PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Data Quality and 30-day Survival for Out-of-Hospital Cardiac Arrest in the UK Out-of-Hospital Cardiac Arrest Registry: A Data Linkage Study
AUTHORS	Rajagopal, Sangeerthana; Booth, Scott; Brown, Terry; Ji, Chen; Hawkes, Claire; Siriwardena, Aloysius; Kirby, Kim; Black, Sarah; Spaight, Robert; Gunson, Imogen; Brace-McDonnell, Samantha; Perkins, Gavin

VERSION 1 – REVIEW

REVIEWER	Ms. Siobhán Masterson HRB Research Fellow, Discipline of General Practice National University of Ireland Galway
REVIEW RETURNED	26-May-2017

GENERAL COMMENTS	This is paper is well-written, easy to follow, with explicit aims and objectives which the reader is appropriately reminded of throughout the paper. Pg.3/32 Lines 5-40: Rationale for study and the issue of dealing with multiple sources of outcome data very well described Pg. 3/32 Line 51: Suggest that some more recent additional references from Europe, US and Asia are used to highlight differences in reported patient survival worldwide. Pg. 3/32 Line 51: It is fair to say that quality of data is a substantial contributor to outcome variation. I am not convinced that it is fair to say data quality is the 'greatest' contributor Pg. 4/32 Line 46: 'attempted by EMS' – is this statutory ambulance services? Might be useful to specify this as EMS structure is so varied worldwide Pg. 5/32 Line 51: This is my primary concern. Does linking with ONS actually confirm survival status or does it solely confirm death? I understand that certified deaths are registered on ONS within 5 days, but what is the process and timeline for obtaining a death certificate in the UK? In some jurisdictions, it is a legal requirement that a death be registered within one year but I don't believe that prosecution for non-certification is common. What about cases that are being investigated by the coroner? Or cases where there is no next-of-kin? Is there less chance of 'efficient' certification of death where english is the family's second language, or where the deceased does not leave a will/estate?

	Are any of these scenarios relevant in the UK context? If they are, the comprehensiveness and accuracy of the ONS may need to be considered in the limitations section Pg. 5/32 Line 6: As above, is it safe to assume 'alive'? Pg. 12/32 Line 29: The improvements in demographic data is very impressive Pg. 13/32 Line 7: As above, can 30-day survival be assumed from NOT being on the ONS? Pg. 13/32 Lines 33-58: I am not sure if the detailed comparison of patient groups adds to your ability to fulfill the study aims. I think it is of most interest to know whether there is a significant difference in the % survival and % missing survival status between the matched and unmatched group. I think that data on other variables and secondary outcomes detracts from the main result of interest. Perhaps a simple chi square of % survival and %missing survival status by matched/unmatched would provide the relevant information? Pg. 15/32 Table 5: As above, I'm not convinced that the level of detail provided adds to fulfilling your study aims. Suggest: Columns: Matched Unmatched Sig Row 1: % Survived Row 2: % missing survival status Pg. 17/32 Line 40: For what proportion of overall cases do you have postcodes? Pg. 18/32 Line 19: Again, your paper shows the value of the NHS number for data linkage, and also the value of data linkage in adding the NHS number to your OHCAO data, great potential for longitudinal work Pg. 18/32 Lines 39-46: The meaning of the sentence beginning "Whilst a study…" is not clear to me Pg. 19/32 Lines 20-26: As above, it is not clear to me what analysis of % bystander CPR, % shockable rhythms etc. is adding to your results. Pg. 19/32 Line 36: Again, can you confirm that patients were alive at the time of data linkage or is it possible that some deaths were not registered? Pg. 20/32 Line 12: As above, does linkage 'confirm' 30-day survival status? Is any further validation need to confirm survival?

REVIEWER	Jan Wnent,MD Deputy Director Institute for Emergency Medicine University Hospital Schleswig-Holstein, Kiel, Germany
REVIEW RETURNED	28-May-2017

GENERAL COMMENTS	thank yoi very much for this manuscript. I have only some amentments: On page 3 line 25: please refer to the EuReCa ONE Study On page 4 in methods setting: please add a short discription of the OHCAO project Table 5: Why are you reporting "not recorded", "missing" or "others" to the first monitored rhythm. Is it not a mandatory data point in the OHCAO dataset? Is it posible to specify these points and re-calculate this into the asystoly, PEA and VF group? Please add a limitation section to the manuscript and discuss the limitations of your study

