time span (STEMI hospitalizations RR 1.17, 95% CI 1.00–1.38; NSTEMI hospitalizations RR 1.30, 95% CI 1.09–1.57).

For other acute CV presentations, there is limited evidence for the impact of the pandemic. A single-centre study reported that

the number of hospitalizations with pericarditis and hypertensive crisis did not increase during the pandemic.<sup>39</sup> A Danish nationwide study of infective endocarditis (IE) hospitalizations found no difference during the pandemic, whereas a Mexican single-centre study showed a 93% reduction.<sup>40,41</sup> One single-centre study reported a decline in hospitalizations with adult congenital heart disease (ACHD) during the pandemic,<sup>42</sup> and two studies



**Figure 4** Summary estimates for analyses across hospitalizations, in-hospital management, diagnostic and interventional procedures, and mortality. The full forest plots for each analysis are available in [Supplementary material online, Figures S1–S18](#). EP, electrophysiology.

demonstrated a significant increase in the incidence of stress cardiomyopathy.<sup>43,44</sup>

## Invasive management of acute myocardial infarction

The number of percutaneous coronary intervention (PCI) procedures for STEMI and NSTEMI declined during the pandemic to a similar extent to the decline in hospitalizations (PCI for STEMI, IRR 0.72, 95% CI 0.67–0.77,  $I^2 = 92.5\%$ ; PCI for NSTEMI, IRR 0.70, 95% CI 0.61–0.80,  $I^2 = 88.1\%$ ) (Figure 4; [Supplementary material online, S6 and S7](#)). However, amongst patients hospitalized for STEMI and NSTEMI, the proportion who received revascularization did not change during the pandemic (PCI for STEMI hospitalizations, RR 0.98, 95% CI 0.96–1.01,  $I^2 = 82.3\%$ ; PCI for NSTEMI hospitalizations, RR 1.05, 95% CI 0.93–1.17,  $I^2 = 88.3\%$ ) ([Supplementary material online, Figures S8 and S9](#)).

The detrimental effect of the pandemic is evident in system delays related to the STEMI care pathway. Whilst door-to-balloon times (D2B) did not increase significantly during the pandemic (WMD 3.33 min, 95% CI  $-0.32$  to 6.98 min,  $I^2 = 94.2\%$ ) we estimated that there was over an hour greater delay between symptoms to first medical contact (S-FMC) during the pandemic (WMD 69.45 min, 95% CI 11.00–127.89 min,  $I^2 = 99.4\%$ ) ([Supplementary material online, Figure S10](#)).

There was divergence by geographic region and country-level income in the management of acute myocardial infarction during the pandemic. Meta-regression demonstrated that the decline in revascularization was greater in LMICs compared with HICs (PCI for STEMI, RR 0.73, 95% CI 0.62–0.87; PCI for NSTEMI, RR 0.69, 95% CI 0.48–0.99) ([Supplementary material online, Table S62](#)). Increases in D2B and S-FMC time were only found to be significant in countries outside of Europe and North America (Table 1). Finally, the proportion of patients treated for STEMI with thrombolysis increased during the pandemic (RR 1.41, 95% CI 1.08–1.84,  $I^2 = 55.3\%$ ) ([Supplementary material online, Figure S8](#)), driven by increased use of thrombolysis in LMICs and countries outside of Europe and North America (Table 1).

## Interventional procedures

Nationwide data from the UK and the USA found that elective PCI decreased by  $>50\%$  during the pandemic,<sup>45,46</sup> and disproportionately affected older ages and Black, Asian, and minority ethnic (BAME) groups.<sup>45</sup> During the pandemic, we observed a reduction in implantations of permanent pacemakers (IRR 0.55, 95% CI 0.44–0.69,  $I^2 = 98.3\%$ ), implantations of all CIEDs (IRR 0.51, 95% CI 0.44–0.59,  $I^2 = 86.0\%$ ), and the overall number of percutaneous catheter ablations performed (IRR 0.42, 95% CI 0.24–0.75,  $I^2 = 99.4\%$ ) (Figure 4; [Supplementary material online, Figure S11](#)). In contrast, we found conflicting reports for rates of transcatheter aortic valve implantations (TAVIs) during the pandemic compared with pre-pandemic

