Association of measures of socioeconomic position with survival following out-of-hospital cardiac arrest: a systematic review

Resuscitation

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Corresponding Author:	Nynke Halbesma, Ph.D. University of Edinburgh Edinburgh, UNITED KINGDOM
First Author:	Rosemary Chamberlain, MPH
Order of Authors:	Rosemary Chamberlain, MPH
	Calum Barnetson, BMedSci; MBChB
	Gareth Clegg, PhD
	Nynke Halbesma, PhD
Abstract:	Background: Survival following out-of-hospital cardiac arrest (OHCA) is low, and poor survival appears associated with low socioeconomic position (SEP). We aimed to synthesise the evidence regarding association of specific SEP measures with OHCA survival, as well as effect modification and potential mediators, with the goal of informing efforts to improve survival by highlighting characteristics of populations requiring additional resources, and identifying modifiable factors. Methods: MEDLINE and Embase databases were searched on 23 May 2019. Quantitative primary studies considering the association of any SEP measure with any OHCA survival measure were eligible. SEP could be measured at the level of the patient, their residential area, or OHCA location. Data on study characteristics and outcomes were extracted and a narrative review performed; this considered the evidence for overall SEP-survival association, variation in association of different SEP measures with survival, effect modification, and mediation. Results: Twenty-three studies were included. These were highly heterogeneous, particularly regarding SEP measures and eligibility criteria. Several studies report a SEP-survival association, with this being almost exclusively in the direction of lower survival with lower SEP. There is some indication that the education-survival association is particularly consistent but further work is needed to increase confidence here. No evidence of effect modification by age, sex or other factors was seen, although few studies considered this. No mediators were conclusively identified. Conclusions: Low SEP is associated with poorer OHCA survival in at least some settings. It may be appropriate to consider populations' socioeconomic characteristics when targeting interventions to improve OHCA survival.

Cover Letter

Dr Nynke Halbesma
Usher Institute, University of Edinburgh
Teviot Place, Edinburgh, EH8 9AG
nynke.halbesma@ed.ac.uk

Reference: RESUS-D-20-00325
Association of measures of socioeconomic position with survival following out-of-hospital cardiac arrest: a systematic review

21 August 2020

Dear Professor Perkins,

We would like to thank you for again taking the time to review our manuscript and giving the opportunity to submit a revision. We have made some changes to address the points raised by the second reviewer, along with a small number of wording changes in order to keep within the word limit. We have also made some very minor formatting and typographical changes to the supplementary materials.

Yours sincerely,

Dr. Nynke Halbesma

Review comments:

Reviewer #2: Thank you for your response to my comments. I agree with the majority of changes made and think that the manuscript is greatly enhanced.

We would like to again thank the reviewer for their previous comments, which we felt to be very constructive and helpful in enhancing the manuscript.

However I don't agree with the idea that area level measures can serve as a proxy for individual level measures as they measure different things. As per Diez Roux (2002) assuming that that variables that span two measurement levels are interchangeable runs the risk of ecological fallacy. The way in which deprivation affects survival at area level (e.g. might be less B-CPR performed or less availability of AEDs in a more deprived area) may differ from the way in which deprivation affects survival at an individual level (e.g. individuals have more comorbidities which impact on individual likelihood of successful resuscitation). I really think this is an important issue that merits comment in your discussion, as the level of measurement has different implications for recommendations.

It is clear from your analysis that measuring the impact of socioeconomic position is complicated - would you offer any recommendations for further research?

We thank the reviewer for highlighting this. We fully agree that the distinction between area-level and individual-level measures is very important to recognise, and that any conclusions and recommendations made must be appropriate for the level of measurement. We consider this point to be an important recommendation for further research. We have extended an existing paragraph in the discussion section to highlight these points. This now reads:

"The previous review also indicated area-level measures of patient SEP may show less consistent associations with survival than individual-level measures.[6] Our findings are consistent with this, with a clear adjusted SEP-survival association observed for one or more SEP indicator in only two of eight studies using area-level measures of home-address SEP, compared to six of nine studies using individual-level measures. While this may indicate a true difference, it may instead reflect misclassification of individual-level SEP by area-level measures, as suggested previously.[6] It also highlights the importance of using the most appropriate level of measurement for each specific research question wherever possible, such as using individual-level measures when focussing on patient-level SEP, both to avoid misclassification from using area-level measures as a proxy, and to avoid the risk of ecological fallacy from drawing conclusions about individuals based on area-level measurements."

TITLE: Association of measures of socioeconomic position with survival following out-of-hospital cardiac arrest: a systematic review

Authors: Rosemary C. Chamberlain[1], Calum Barnetson[2], Gareth R. Clegg[3], Nynke Halbesma[1,3]

1. Usher Institute, University of Edinburgh, United Kingdom
2. NHS Lothian, United Kingdom
3. Resuscitation Research Group, University of Edinburgh, United Kingdom

Correspondence address:
Dr Nynke Halbesma
Usher Institute, University of Edinburgh
Teviot Place Edinburgh EH8 9AG
nynke.halbesma@ed.ac.uk

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Abstract

Background: Survival following out-of-hospital cardiac arrest (OHCA) is low, and poor survival appears associated with low socioeconomic position (SEP). We aimed to synthesise the evidence regarding association of specific SEP measures with OHCA survival, as well as effect modification and potential mediators, with the goal of informing efforts to improve survival by highlighting characteristics of populations requiring additional resources, and identifying modifiable factors.

Methods: MEDLINE and Embase databases were searched on 23 May 2019. Quantitative primary studies considering the association of any SEP measure with any OHCA survival measure were eligible. SEP could be measured at the level of the patient, their residential area, or OHCA location. Data on study characteristics and outcomes were extracted and a narrative review performed; this considered the evidence for overall SEP-survival association, variation in association of different SEP measures with survival, effect modification, and mediation.

Results: Twenty-three studies were included. These were highly heterogeneous, particularly regarding SEP measures and eligibility criteria. Several studies report a SEP-survival association, with this being almost exclusively in the direction of lower survival with lower SEP. There is some indication that the education-survival association is particularly consistent but further work is needed to increase confidence here. No evidence of effect modification by age, sex or other factors was seen, although few studies considered this. No mediators were conclusively identified.

Conclusions: Low SEP is associated with poorer OHCA survival in at least some settings. It may be appropriate to consider populations' socioeconomic characteristics when targeting interventions to improve OHCA survival.

Introduction

Cardiac arrest refers to sudden halting of cardiac mechanical activity, indicated by absence of signs of circulation.[1] This may have a cardiac cause such as myocardial infarction, or non-cardiac cause such as drug overdose or airway obstruction.[2] Out-of-hospital cardiac arrest (OHCA) is a particular healthcare challenge due to the need for rapid action and co-ordination of bystanders, emergency medical services (EMS), and hospital.[3] The proportion of patients that survive OHCA varies between countries, but is generally low; a multicentre European study reported survival to hospital discharge in only 8% of patients who received cardiopulmonary resuscitation (CPR) (0-18% inter-country range).[4]

Work to understand predictors of OHCA survival may identify factors that could be targeted to improve survival, or highlight characteristics of populations with poor survival where interventions could be focused. Socioeconomic factors are one characteristic of interest. A recent systematic review found a generally consistent pattern of decreased OHCA survival in patients of lower socioeconomic position (SEP), such as 70% improved odds of 30-day survival in the most highly educated quintile relative to least,[5] although several studies observed no such SEP-OHCA survival association.[6] This was in addition to higher OHCA incidence in low SEP areas.[6]

Understanding which SEP measures, such as education or income, best identify likelihood of poor OHCA survival may help elucidate SEP-survival causal pathways and further guide targeting of interventions to subpopulations. Understanding whether the SEP-OHCA survival relationship differs by factors such as age and sex (effect modification) may also be informative here. While the previous review found insufficient evidence to draw conclusions around either of these aspects,[6] we identified several additional relevant papers and therefore aimed to consider both aspects in more detail. We also considered the evidence for potential factors mediating any SEP-survival relationship, aiming to identify further potentially modifiable factors.

While population characteristics such as race and ethnicity may also be related to SEP in some settings, this is likely to vary significantly between countries. As we intended to review the global literature, we focused on economic factors such as education and income, considering these to be of broadest relevance.

Methods

Eligibility criteria

Eligibility criteria are detailed in Table 1. Briefly, primary studies considering the association of any SEP measure with any OHCA survival measure were eligible.

Study selection

MEDLINE and Embase databases were searched via Ovid using comprehensive search strategies (see supplementary materials), on 23 May 2019. All records were transferred into EndNote, duplicates removed, and initially screened by title or abstract to remove those clearly ineligible according to the Table 1 criteria. Full texts of remaining records were then assessed fully against the

same criteria. Reference lists of all included records were also reviewed to identify further eligible records.

Data extraction

The full text and supplementary materials of eligible records were read, and specific data elements extracted (Table 2). This was performed by one reviewer (RC) and corroborated by a second (CB). Where a study assessed survival to 30-days or to discharge, this was considered the main outcome of interest and these were recorded in Table S3 (supplementary) and summarised in Table 4 (main text). If neither of these were assessed, other survival outcomes were recorded in Tables 4/S3. Results for outcomes not included in Tables 4/S3 are included in Table S4 (supplementary) for completeness. Potentially problematic aspects of methods were noted (Table S6, supplementary) and results interpreted in light of these.