REVIEWER	Helle Søholm Copenhagen University Hospital, Rigshospitalet, Denmark
REVIEW RETURNED	01-Jun-2017

GENERAL COMMENTS	Review ” Improving Data Quality in a UK Out-of-Hospital Cardiac Arrest Registry Through Data Linkage Between the Out-of-Hospital Cardiac Arrest Outcomes (OHCAO) Project and NHS Digital” Thank you for the opportunity to review the manuscript Improving Data Quality in a UK Out-of-Hospital Cardiac Arrest Registry Through Data Linkage Between the Out-of-Hospital Cardiac Arrest Outcomes (OHCAO) Project and NHS Digital. The study covers establishment of a registry including patients with out-of-hospital cardiac arrest during 2014 by linking demographic data and date of death data to improve data quality and establish accurate 30-day survival outcomes for OHCA. General comments The manuscript is in general well-written and covers and important and interesting subject. In general the manuscript is very focused on the UK data, which could be reduced and instead a more international angle could be enhanced to make the manuscript more interesting for the international/non-UK reader. For example a reference to the Danish registries (Dansk Hjertestopregister: http://genoplivning.dk/wp-content/uploads/2016/05/Rapport-fra-Dansk-Hjertestopregister-2001-2014.pdf) and the national registration of all citizens, which enables outcome data on all citizens (Wissenberg M, Lippert FK, Folke F, Weeke P, Hansen CM, Christensen EF, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA 2013;310:1377-84).

	Specific comments Abstract: The abstract is well-written, however I find the section “design and setting” a bit hard to follow. The sentence “Of these, a randomly selected sample of 3120 cases were securely transferred to the NHS Digital list cleaning service to be matched using OHCAO patient demographic data to return previously missing data and provide Office for National Statistics (ONS) mortality data.” should be easier to read for the non-UK reader. I do not know what the “NHS Digital list cleaning service” is for example. Why was a random sample selected? Please explain. Introduction: The introduction is fairly long and could be improved by saving some of the discussion points for the discussion section and limiting the introduction to a background and introduction to the subject – OHCA, survival and difficulties with international comparisons of outcome data. For example outcome data from different countries could be highlighted. Methods: “Setting “ - Please include the percentage of coverage of the UK population. - Please indicate the incidence of OHCA in the current study (for international comparison). - Please indicate the number of each exclusion criteria: “presence of a do not attempt resuscitation order (n =, %)”, “signs incompatible with life (n =, %)” and “where resuscitation attempts would be futile (n =, %)” “Aims & Objectives” - please indicate why not all OHCA-patients were matched “OHCA data collection” - Please indicate how precise the “EMS personnel identified OHCAs by searching case records for confirmed arrests”, what is the sensitivity and specificity of the search? Results: “Comparison of patient groups” - Line 37: Please be more precise “died” after 30 days or during hospital admission? - Line 50: Please indicate the actual numbers instead of stating “Additionally the bystander CPR rate was at least 10% higher ” - Line 56: “However those not matched in the survival to hospital discharge groups showed comparatively higher rates of defibrillator usage (20.0% vs. 5.7%) with lower rates of shockable rhythms (32.0% vs. 61.0%) compared to the matched group. However these figures are based on very few patients.” Why is the numbers based on very few patients? And why was not all patients matched, when there is differences in the pre-hospital factors known to provide important information with regards to survival? - Figure 1: Please provide the reason for not manually submitting the 430 patients in the figure or as a foot-note. - Table 5: Please indicate p-values or a * when there is significant differences between matched and unmatched patients.

	Age can be provided only as median (IQR). - Please provide data for patients not selected for matching – is the sample truly random? - With regards to survival calculations (table 4) after matching please provide best and worse case scenarios – is all patients with missing 30 day survival was alive and dead, respectively. Discussion: - The first section of the discussion repeats too many details of the results. Please provide an overview of the found results of the current study. - Please explain “multiple deprivation index effect” - With regards to “The variability of cardiac arrest survival is well documented.” please be more specific. The reference refers to an editorial covering UK circumstances. The survival may not vary but so does the registries. Please discuss in further detail and provide international references as well. - “The best data point provided by ambulance services to identify cases is the NHS number.” add “in the UK” - “These findings are in line with research showing that OHCA databases in different countries can successfully link OHCA patients to outcome databases where unique patient identifiers are readily available.12,13” The Danish reference is not correct in this setting. There is 100% availability of outcome data due to the unique civil registration number provided to all Danish citizens. Please discuss. - “Half (50.8%) of OHCAs with attempted resuscitation died with no ROSC at anytime while 37.9% achieved ROSC at anytime but were not discharged from hospital.” How many patients were found dead (with obvious signs of death) and were not attempted resuscitated? - Please include a statistically discussion of acceptable missing data. - Please provide a more thorough discussion of the UK registries from the current study with international registries.