**Table 1** Summary estimates for all outcomes by subgroups of geographical region and country-level income classification

	Geographic region												Country-level income						
	All data			Europe			North America			Other countries			High-income countries			Low-middle income countries			
	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	
<b>Hospitalization (IRR)</b>																			
STEMI	65	0.78 (0.72–0.85)	39	0.80 (0.74–0.87)	7	0.83 (0.73–0.94)	19	0.72 (0.58–0.89)	48	0.82 (0.77–0.88)	17	0.68 (0.54–0.85)							
NSTEMI	43	0.66 (0.60–0.72)	29	0.68 (0.60–0.76)	3	0.71 (0.66–0.75)	11	0.60 (0.51–0.71)	32	0.68 (0.61–0.76)	11	0.58 (0.49–0.69)							
Unstable angina	9	0.80 (0.66–0.98)	6	0.77 (0.63–0.95)	0		3	0.88 (0.53–1.49)	7	0.78 (0.60–1.02)	2	0.85 (0.69–1.03)							
Heart failure	19	0.66 (0.59–0.73)	12	0.70 (0.65–0.74)	5	0.58 (0.41–0.84)	2	0.65 (0.39–1.08)	17	0.66 (0.58–0.74)	2	0.65 (0.39–1.08)							
Arrhythmias	6	0.70 (0.57–0.85)	5	0.73 (0.59–0.90)	0		1	0.51 (0.36–0.72)	4	0.75 (0.58–0.99)	2	0.61 (0.49–0.77)							
<b>AMI management (IRR or RR)</b>																			
STEMI (PCI procedures, IRR)	47	0.72 (0.67–0.77)	28	0.75 (0.70–0.80)	3	0.75 (0.58–0.97)	16	0.66 (0.54–0.79)	37	0.76 (0.71–0.81)	10	0.60 (0.49–0.72)							
NSTEMI (PCI procedures, IRR)	15	0.70 (0.61–0.80)	10	0.72 (0.66–0.78)	2	0.75 (0.67–0.83)	3	0.59 (0.31–1.13)	12	0.72 (0.67–0.77)	3	0.59 (0.31–1.13)							
STEMI (thrombolysis rate, RR)	13	1.41 (1.08–1.84)	6	1.02 (0.80–1.29)	0		7	2.18 (1.10–4.31)	7	1.07 (0.87–1.33)	6	2.70 (1.07–6.86)							
STEMI (PCI rate, RR)	17	0.98 (0.96–1.01)	9	0.99 (0.96–1.02)	1	1.04 (1.00–1.09)	7	0.96 (0.93–1.00)	12	0.99 (0.97–1.02)	5	0.89 (0.72–1.10)							
NSTEMI (PCI rate, RR)	10	1.05 (0.93–1.17)	4	1.06 (0.88–1.29)	2	1.15 (0.91–1.46)	4	0.99 (0.80–1.22)	6	1.02 (0.95–1.10)	4	1.12 (0.83–1.52)							
<b>Delays in STEMI care (WMD, minutes)</b>																			
Symptom to first medical contact time	12	69.5 (11.0 to 127.9)	5	14.6 (–11.1 to 40.3)	2	225.1 (–23.1–473.2)	5	48.0 (7.1–88.9)	7	85.4 (14.5–185.3)	5	48.0 (7.1–88.9)							
Door-to-balloon time	22	3.3 (–0.3 to 7.0)	11	0.9 (–2.8 to 4.8)	2	–1.7 (–4.5 to 1.2)	9	8.4 (0.6–16.2)	17	0.9 (–2.2 to 4.0)	5	9.5 (–0.5 to 19.4)							
<b>Cardiac surgery and TAVI (IRR)</b>																			
Cardiac surgery	11	0.66 (0.55–0.79)	5	0.59 (0.41–0.84)	2	0.66 (0.61–0.72)	4	0.87 (0.85–0.88)	9	0.64 (0.53–0.79)	2	0.76 (0.49–1.18)							
CABG	9	0.58 (0.44–0.76)	4	0.45 (0.33–0.61)	2	0.78 (0.39–1.55)	3	0.62 (0.39–1.00)	7	0.59 (0.42–0.82)	2	0.54 (0.29–1.03)							
Valve surgery	5	0.57 (0.34–0.96)	3	0.53 (0.29–0.96)	2	0.59 (0.17–2.02)	0		5	0.57 (0.34–0.96)	0								
Aortic valve surgery	7	0.59 (0.48–0.73)	6	0.56 (0.47–0.67)	0		1	1.13 (0.57–2.27)	7	0.59 (0.48–0.73)	0								
TAVI	7	0.76 (0.43–1.33)	6	0.65 (0.37–1.14)	1	1.83 (1.67–2.00)	0		7	0.76 (0.43–1.33)	0								
<b>EP procedures (IRR)</b>																			
PPM	8	0.55 (0.44–0.69)	6	0.54 (0.45–0.64)	0		2	0.58 (0.23–1.44)	6	0.54 (0.45–0.64)	2	0.58 (0.23–1.44)							
All CIED	5	0.51 (0.44–0.59)	5	0.51 (0.44–0.59)	0		0		5	0.51 (0.44–0.59)	0								
Percutaneous catheter ablation	5	0.42 (0.24–0.75)	3	0.47 (0.22–0.97)	1	0.20 (0.17–0.24)	1	0.68 (0.46–1.03)	5	0.42 (0.24–0.75)	0								