Results

The database searches yielded 3,642 unique records, with 20 meeting the eligibility criteria. Reviewing their references yielded three more records. Figure 1 outlines the number of records at each stage.

Characteristics of included studies

Study characteristics are summarised in Table 3, with further details in Table S2 (supplementary). The included studies were highly heterogeneous in several respects. Firstly, there was variation in whether the SEP measures referred to the OHCA patient, either as individual-level measures for the patient or their household[7–15] or area-level measures based on the patient's residential address,[5,13,15–20] or whether they referred to area-level SEP at the OHCA location.[21–28] Several different SEP measures were used, including measures of income,[5,7,13,14,17–21,26,27] poverty,[15,21,23] education,[5,9,14,26] property value,[11–13,27] employment,[10,15,21] occupation,[9] crime rate,[16] and housing.[8] Others used a composite measure incorporating several indicators.[22,24,25,28] Several studies considered multiple measures. The SEP measures were variously categorised into between two and five categories for analysis. Regarding outcome measures, most studies reported survival to discharge or to 30 days post-OHCA;[5,8,9,11,13,14,16–18,20–25,27,28] other outcomes included return of spontaneous circulation,[7,8,14,16,21,24,27,28] survival with good neurological outcome,[12,15,25,27] or survival to hospital admission,[9,10] one day post-OHCA[5] or one year post-OHCA.[5,14] Eligibility criteria also varied greatly, with variation in inclusion of OHCAs in paediatrics, in public locations, EMS-witnessed, of non-cardiac or traumatic aetiology, with non-shockable initial rhythm and where the patient was pronounced dead at the scene.

The included studies also varied in analytical approaches to handling potential confounding and mediating variables. Only five[13,14,19,24,25] reported effect estimates after adjustment for potential confounders without co-adjustment for potential mediators, where potential mediators are defined as post-exposure variables, such as OHCA-related medical treatment. Adjusting for variables on the causal pathway between exposure and outcome may prevent valid estimation of the total association, as this can 'control away' association mediated through that variable.[29]

Many of the included studies were conducted in the USA,[9,12,13,15,17–20,23,26] with the others in Canada,[8,11,16] South Korea,[24,25] Taiwan,[7,27] Denmark,[10,14] France,[21] Sweden,[5] Singapore[22] and New Zealand.[28] Some studies from the same locations report data for overlapping time periods, but mostly these considered different SEP measures, so each period contributes singularly to the consideration of each measure. The exceptions are two studies each in Michigan, USA[17,18] and South Korea;[24,25] these are indicated below where relevant.

The findings of the included studies are reviewed below, divided first by whether they considered SEP of the patient or OHCA location, and then by the SEP aspects. See Table 4 for a summary of the main results, and Tables S3-5 (supplementary) for further detail including effect sizes, effect modification and model specifications.

SEP measures referring to the OHCA patient

Education

A Danish study of patients aged under 21 years considered parental education level for the individual patients, and reported notably higher 30-day survival in the highest parental education tertile relative to the lowest, after adjustment for age and sex (OR 3.48, 95%CI 1.27-9.41).[14] Further adjustment for several potential mediators substantially attenuated this to 1.83 (95%CI 0.54-6.20).[14]

A Swedish study considered the proportion of university-educated residents within the patient's residential area, reporting evidence of a notable association with 30-day survival after adjusting for age, sex and several potential mediators (OR 1.93, 95%CI 1.41-2.64 for highest education quintile relative to lowest), with only moderate attenuation after further adjustment for median disposable family income (OR 1.70, 95%CI 1.15-2.51).[5] A study in Washington State, USA considered the patient's own education, and reported higher odds of survival to discharge with >4 years of college relative to not receiving a high school diploma (OR 2.02, 95%CI 1.27-3.23), in an analysis adjusted for age, sex, race and some potential mediators. Further adjustment for occupation had little impact.[9]

Income

Another study in Washington State, USA considered the median household income (MHI) in the patient's home census tract, finding no evidence of a survival difference between the highest and lowest income quartile, after adjustment for age and sex (OR 1.03, 95%CI 0.67-1.39).[13] The aforementioned Danish study in a population aged under 21 years considered individual household income and reported OR 2.40 (95%CI 0.88-6.53) for the highest tertile relative to lowest, adjusted for age and sex.[14] This is not statistically significant, although the wide confidence intervals and small sample (n=459) indicate the study may be underpowered. There was a statistically significant association in the unadjusted analysis.[14] A study in New York City focused on ethnic disparities in OHCA survival but included home census tract MHI as a covariate.[19] The MHI association is not statistically significant (OR 1.7, 95%CI 0.8-3.5, for MHI >$50,000 relative to <$25,000, after adjustment for age, sex and ethnicity).[19]

Three papers considered area-level measures of household income at the patient's home address only within analyses co-adjusted for potential confounding and mediating variables. The first of these, the aforementioned Swedish study, reported evidence of an association of median disposable family income with 30-day survival (OR 1.88, 95%CI 1.36-2.59 for highest quintile relative to lowest), after adjustment for age, sex and some potential mediators. This was partly attenuated after further adjustment for the proportion of university-educated residents (OR 1.31, 95%CI 0.87-1.98).[5] Two other papers considered MHI, both using data from Michigan, USA. The first used 1991-1996 data from seven cities and considered MHI of the patient's home census tract, dichotomised at the state median. They reported OR 1.51 (95%CI 0.80-2.80) for survival to discharge with MHI above the state median relative to below; thus this is not statistically significant.[17] This analysis was adjusted for race and some potential mediators, but not age or sex. The second used 1991-1994 data from nine hospitals across three counties and considered average household income of the patient's ZIP code, in $10,000 increments. This showed evidence of a small association with survival to discharge (OR 1.24, 95%CI 1.03-1.51 for $10,000 increase), adjusted for age, sex, race and some potential mediators.[18]

Also considering home address income, an ecological-level comparison of survival in the 20 highest-income census tracts in Portland, Oregon compared to the 20 lowest-income tracts observed no clear evidence of a survival disparity.[20] No adjusted analysis was performed. Finally, a study in Taiwan used individual-level income and found no clear association, reporting hazard ratio 1.03 (95%CI 0.92-1.16) for the highest income group relative to no income, after adjustment for age, sex and some potential mediators, although with small statistically significant associations in intermediate income groups. These appear to be in the direction of higher mortality with higher income though some lack of clarity in the description of methods and results casts some doubt on this (Table S6).[7]

Property value

An aforementioned study in Washington State**,** USA also considered the patient's home property value, reporting the highest quartile to be associated with notably higher survival to discharge relative to the lowest quartile, after adjusting for age and sex (OR 1.81, 95%CI 1.21-2.42).[13] Further adjustment for some potential mediators had little impact (OR 1.73, 95%CI 1.16-2.30), but further adjustment for census tract MHI did cause attenuation (OR 1.48, 95%CI 0.91-2.41);[13] this could indicate either confounding or mediation by income.

Two further studies considered property value. Another in Washington State, USA reported evidence of some association with increased survival, with a relative risk of 1.6 (95%CI 1.1-2.4) per $50,000 increase, adjusted for age, sex and some potential mediators.[12] In contrast, a Canadian study reported an association of increased property value with *decreased* survival, with OR 0.77 (95%CI 0.61-0.97) per $100,000 increase, adjusted for age and some potential mediators.[11]

Other SEP measures

Three papers reported on other SEP measures related to the OHCA patient. These were all analyses co-adjusted for potential confounders and mediators. The first reported no clear evidence of an

association of violent crime rate or material deprivation in the patient's home census tract with survival to discharge (OR 1.11, 95%CI 0.73-1.69 for lowest crime quintile relative to highest, OR 1.09, 95%CI 0.74-1.61 for least materially deprived quintile relative to most).[16] The second reported no clear relationship of any occupational group with survival to discharge, relative to 'blue-collar' work.[9] The third, a study in Ontario, Canada considered the association of floor of residence with survival to discharge, finding a possible small survival decrease associated with residence on or above the third floor relative to below the third (OR 0.70, 95%CI 0.50-0.99).[8] Residence in high-rise buildings is associated with low income in this location.[30]

A study in Pittsburgh, USA assessed the association of individual employment status and area poverty level with survival with good neurological outcome; both variables were excluded from the multivariable model by automated variable selection, although being unemployed/disabled was associated with decreased survival in unadjusted analysis (OR 0.39, 95%CI 0.18–0.84, relative to employed).[15] Another study reported no clear association of employment status with survival to hospital admission (OR 1.17, 95%CI 0.89-1.56 for employed relative to unemployed) in an analysis adjusted for age, sex and potential mediators, although unadjusted analysis indicated an association of employment with both survival to hospital admission and from admission to discharge.[10]

SEP measures referring to OHCA location

Composite indices

Two papers reported results from South Korea, both assessing OHCA-location SEP using the Carstairs Index.[24,25] One reports risk-adjusted survival to discharge rates from 2006-2015 adjusted for age and sex, with likely evidence of poorer survival in the most deprived quintile compared to least (2006: 2.3% vs. 3.5%, 2015: 6.2% vs. 9.9%); statistical significance is not reported but a difference of similar magnitude is found in the unadjusted analysis and is significant.[25] The other reported from the same database for 2006-2007 only, also finding evidence of poorer survival to discharge in the most deprived quintile relative to least (OR 0.57, 95%CI 0.45-0.72) adjusted for age and sex. Further adjustment for mediators made no impact.[24]

A Singaporean study assessed OHCA-location SEP using the Singapore Socioeconomic Disadvantage Index (SEDI). An analysis adjusted for age, sex, ethnicity and several potential mediators showed no clear association of SEDI category with 30-day mortality (OR 0.74, 95%CI 0.44–1.23, most deprived tertile relative to least).[22] A New Zealand study measured OHCA-location SEP using the NZDep index; only an unadjusted analysis was reported, which showed no clear survival disparity.[28]

Other SEP measures

OHCA-location neighbourhood poverty rate was considered by one study in Arizona, USA[23] and one in Paris, France.[21] The latter study also considered neighbourhood unemployment and income. Neither study saw evidence of an association of any of these measures with survival, in analyses co-adjusted for possible confounders and mediators.