REVIEWER	Ben Beck Monash University, Australia
REVIEW RETURNED	02-Jun-2017

GENERAL COMMENTS	I have a number of minor comments that I have outlined below. 1. Page 2, line 8: The study does not “aim to establish the feasibility of producing a registry”; it is the supplementation of missing data. Please edit. 2. Page 2, line 56: The last dot point of ‘strengths and limitations’ needs clarification. 3. Page 3, lines 12-15: Please separate this sentence as it is discussing two separate issues. 4. Page 3, lines 17-24: I would like to see an expansion on the strengths and weaknesses of collecting survival to hospital discharge vs 30 day survival. What do other international registries use? Also, I’m not convinced that survival to hospital discharge is easier to collect than 30-day survival. Often 30 day survival is reliant on data linkage with national registries, but this is often easier than manual follow-up of patients (or medical records) to determine survival to hospital discharge. 5. Page 3, line 19: I’m not sure that “cultural differences” is the most appropriate term. Perhaps “differences in discharge practices”?

	6. Page 3, line 36: Please explain what “central records centres” are. 7. Page 3, line 38: And potentially varying capture rates. 8. Page 5, line 8: Please explain the “NHS Digital list cleaning service”. 9. Page 5, line 12: What is meant by this “success rate”? Is this compared to ambulance records? 10. Page 6, line 19: Validation “was”…. 11. Page 7, line 33: How is this date of death/discharge collected in the OHCAO? I would like to see greater explanation of data collection methods in the OHCAO. 12. Page 8, line 12: Should “ROSC at anytime” actually be “ROSC in the prehospital setting”? 13. Page 8, line 23: Place the last sentence of this paragraph earlier to explain why you are comparing these three groups. 14. Page 9, line 55: Just to confirm – there were no errors with the originally recorded NHS number? Ie. These were all correct linkages? 15. Page 17, line 40: This last sentence does not make sense. Additionally, how does having the postcode assist in the determination of arrests that occur at home vs those in public places? It may aid in determining whether an arrest occurs outside of the primary residence, but it may still occur in a ‘home’. 16. Discussion: I’d like to see some additional commentary around the reliance of data capture in the prehospital setting with respect to the linkage methods outlined in this study. The only way that these linkage methods will improve is through improved data capture in the prehospital setting (and there are obvious challenges with this).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1. Reviewer Name: Ms. Siobhán Masterson

Comment: Pg. 3/32 Line 51: Suggest that some more recent additional references from Europe, US and Asia are used to highlight differences in reported patient survival worldwide.

Response: Thank you. We have added the following more recent additional references from US, Asia and Europe that highlight regional variation in reported patient survival across the world:

Girotra S, van Diepen S, Nallamothu BK, Carrel M, Vellano K, Anderson ML, et al. Regional variation in out-of-hospital cardiac arrest survival in the United States. Circulation. 2016;doi:10.1161/circulationaha.115.018175

Okubo M, Kiyohara K, Iwami T, Callaway CW, Kitamura T. Nationwide and regional trends in survival from out-of-hospital cardiac arrest in Japan: A 10-year cohort study from 2005 to 2014. Resuscitation. 2017;115;120-28.

Stromsoe A, Svensson L, Axelsson AB, Claesson A, Goransson KE, Nordberg P, et al. Improved outcome in Sweden after out-of-hospital cardiac arrest and possible association with improvements in every link in the chain of survival. Eur Heart J. 2015;36;863-71.

Comment: Pg. 3/32 Line 51: It is fair to say that quality of data is a substantial contributor to outcome variation. I am not convinced that it is fair to say data quality is the ‘greatest’ contributor.

Response: We have amended the text to now state:

“Lilford et al highlighted that an important source of variation in reporting outcomes can be traced to the quality of data that results are based on.”

Comment: Pg. 4/32 Line 46: ‘attempted by EMS’ – is this statutory ambulance services? Might be useful to specify this as EMS structure is so varied worldwide.

Response: Text updated with “statutory”.