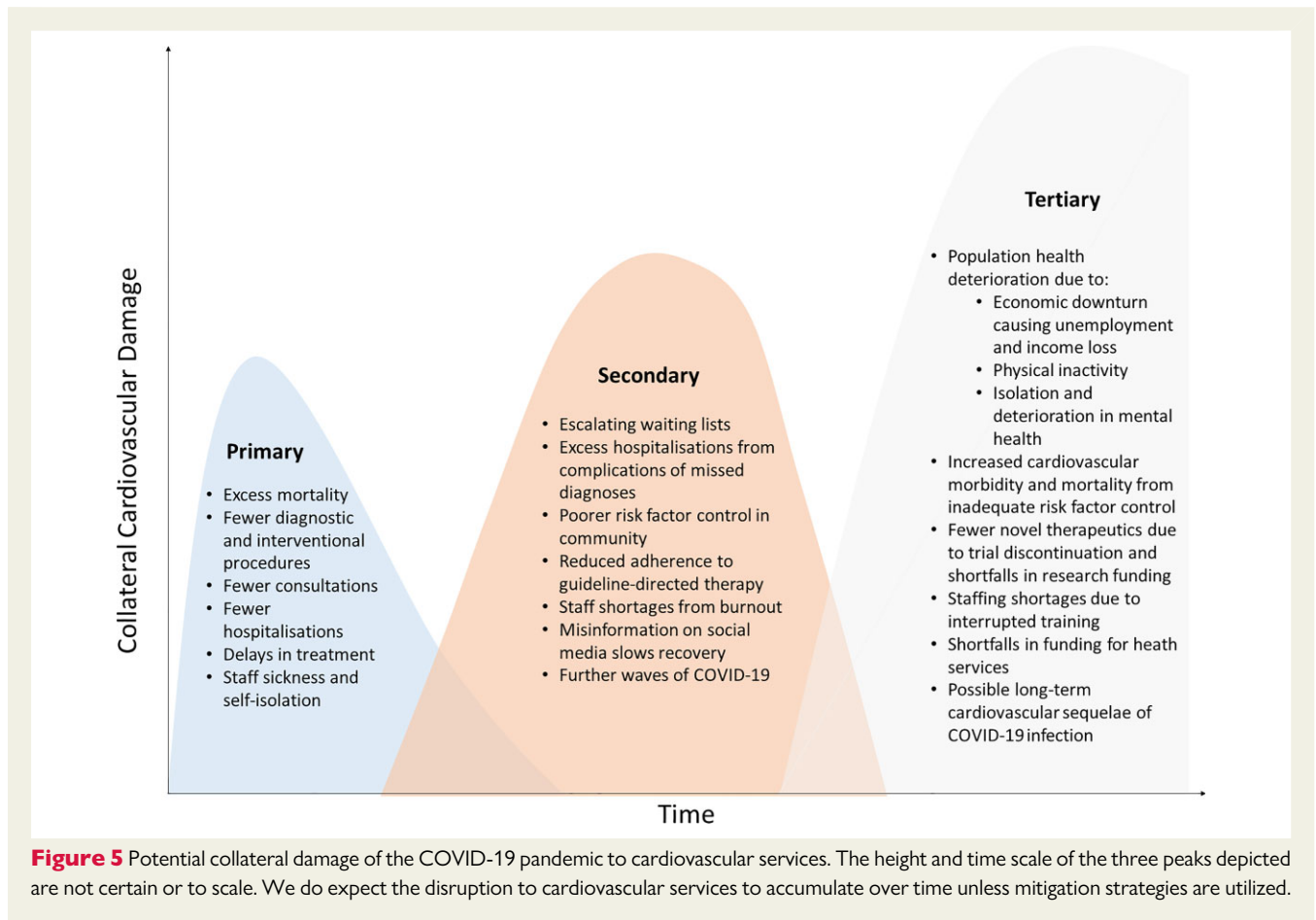
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**Table 1 Continued**