Studies in Taiwan[27] and Florida, USA[26] considered property value and income, and education and income respectively, as OHCA-location SEP measures. Both only reported unadjusted analyses, which showed evidence of poorer survival with lower SEP in each case.

Effect modification

Three papers assessed effect modification. One found no evidence of sex being an effect modifier of the relationship of either home area-level education or income with survival,[5] and another found no evidence of effect modification of the individual-level education-survival relationship by sex, or occupation-survival relationship by education.[9] The third found no evidence of effect modification of the individual-level property value-survival relationship by age, sex, home/public location or initial cardiac rhythm.[13]

Discussion

SEP-survival association

In almost all of the included studies, any association observed between a SEP measure and OHCA survival was in the direction of low SEP with decreased survival. The two exceptions are one study reporting an association of increased property value with decreased survival,[11] and one reporting possible decreased survival in an intermediate income level relative to no income, but no association when comparing the most extreme categories.[7] Though notably, several studies found no evidence of an association in either direction. Therefore, after our synthesis of evidence including ten additional papers, the generally consistent association of lower SEP with decreased survival agrees with the previous review's conclusions.[6]

While including these additional papers allowed further consideration of the specific aspects of SEP, the high heterogeneity in study designs and the range of SEP aspects considered means there is still limited evidence for any single aspect being especially consistently associated with OHCA survival.

For patient SEP, there is most consistency regarding education, an association with survival being reported in all three studies which considered it.[5,9,14] The evidence regarding income is more mixed. Of the eight relevant studies, two report an association,[5,18] one reports possible decreased survival in an intermediate but not the highest income level relative to no income,[7] and five report no clear association in adjusted analyses.[13,14,17,19,20] Possible reasons for these different findings are numerous, given the methodological heterogeneity. Notably however, the estimates from three of the studies where no effect was found were not adjusted for mediators,[13,14,19] so over-adjustment could not explain their null findings.

The evidence around property value is also mixed, with two studies reporting an association of higher property value with higher survival,[12,13] but one reporting the opposite.[11] However, these studies have several methodological differences, such as the latter including only OHCAs occurring in private residences, and excluding those in apartments or condominiums;[11] OHCAs in lower value properties are therefore likely underrepresented. One of the former studies also only included patients with initial shockable rhythm.[12] Both studies considering patients' employment status found a univariable

association with survival, attenuated after adjustment.[10,15] Being considered in single studies, little can be concluded regarding patients' occupation, housing, neighbourhood poverty level or crime rate.

The previous review also indicated area-level measures of patient SEP may show less consistent associations with survival than individual-level measures.[6] Our findings are consistent with this, with a clear adjusted SEP-survival association observed for one or more SEP indicator in only two of eight studies using area-level measures of home-address SEP, compared to six of nine studies using individual-level measures. While this may indicate a true difference, it may instead reflect misclassification of individual-level SEP by area-level measures, as suggested previously.[6] It also highlights the importance of using the most appropriate level of measurement for each specific research question wherever possible, such as using individual-level measures when focussing on patient-level SEP, both to avoid misclassification from using area-level measures as a proxy, and to avoid the risk of ecological fallacy from drawing conclusions about individuals based on area-level measurements.

With sparse literature, the picture is also unclear regarding OHCA-location SEP. Of the multivariable analyses, only two report a SEP-survival association (and these use the same database),[24,25] while three report no association.[21–23] While this could indicate the composite index used by the first two studies best captures the association, several other factors could explain the difference; notably the first two use quintiles of the SEP measure,[24,25] while the other three use measures with two or three categories.[21–23] The small number of studies and methodological heterogeneity limits further conclusions.

It is also possible that the inter-study differences in results partly reflect differing socioeconomic inequality between settings. SEP is generally defined relative to the range within that study, such as by comparing extreme quintiles. Theoretically therefore, a setting with less extreme inequality could expect to see less of a SEP-survival association.

There are several possible causal pathways between SEP aspects and survival. Education may improve cognitive function, communication with health services and awareness of health education,[31] potentially leading to faster symptom recognition, more effective EMS-communication, and increasing bCPR likelihood.[5] Unemployment may make OHCA more likely to occur at home and be unwitnessed, without rapid initiation of bCPR or EMS-communication. Income influences access to services and commodities, including food and activities,[31] the impact on overall health may influence co-morbidity, which may be associated with OHCA survival.[32,33]

Mediators

This review also aimed to consider the evidence for any specific mediators in the SEP-survival relationship, that is factors on the causal pathway. The 'difference method' is one approach to identifying mediators; this considers whether the exposure-outcome effect estimate differs between models which do and do not adjust for the potential mediators.[34] Regarding OHCA location, only one study reports separate estimates for analyses adjusting for potential confounders and after further

adjustment for potential mediators. Here, the further adjustment made little difference.[24] This may indicate the factors adjusted for in the further analysis (witness, bCPR, initial rhythm, and call-scene arrival and call-hospital arrival intervals) are not mediators, but the other studies provide no evidence for or against this.

Regarding patient SEP, of the three studies reporting separate estimates for analyses adjusted only for potential confounders, and after further adjustment for potential mediators[13,14,19] only one reports attenuation.[14] However, there is little difference evident in the variable sets adjusted for, meaning no particular variable can be identified as a mediator. This may indicate a real inter-study difference in mediation mechanism. Notably, the study where adjustment for mediators caused attenuation was restricted to patients younger than 21 years, and used parental SEP measures.[14] This may suggest some of the variables adjusted for (location, witness, bCPR, initial rhythm, incident year, and arrest recognition-rhythm analysis interval) are mediators specifically in the parental SEP-child survival relationship.

However, the validity of identifying mediators by the 'difference method' depends on controlling for confounding of the mediator-outcome, as well as exposure-outcome relationship.[34] This assumption is not discussed explicitly by any of the included studies and the possibility remains of residual confounding of mediator-outcome relationships distorting these results. Potential mediators may also show different socioeconomic patterning between settings, and therefore mediate the SEP-survival relationship in specific settings only.

Other work indicates likelihood of receiving bCPR as one plausible mediator, being associated both with improved survival,[35] and higher OHCA-location SEP.[6] This may be partly due to socioeconomic patterning of CPR training, with individuals in manual or unskilled occupations or long-term unemployment less likely to be trained than professional, managerial or non-manual occupations.[36] Use of an automated external defibrillator is another candidate, with evidence of association with both higher SEP[37] and survival.[38] Underlying health status is another, given extensive evidence of socioeconomic patterning of morbidity,[39] and of co-morbidity being associated with decreased OHCA survival.[32,33] These factors could be usefully considered in future studies.

Effect modification

With only three papers considering effect modification (differences in SEP-survival association between groups defined by an 'effect modifier'), the evidence remains sparse. There is most evidence regarding sex, with all three considering it but finding no evidence in support.[5,9,13] However, these assessments were all within analyses co-adjusted for potential confounders and mediators, raising the question of whether the finding would be maintained without mediator adjustment. One study also considered effect modification by age, private/public location and initial rhythm,[13] and another considered occupation as an effect modifier of the education-survival relationship.[9] While no evidence was found for any of these, this should be interpreted cautiously given they were assessed by single studies.

Quality of evidence

As described above, high methodological heterogeneity limits the capacity for inter-study comparisons. Some specific aspects also raise concerns about quality. Firstly, the potential for bias due to missing data is generally unclear; several studies exclude >20% cases,[12,15,17,18,] and in others the extent of missing data is unclear.[7,10,11,25,27]

Secondly, there is notable inter-study variation in overall survival (Table S3), from 2.2% survival to discharge[19] to 50.4% 'overall survival' (period unspecified).[26] While this may be partly explained by differing eligibility criteria, such as high survival in studies restricted to cases presenting with shockable rhythm,[9,12] in some studies the reason for unusually high or low survival is unclear.[7,19,26] This raises questions regarding study population representativeness and generalisability.

Limitations of this review

Although extensive search strategies were used, unpublished and non-English language literature was excluded. We were also unable to assess potential for publication bias; funnel plots were not appropriate due to the heterogeneity in SEP measures considered and in their categorisation.

