Mediators of the Association Between Socioeconomic Status and Survival After Out-of-Hospital Cardiac Arrest: A Systematic Review

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Main Findings

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**Objective**

Identify and quantify mediators of the association between SES and survival after OHCA.

**Indirect Effect**

Intermediate Variable (Mediator)

**Direct Effect**

Survival

**Conclusions**

To mitigate socioeconomic disparities in outcomes after OHCA, public health interventions should target potentially modifiable mediators, such as initial rhythm (through the promotion of prompt resuscitation).

**Main Findings**

- Initial rhythm (n=6): 37.4\% (28.6\%-40\%), 41.8\%*
- Bystander CPR/AED use (n=4): 8.6\%-18.8\%, 4.8\%*, (0.1\%-0.2\%)*
- EMS response time (n=5): 14.4\% (6.9\%-20.0\%)
- Witnessed status (n=2): 3.6\%-18.8\%, 4.8\%*, (0.1\%-0.2\%)*

**Mediation measures:** percent excess risk explained by the mediator – median (range), *mediation proportion, †eliminated SES disparity by mediator – (range), n= number of studies

**ABSTRACT**

Low socioeconomic status (SES) is associated with poor outcomes after out-of-hospital cardiac arrest (OHCA). Patient characteristics, care processes, and other contextual factors may mediate the association between SES and survival after OHCA. Interventions that target these mediating factors may reduce disparities in OHCA outcomes across different socio-economic groups.

**RÉSUMÉ**

Le faible statut socioéconomique (SSE) est associé à de mauvais résultats après un arrêt cardiaque hors de l’hôpital (ACHH). Les caractéristiques du patient, les processus de soins et les autres facteurs contextuels peuvent médiatiser l’association entre le SSE et la survie après un ACHH. Les interventions qui visent les facteurs médiateurs...
the socioeconomic spectrum. This systematic review identified and quantified mediators of the SES–survival after OHCA association. Electronic databases (MEDLINE, Embase, PubMed, Web of Science) and grey literature sources were searched from inception to July or August 2023. Observational studies of OHCA patients that conducted mediation analyses to evaluate potential mediators of the association between SES (defined by income, education, occupation, or a composite index) and survival outcomes were included. A total of 10 studies were included in this review. Income (n = 9), education (n = 4), occupation (n = 1), and composite indices (n = 1) were used to define SES. The proportion of OHCA cases that had bystander involvement, presented with an initial shockable rhythm, and survived to hospital discharge or 30 days increased with higher SES. Common mediators of the SES-survival association that were evaluated included initial rhythm (n = 6), emergency medical services response time (n = 5), and bystander cardiopulmonary resuscitation (n = 4). Initial rhythm was the most important mediator of this association, with a median percent excess risk explained of 37.4% (range 28.6%-40.0%; n = 5; 1 study reported no mediation) and mediation proportion of 41.8% (n = 1). To mitigate socioeconomic disparities in outcomes after OHCA, interventions should target potentially modifiable mediators, such as initial rhythm, which may involve improving bystander awareness of OHCA and the need for prompt resuscitation.

Out-of-hospital cardiac arrest (OHCA) is a global public health concern that is associated with significant morbidity and mortality.1-4 Outcomes after OHCA are poor worldwide, with significant variation reported between continents and within countries.1,5-7 Survival after OHCA is influenced by a complex interplay of factors, including patient and arrest characteristics, pre-hospital interventions, and post-arrest care.8-10 Numerous studies have shown differences in the provision of care and outcomes after OHCA by various social determinants of health, such as sex,11 race/ethnicity,12-14 and geographic location (of arrest).15

Socioeconomic status (SES) is a multidimensional construct that represents the combined social and economic background of an individual or group.16,17 It is well established that SES, typically measured through income level, educational attainment, or employment status, is associated with incident cardiovascular disease and all-cause mortality.18-20 Previous reviews have consistently demonstrated that lower SES is associated with an increased incidence of OHCA and a reduced probability of survival.21-23 It has been hypothesised that disparities in OHCA outcomes may be explained, at least in part, by the impact of SES on crucial actions throughout the resuscitation pathway, commonly referred to as the Chain of Survival.24 Lower SES has been linked to longer dispatcher recognition times,25 reduced odds of receiving bystander interventions,26-29 and lower rates of post-arrest care, such as targeted temperature management and coronary angiography.27,28

Achieving meaningful and sustainable improvements in SES at the societal level is difficult, given the need for long-term strategies that address multiple interconnected issues. Intervening on SES involves the development of policies to redistribute economic resources, improve educational opportunities, generate job availability, and ensure access to health care services.29 Understanding the mechanisms by which SES indirectly influences survival after OHCA may help to identify modifiable factors to target through future public health interventions. As part of a multipronged approach to addressing OHCA inequities, intervening on these mediating factors may be a beneficial strategy to reduce OHCA outcome disparities across the socioeconomic spectrum. Accordingly, the objective of this systematic review was to identify and quantify potential mediators of the association between SES and survival after OHCA.