Comment: Pg. 5/32 Line 51: This is my primary concern. Does linking with ONS actually confirm survival status or does it solely confirm death? I understand that certified deaths are registered on ONS within 5 days, but what is the process and timeline for obtaining a death certificate in the UK? In some jurisdictions, it is a legal requirement that a death be registered within one year but I don’t believe that prosecution for non-certification is common. What about cases that are being investigated by the coroner? Or cases where there is no next-of-kin? Is there less chance of ‘efficient’ certification of death where English is the family’s second language, or where the deceased does not leave a will/estate? Are any of these scenarios relevant in the UK context? If they are, the comprehensiveness and accuracy of the ONS may need to be considered in the limitations section.

Response: Thank you for raising these points. Linking with ONS does technically only confirm death and an absence of death being recorded cannot guarantee that the patient is alive, just that the death has not been registered.

The process in England and Wales is that, following certification (usually by a medical practitioner), there is a legal requirement for deaths to be registered with the registrar and this is meant to be within 5 days. ONS data shows that for 2011, 77.7% of deaths were registered within 5 days, 94% of deaths were registered within one month and 95.4% of deaths were registered within 3 months of the date of death.

There may of course be delays to the registration of a death mainly as a result of referral to the coroner. However, most cases that go to the coroner do not require a full inquest with ONS data showing that for 2014-2015 only 6.1% of deaths required a coroner’s inquest. Furthermore, data from ONS shows that the average time for completion of a coroner’s inquest was 24 weeks for 2014-2015.

It is plausible that there could be a delay to the registration of a death where there is no next-of-kin, although the law states that in this scenario the death should then be registered by (in order of priority) a relative living in the district where the death took place, anyone else present at the death, an owner or occupier of the building where the death took place and who was aware of the death, or the person arranging the funeral (but not the funeral director).

It is also plausible that may be less chance of an ‘efficient’ registration of death where English is the family’s second language. However, the deceased not leaving a will/estate should not impact on the registration of a death in England and Wales.

To calculate 30-day survival for the sample we needed confirmation of registration of deaths (or absence of registration of deaths) up until 31st January 2015 and the data was provided by NHS Digital in March 2016 (for the automatic matched cases) and June 2016 (for the manual matched cases) so at least 13 months after the last deaths would have been expected to be registered if there were no delays.

Based on this information it is likely that the ONS mortality data provides an accurate reflection of death/30-day survival status within the linked sample, but with the caveat that there is always the chance that some deaths were still not registered at the time of linkage.

As such, we have added more text in the methods under ‘ONS date of death data’ to provide more information on the process regarding registration of deaths in England and Wales and we have added further text in the discussion to note that the absence of registered death could mean delay in registration of a death but it is likely that ONS mortality data provided an accurate reflection of 30-day survival status in this study.

Comment: Pg. 5/32 Line 6: As above, is it safe to assume ‘alive’?

Response: Question answered above.

Comment: Pg. 13/32 Line 7: As above, can 30-day survival be assumed from NOT being on the ONS?

Response: Question answered above.

Comment: Pg. 13/32 Lines 33-58: I am not sure if the detailed comparison of patient groups adds to your ability to fulfil the study aims. I think it is of most interest to know whether there is a significant difference in the % survival and % missing survival status between the matched and unmatched group. I think that data on other variables and secondary outcomes detracts from the main result of interest. Perhaps a simple chi square of % survival and %missing survival status by matched/unmatched would provide the relevant information?

Response: We agree that Table 5 does not enhance the paper and have deleted it, as well as deleting related text from the methods, results and discussion.

With regards to a comparison of known and unknown survival status between the unmatched and matched groups, a Fisher’s exact test is significant ($p < .05$) indicating the difference in known survival status (30-day survival) between the matched and unmatched groups; however, on reflection we do not feel that this adds anything above what is already shown in Table 4 which shows the overall improvement in the OHCAO data.

Comment: Pg. 15/32 Table 5: As above, I’m not convinced that the level of detail provided adds to fulfilling your study aims. Suggest:
Columns: Matched Unmatched Sig
Row 1: % Survived
Row 2: % missing survival status

Response: Thank you – answered above.

Comment: Pg. 17/32 Line 40: For what proportion of overall cases do you have postcodes?

Response: We have added an extra row to Table 1 to show the percentage of available demographic data points available in all 28,729 2014 OHCAO cases. We have added the following text in the preceding paragraph:
“The percentage of each available demographic data point in the random sample of 3120 cases was similar to the percentage of each available demographic data point in all 28,729 cases for 2014 (Table 1).”