Conclusions

The current literature is generally supportive of any association of SEP with OHCA survival being in the direction of decreased survival with lower SEP, although an association is not seen in all studies. This further supports the need to reduce socioeconomic deprivation in society. It also suggests it may be appropriate to consider socioeconomic characteristics of populations when targeting CPR training and other resources to improve survival, especially given evidence of lower SEP being associated with higher OHCA incidence[6] and lower rates of CPR training.[36] Regarding particular SEP aspects, there is some coherent evidence for a higher education level of the patient or their residential area being associated with improved survival, though further work would be required to increase confidence in this finding. No mediators of the SEP-survival relationship have been clearly identified. A small number of studies have considered effect modification, finding no evidence of any factors with this effect; there is most evidence against sex as an effect modifier, with other factors having only been considered in single studies. The certainty and generalisability of the conclusions from this body of evidence are restricted by methodological heterogeneity.

Conflicts of interest

None.

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TITLE: Association of measures of socioeconomic position with survival following out-of-hospital cardiac arrest: a systematic review

Authors: Rosemary C. Chamberlain[1], Calum Barnetson[2], Gareth R. Clegg[3], Nynke Halbesma[1,3]

1. Usher Institute, University of Edinburgh, United Kingdom
2. NHS Lothian, United Kingdom
3. Resuscitation Research Group, University of Edinburgh, United Kingdom

Correspondence address:

Dr Nynke Halbesma

Usher Institute, University of Edinburgh

Teviot Place Edinburgh EH8 9AG

nynke.halbesma@ed.ac.uk

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Abstract

Background: Survival following out-of-hospital cardiac arrest (OHCA) is low, and poor survival appears associated with low socioeconomic position (SEP). We aimed to synthesise the evidence regarding association of specific SEP measures with OHCA survival, as well as effect modification and potential mediators, with the goal of informing efforts to improve survival by highlighting characteristics of populations requiring additional resources, and identifying modifiable factors.

Methods: MEDLINE and Embase databases were searched on 23 May 2019. Quantitative primary studies considering the association of any SEP measure with any OHCA survival measure were eligible. SEP could be measured at the level of the patient, their residential area, or OHCA location. Data on study characteristics and outcomes were extracted and a narrative review performed; this considered the evidence for overall SEP-survival association, variation in association of different SEP measures with survival, effect modification, and mediation.

Results: Twenty-three studies were included. These were highly heterogeneous, particularly regarding SEP measures and eligibility criteria. Several studies report a SEP-survival association, with this being almost exclusively in the direction of lower survival with lower SEP. There is some indication that the education-survival association is particularly consistent but further work is needed to increase confidence here. No evidence of effect modification by age, sex or other factors was seen, although few studies considered this. No mediators were conclusively identified.

Conclusions: Low SEP is associated with poorer OHCA survival in at least some settings. It may be appropriate to consider populations' socioeconomic characteristics when targeting interventions to improve OHCA survival.

Introduction

Cardiac arrest refers to sudden halting of cardiac mechanical activity, indicated by absence of signs of circulation.[1] This may have a cardiac cause such as myocardial infarction, or non-cardiac cause such as drug overdose or airway obstruction.[2] Out-of-hospital cardiac arrest (OHCA) is a particular healthcare challenge due to the need for rapid action and co-ordination of bystanders, emergency medical services (EMS), and hospital.[3] The proportion of patients that survive OHCA varies between countries, but is generally low; a multicentre European study reported survival to hospital discharge in only 8% of patients who received cardiopulmonary resuscitation (CPR) (0-18% inter-country range).[4]

Work to understand predictors of OHCA survival may identify factors that could be targeted to improve survival, or highlight characteristics of populations with poor survival where interventions could be focused. Socioeconomic factors are one characteristic of interest. A recent systematic review found a generally consistent pattern of decreased OHCA survival in patients of lower socioeconomic position (SEP), such as 70% improved odds of 30-day survival in the most highly educated quintile relative to least,[5] although several studies observed no such ~~evidence of a~~ SEP-OHCA survival association.[6] This was in addition to higher OHCA incidence in low SEP areas.[6]

Understanding which SEP measures, such as education or income, best identify likelihood of poor OHCA survival may help elucidate SEP-survival causal pathways and further guide targeting of interventions to subpopulations. Understanding whether the SEP-OHCA survival relationship differs by factors such as age and sex (effect modification) may also be informative here. While the previous review found insufficient evidence to draw conclusions around either of these aspects,[6] we identified several additional relevant papers and therefore aimed to consider both aspects in more detail. We also considered the evidence for potential factors mediating any SEP-survival relationship, aiming to identify further potentially modifiable factors.

While population characteristics such as race and ethnicity may also be related to SEP in some settings, this is likely to vary significantly between countries. As we intended to review the global literature, we focused on economic factors such as education and income, considering ~~as we considered~~ these to be of broadest relevance.

Methods

Eligibility criteria

Eligibility criteria are detailed in Table 1. Briefly, primary studies considering the association of any SEP measure with any OHCA survival measure were eligible.

Study selection

MEDLINE and Embase databases were searched via Ovid using comprehensive search strategies (see supplementary materials), on 23 May 2019. All records were transferred into EndNote, duplicates removed, and initially screened by title or abstract to remove those clearly ineligible according to the Table 1 criteria. Full texts of remaining records were then assessed fully against the

same criteria. Reference lists of all included records were also reviewed to identify further eligible records.

Data extraction

The full text and supplementary materials of eligible records were read, and specific data elements extracted (Table 2). This was performed by one reviewer (RC) and corroborated by a second (CB). Where a study assessed survival to 30-days or to discharge, this was considered the main outcome of interest and these were recorded in Table S3 (supplementary) and summarised in Table 4 (main text). If neither of these were assessed, other survival outcomes were recorded in Tables 4/S3. Results for outcomes not included in Tables 4/S3 are included in Table S4 (supplementary) for completeness. Potentially problematic aspects of methods were noted (Table S6, supplementary) and results interpreted in light of these.

Results

The database searches yielded 3,642 unique records, with 20 meeting the eligibility criteria. Reviewing their references yielded three more records. Figure 1 outlines the number of records at each stage.

Characteristics of included studies

Study characteristics are summarised in Table 3, with further details in Table S2 (supplementary). The included studies were highly heterogeneous in several respects. Firstly, there was variation in whether the SEP measures referred to the OHCA patient, either as individual-level measures for the patient or their household[7–15] or area-level measures based on the patient's residential address,[5,13,15–20] or whether they referred to area-level SEP at the OHCA location.[21–28] Several different SEP measures were used, including measures of income,[5,7,13,14,17–21,26,27] poverty,[15,21,23] education,[5,9,14,26] property value,[11–13,27] employment,[10,15,21] occupation,[9] crime rate,[16] and housing.[8] Others used a composite measure incorporating several indicators.[22,24,25,28] Several studies considered multiple measures. The SEP measures were variously categorised into between two and five categories for analysis. Regarding outcome measures, most studies reported survival to discharge or to 30 days post-OHCA;[5,8,9,11,13,14,16–18,20–25,27,28] other outcomes included return of spontaneous circulation ~~(ROSC)~~,[7,8,14,16,21,24,27,28] survival with good neurological outcome,[12,15,25,27] or survival to hospital admission,[9,10] one day post-OHCA[5] or one year post-OHCA.[5,14] Eligibility criteria also varied greatly, ~~leading to~~with variation in inclusion of OHCAs in paediatrics, in public locations, EMS-witnessed, of non-cardiac or traumatic aetiology, with non-shockable initial rhythm and where the patient was pronounced dead at the scene.

The included studies also varied in analytical approaches to handling potential confounding and mediating variables. Only five[13,14,19,24,25] reported effect estimates after adjustment for potential confounders without co-adjustment for potential mediators, where potential mediators are defined as post-exposure variables, such as OHCA-related medical treatment. Adjusting for variables on the causal pathway between exposure and outcome may prevent valid estimation of the total association, as this can 'control away' association mediated through that variable.[29]

Many of the included studies were conducted in the USA,[9,12,13,15,17–20,23,26] with the others in Canada,[8,11,16] South Korea,[24,25] Taiwan,[7,27] Denmark,[10,14] France,[21] Sweden,[5] Singapore[22] and New Zealand.[28] Some studies from the same locations report data for overlapping time periods, but mostly. However, in most cases, these each considered different SEP measures, so each period contributes singularly to the consideration of each measure. The exceptions are two studies each in Michigan, USA[17,18] and South Korea;[24,25] these are indicated below where relevant.

The findings of the included studies are reviewed below, divided first by whether they considered SEP of the patient or OHCA location, and then by the SEP aspects. See Table 4 for a summary of the main results, and Tables S3-5 (supplementary) for extensive further detail including effect sizes, effect modification and model specifications.