	Geographic region																	
	All data			Europe			North America			Other countries			High-income countries			Low-middle income countries		
	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)	Study	Estimate (95% CI)
<b>Diagnostic procedures (IRR)</b>																		
Transthoracic echo	6	0.29 (0.19–0.46)	4	0.28 (0.16–0.47)	0		2	0.33 (0.11–1.00)	4	0.28 (0.16–0.47)	2	0.33 (0.11–1.00)	2	0.33 (0.11–1.00)	2	0.33 (0.11–1.00)	2	0.33 (0.11–1.00)
ECG	4	0.21 (0.08–0.57)	2	0.22 (0.08–0.60)	0		2	0.19 (0.02–1.82)	2	0.22 (0.08–0.60)	2	0.22 (0.08–0.60)	2	0.22 (0.08–0.60)	2	0.22 (0.08–0.60)	2	0.19 (0.02–1.82)
ABPM	3	0.12 (0.03–0.50)	1	0.22 (0.14–0.33)	0		2	0.08 (0.01–0.93)	1	0.22 (0.14–0.33)	2	0.08 (0.01–0.93)	2	0.22 (0.14–0.33)	2	0.08 (0.01–0.93)	2	0.08 (0.01–0.93)
Ambulatory ECG monitoring	4	0.25 (0.12–0.51)	2	0.28 (0.23–0.34)	0		2	0.19 (0.03–1.39)	2	0.28 (0.23–0.34)	2	0.19 (0.03–1.39)	2	0.28 (0.23–0.34)	2	0.28 (0.23–0.34)	2	0.19 (0.03–1.39)
Exercise tolerance tests	3	0.32 (0.17–0.61)	1	0.47 (0.32–0.69)	0		2	0.26 (0.10–0.66)	1	0.47 (0.32–0.69)	2	0.26 (0.10–0.66)	1	0.47 (0.32–0.69)	2	0.26 (0.10–0.66)	2	0.26 (0.10–0.66)
<b>Mortality (RR)</b>																		
STEMI	37	1.17 (1.07–1.28)	18	1.20 (1.04–1.38)	3	0.97 (0.56–1.69)	16	1.14 (1.04–1.26)	23	1.11 (0.97–1.28)	14	1.22 (1.10–1.37)	4	1.06 (0.55–2.05)	4	1.06 (0.55–2.05)	4	1.06 (0.55–2.05)
NSTEMI	8	0.94 (0.83–1.07)	5	0.94 (0.82–1.07)	0		3	1.12 (0.44–2.86)	4	0.94 (0.82–1.07)	4	1.12 (0.44–2.86)	4	0.94 (0.82–1.07)	4	0.94 (0.82–1.07)	4	1.06 (0.55–2.05)
Heart failure	6	1.11 (1.03–1.20)	4	1.13 (0.99–1.29)	0		2	1.08 (1.04–1.12)	4	1.13 (0.99–1.29)	2	1.08 (1.04–1.12)	4	1.13 (0.99–1.29)	2	1.08 (1.04–1.12)	2	1.08 (1.04–1.12)
OHCA medical cause	4	0.78 (0.58–1.04)	3	0.70 (0.52–0.95)	1	1.03 (0.92–1.15)	0		0	1.03 (0.92–1.15)	0		4	0.78 (0.58–1.04)	0		0	
OHCA cardiac cause	6	1.04 (0.76–1.40)	2	0.91 (0.36–2.27)	2	1.27 (0.79–2.03)	2	0.95 (0.78–1.17)	6	1.04 (0.76–1.40)	2	0.95 (0.78–1.17)	6	1.04 (0.76–1.40)	0		0	