**Methods**

**Registration**

The methodology and reporting of this systematic review was conducted in accordance with the Preferred
The protocol for this systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) on August 7, 2023 (registration no. CRD42023447292).

**Eligibility criteria**

**PECOS framework.** The PECOS (Population, Exposure, Comparator, Outcome, Study Design) framework was used to guide study eligibility decisions for this review. Observational research studies of OHCA cases (Population) that stratified their sample according to SES (Exposure) were included. The main socioeconomic indicators of interest included income, education, and occupation, as measured in isolation (ie, actual indicators or proxy measures) or as a component of a composite index. These factors are the most frequently used indicators of SES in health research and can be measured at the area level (eg, neighbourhoods or communities) or the individual level (ie, pertaining to specific persons). A comparison group for the main exposure (eg, individuals in the lowest or highest income group) was required for study inclusion (Comparator). Only studies that reported survival outcomes, including pre-hospital return of spontaneous circulation, survival to hospital admission, survival to hospital discharge, or long-term survival (eg, survival at 30 days or 1 year), were included (Outcome). Finally, studies were restricted to those published in English, with a sample size > 100. Case reports, case series, and conference abstracts were excluded owing to the inability to evaluate their methodologic rigour and risk of bias (Study Design).

**Methodologic eligibility requirements.** To be eligible for inclusion, studies were required to report results from traditional mediation approaches (eg, difference method) or modern causal inference-based mediation approaches (eg, structural equation modelling). In the context of this review, mediation refers to the extent to which the effect of SES on survival after OHCA (referred to as the total effect) is explained by an intermediate variable or set of intermediate variables (referred to as the indirect effect). These intermediate variables are commonly referred to as mediators. Potential mediators that were conceptualized from eligible studies included intermediate variables that temporally succeeded the exposure (SES), preceded the outcome (survival), and could potentially affect the outcome (survival). The conceptual framework for the mediation analysis in this review is shown in Figure 1. Mediators are different than confounders. Confounding variables (confounders) are variables that affect both exposure and outcome. Confounders may introduce confounding, a form of bias that is defined as a distortion of the true exposure-outcome relationship due to the presence of confounders. For a thorough overview of the unique motivations and conceptual differences between mediators and confounders, as well as other epidemiologic concepts, such as effect modification and interaction, interested readers should consult Babyak and Corraineri et al. (2017). Detailed overviews of mediation analysis techniques have been described elsewhere. In brief, the difference method is a regression-based approach that compares a measure of association between a model that includes a specific mediator (or set of mediators) and one that does not include the mediator(s). Attenuation of the measure of association after including the mediator(s) in the model is indicative of mediation; this suggests that the mediator explains some of the total effect of the exposure on the outcome. In comparison, an example of a modern causal inference-based approach to mediation is structural equation modelling, which is a statistical method that can be used to examine the relationships between multiple variables, thus providing a useful inference framework for mediation analyses. Media- tion proportions can be calculated from this approach, which quantify the percentage change of the regression coefficients when a mediator is included in the model. In other words, the mediation proportion quantifies how important the pathway through the mediator is in explaining the effect of the exposure on the outcome. Other modern approaches to mediation have been applied in health disparities research, such as the estimation of counterfactual disparity measures, which can be used to quantify the proportion of disparity that would be eliminated if a mediator was changed.

**Information sources and search strategies**

Electronic literature searches were conducted in MEDLINE (from 1946), Embase (from 1947), PubMed (from 1966), and Web of Science (from 1900) on July 23, 2023, A focused search of Google Scholar (first 300 results, sorted by relevance), as previously suggested, was performed in August 2023 to capture sources of evidence within grey literature. The electronic search strategies that were used for each database are outlined in the Supplemental Appendix S2.