SEP measures referring to the OHCA patient

Education

A Danish study of patients aged under 21 years considered parental education level for the individual patients, and reported notably higher 30-day survival in the highest parental education tertile relative to the lowest, after adjustment for age and sex (OR 3.48, 95%CI 1.27-9.41).[14] Further adjustment for several potential mediators substantially attenuated this to 1.83 (95%CI 0.54-6.20).[14]

A Swedish study considered the proportion of university-educated residents within the patient's residential area, reporting evidence of a notable association with 30-day survival after adjusting for age, sex and several potential mediators (OR 1.93, 95%CI 1.41-2.64 for highest education quintile relative to lowest), with only moderate attenuation after further adjustment for median disposable family income (OR 1.70, 95%CI 1.15-2.51).[5] A study in Washington State, USA considered the patient's own education level, and reported higher odds of survival to discharge with >4 years of college relative to not receiving a high school diploma (OR 2.02, 95%CI 1.27-3.23), in an analysis adjusted for age, sex, race and some potential mediators. Further adjustment for occupation had little impact.[9]

Income

Another study in Washington State, USA considered the median household income (MHI) in the patient's home census tract, finding no evidence of a survival difference between the highest and lowest income quartile, after adjustment for age and sex (OR 1.03, 95%CI 0.67-1.39).[13] The aforementioned Danish study in a population aged under 21 years considered individual household income and reported OR 2.40 (95%CI 0.88-6.53) for the highest tertile relative to lowest, adjusted for age and sex.[14] This is not statistically significant, although the wide confidence intervals and small sample size (n=459) indicate the study may be underpowered. There was a statistically significant association in the unadjusted analysis.[14] A study in New York City focused on ethnic disparities in OHCA survival but included home census tract MHI as a covariate.[19] The MHI association is not statistically significant (OR 1.7, 95%CI 0.8-3.5, for MHI >$50,000 relative to <$25,000, after adjustment for age, sex and ethnicity).[19]

Three papers considered area-level measures of household income at the patient's home address only within analyses co-adjusted for potential confounding and mediating variables. The first of these, the aforementioned Swedish study ~~mentioned above~~, reported evidence of an association of median disposable family income with 30-day survival (OR 1.88, 95%CI 1.36-2.59 for highest quintile relative to lowest), after adjustment for age, sex and some potential mediators. This was partly attenuated after further adjustment for the proportion of university-educated residents (OR 1.31, 95%CI 0.87-1.98).[5] Two other papers considered MHI, both using data from Michigan, USA. The first used 1991-1996 data from seven cities and considered MHI of the patient's home census tract, dichotomised at the state median. They reported OR 1.51 (95%CI 0.80-2.80) for survival to discharge with MHI above the state median relative to below; thus this is not statistically significant.[17] This analysis was adjusted for race and some potential mediators, but not age or sex. The second used 1991-1994 data from nine hospitals across three counties and considered average household income of the patient's ZIP code, in $10,000 increments. This showed evidence of a small association with survival to discharge (OR 1.24, 95%CI 1.03-1.51 for $10,000 increase), adjusted for age, sex, race and some potential mediators.[18]

Also considering home address income, an ecological-level comparison of survival in the 20 highest-income census tracts in Portland, Oregon compared to the 20 lowest-income tracts observed no clear evidence of a survival disparity.[20] No adjusted analysis was performed. Finally, a study in Taiwan used individual-level income and found no clear association, reporting hazard ratio 1.03 (95%CI 0.92-1.16) for the highest income group relative to no income, after adjustment for age, sex and some potential mediators, although with small statistically significant associations in intermediate income groups. These appear to be in the direction of higher mortality with higher income though some lack of clarity in the description of methods and results casts some doubt on this (Table S6).[7]

Property value

An aforementioned study in Washington State**,** USA also considered the patient's home property value, reporting the highest quartile to be associated with notably higher survival to discharge relative to the lowest quartile, after adjusting for age and sex (OR 1.81, 95%CI 1.21-2.42).[13] Further adjustment for some potential mediators ~~made~~ had little impact ~~change to the estimate~~ (OR 1.73, 95%CI 1.16-2.30), but ~~it was attenuated by~~ further adjustment for census tract MHI did cause attenuation (OR 1.48, 95%CI 0.91-2.41);[13] this could indicate ~~–~~ either confounding or mediation by income.

Two further studies considered property value. Another in Washington State, USA reported evidence of some association with increased survival, with a relative risk of 1.6 (95%CI 1.1-2.4) per $50,000 increase, adjusted for age, sex and some potential mediators.[12] In contrast, a Canadian study reported an association of increased property value with *decreased* survival, with OR 0.77 (95%CI 0.61-0.97) per $100,000 increase, adjusted for age and some potential mediators.[11]

Other SEP measures

Three papers reported on other SEP measures related to the OHCA patient. These were all analyses co-adjusted for potential confounders and mediators. The first reported no clear evidence of an association of violent crime rate or material deprivation in the patient's home census tract with survival to discharge (OR 1.11, 95%CI 0.73-1.69 for lowest crime quintile relative to highest, OR 1.09, 95%CI 0.74-1.61 for least materially deprived quintile relative to most).[16] The second reported no clear relationship of any occupational group with survival to discharge, relative to 'blue-collar' work.[9] The third, a study in Ontario, Canada considered the association of floor of residence with survival to discharge, finding a possible small survival decrease associated with residence on or above the third floor relative to below the third (OR 0.70, 95%CI 0.50-0.99).[8] Residence in high-rise buildings is associated with low income in this location.[30]

A study in Pittsburgh, USA assessed the association of individual employment status and area poverty level with survival with good neurological outcome; both variables were excluded from the multivariable model by automated variable selection, although being unemployed/disabled was associated with decreased survival in unadjusted analysis (OR 0.39, 95%CI 0.18–0.84, relative to employed).[15] Another study reported no clear association of employment status with survival to hospital admission (OR 1.17, 95%CI 0.89-1.56 for employed relative to unemployed) in an analysis adjusted for age, sex and potential mediators, although unadjusted analysis indicated an association of employment with both survival to hospital admission and from admission to discharge.[10]

SEP measures referring to OHCA location

Composite indices

Two papers reported results from South Korea, both assessing ~~SEP at the~~ OHCA-~~-~~location SEP using the Carstairs Index.[24,25] One ~~paper~~ reports risk-adjusted survival to discharge rates from 2006-2015 adjusted for age and sex, with likely evidence of poorer survival in the most deprived quintile compared to ~~the~~ least (2006: 2.3% vs. 3.5%, 2015: 6.2% vs. 9.9%); statistical significance is not reported but a difference of similar magnitude is found in the unadjusted analysis and is significant.[25] The other reported from the same database for 2006-2007 only, also finding evidence of poorer survival to discharge in the most deprived quintile relative to least (OR 0.57, 95%CI 0.45-0.72) adjusted for age and sex. Further adjustment for mediators made no impact.[24]

A Singaporean study assessed OHCA-~~—~~location SEP using the Singapore Socioeconomic Disadvantage Index (SEDI). An analysis adjusted for age, sex, ethnicity and several potential mediators showed no clear association of SEDI category with 30-day mortality (OR 0.74, 95%CI 0.44–1.23, most deprived tertile relative to least).[22] A New Zealand study measured OHCA-~~-~~location SEP using the NZDep index; only an unadjusted analysis was reported, which showed no clear survival disparity.[28]

Other SEP measures

OHCA-~~-~~location neighbourhood poverty rate was considered by one study in Arizona, USA[23] and one in Paris, France.[21] The latter study also considered neighbourhood unemployment and income.

Neither study saw evidence of an association of any of these measures with survival, in analyses co-adjusted for possible confounders and mediators.

Studies in Taiwan[27] and Florida, USA[26] considered property value and income, and education and income respectively, as ~~measures of~~ OHCA-location SEP measures. Both only reported unadjusted analyses, which ~~with these showing~~ showed evidence of poorer survival with lower SEP in each case.

Effect modification

Three papers assessed effect modification. One found no evidence of sex being an effect modifier of the relationship of either home area-level education or income with survival,[5] and another found no evidence of effect modification of the individual-level education-survival relationship by sex, or occupation-survival relationship by education.[9] The third found no evidence of effect modification of the individual-level property value-survival relationship by age, sex, home/public location or initial cardiac rhythm.[13]

Discussion

SEP-survival association

In almost all of the included studies, ~~where~~ any association ~~was~~ observed between a SEP measure and OHCA survival ~~this~~ was in the direction of low SEP with decreased survival. The two exceptions are one study reporting an association of increased property value with decreased survival,[11] and one reporting possible decreased survival in an intermediate income level relative to no income, but no association when comparing the most extreme categories.[7] Though notably, several studies found no evidence of an association in either direction. Therefore, after our synthesis of evidence including ten additional papers, the generally consistent association of lower SEP with decreased survival agrees~~is in agreement~~ with the previous review's conclusions.[6]

While including these additional papers allowed further consideration of the specific aspects of SEP, the high heterogeneity in study designs and the range of SEP aspects considered means there is still limited evidence for any single aspect being especially consistently associated with OHCA survival.

For patient SEP, there is most consistency regarding education, an association with survival being reported in all three studies which considered it.[5,9,14] The evidence regarding income is more mixed. ~~Out o~~Of the eight relevant studies, two report an association,[5,18] one reports possible decreased survival in an intermediate but not the highest income level relative to no income,[7] and five report no clear association in adjusted analyses.[13,14,17,19,20] ~~The~~ Ppossible reasons for these different findings are numerous, given the methodological heterogeneity. Notably however, the estimates from three of the studies where no effect was found were not adjusted for mediators,[13,14,19] so over-adjustment could not explain their null findings.