ABPM, ambulatory blood pressure monitoring; AMI, acute myocardial infarction; CABG, coronary artery bypass graft; CI, confidence interval; CIED, cardiac implantable electronic device; ECG, electrocardiogram; EP, electrophysiology; IRR, incidence rate ratio; NSTEMI, non-ST-elevation myocardial infarction; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; PPM, permanent pacemaker; RR, relative risk; STEMI, ST-elevation myocardial infarction, TAVI, transcatheter aortic valve implantation; WMD, weighted mean difference.



(IRR 0.76, 95% CI 0.43–1.33,  $I^2 = 99.2\%$ ) (Supplementary material online, Figure S12). Whilst reports from most of Europe showed a decline in TAVI rates,<sup>1,47–50</sup> there was an increase in the number of TAVI procedures performed during the pandemic in Poland and Ontario, Canada.<sup>51,52</sup>

The total number of cardiac surgical operations fell during the pandemic (IRR 0.66; 95% CI 0.55–0.79,  $I^2 = 99.6\%$ ) (Supplementary material online, Figure S12). There were clear declines in coronary artery bypass graft (CABG) operations (IRR 0.58, 95% CI 0.44–0.76,  $I^2 = 99.0\%$ ) and surgical interventions for the aortic valve (IRR 0.59, 95% CI 0.48–0.73,  $I^2 = 85.6\%$ ).

## Diagnostic procedures

Observational studies reporting a comparison of the number of diagnostic CV procedures during and pre-pandemic were infrequent. Available studies reported declines in exercise tolerance tests (IRR 0.32, 95% CI 0.17–0.61,  $I^2 = 92.9\%$ ), ambulatory ECG monitoring (IRR 0.25, 95% CI 0.12–0.51,  $I^2 = 96.6\%$ ), ambulatory blood pressure monitoring (IRR 0.12, 95% CI 0.03–0.50,  $I^2 = 97.1\%$ ), 12-lead ECGs (IRR 0.21, 95% CI 0.08–0.57,  $I^2 = 99.3\%$ ), and transthoracic echocardiograms (IRR 0.29, 95% CI 0.19–0.46,  $I^2 = 98.1\%$ ) during the pandemic (Figure 4; Supplementary material online, S13). The use of diagnostic invasive coronary angiography has been reported to fall by as much as 74%.<sup>53</sup> Single-centre studies demonstrated that transoesophageal echocardiograms, computed tomography coronary

angiograms, and myocardial perfusion scans either ceased or sharply declined.<sup>27,54,55</sup>

## Outpatient and community consultations

During the pandemic, we found a marked decline in in-person outpatient consultations (IRR 0.27, 95% CI 0.09–0.75,  $I^2 = 100\%$ ) (see Supplementary material online, Figure S14). Five studies reported an increase in telemedicine cardiology outpatient appointments in both HICs and LMICs during the pandemic.<sup>54,56–59</sup> However, multi-centre reports from the USA and Germany suggested overall deficits of 61%, 33%, and 5% in outpatient CV consultations even after including telemedicine appointments.<sup>56,58,60</sup> Surveys showed that almost half of all exercise-based cardiac rehabilitation programmes closed during the pandemic,<sup>61–63</sup> and of programmes that continued many used technology to provide virtual consultations.<sup>62–64</sup>

## Mortality

### In-hospital all-cause mortality

For patients hospitalized with acute CV disease, in-hospital all-cause mortality was reported frequently and 30-day all-cause mortality rarely. For both STEMI and HF, in-hospital mortality increased during the pandemic (STEMI, RR 1.17, 95% CI 1.07–1.28,  $I^2 = 23.3\%$ ; HF, RR 1.11, 95% CI 1.03–1.20,  $I^2 = 63.9\%$ ) and did not differ for NSTEMI (RR 0.94, 95% CI 0.83–1.07,  $I^2 = 0.0\%$ ) (Figure 4; Supplementary

material online, S15 and S16). For both STEMI and HF, in-hospital mortality increased during the pandemic in LMICs but not in HICs (Table 1).