**Study selection process**

The systematic review management platform Covidence (Melbourne, Australia) was used to perform study selection. Any duplicate records were automatically identified and removed by this platform, which has demonstrated high accuracy in the identification of duplicate records. Abstract screening and full-text review were performed independently.
by 2 reviewers (N.G. and B.H.). Any conflicts regarding the inclusion or exclusion of articles at each stage were discussed until a consensus was reached. Cohen’s kappa (κ) statistic and a 95% confidence interval (CI) for interrater reliability was calculated at the abstract screening stage. A single reviewer (B.H.) examined the reference lists of included articles to identify additional articles that may be relevant, which were judged for inclusion by the same processes outlined above.

Data collection process and data items

Data extraction was performed by 2 independent reviewers (N.G. and B.H.). One reviewer extracted data and the other reviewer assessed data for accuracy and completeness. A standardised data collection form was used to extract study characteristics, patient and OHCA characteristics, and mediation analysis results. Study characteristics included first author’s name, year of publication, study design, location, time period, sample description, sample size, and SES indicator information (type, description, and level of measurement). Patient and OHCA characteristics included sex, age, bystander interventions, witnessed status, location of arrest, initial shockable rhythm, emergency medical services (EMS) response time, and survival outcomes. A summary of mediation analysis findings was extracted from each study, which included the mediator(s) evaluated, method used, and key quantitative results (eg, measures of association, mediation measures).

Study risk of bias assessment

The risk of bias in included studies was evaluated by means of the Newcastle-Ottawa Scale for cohort studies, which uses a star-based system to score studies from 0 (lowest quality) to 9 (highest quality). Stars are awarded based on the selection of the study groups (maximum 4 stars), comparability of the groups (maximum 2 stars), and ascertainment of the outcome of interest (maximum 3 stars). To fit the scope of this systematic review, a modified version of this assessment scale was used to assess the risk of bias of the included studies (Supplemental Table S1).

Synthesis approach

Because mediation analyses focus on assessing the relative magnitude of indirect effects, meta-analyses of mediation studies are methodologically complex. Common complications include differences in analytic techniques for mediation analysis, a high risk of selective reporting of mediation results (leading to publication bias), and significant heterogeneity across eligible studies in terms of confounder adjustment and mediator measurement. For these reasons, a formal meta-analysis was not feasible for this review.

Review findings were summarised using tabular and descriptive synthesis approaches. In this review, frequency counts refer to the number of studies, whereas medians and ranges were used to summarise study characteristics and other review results. Survival outcomes, stratified by SES indicator level (low, medium, and high), were summarised by calculating the median and range across studies with similar samples. For studies that used more than 3 subgroups to ascertain SES subgroups, middle levels were combined into a weighted average.

All mediation measures were reported as presented in the individual studies. When possible, the percent excess risk explained by the mediator(s) was calculated. This was determined by comparing the measure of association between the exposure and outcome before (U) and after (A) adjusting for the mediator(s) of interest. The equation for the measure, which has been previously described, is:

\[
\text{Percent Excess Risk Explained} = \frac{RR_U - RR_A}{RR_U - 1} \times 100\%
\]

RR refers to the relative risk. This measure provides an approximate indication of the degree to which the mediator(s) of interest could explain the SES-survival association. For the calculation of this measure, studies that presented odds ratios (ORs) were approximated as RRs. The measure of association that compared the lowest SES category (reference) with the highest SES category was used to calculate the percent excess risk explained (reciprocal measures were calculated as necessary for studies that used opposite reference coding). All analyses were conducted in Microsoft Excel (Redmond, Washington, United States).

Results

Study selection

A total of 5824 studies from electronic databases and grey literature sources were retrieved, of which 3829 were screened by 2 reviewers (κ = 0.87, 95% CI 0.80-0.94), and 10 retrospective cohort studies were ultimately included (Fig. 2). Two additional studies were identified from citation searching, both of which were not eligible for inclusion.

Study characteristics

Study characteristics are shown in Table 1. Studies were conducted in the United States (n = 3), South Korea (n = 2), Sweden (n = 2), Denmark (n = 2), and the Netherlands (n = 1). The median sample size was 15,413 (range 459-169,502), and the median study duration was 84 months (range 24-163 months). Years of study coverage ranged from 1999 to 2020. Primary outcomes included survival to hospital discharge (n = 6; n = 1 with good neurologic recovery) and 30-day survival (n = 4). All studies scored high (8/9 or 9/9) on the Newcastle-Ottawa Scale, suggesting minimal risk of bias (Supplemental Table S2).