The evidence around property value is also mixed, with two studies reporting an association of higher property value with higher survival,[12,13] but one reporting the opposite ~~relationship~~.[11] However, these studies have several methodological differences, such as the latter including only OHCAs occurring in private residences, and excluding those in apartments or condominiums;[11] OHCAs in lower value

properties are therefore likely underrepresented. One of the former studies also only included patients with initial shockable rhythm.[12] Both studies considering patients' employment status found a univariable association with survival, attenuated after adjustment.[10,15] Being considered in single studies, little can be concluded regarding patients' occupation, housing, neighbourhood poverty level or crime rate.

The previous review also indicated area-level measures of patient SEP may show less consistent associations with survival than individual-level measures.[6] Our findings are consistent with this, with a clear adjusted SEP-survival association observed for one or more SEP indicator in only two of eight studies using area-level measures of home-address SEP, compared to six of nine studies using individual-level measures. While this may indicate a true difference, it may instead ~~This may~~ reflect misclassification of individual-level SEP by area-level measures, as suggested previously.[6] ~~and indicate individual-level measures are preferable for studies focussing on individual-level SEP.~~

It also highlights the importance of using the most appropriate level of measurement for each specific research question wherever possible, such as using individual-level measures when focussing on patient-level SEP, both to avoid misclassification from using area-level measures as a proxy, and to avoid the risk of ecological fallacy from drawing conclusions about individuals based on area-level measurements.

With sparse literature, the picture is also unclear regarding OHCA-location SEP. Of the multivariable analyses, only two report a SEP-survival association (and these ~~are from~~use the same database),[24,25] while three report no association.[21–23] While this could indicate the composite index used by the first two studies best captures the association ~~most effectively~~, several other factors could explain the difference; notably the first two use quintiles of the SEP measure,[24,25] while the other three use measures with two or three categories.[21–23] The small number of studies and methodological heterogeneity limits further conclusions.

It is also possible that the inter-study differences in results partly reflect differing socioeconomic inequality between settings. SEP is generally defined relative to the range within that study, such as by comparing extreme quintiles. Theoretically therefore, a setting with less extreme inequality could expect to see less of a SEP-survival association.

There are several possible causal pathways between SEP aspects and survival. Education may improve cognitive function, communication with health services and awareness of health education,[31] potentially leading to faster symptom recognition, more effective EMS-communication, and increasing bCPR likelihood ~~of bCPR~~.[5] Unemployment may make OHCA more likely to occur at home and be unwitnessed, without rapid initiation of bCPR or EMS-communication. Income influences access to services and commodities, including food and activities,[31] the impact on overall health may influence co-morbidity, which may be associated with OHCA survival.[32,33]

Mediators

This review also aimed to consider the evidence for any specific mediators in the SEP-survival relationship, that is factors on the causal pathway. The 'difference method' is one approach to identifying mediators; this considers whether the exposure-outcome effect estimate differs between models which do and do not adjust for the potential mediators.[34] Regarding OHCA location, only one study reports separate estimates for analyses adjusting for potential confounders and after further adjustment for potential mediators. Here, the further adjustment made little difference.[24] This may indicate the factors adjusted for in the further analysis (witness, bCPR, initial rhythm, and call-scene arrival and call-hospital arrival intervals) are not mediators, but the other studies provide no evidence for or against this.

Regarding patient SEP, of the three studies ~~that report~~reporting separate estimates for analyses adjusted only for potential confounders, and after further adjustment for potential mediators[13,14,19] only one reports attenuation.[14] However, there is little difference evident in the variable sets adjusted for, meaning no particular variable can be identified as a mediator. This may indicate a real inter-study difference in mediation mechanism~~ between the studies~~. Notably, the study where adjustment for mediators caused attenuation was restricted to patients younger than 21 years, and used parental SEP measures.[14] This may suggest ~~one or more~~some of the variables adjusted for (location, witness, bCPR, initial rhythm, incident year, and~~–~~ arrest recognition-rhythm analysis interval) are mediators specifically in the parental SEP-child survival relationship.

However, the validity of identifying mediators by the 'difference method' depends on controlling for confounding of the mediator-outcome, as well as exposure-outcome relationship.[34] This assumption is not discussed explicitly by any of the included studies and the possibility remains of residual confounding of ~~the~~ mediator-outcome relationships distorting these results. Potential mediators may also show different socioeconomic patterning between settings, and therefore mediate the SEP-survival relationship in specific settings only.

Other work indicates likelihood of receiving bCPR as one plausible mediator, being associated both with improved survival,[35] and higher ~~SEP at the~~ OHCA~~–~~ location SEP.[6] This may be partly due to socioeconomic patterning of CPR training, with individuals in manual or unskilled occupations or long-term unemployment less likely to be trained than professional, managerial or non-manual occupations.[36] Use of an automated external defibrillator is another candidate, with evidence of association with both higher SEP[37] and survival.[38] Underlying health status is another, given extensive evidence of socioeconomic patterning of morbidity,[39] and of co-morbidity being associated with decreased OHCA survival.[32,33] These factors could be usefully considered in future studies.

Effect modification

With only three papers considering effect modification (differences in SEP-survival association between groups defined by an 'effect modifier'), the evidence remains~~is still~~ sparse. There is most evidence regarding sex, with all three considering it but finding no evidence in support.[5,9,13] However, these assessments were all within analyses co-adjusted for potential confounders and mediators, raising the question of whether the finding would be maintained without mediator~~-~~ adjustment. One

study also considered effect modification by age, private/public location and initial rhythm,[13] and another considered occupation as an effect modifier of the education-survival relationship.[9] While no evidence was found for any of these, this should be interpreted cautiously given they were assessed by single studies.

Quality of evidence

As described above, high methodological heterogeneity limits the capacity for inter-study comparisons. Some specific aspects also raise concerns about quality. Firstly, ~~One aspect is~~ the~~at~~ potential for bias due to missing data is generally unclear; ~~with~~ several studies exclud~~eing~~ >20% cases,[12,15,17,18,] and in others the extent of missing data is unclear.[7,10,11,25,27]

Secondly, ~~A second aspect is~~ there is notable inter-study variation in overall survival (Table S3), from 2.2% survival to discharge[19] to 50.4% 'overall survival' (period unspecified).[26] While this may be partly explained by differing eligibility criteria, such as high survival in studies restricted to cases presenting with shockable rhythm,[9,12] in some studies the reason for unusually high or low survival is unclear.[7,19,26] This raises questions regarding study population representativeness and generalisability.

Limitations of this review

Although extensive search strategies were used, unpublished and non-English language literature was excluded. We were also unable to assess potential for publication bias; funnel plots were not appropriate due to the heterogeneity in SEP measures considered and in their categorisation.

Conclusions

The current literature is generally supportive of any association of SEP with OHCA survival being in the direction of decreased survival with lower SEP, although an association is not seen in all studies. This ~~provides~~ further supports ~~for~~ the need to reduce socioeconomic deprivation in society. It also suggests it may be appropriate to consider socioeconomic characteristics of populations when targeting CPR training and other resources to improve survival, especially given evidence of lower SEP being associated with higher OHCA incidence[6] and lower rates of CPR training.[36] Regarding particular SEP aspects, there is some coherent evidence for a higher education level of the patient or their residential area being associated with improved survival, though further work would be required to increase confidence in this finding. No mediators of the SEP-survival relationship have been clearly identified. A small number of studies have considered effect modification, finding no evidence of any factors with this effect; there is most evidence against sex as an effect modifier, with~~hile~~ other factors having~~have~~ only been considered in single studies. The certainty and generalisability of the conclusions from this body of evidence are restricted by methodological heterogeneity.

Conflicts of interest

None.

Acknowledgements

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Tables

Table 1: Eligibility criteria for study inclusion

	Inclusion	Exclusion
Study design	• Observational studies reporting primary findings	• Case reports • Intervention studies • Qualitative research • Reviews
Participants	• Cardiac arrest cases of any aetiology, occurring in any non-hospital location (including specific locations such as home or workplace)	• Myocardial infarction without cardiac arrest • Sudden cardiac death without separating incidence and survival • In-hospital cardiac arrests unless OHCA results reported separately

Exposure	• Any area or individual-level measure of socioeconomic position or deprivation
	• May be a composite index measure or a specific indicator, including but not limited to:
	  ○ Income
	  ○ Education/skills/training
	  ○ Employment
	  ○ Housing
	  ○ Crime
	  ○ Access to services
	  ○ 'Social class'
	• The measure may refer to the OHCA patient or OHCA location
	• The measure may be the primary focus of the paper or included as a covariate, as long as an effect estimate of socioeconomic position or deprivation is reported
		• Population density or physician density not considered a measure of socioeconomic position or deprivation
		• Neighbourhood characteristics, such as urban vs. rural, without consideration of some aspect of socioeconomic position or deprivation
		• Race/ethnicity, without consideration of some aspect of socioeconomic position or deprivation

Outcome	• Any measure of OHCA survival, including but not limited to return of spontaneous circulation, survival to hospital, discharge from hospital, discharge with neurologically favourable outcomes, survival to 30-days, or survival at a longer follow-up point	• Assessment of longer-term outcomes in a population restricted to OHCA survivors
Other	• Any date of publication	• Records published in a language other than English • Results reported only in conference abstracts

Table 1: Eligibility criteria for study inclusion

Abbreviations: OHCA, out-of-hospital cardiac arrest.