Comment: Pg. 18/32 Lines 39-46: The meaning of the sentence beginning “Whilst a study…” is not clear to me

Response: The sentence before has been amended to put this sentence into better context. We are providing examples of international research to illustrate the importance of good quality data to ensure successful data linkage. Specifically the Danish experience which is able to link 100% of OHCAO patients due to 100% provision of a unique patient identifier. In comparison the Mumma et al study shows very poor data linkage results when there is no unique patient identifier and the demographic data is of not high quality. This is supported by the results of our study which show the importance of having a unique patient identifier (NHS number) and/or 3 to 4 other demographic variables. The complete text now states:

“Our findings support previous research showing that the ability to successfully link international OHCA databases to outcome data is dependent on the provision and completeness of patient identifiers. For example, the Danish Cardiac Arrest Registry was able to link to the Danish Civil Registration System to confirm 30-day survival for 100% of OHCA patients due to 100% provision of a unique Civil Registration Number.20 Conversely, a study from the United States showed limited feasibility for linking OHCA patients to longitudinal outcomes when there was no unique patient identifiers available and there was variability in completeness of patient demographic data, resulting in a linkage rate of only 34.2%.33”

Comment: Pg. 19/32 Lines 20-26: As above, it is not clear to me what analysis of % bystander CPR, % shockable rhythms etc. is adding to your results.

Response: As above text relating to Table 5 has now been deleted.

Comment: Pg. 19/32 Line 36: Again, can you confirm that patients were alive at the time of data linkage or is it possible that some deaths were not registered?

Response: Thank you - question answered above.

Comment: Pg. 20/32 Line 12: As above, does linkage ‘confirm’ 30-day survival status? Is any further validation need to confirm survival?

Response: Thank you - question answered above.

Reviewer: 2

Reviewer Name: Jan Wnent, MD
Institution and Country: Deputy Director, Institute for Emergency Medicine, University Hospital Schleswig-Holstein, Kiel, Germany

Comment: On page 3 line 25: please refer to the EuReCa ONE Study.

Response: The introduction has been amended based on reviewer comments and does now include a reference to the EuReCa ONE study.

Comment: On page 4 in methods setting: please add a short description of the OHCAO project.

Response: A short description is given of the OHCAO project at the end of the introduction and a very brief description of the OHCAO project has now been added under methods ‘setting’. The text states:

“The OHCAO project established a national UK OHCA registry to collect process and outcome data to facilitate OHCA research and quality improvement. Detailed information about the OHCAO project is available in the study protocol.21”

Comment: Table 5: Why are you reporting "not recorded", "missing" or "others" to the first monitored rhythm. Is it not a mandatory data point in the OHCAO dataset? Is it possible to specify these points and re-calculate this into the asystole, PEA and VF group?

Response: Table 5 has been deleted as we are in agreement with Reviewer 1 that this table did not enhance the paper.

Comment: Please add a limitation section to the manuscript and discuss the limitations of your study

Response: A limitations section has been added to the end of the discussion discussing the limitations of the study.

Reviewer: 3
Reviewer Name: Helle Søholm
Institution and Country: Copenhagen University Hospital, Rigshospitalet, Denmark

General comments
In general the manuscript is very focused on the UK data, which could be reduced and instead a more international angle could be enhanced to make the manuscript more interesting for the international/non-UK reader. For example a reference to the Danish registries (http://genoplivning.dk/wp-content/uploads/2016/05/Rapport-fra-Dansk-Hjertestopregister-2001-2014.pdf) and the national registration of all citizens, which enables outcome data on all citizens (Wissenberg et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest).

Response: Thank you. The introduction has been amended to give more of an international context.

Specific comments
Abstract:
The abstract is well-written, however I find the section “design and setting” a bit hard to follow. The sentence “Of these, a randomly selected sample of 3120 cases were securely transferred to the NHS Digital list cleaning service to be matched using OHCAO patient demographic data to return previously missing data and provide Office for National Statistics (ONS) mortality data.” should be easier to read for the non-UK reader. I do not know what the “NHS Digital list cleaning service” is for example. Why was a random sample selected? Please explain.

Design and setting and been amended. NHS Digital list cleaning service has been amended to “NHS Digital” and a brief description of NHS Digital has also been added to the abstract. Whilst we are constrained by the word limit in the abstract more detail has been added to the methods.

Response: Text in the abstract now states:

“Data linkage was carried out using a data linkage service provided by NHS Digital, a national provider of health-related data.”