SES indicators

The SES indicators used across included studies are summarized in Table 2. Measures of SES included income (n = 9), education (n = 4), occupation (n = 1), and a composite measure (n = 1). Five studies (n = 5) used more than 1 SES indicator. Indicators were measured at either the area level (n = 4), using census tracts (United States) or districts (South Korea), or the individual level (n = 6).
Patient and OHCA characteristics

Patient and OHCA characteristics for each study sample, stratified by SES, are presented in Supplemental Table S3. In general, the proportion of OHCA patients that were female was similar across SES strata. Most samples were composed of middle-aged adult OHCA patients, apart from 2 studies that included child and adolescent OHCA cases.50,56 A greater proportion of OHCA patients in high income or high education strata had their arrest witnessed by a bystander than those in low income or low education strata. Bystander cardiopulmonary resuscitation (CPR) was reported by all studies (n = 10), whereas bystander automated external defibrillator (AED) use was reported by 3 studies. The proportion of OHCA patients who received bystander interventions appeared to increase as income and educational level increased. The proportion of OHCA events with an initial shockable rhythm appeared to increase as income and educational level increased. The EMS response time for OHCA events was similar across SES levels.

Outcomes

Summary measures of survival outcomes by SES indicator level are shown in Figure 3 (individual outcome measures by SES are presented in Supplemental Table S3). All summary measures were calculated after excluding 2 studies that included child and adolescent OHCA cases.50,56 A greater proportion of OHCA patients in high income or high education strata had their arrest witnessed by a bystander than those in low income or low education strata. Bystander cardiopulmonary resuscitation (CPR) was reported by all studies (n = 10), whereas bystander automated external defibrillator (AED) use was reported by 3 studies. The proportion of OHCA patients who received bystander interventions appeared to increase as income and educational level increased. The proportion of OHCA events with an initial shockable rhythm appeared to increase as income or educational level increased. Among 4 studies, the proportions of OHCA patients that survived to hospital discharge for low, medium, and high incomes were 10.0% (range 4.5%-16.1%), 13.6% (range 8.4%-19.2%), and 14.0% (range 7.2%-28.6%), respectively. Among 3 studies, the proportions of OHCA patients that achieved 30-day survival for low, medium, and high incomes were 4.7% (range 4.2%-6.6%), 7.7% (range 7.5%-8.1%), and 14.8% (range 11.4%-19.4%), respectively. Among 3 studies, the proportions of OHCA patients that achieved 30-day survival for low, medium, and high educational levels were 6.4% (range 4.9%-7.2%), 9.7% (range 8.7%-11.9%), and 14.7% (range 13.1%-15.9%), respectively. Notable differences in the rate of survival across SES levels were observed among included studies, with differences between the lowest and highest rates ranging from 1.3% to 25.1% (Supplemental Table S4).