### 30-day all-cause mortality

Only six studies reported 30-day all-cause mortality for NSTEMI, STEMI, or HF.<sup>65–70</sup> Three studies showed that 30-day mortality increased during the pandemic for NSTEMI but not STEMI.<sup>65–67</sup> In one report, higher 30-day mortality for NSTEMI was correlated with concurrent SARS-CoV-2 infection.<sup>67</sup> For the other two studies, infection status was not reported but primary PCI (PPCI) was 'protected' during the pandemic whilst patients admitted for NSTEMI received lower rates of and a greater delay to angiography.<sup>65,66</sup> An analysis of nationwide health records described increased odds of 30-day mortality following admission with HF.<sup>70</sup> Notably, studies of mortality in the mid- to long term suggest that these trends may continue. One-year cardiac-related mortality for patients admitted for STEMI during the pandemic was reported to be no different from a historical control group, in spite of worse in-hospital outcomes.<sup>71</sup> Patients admitted for NSTEMI during the pandemic, who on average waited longer for revascularization, have been reported to have over twice as high a risk of all-cause mortality and a 20-fold increased risk of hospitalization with HF at 6 months compared with historical controls.<sup>72</sup> Patients surviving hospitalization for HF during the pandemic also have higher all-cause mortality at 1 year compared with patients hospitalized in 2019, correlated with fewer receiving their inpatient care on specialist cardiology wards.<sup>73</sup>

### Out-of-hospital cardiac arrest

We found no evidence for an increase during the pandemic period of out-of-hospital cardiac arrest (OHCA) of presumed medical or cardiac cause—as defined by attending emergency medical service personnel (OHCA medical cause, IRR 0.78, 95% CI 0.58–1.04,  $I^2 = 95.1\%$ ; OHCA cardiac cause, IRR 1.04, 95% CI 0.76–1.40,  $I^2 = 98.6\%$ ) (Figure 4; Supplementary material online, S17 and S18).

### Population-level cardiovascular mortality

Four studies using UK nationwide data reported increased non-COVID-19 acute CV mortality compared with the historical average in the early months of the pandemic,<sup>74–77</sup> with a 'displacement of death' occurring in homes (30.9% vs. 23.5%) and care homes (15.7% vs. 13.5%).<sup>77</sup> In the USA, two studies demonstrated increased deaths from heart disease during the pandemic compared with previous years,<sup>78,79</sup> with a greater excess in areas of higher density of COVID-19 infection.<sup>78</sup> This pattern was also noted in LMICs, with the greatest excess CV mortality reported in the most deprived cities.<sup>80,81</sup>

## Discussion

This systematic review and meta-analysis of the effect of the COVID-19 pandemic on CV services has identified a number of important points. First, the COVID-19 pandemic witnessed a substantial global decline in hospitalizations with acute CV disease, fewer diagnostic and interventional procedures, and fewer outpatient and

community consultations. Second, we found no difference in the decline in hospitalizations for STEMI, NSTEMI, and HF during the second wave compared with the first wave. Third, there is disparity in the severity of collateral CV damage across geographic and economic boundaries. Across LMICs and countries outside of Europe and North America, we observed a more severe decline in hospitalizations and revascularization for STEMI, greater delays in STEMI care pathways with more frequent use of thrombolysis, and elevated in-hospital mortality for both STEMI and HF (Structured Graphical Abstract).

Previous reviews have observed a decline in hospitalizations for ACS during the pandemic,<sup>8–10</sup> but here we extend the quantitative analysis of hospitalization rates to HF and arrhythmias, and demonstrate similar patterns. Other authors have shown that in-hospital mortality rose during the pandemic when studies reporting different CV diseases are combined,<sup>17</sup> and specifically in patients who underwent PPCI for STEMI.<sup>9</sup> In this analysis, we are able to demonstrate elevated in-hospital mortality during the pandemic for both STEMI and HF, and demonstrate variation across geographic regions and by country economic development. Finally, we provide the first estimates of the detrimental effect of the pandemic on interventional procedures, diagnostic procedures, and outpatient consultations.