Table 2: Data elements sought for extraction

Setting	• Years covered • Location (country and cities/states/counties as appropriate)
Participants	• Number of participants • Exclusion/inclusion criteria

Variables	• Socioeconomic position variable
	  ○ OHCA location or OHCA patient characteristic?
	  ○ Individual level or area-level?
	  ○ Definition of variable, and how it was measured
	• Outcome variable

Results	• Overall survival • Crude association or disparity, unadjusted for other variables • Association adjusted for possible confounders and/or possible mediators noting the variables adjusted for in each case • Any investigation of effect modification
Other	• Analysis method used • Data source

Table 2: Data elements sought for extraction

Abbreviations: OHCA, out-of-hospital cardiac arrest.

Table 3: Characteristics of included studies

a) Studies using SEP measures referring to the OHCA patient or their area of residence						
Reference	**Country**	**Study period**	**N***	**Inclusion criteria****	**SEP measure(s)*****	**Outcome measures******
Jonsson *et al.*, 2019[5]	Sweden	2006–2015	7,431	Any age, EMS-treated, not EMS-witnessed.	• Income [◊] • Education [◊]	• 30-day survival† • 1 day survival • 1 year survival
Chen *et al.,* 2017[7]	Taiwan	2005–2012	5,338	Age ≥18 years, non-traumatic aetiology, transported to hospital and resuscitation attempted in ED.	• Income [‡]	• Hospital survival† • ROSC
Drennan *et al.,* 2016[8]	Canada	2007–2012	7,842	Age ≥18 years, presumed cardiac aetiology, not EMS-witnessed, occurring in a residential building.	• Housing: Floor number [‡]	• Survival to discharge† • ROSC
Wells *et al.,* 2016[9]	USA	1999-2005	1,390	Age ≥18 years, non-traumatic aetiology, EMS-treated, presenting with shockable rhythm.	• Education [‡] • Occupation [‡]	• Survival to discharge† • Survival to admission
Soholm *et al.,* 2015[10]	Denmark	2007–2011	2,527	Age ≥18 years, any aetiology, EMS-attended, CPR attempted, without obvious signs of death.	• Employment [‡]	• Survival to admission† • Survival from admission to discharge
Vaillancourt *et al.,* 2008[11]	Canada	1995 –1999	3,600	Any age, cardiac aetiology, not EMS-witnessed, occurring in a private residence, excluding apartments and condominiums.	• Property value [‡]	• Survival to discharge†
Hallstrom *et al.,* 1993[12]	USA	1986 –1988	183	Any age, cardiac aetiology, presenting with VF. CPR instructions given to bystander by telephone.	• Property value [‡]	• Survival to discharge without obvious neurological deficit†
Clarke *et al.,* 2005[13]	USA	1999 – 2003	1,789	Age ≥18 years, cardiac aetiology. Nursing home, trailer park, motel/hotel and non-county residents excluded.	• Property value [‡] • Income [◊]	• Survival to discharge†
Rajan *et al.,* 2015[14]	Denmark	2001–2010	459	Age ≤21 years, any aetiology, CPR attempted (by bystander or EMS).	• Income [‡] • Parental education [‡]	• 30-day survival† • ROSC on hospital arrival • 1-year survival
Uray *et al.,* 2015[15]	USA	2010–2012	234	Age 18-65 years, any aetiology, not pronounced dead at scene.	• Poverty [◊] • Employment [‡]	• Good neurological outcome (CPC 1/2) †
Buick *et al.,* 2016[16]	Canada	2006–2014	9,485	Age ≥20 years, Toronto resident, non-traumatic aetiology, not EMS-witnessed, EMS-treated, no DNR, no sign of obvious death.	• Material deprivation [◊] • Crime [◊]	• Survival to discharge† • ROSC on hospital arrival
Sayegh *et al.,* 1999[17]	USA	1991-1996	1,317	Age ≥18 years, cardiac aetiology, no DNR, resuscitation attempted.	• Income [◊]	• Survival to discharge†

Table 3: Characteristics of included studies (cont.)

Reference	Country	Study period	N*	Inclusion criteria**	SEP measure(s)***	Outcome measures****
Chu *et al.,* 1998[18]	USA	1991 –1994	1,197	Age ≥18 years, cardiac aetiology, resuscitation attempted, no DNR.	• Income [◊]	• Survival to discharge†
Galea *et al.,* 2007[19]	USA	2002–2003	3,891	Age ≥18 years, cardiac aetiology, not EMS-witnessed, EMS resuscitation attempted, NYC resident.	• Income [◊]	• Survival to 30 days post-discharge†
Feero *et al.,* 1995[20]	USA	1991	322	Any age, cardiac aetiology, EMS-resuscitation attempted, within Portland.	• Income [◊]	• Survival to discharge†
b) Studies using SEP measures referring to the OHCA location						
Reference	**Country**	**Study period**	**N***	**Inclusion criteria****	**SEP measure(s)*****	**Outcome measures********
Chocron *et al.,* 2019[21]	France	2011-2016	8,754	Age ≥18 years, presumed cardiac aetiology, resuscitation attempted.	• Employment [◊] • Poverty [◊] • Income [◊]	• Survival to discharge† • ROSC
Rakun *et al.,* 2019[22]	Singapore	2010-2015	8,900	Any age, Chinese, Malay or Indian ethnicity, EMS-transported or ED-presentation, no obvious sign of death.	• Singapore Socioeconomic Disadvantage Index [◊]	• Survival to 30 days or discharge†
Moon *et al.,* 2014[23]	USA	2010-2012	4,821	Age ≥18 years, non-traumatic aetiology, non EMS-witnessed, no DNR, EMS-resuscitation attempted. Excluding airport/jail/government building location.	• Poverty [◊]	• Survival to discharge†
Ahn *et al.,* 2011[24]	South Korea	2006-2007	34,227	Any age, any aetiology, EMS-attended.	• Carstairs index [◊]	• Survival to discharge† • Survival to hospital admission • ROSC
Lee *et al.,* 2018[25]	South Korea	2006 – 2015	120,365	Age ≥18 years, cardiac aetiology, non-EMS-witnessed, EMS attended, resuscitation attempted.	• Carstairs index [◊]	• Survival to discharge† • Good neurological outcome (CPC 1/2)
Rivera *et al.,* 2016[26]	USA	25-month period, years not specified	125	All ages, cardiac aetiology, not HCP-witnessed. Excluding airport/jail location.	• Income [◊] • Education [◊]	• 'Overall survival' (undefined)†
Chiang *et al.,* 2014[27]	Taiwan	2008–2009	3,573	Age ≥18 years, non-traumatic aetiology, no DNR, no obvious signs of death, EMS-resuscitation attempted, transported to hospital.	• Property value [◊] • Income [◊]	• Survival to discharge† • ROSC (>2 hours) • Good neurological outcome (CPC 1/2)
Fake *et al.,* 2013[28]	New Zealand	2007-2010	413	Age ≥16 years, non-traumatic aetiology, not EMS-witnessed, EMS-resuscitation attempted.	• NZDep2006 index of deprivation [◊]	• Survival to discharge† • ROSC

Table 3: Characteristics of included studies

Records are arranged by reference number. Only exposure variables related to socioeconomic position are recorded. Further details of how the SEP measures are defined in each study are detailed in Table S2 (supplementary).

*The listed sample size refers to the number of OHCAs included in the multivariable analysis (or unadjusted analysis if no multivariable analysis was performed), without those excluded due to missing data (where this information is given). For studies with missing data in relevant variables, this number is smaller than the total number of eligible OHCAs and therefore may be smaller than the main sample size quoted by the study authors. **If a characteristic is not mentioned in these criteria (e.g. aetiology), the authors did not report exclusion/inclusion of OHCAs on these criteria. ***Diamond symbol [◊] indicates an area-level variable, double dagger [‡] indicates an individual-level variable. ****A single dagger (†) is used to indicate the outcome for which results are summarised in Table 4; this is 30-day survival or survival to discharge where this was assessed by the study, otherwise any other survival outcome that is reported.

Abbreviations: bCPR, bystander CPR; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; DNR, "do not resuscitate" advanced directive; ED, emergency department; EMS, emergency medical services; HCP, healthcare professional; OHCA, out-of-hospital cardiac arrest; NYC, New York City; ROSC, return of spontaneous circulation; SEP, socioeconomic position; VF, ventricular fibrillation.