Mediators and mediation results

A summary of the mediation analyses across included studies is presented in Table 3, whereas study-specific results are presented in Supplemental Table S5. Mediation analyses were conducted using the difference method (n = 8), structural equation modelling (n = 1), and a counterfactual disparity approach (n = 1). All studies (n = 10) evaluated at least 1 mediator individually, whereas 5 studies additionally evaluated mediator variable sets (Supplemental Table S6). Common mediators of the SES-survival association that were evaluated individually included initial rhythm (n = 6), EMS response time (n = 5), bystander CPR (n = 4), witnessed...
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<tr>
<th>Study</th>
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<th>Sample description</th>
<th>Primary outcome</th>
<th>Sample size</th>
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<tr>
<td>Ahn et al.50</td>
<td>South Korea</td>
<td>2006-2007 (24 mo)</td>
<td>EMS-assessed OHCA cases that were transported to all levels of EDs</td>
<td>Survival to hospital discharge</td>
<td>34,227</td>
<td>9/9</td>
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<tr>
<td>Chan et al.51</td>
<td>United States</td>
<td>2013-2017 (60 mo)</td>
<td>EMS-assessed adult (≥18 y) OHCA cases where resuscitation was attempted</td>
<td>Survival to hospital discharge</td>
<td>169,502</td>
<td>9/9</td>
</tr>
<tr>
<td>Choi et al.52</td>
<td>South Korea</td>
<td>2013-2019 (84 mo)</td>
<td>EMS-treated adult (≥18 y) OHCA cases of presumed cardiac etiology</td>
<td>Survival to hospital discharge</td>
<td>121,516</td>
<td>9/9</td>
</tr>
<tr>
<td>Clarke et al.53</td>
<td>United States (King County, Washington)</td>
<td>1999-2003 (60 mo)</td>
<td>EMS-treated adult (≥18 y) OHCA cases who had an underlying etiology of heart disease</td>
<td>Survival to hospital discharge</td>
<td>1789</td>
<td>9/9</td>
</tr>
<tr>
<td>Huebinger et al.28</td>
<td>United States (Texas)</td>
<td>2014-2020 (84 mo)</td>
<td>EMS-assessed adult (≥18 y) OHCA cases where resuscitation was attempted and the patient survived to hospital admission</td>
<td>Survival to hospital discharge with good neurologic recovery</td>
<td>9346</td>
<td>9/9</td>
</tr>
<tr>
<td>Jonsson et al.54</td>
<td>Sweden</td>
<td>2010-2017 (96 mo)</td>
<td>Adult (≥25 y) OHCA cases</td>
<td>30-day survival</td>
<td>31,373</td>
<td>9/9</td>
</tr>
<tr>
<td>Lagedal et al.27</td>
<td>Sweden</td>
<td>2008-2013 (72 mo)</td>
<td>Adult (≥18 y) OHCA cases who survived to hospital admission</td>
<td>30-day survival</td>
<td>3906</td>
<td>9/9</td>
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<tr>
<td>Møller et al.55</td>
<td>Denmark</td>
<td>2001-2014 (163 mo)</td>
<td>Adult (≥30 y) OHCA cases of presumed cardiac etiology where resuscitation was attempted</td>
<td>30-day survival</td>
<td>21,480</td>
<td>8/9</td>
</tr>
<tr>
<td>Rajan et al.56</td>
<td>Denmark</td>
<td>2001-2010 (115 mo)</td>
<td>EMS-assessed child/adolescent (≥12 y) OHCA cases where resuscitation was attempted</td>
<td>30-day survival</td>
<td>459</td>
<td>9/9</td>
</tr>
<tr>
<td>van Dongen et al.57</td>
<td>Netherlands (North Holland)</td>
<td>2009-2015 (84 mo)</td>
<td>EMS-assessed adult (≥25 y) OHCA cases of presumed cardiac etiology where resuscitation was attempted</td>
<td>Survival to hospital discharge</td>
<td>5395</td>
<td>9/9</td>
</tr>
</tbody>
</table>

ED, emergency department; EMS, emergency medical services; NOS, Newcastle-Ottawa Scale; OHCA, out-of-hospital cardiac arrest.
status (n = 2), and hospital/emergency department type (n = 2).

Initial rhythm appeared to be the strongest mediator, with a median percent excess risk explained of 37.4% (range 28.6%-40.0%; 5 studies; 1 study reported no mediation). Using a structural equation modelling approach, Choi et al. (2023) identified initial rhythm as the most important mediator of the SES-survival association (mediation proportion: 41.8%).52 Mediation of the SES-survival association by EMS response time was weaker, with a median percent excess risk explained of 14.4% (range 6.9%-20.0%; 5 studies; 3 studies reported no mediation). The median percent excess risk explained by bystander CPR ranged from 8.6% to 18.8% (2 studies). The mediation proportion of bystander CPR as quantified by Choi et al. (2023) was 4.8%.52 Møller et al. (2021) calculated the SES disparity in 30-day survival that would have occurred given the entire population had the same chances of bystander CPR as the highest income group, which was almost zero (0.1%-0.2%), suggesting no to minimal mediation by this factor.55

Discussion
This systematic review of 10 studies identified and quantified various mediators of the association between SES and survival after OHCA. As SES increased, a greater proportion of OHCA cases had a bystander witness their arrest, received bystander interventions, and presented with an initial shockable rhythm. The proportion of patients who survived an OHCA increased with higher income and education, highlighting SES-related outcome disparities. Commonly evaluated mediators of the SES-survival association included initial rhythm, EMS response time, and bystander CPR. The most important mediator of this association appeared to be initial rhythm.