We found that the decline in hospitalization for acute CV disease occurred across the breadth of CV diseases, and reports suggest that reductions occurred irrespective of formal restrictions on movement,<sup>65,82,83</sup> or the extent of COVID-19 diagnoses within the local population.<sup>84</sup> We observed delays to seeking help and receiving medical attention, independent reports of increased CV deaths in homes and care homes, and reports of increased case severity amongst those who did reach hospital.<sup>3,42,85–87</sup> One may infer that fear of the contagion, 'stay at home campaigns', and overwhelmed emergency medical services prevented and delayed hospitalization of unwell patients. The scale of disruption to public interaction with CV services was not fully anticipated before the pandemic. In response, information campaigns, such as 'You can't pause a heart' by the European Society of Cardiology (ESC),<sup>88</sup> aimed to equilibrate public health messaging by accentuating the importance of expeditiously seeking medical attention for symptoms of acute CV disease. Whilst some studies reported that information campaigns quickened recovery in rates of hospitalization for acute myocardial infarction,<sup>82,83,89,90</sup> we did not find a significant difference in the decline of hospitalization rates between the first and second wave across STEMI, NSTEMI, and HF. However, we did observe that studies reporting a longer time span of the pandemic period, and thus better reflecting both 'decline' and 'recovery' phases of hospitalization rates related to public health restrictions,<sup>65</sup> evidenced a less extreme decline in hospitalizations for acute CV disease. Initial evidence on the Omicron variant suggests that it is more easily spread, but generally causes less severe disease, than previous SARS-CoV-2 variants.<sup>91</sup> As the public and healthcare services become more familiar with 'living with' COVID-19 and widespread vaccination in HICs limits morbidity and mortality directly related to SARS-CoV-2 infection,<sup>92</sup> it remains to be seen if hospitalization rates for acute CV disease will be robust to future waves.

There were comparatively few available data for the effect of the pandemic on CV services in LMICs. Only for hospitalizations, STEMI care pathways, and in-hospital mortality were we able to investigate for disparities compared with HICs, and we consistently found more

severe collateral CV damage. The 143 LMICs constitute 80% of the world's population—approximately 6 billion people—and the World Health Organization (WHO) estimates that 80% of all CV deaths now occur in LMICs.<sup>93</sup> Whilst guideline-based therapy for STEMI has dramatically improved outcomes in HICs, regional systems of care for STEMI in LMICs are sparse. There are few emergency medical services, catheterization labs tend to be clustered in urban centres, and poor insurance coverage for the majority of the population limits the applicability of expensive procedures, leaving fibrinolysis as the most common treatment of STEMI.<sup>94</sup> Historically, inpatients with acute HF in North America and Europe have had lower mortality rates than patients in South America and Asia,<sup>95</sup> and 6-month mortality rates of almost 20% after HF hospitalization have been reported in sub-Saharan Africa.<sup>96</sup> Access to diagnostic and interventional cardiac procedures is limited in LMICs,<sup>97</sup> as is the ability to be able to provide guideline-directed management for other CV diseases.<sup>98</sup> The pandemic exacerbated established challenges to the delivery of STEMI and HF care in LMICs. We are concerned that the gap in CV care and outcomes between HICs and LMICs may have widened during the pandemic across the breadth of CV diseases and services, yet data are not available to evidence this notion.

Collateral CV damage from missed diagnoses and delayed treatments will continue to accrue unless mitigation strategies are speedily implemented (Figure 5). The deferral of interventional procedures, especially for structural heart disease, leaves many patients at high risk of adverse outcomes.<sup>99</sup> Risk stratification and prioritization will be needed to avert substantial excess mortality,<sup>100,101</sup> and the pragmatic use of percutaneous over surgical options should be considered.<sup>102–104</sup> A digital transformation in the healthcare model could cut the deficit in outpatient care and improve risk factor control. During the pandemic, there have been fewer contacts for CV diagnoses and risk factor monitoring,<sup>105,106</sup> and lockdowns led to a significant decline in physical activity, weight gain, and worsening psychological health.<sup>107,108</sup> Virtual consultations and tele-rehabilitation can provide better patient engagement with similar outcomes to in-person interactions, and patients can be empowered to manage their CV health by integrating home health equipment into routine clinical practice.<sup>59,109,110</sup> Nonetheless, inequitable access to telemedicine and digital technology has been described for female, non-English-speaking, older, and poorer patients, and we must guard against reinforcing such inequities in healthcare.<sup>111</sup>