“To assess data linkage feasibility a random sample of 3120 cases was selected.”

Text in the methods under ‘OHCAO data linkage to ONS mortality data’ now states:

“NHS Digital is the national provider of data relating to health and social care in England. OHCAO used the NHS Digital list cleaning and patient status service. The list cleaning service was used to validate submitted demographic data to ensure accuracy and improve data linkage outcomes. Validation was achieved by NHS Digital matching submitted demographic variables to NHS patient demographic data held on the PDS database. The PDS database is a national electronic database containing NHS patient demographic information, including NHS number, name and address. For each matched case NHS Digital were asked to provide OHCAO with the following patient demographic information: NHS number, surname, forename, and home postcode. These data were used to improve the percentage of missing data for these variables in the OHCAO sample.”

The text in the methods has also been amended to explain that a random sample was chosen to reduce costs associated with data linkage as the primary aim of this study was to assess initial feasibility of data linkage. Random sampling was chosen to avoid selection bias. Table 1 in the methods has also been amended to show the percentage of available demographic data points available in all 28,729 2014 OHCAO cases compared with the 10% random sample and showing that the percentage of each available demographic data point in the random sample of 3120 cases was similar to the percentage of each available demographic data point in all 28,729 cases for 2014. The text in the methods under ‘OHCAO data sample’ now states:

“To assess feasibility whilst minimising costs associated with data linkage, the analysis presented here represents a 10.9% sample of the 2014 OHCAO data, comprising 3120 OHCA patients. To avoid selection bias the sample was selected using simple random sampling and stratified by ambulance service.”

Introduction:
The introduction is fairly long and could be improved by saving some of the discussion points for the discussion section and limiting the introduction to a background and introduction to the subject – OHCA, survival and difficulties with international comparisons of outcome data. For example outcome data from different countries could be highlighted.

Response: Thank you. We agree and the introduction has been amended to make it more concise.

Methods:
“Setting “
Comment: Please include the percentage of coverage of the UK population.

Response: Text added stating:
... “equating to 99.7% of the England population and 83.9% of the UK population.23”

Comment: Please indicate the incidence of OHCA in the current study (for international comparison).

Response: Text added stating:
... “(an incidence rate of 53.2 per 100,000 of the English population).22”

Comment: Please indicate the number of each exclusion criteria: “presence of a do not attempt resuscitation order (n =, %)”, “signs incompatible with life (n =, %)” and “where resuscitation attempts would be futile (n =, %)”

Response: Text amended to state:
“This figure was reached after excluding individuals who achieved ROSC before arrival of EMS (n=1711) and where resuscitation was not attempted as per national guidelines due to the presence of a do not attempt resuscitation order (n=387), or signs incompatible with life or where resuscitation attempts would be futile (n=5403).”

“Aims & Objectives”
Comment: Please indicate why not all OHCA-patients were matched

Response: As above the text in the methods has been amended to explain that a random sample was chosen to reduce costs associated with data linkage as the primary aim of this study was to assess initial feasibility of data linkage.

“OHCA data collection”
Please indicate how precise the “EMS personnel identified OHCAs by searching case records for confirmed arrests”, what is the sensitivity and specificity of the search?

The ambulance services are asked to submit cases that match the OHCAO inclusion/exclusion criteria. However, methods for case ascertainment are not standardised across the participating services.
The text has been amended to provide more detail:
“Each ambulance service has their own methods for OHCA case ascertainment e.g. electronic searches of patient report form databases for diagnostic codes indicating cardiac arrest. A trained member of the ambulance service clinical audit team entered eligible cases into a cardiac arrest database, followed by data cleaning and verification processes. Survival to hospital discharge data was collected directly from hospitals by the clinical audit team if data sharing protocols were in place. Each ambulance service uploaded their data via a secure server to the OHCAO registry which is stored at the University of Warwick.”

Work is currently ongoing by a member of the team to evaluate current strategies for case ascertainment for OHCA in UK ambulance services which will report on the sensitivity and specificity of the different search methods.

Results:
“Comparison of patient groups”
Comment: Line 37: Please be more precise “died” after 30 days or during hospital admission?

Response: This paragraph has been deleted as the text related specifically to Table 5 which has now been deleted.

Comment: Line 50: Please indicate the actual numbers instead of stating “Additionally the bystander CPR rate was at least 10% higher ”

Response: This paragraph has been deleted as the text related specifically to Table 5 which has now been deleted.