Three previous systematic reviews have evaluated the relationship of SES with pre-hospital care and survival after OHCA.21-23 A review of 32 studies by van Nieuwenhuizen et al. (2019) found that individuals of low SES had an increased risk of OHCA incidence, decreased chance of receiving bystander CPR, and poorer survival outcomes than individuals of high SES.22 A review by Chamberlain et
(2020) corroborated those findings, noting that the association between SES and OHCA survival was in the direction of decreased survival with lower SES.21 In a meta-analysis by Lee et al. (2021), OHCA patients residing in low-SES communities had reduced odds of bystander CPR (OR 0.67, 95% CI 0.51-0.89) and survival to hospital discharge (OR 0.60, 95% CI 0.35-1.02) compared with those residing in high-SES communities.23 Only 1 review explored potential mediators of the SES-survival association.21 However, very few of the articles included in that review were designed to evaluate mediation, and therefore no mediators could be clearly identified.

The unique contribution of the present review is a focus on identifying mediators of the relationship between SES and survival after OHCA. Among the 10 included studies in this review, 8 were published after, and therefore not captured, in earlier reviews.21-23 Various mediators of the SES-survival association were identified in the present review, including initial rhythm, EMS response time, and bystander CPR. Following careful feasibility and cost-effectiveness assessments, community-based public health interventions that intervene on these factors may help to reduce socioeconomic disparities in OHCA outcomes. Furthermore, the present review provides methodologic considerations to guide future studies aimed at evaluating mediators of the SES-survival association.

Interestingly, initial rhythm was the most important mediator of the SES-survival association, and it appeared to be more influential than other resuscitation factors, such as EMS response time, bystander CPR, and witnessed status. A recent study confirmed that an initial shockable rhythm was the strongest predictor of survival in OHCA, with a relative importance that was more than 3-fold greater than other resuscitation factors.58 An initial shockable rhythm is also considered to be a marker for a short duration between collapse and initiation of CPR, referred to as no-flow time.59-61 As observed in this systematic review, the proportion of OHCA events with an initial shockable rhythm demonstrated a socioeconomic gradient. This may suggest an inversely proportional relationship between no-flow time and SES as a result of time delays to resuscitation within disadvantaged communities. Because prolonged no-flow intervals are associated with lower odds of survival after OHCA,62 public health interventions aimed at promoting the importance of time to CPR and defibrillation after OHCA may help to reduce outcome disparities in low-SES communities. According to survey data from the United States, there is a general lack of awareness concerning the urgency of care after cardiac arrest.63 Tailored messaging for OHCA initiatives should be considered to promote prompt bystander intervention, particularly in underserviced and disadvantaged communities. Improving the accessibility and maintenance of AEDs, which are disproportionately placed in areas of higher community-level SES within many countries,64-66 should be a focal point of health resource allocation decision making.

Mediation of the SES-survival association by initial shockable rhythm could also be a function of OHCA etiology, considering that arrests of noncardiac etiology are less likely to be initially shockable than arrests of cardiac etiology.67 Noncardiac etiologies, such as those caused by drug overdose or drowning, are more common in communities of lower SES68,69 and are associated with less favourable outcomes after OHCA.70,71

Bystander CPR is integral to optimising outcomes after OHCA,8,72 but this factor appeared to explain only a small amount of the effect of SES on survival. All studies in this review captured only the receipt of bystander CPR, whereas timing and proper technique are key factors to achieving favourable outcomes.73 Evidence from Japan has found that for every incremental minute of CPR delay, the probabilities of neurologically favourable 1-month survival decreased by
<table>
<thead>
<tr>
<th>Study</th>
<th>SES indicator</th>
<th>Mediators evaluated</th>
<th>Initial rhythm</th>
<th>Witnessed status</th>
<th>Location</th>
<th>Bystander CPR</th>
<th>AED connected</th>
<th>Comorbidities</th>
<th>EMS response time</th>
<th>Hospital/ED type</th>
<th>CAG</th>
<th>TTM</th>
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<tbody>
<tr>
<td>Ahn et al.50 (2011)</td>
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<td></td>
<td></td>
<td>NA</td>
<td></td>
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<tr>
<td>Chan et al.51 (2020)</td>
<td>Income</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
<td></td>
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<tr>
<td>Choi et al.52 (2023)*</td>
<td>Income</td>
<td></td>
<td>41.8%</td>
<td>15.1%</td>
<td></td>
<td>4.8%</td>
<td></td>
<td></td>
<td>9.4%</td>
<td>20.2%±</td>
<td>4.2%±</td>
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<td>Clarke et al.53 (2005)</td>
<td>Income</td>
<td></td>
<td>NA</td>
<td></td>
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<td></td>
<td></td>
<td>NA (Charlson index)</td>
<td>NA (Charlson index)</td>
<td>20.0%±</td>
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<tr>
<td>Huebinger et al.28 (2023)</td>
<td>Income, Education, Occupation</td>
<td></td>
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<td>85.0%</td>
<td>54.6%</td>
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<tr>
<td>Jonsson et al.54 (2021)</td>
<td>Income</td>
<td></td>
<td>39.3%</td>
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<td></td>
<td>NA (Charlson index)</td>
<td>NA</td>
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<tr>
<td>Lagedal et al.27 (2020)</td>
<td>Income</td>
<td></td>
<td>37.0%</td>
<td></td>
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<td></td>
<td></td>
<td>NA (Charlson index)</td>
<td>20.0%±</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Møller et al.55 (2021)</td>
<td>Income, Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.2%±</td>
<td>0.1%±</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rajan et al.56 (2015)</td>
<td>Income</td>
<td></td>
<td>40.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>van Dongen et al.57 (2022)*</td>
<td>Income</td>
<td></td>
<td>37.7%</td>
<td>4.9%</td>
<td>14.0%</td>
<td>8.6%±</td>
<td>1.7%±</td>
<td></td>
<td>14.4%±</td>
<td>6.9%±</td>
<td></td>
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</tr>
</tbody>
</table>