As this review reveals, there is limited information about CV health and care from LMICs (data gaps exist in the African, South American, and Western Pacific regions). There are a few nationwide initiatives to systematically collect and report data on CV health in LMICs,<sup>112</sup> and the WHO is engaging with member states and technology partners to strengthen their local health information systems.<sup>113</sup> The ESC Atlas of Cardiology provides an enviable resource for data relating to population health in Europe.<sup>114</sup> A global living collaborative network focusing on CV care during the pandemic at an institutional level could be established,<sup>115</sup> and internationally harmonized CV data available in a responsive fashion could enable a 'global barometer' of the consequences of the pandemic as well as the opportunity to prepare for future major health crises.<sup>116</sup>

There are limitations to our analysis. The evidence base is skewed to HICs in Europe and North America, the earlier part of the

pandemic, certain CV diseases, and short-term outcome measures, which limit quantitative insights. We classified most studies as being at severe or moderate risk of bias across all outcomes, which is in agreement with previous reports of the methodological quality of publications during the COVID-19 pandemic.<sup>17,117</sup> Many studies did not report the number or proportion of included patients that had co-existent COVID-19 infection, which introduces bias and prohibits detailed analysis of what contribution the direct effect of COVID-19 on the CV system may have had on our estimates for in-hospital mortality and hospitalizations. Nonetheless, a meta-analysis including >27 000 patients demonstrated that in-hospital mortality in CV disease was increased during the pandemic independent of co-infection with COVID-19, and the direction of effect was consistent between studies at moderate and severe risk of bias.<sup>17</sup> Furthermore, the direct CV consequences of COVID-19 include myocarditis, HF, arrhythmias, and acute myocardial injury,<sup>118</sup> so the number of hospitalizations for acute CV disease would probably increase if direct COVID-19 pathology was the predominant factor, in contrast to our findings.

Heterogeneity was high in most analyses, which we investigated through meta-regression for a range of factors in outcomes of hospitalizations, invasive management of acute myocardial infarction, and in-hospital mortality. We found that geographic region, income classification, and whether the first or second wave was reported introduced variability in effect size, as did study characteristics such as the data source, presence of a matched comparator period, the length of the pandemic study period, and the time point at which data collection started during the pandemic period (Supplementary material online, Table S62). Significance was often not reached for individual factors due to the small number of studies. The smaller number of studies reporting procedures and outpatient consultations precluded meta-regression to investigate heterogeneity. Nevertheless, the direction of association is consistent across outcomes (Supplementary material online, Figures S1–S18), suggesting that the conclusions we draw for trends during the pandemic are reliable.

## Conclusions

This systematic review with a meta-analysis provides, to date, the most comprehensive summary of the effect of the COVID-19 pandemic on CV services and individuals with CV disease. From 189 articles, we show evidence of fewer hospitalizations, procedures, and consultations with increased mortality amongst in-hospital and community populations. We identified disparity by geographical region and country income classification in the availability of data and the severity of the detrimental effect of the pandemic on CV services, and presently there are insufficient data to fully characterize the effects to CV services in LMICs. Notwithstanding this, we provide synthesized evidence that the COVID-19 pandemic resulted in substantial global collateral CV damage.

## Author contributions

C.P.G. conceived the idea of the study. R.N. and B.H. screened the studies and reviewed the selected articles. R.N. and B.H. undertook



data extraction. J.W. carried out the statistical analysis. R.N., J.W., and C.P.G. interpreted the findings, and R.N. drafted the manuscript. J.W., B.H., S.A., D.L.B., G.B.Z., L.S.M., C.V.S.R., A.P.L.R., H.G.C.V.S., J.E.D., T.F.L., M.M., and C.P.G. critically reviewed the manuscript, and R.N. revised the manuscript for final submission. All authors have approved the final draft of the manuscript. R.N. is the guarantor. R.N. accepts full responsibility for the work and the conduct of the review, had access to the data, and controlled the decision to publish. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

## Supplementary material

Supplementary material is available at *European Heart Journal* online.

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**Conflict of interest:** none declared.

## Ethical approval

Ethical approval was not required.

## Data sharing

Data are available on reasonable request. The technical appendix, statistical code, and dataset are available from the corresponding author at [r.nadarajah@leeds.ac.uk](mailto:r.nadarajah@leeds.ac.uk).

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