Comment: Line 56: “However those not matched in the survival to hospital discharge groups showed comparatively higher rates of defibrillator usage (20.0% vs. 5.7%) with lower rates of shockable rhythms (32.0% vs. 61.0%) compared to the matched group. However these figures are based on very few patients.” Why is the numbers based on very few patients? And why was not all patients matched, when there is differences in the pre-hospital factors known to provide important information with regards to survival?

Response: This paragraph has been deleted as the text related specifically to Table 5 which has now been deleted.

Comment: Figure 1: Please provide the reason for not manually submitting the 430 patients in the figure or as a footnote.

Response: There was a footnote under Figure 1 on page 9. The text in the footnote has been amended to make clearer. It now states:
“* Cases not resubmitted due to insufficient OHCAO data points to enable NHS Digital to match OHCAO cases to the NHS PDS database.”
A small amendment is made in the main text on page 8 to clarify that cases were not “resubmitted” for manual matching. It previously stated that cases were not submitted for manual matching.

Comment: Table 5: Please indicate p-values or a * when there is significant differences between matched and unmatched patients. Age can be provided only as median (IQR).

Response: Table 5 has been deleted as we are in agreement with Reviewer 1 that this table did not enhance the paper.

Comment: Please provide data for patients not selected for matching – is the sample truly random?

Response: We have added an extra row to Table 1 to show the percentage of available demographic data points available in all 28,729 2014 OHCAO cases. We have added the following text in the preceding paragraph:
“The percentage of each available demographic data point in the random sample of 3120 cases was similar to the percentage of each available demographic data point in all 28,729 cases for 2014 (Table 1).”

Comment: With regards to survival calculations (table 4) after matching please provide best and worst case scenarios – is all patients with missing 30 day survival was alive and dead, respectively.

Response: Thank you. The following text has been added to the discussion under limitations:
“Secondly, following linkage 30-day survival status remained unknown for 264 (8.5%) cases. Data not missing completely at random can bias results.40 For example, if those 264 patients survived to 30 days the overall 30-day survival rate would be 17.8% (584 cases) instead of 9.3% (290 cases).”

Discussion:
Comment: The first section of the discussion repeats too many details of the results. Please provide an overview of the found results of the current study.

Response:The first paragraph has been edited to provide a more concise overview of the study results.

Comment: Please explain “multiple deprivation index effect”

The paragraph has been amended to explain better the potential benefit of receiving further postcodes.

Response: The term “multiple deprivation index” may be more easily understood within the UK so it has been changed to “social deprivation”.

Comment: With regards to “The variability of cardiac arrest survival is well documented.” please be more specific. The reference refers to an editorial covering UK circumstances. The survival may not vary but so does the registries. Please discuss in further detail and provide international references as well.

Response: We have added text to make it clear that the first sentence is referring specifically to variability between ambulance services in England. The lead author has added this paragraph to highlight that other methods (such as core outcome sets) have been developed to tackle the issue of data collection variability and missing data. With regards to international registries the paragraph refers to the review by Nishiyama et al (2014: Resuscitation 85: 1599-1609) showing that there are differences in measurement of data relating to OHCA across international registries.

Comment: “The best data point provided by ambulance services to identify cases is the NHS number.” add “in the UK”

Response: We have added “in the UK”

Comment: “These findings are in line with research showing that OHCA databases in different countries can successfully link OHCA patients to outcome databases where unique patient identifiers are readily available.12,13” The Danish reference is not correct in this setting. There is 100% availability of outcome data due to the unique civil registration number provided to all Danish citizens. Please discuss.

Response: Thank you. The sentence has been amended to make the point that in Denmark they have the ability to complete data linkage for 100% of OHCA patients as a result of the 100% provision of a unique patient identifier. This is in contrast to the UK experience.

“Our findings support previous research showing that the ability to successfully link international OHCA databases to outcome data is dependent on the provision and completeness of patient identifiers. For example, the Danish Cardiac Arrest Registry was able to link to the Danish Civil Registration System to confirm 30-day survival for 100% of OHCA patients due to 100% provision of a unique Civil Registration Number.20”

Comment: “Half (50.8%) of OHCAs with attempted resuscitation died with no ROSC at anytime while 37.9% achieved ROSC at anytime but were not discharged from hospital.” How many patients were found dead (with obvious signs of death) and were not attempted resuscitated?

Response: This paragraph has been deleted as the text related specifically to Table 5 which has now been deleted.

Please include a statistically discussion of acceptable missing data.
Comment: Please provide a more thorough discussion of the UK registries from the current study with international registries.