Table 4: Summary of relevant results reported by included studies

a) Studies using SEP measures referring to the OHCA patient or their area of residence									
Reference	**N***	**Model**	**Composite**	**Income**	**Education**	**Employment**	**Property value**	**Poverty**	**Other (specified)**
Jonsson *et al.*, 2019[5]	7,431	*Unadj.*	-	✓	✓	-	-	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	✓	✓	-	-	-	-
Chen *et al.,* 2017[7]	5,338	*Unadj.*	-	**?** †	-	-	-	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	**?** †	-	-	-	-	-
Drennan *et al.,* 2016[8]	7,842	*Unadj.*	-	-	-	-	-	-	✓ (Housing floor)
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	-	-	✓ (Housing floor)
Wells *et al.,* 2016[9]	1,390	*Unadj.*	-	-	✓	-	-	-	**?** (Occupation)
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	✓	-	-	-	**X** (Occupation)
Soholm *et al.,* 2015[10]	2,527	*Unadj.*	-	-	-	✓	-	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	**X**	-	-	-
Vaillancourt *et al.,* 2008[11]	3,600	*Unadj.*	-	-	-	-	**?**	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	✓ (**)	-	-
Hallstrom *et al.,* 1993[12]	183	*Unadj.*	-	-	-	-	✓	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	✓	-	-
Clarke *et al.,* 2005[13]	1,789	*Unadj.*	-	**X**	-	-	✓	-	-
		Adj. (A)	-	**X**	-	-	✓	-	-
		Adj. (B)	-	**X**	-	-	✓	-	-
Rajan *et al.,* 2015[14]	459	*Unadj.*	-	✓	✓	-	-	-	
		Adj. (A)	-	**X**	✓	-	-	-	
		Adj. (B)	-	**X**	**X**	-	-	-	
Uray *et al.,* 2015[15]	234	*Unadj.*	-	-	-	✓	-	**X**	
		Adj. (A)	-	-	-	-	-	-	
		Adj. (B)	-	-	-	**X**	-	-	
Buick *et al.,* 2016[16]	9,485	*Unadj.*	-	-	-	-	-	-	**?** (Crime); **?** (Material deprivation)
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	-	-	**X** (Crime); **X** (Material deprivation)

Table 4: Summary of relevant results reported by included studies (cont.)

Reference	N*	Model	Composite	Income	Education	Employment	Property value	Poverty	Other (specified)
Sayegh *et al.,* 1999[17]	1,317	*Unadj.*	-	-	-	-	-	-	
		Adj. (A)	-	-	-	-	-	-	
		Adj. (B)	-	**X**	-	-	-	-	
Chu *et al.,* 1998[18]	1,197	*Unadj.*	-	-	-	-	-	-	
		Adj. (A)	-	-	-	-	-	-	
		Adj. (B)	-	✓	-	-	-	-	
Galea *et al.,* 2007[19]	3,891	*Unadj.*	-	-	-	-	-	-	
		Adj. (A)	-	**X**	-	-	-	-	
		Adj. (B)	-	**X**	-	-	-	-	
Feero *et al.,* 1995[20]	322	*Unadj.*	-	**X**	-	-	-	-	
		Adj. (A)	-	-	-	-	-	-	
		Adj. (B)	-	-	-	-	-	-	
b) Studies using SEP measures referring to the OHCA location									
Reference	**N***	**Model**	**Composite**	**Income**	**Education**	**Employment**	**Property value**	**Poverty**	**Other (specified)**
Chocron *et al.,* 2019[21]	8,754	*Unadj.*	-	-	-	-	-	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	**X**	-	**X**	-	**X**	-
Rakun *et al.,* 2019 [22]	8,900	*Unadj.*	**X**	-	-	-	-	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	**X**	-	-	-	-	-	-
Moon *et al.,* 2014[23]	4,821	*Unadj.*	-	-	-	-	-	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	-	**X**	-
Ahn *et al.,* 2011[24]	34,227	*Unadj.*	✓	-	-	-	-	-	-
		Adj. (A)	✓	-	-	-	-	-	-
		Adj. (B)	✓	-	-	-	-	-	-
Lee *et al.,* 2018[25]	120,365	*Unadj.*	✓	-	-	-	-	-	-
		Adj. (A)	**?**	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	-	-	-
Rivera *et al.,* 2016[26]	125	*Unadj.*	-	✓	✓	-	-	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	-	-	-
Chiang *et al.,* 2014[27]	3,573	*Unadj.*	-	✓	-	-	✓	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	-	-	-
Fake *et al.,* 2013[28]	413	*Unadj.*	**X**	-	-	-	-	-	-
		Adj. (A)	-	-	-	-	-	-	-
		Adj. (B)	-	-	-	-	-	-	-

Table 4: Summary of relevant results reported by included studies

Full details of the effect estimates, effect modification, and variables adjusted for are detailed in Table S3 (supplementary).

Adj. (A): Adjusted for potential confounders only

Adj. (B): Co-adjusted for potential confounders and mediators (except adjustment for other measures of SEP if this adjustment is reported separately)

✓: Statistically significant association (5% threshold) in most extreme category e.g. lowest income quintile relative to highest. This is in the direction of association of lower SEP with poor outcome, unless marked by (**).

X: Not statistically significant (including exclusion by automated variable selection e.g. backwards stepwise regression)

?: Not clear (statistically significant association in an intermediate quintile but not the most extreme, or no statistical test performed)

*The listed sample size refers to the number of OHCAs included in the multivariable analysis (or unadjusted analysis if no multivariable analysis was performed), without those excluded due to missing data (where this information is given). For studies with missing data in relevant variables, this number is smaller than the total number of eligible OHCAs and therefore may be smaller than the main sample size quoted by the study authors. †Lack of detail in methods, and possible contradiction of results and authors' interpretation casts some doubt on direction of effect.

Records are arranged by reference number. Where 30-day survival or survival to discharge was assessed in the study, only these results are referred to in Table 4. If one of these outcomes were not assessed, any other survival outcome assessed in the study is instead summarised here. Other survival outcomes are reported in Table S4 (supplementary). Only exposure variables related to socioeconomic position are summarised. Where a paper reports results for both the main study population and a subgroup (e.g. Utstein comparator subgroup), the Table 4 summary refers to the main study population. The subgroup results are included in Table S5 (supplementary).

Abbreviations: OHCA, out-of-hospital cardiac arrest; SEP, socioeconomic position.

Figure 1: PRISMA flowchart indicating number of records at each review stage

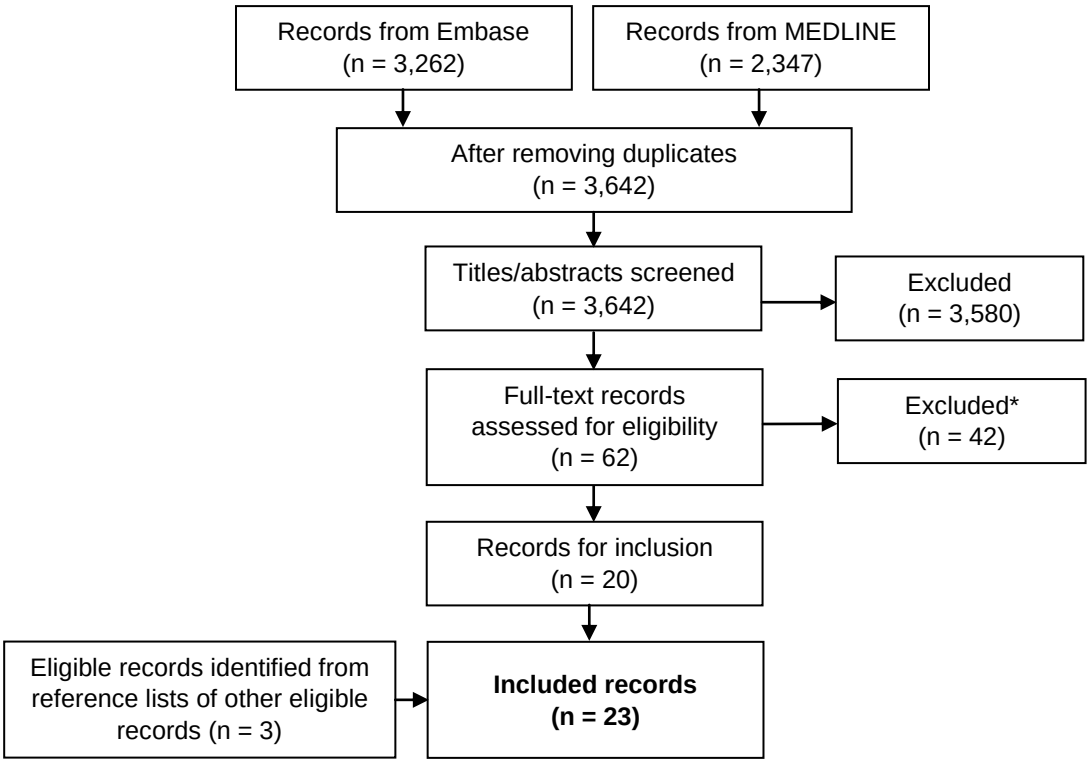

Figure 1: PRISMA flowchart indicating number of records at each review stage

Adapted from Liberati *et al.*, (2009).

*Reasons for exclusion of records at this stage are detailed in Table S1 (supplementary material).

Conflicts of interest

Conflicts of interest: None.

CRediT author statement

RC: Conceptualisation, Methodology, Data Curation, Analysis, Writing - Original Draft, Writing - Review & Editing. *CB:* Validation, Writing - Review & Editing. *GC:* Conceptualisation, Writing – Review & Editing. *NH:* Conceptualisation, Methodology, Writing - Review & Editing, Supervision.