All values presented are the percent excess risk explained by the mediator(s) in the SES-survival association (calculated among studies that used the difference method to compare the lowest SES category with the highest SES category). Mediators were evaluated either individually or through mediator sets. Mediation metrics provide an indication of the degree to which the mediators of interest could explain the SES-survival association (higher values suggest greater importance).

CAG, coronary angiography; CPR, cardiopulmonary resuscitation; ED, emergency department; EMS, emergency medical services; NA, no attenuation reported; SES, socioeconomic status; TTM, targeted temperature management.

* Mediation metrics used by Choi et al. (2023) are mediation proportions.
± Values derived from subsample with complete data (proxy for EMS response time: distance to nearest hospital).
# Only male subgroup reported attenuation.
|| Proxy for EMS response time: time interval from recognition of arrest to rhythm analysis by EMS.
8.3%, 4.4%, and 6.4% for patients with shockable rhythms, pulseless electric activity, and asystole, respectively. Achieving the appropriate depth and rate of compressions also greatly improves outcomes after OHCA. The recognition of OHCA, activation of the emergency response, and quality of bystander CPR depends on the person who intervenes, which may differ by SES. It is possible that these unmeasured factors may provide a more comprehensive explanation of the SES-survival association, rather than the receipt of bystander CPR alone. Various training disparities and barriers to administering CPR exist in socioeconomically deprived communities, which may reduce the promptness and effectiveness of resuscitation manoeuvres, thus contributing to this hypothesis. Although the mediating role of bystander CPR may differ according to witnessed status and arrest location (public vs private), Muller et al. (2021) found similar measures for mediation across these subgroups (all < 1%). Further research is needed to elucidate the characteristics of bystanders and the quality of bystander resuscitation during OHCA across the socioeconomic spectrum.

The mediating role of other contextual factors, such as witnessed status and EMS response time, was also evaluated by some included studies in this review. As identified in this review and through other studies, low SES was linked to a lower proportion of OHCA events that were witnessed by a bystander. For example, educational attainment has the potential to enhance health-related knowledge and improve communication with health care providers among bystanders. This in turn may contribute to quicker OHCA symptom recognition, more efficient communication with EMS, and an increased likelihood of high-quality bystander CPR. Conversely, unemployment can increase the risk of OHCA incidents occurring at home, which often go unnoticed, thus resulting in delays to emergency response activation and resuscitation. The mediating role of EMS response time was less clear, with some included studies reporting that SES-related survival differences were explained partially by EMS response time, and others reporting that they were not. As EMS response time may be more closely correlated with geographic remoteness than SES (eg, low-SES community in a highly urban area), the mediation mechanism of this factor within the SES-survival association is likely complex and warrants further investigation.

Two studies in this review investigated potential mediation of the SES-survival association by receiving hospital or emergency department and post-arrest care. Among patients who survived to hospital admission, Choi et al. (2023) found that a significant portion of socioeconomic disparities were explained through the emergency department level (mediation proportion 10.7%), coronary angiography (mediation proportion 20.2%), and targeted temperature management (mediation proportion 4.2%). After adjusting for clustering by receiving hospital, Huebinger et al. (2022) noted that SES disparities in survival to hospital discharge with functional neurological recovery were substantially attenuated. These findings suggest that the effect of SES on survival may be mediated through hospital-specific care patterns. Although interhospital variability in care processes after OHCA has been observed in various countries, SES disparities in post-arrest care are largely unexplored.

Because most research to date has focused on identifying SES disparities in bystander interventions and survival, there is an urgent need for additional studies to uncover potential inequities among later Chain of Survival components. Specifically, further evaluation of socioeconomic disparities in post-arrest care processes and other advanced interventions, such as airway management, medication administration, and dispatcher-assisted CPR, is needed. New evidence may help to inform quality improvement initiatives for such interventions within disadvantaged communities.

Methodologic implications
For mediation analyses to be interpreted causally, strong confounding assumptions are required. These assumptions include adequate control for exposure-outcome confounding, mediator-outcome confounding, and exposure-mediator confounding. It is also assumed that no mediator-outcome confounder is affected by the exposure. None of the studies included in this review described these assumptions explicitly when selecting potential confounders. Almost all included studies used the difference approach to assess for mediation. This approach has been criticized for its reliability in effect decomposition analysis, which is only valid for the difference contrast as the measure of causal effect (as opposed to ratio measures). However, under the appropriate mediation assumptions, the difference method can be used to provide conservative evidence for the presence of mediation in logistic regression. In addition, many studies compared measures of association before and after adjustment for sets of variables, some of which included multiple mediators and potential confounders (eg, age, arrest etiology). In these situations, it was not possible to quantify the degree to which a single mediator explained the SES-survival association. The primary objective of some studies included in this review was not to quantify mediators of the SES-survival association, so certain design considerations and reporting requirements may have been overlooked. As a result, the findings of this review should be interpreted with caution.

Limitations
This systematic review is subject to several limitations. First, although levels of income, education, and occupation are correlated, they measure unique phenomena and may represent different causal mechanisms of social inequalities. As certain review findings were synthesized across socioeconomic dimensions, the potential for differential selection biases, measurement error, and status inconsistency (eg, high income and relatively low level of education) by SES indicator is possible. Where applicable, indicator-specific summary measures were calculated. Second, some studies relied on area-level measures of SES to capture individuals’ SES, which may be prone to the ecologic fallacy. Similarly, proxy measures for SES indicators, including health insurance premiums, deprivation indexes, and parental income/education (ie, proxy for SES of child), were used in several studies, which may not adequately reflect actual SES. Third, this review focused on traditional economic indicators of SES. Other social determinants of health, such as sex, gender, race/ethnicity, and region of residence, were not considered because their influence on SES differs considerably according
to the region or country of study. Fourth, most included studies did not include cases where resuscitative efforts were not initiated or terminated. Resuscitation decision making may have been influenced by pre-arrival impressions of EMS personnel regarding the socioeconomic context of an OHCA location.101 Fifth, 3 studies were excluded from this review owing to methodologic approaches that prevented meaningful inferences of mediation.102-104 Those studies evaluated mediators only within sets of variables or assessed another dimension of SES as a potential mediator. Finally, the literature search for this review was designed to capture English-language studies that were indexed in academic databases. However, a previously recommended grey literature search strategy22 was used to capture other sources of evidence that may have been disseminated outside of the research domain.

Conclusion

Initial rhythm was the most important mediator of the association between SES and survival after OHCA. This review did not find consistent evidence supporting EMS response time, bystander CPR, or witnessed status as strong mediators of the association between SES and survival; however, the importance of these factors in improving OHCA outcomes should not be discounted. To reduce SES-related outcome disparities in OHCA, public health interventions and quality improvement initiatives should target potentially modifiable mediators, including initial rhythm (through the promotion of prompt resuscitation) and in-hospital care factors. These tailored interventions should be evaluated through rigorous cost-benefit assessments to determine the most effective strategy for achieving health equity in OHCA. Future studies should quantify the indirect effect of SES on survival after OHCA through intervention-specific mediators, such as bystander AED use, CPR quality, and time to initiation of resuscitation.

Ethics Statement

The research reported in this article did not require ethics approval.

Patient Consent

The authors confirm that patient consent is not applicable to this article. This systematic review involved the synthesis of aggregated and de-identified data from previously published studies.

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Disclosures

The authors have no conflicts of interest to disclose.

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**Supplementary Material**

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjca.ca and at https://doi.org/10.1016/j.cjca.2024.01.002.