Response: We have added some text in the discussion under limitations which states:

“Firstly, only 868 (27.8%) cases had all 5 OHCAO data points, whilst 178 (5.7%) cases had missing data for all OHCAO data points. Missing data is an issue in OHCA registries,32 and improved data linkage in the OHCAO project is reliant on improved data capture of patient demographic data by ambulance services. Whilst NHS numbers were provided for only 989 (31.7%) OHCAO cases, one ambulance service provided NHS numbers for 100% of their cases. This suggests potential for the OHCAO project to work with ambulance services to increase provision of patient demographic data to improve data linkage.”

Reviewer: 4
Reviewer Name: Ben Beck
Institution and Country: Monash University, Australia

Comment: Page 2, line 8: The study does not “aim to establish the feasibility of producing a registry”; it is the supplementation of missing data. Please edit.

Response: Text amended to now state:
“This data linkage study is a sub-project of OHCAO. The aim was to establish the feasibility of linking OHCAO data to National Health Service (NHS) patient demographic data and Office for National Statistics (ONS) date of death data held on the NHS Personal Demographics Service (PDS) database to improve OHCAO demographic data quality and enable analysis of 30-day survival from OHCA.”

Comment: Page 2, line 56: The last dot point of ‘strengths and limitations’ needs clarification.

Response: Thank you. The last dot point has been amended to say:
“Improved data linkage is reliant on improved data capture of patient demographic data by ambulance services.”

Comment: Page 3, lines 12-15: Please separate this sentence as it is discussing two separate issues.

Response: This paragraph has been amended. The sentence now reads:
“This group suffers significant mortality and morbidity,3,4 and improving outcomes from OHCA remains a worldwide research priority.5”

Comment: Page 3, lines 17-24: I would like to see an expansion on the strengths and weaknesses of collecting survival to hospital discharge vs 30 day survival. What do other international registries use? Also, I’m not convinced that survival to hospital discharge is easier to collect than 30-day survival. Often 30 day survival is reliant on data linkage with national registries, but this is often easier than manual follow-up of patients (or medical records) to determine survival to hospital discharge.

Response: Thank you. The introduction has been amended to consider survival to discharge and 30-day survival in an international context. We agree with your point that survival to hospital discharge may not be easier to collect than 30-day survival (through data linkage). Text has been added to the introduction to make the point that ambulance services find it challenging to collect survival to discharge data directly from hospitals, and the updated Utstein guidelines recommend collecting either survival to hospital discharge or 30-day survival. It is also noted in the introduction that research indicates that most international registries can collect either of these survival outcomes. The discussion has also been amended to make the point that utilising data linkage to confirm survival status may be an alternative to ambulance services collecting survival to discharge data directly from hospitals.

Comment: Page 3, line 19: I'm not sure that "cultural differences" is the most appropriate term. Perhaps "differences in discharge practices"?

Response: The introduction has been amended based on reviewer comments and the term "cultural differences" has been removed.

Comment: Page 3, line 36: Please explain what "central records centres" are.

Response: The introduction has been amended based on reviewer comments and the term "central records centres" has been removed.

Comment: Page 3, line 38: And potentially varying capture rates.

Response: We agree. However, based on other reviewer comments this sentence has been removed from the introduction to make the introduction more concise.

Comment: Page 5, line 8: Please explain the "NHS Digital list cleaning service".

Response: Text has been added to the methods to better explain the NHS Digital list cleaning service which is now referred to throughout as "NHS Digital list cleaning and patient status service". The explanation is given in the methods section under 'OHCAO data linkage to ONS mortality data'. The text states:

"NHS Digital is the national provider of data relating to health and social care in England. OHCAO used the NHS Digital list cleaning and patient status service. The list cleaning service was used to validate submitted demographic data to ensure accuracy and improve data linkage outcomes. Validation was achieved by NHS Digital matching submitted demographic variables to NHS patient demographic data held on the PDS database. The PDS database is a national electronic database containing NHS patient demographic information, including NHS number, name and address. For each matched case NHS Digital were asked to provide OHCAO with the following patient demographic information: NHS number, surname, forename, and home postcode. These data were used to improve the percentage of missing data for these variables in the OHCAO sample."

Comment: Page 5, line 12: What is meant by this "success rate"? Is this compared to ambulance records?

Response: The success rate is the match rate for the different combinations of OHCAO patient demographic variables to enable linkage to the NHS PDS database (as shown in Table 2 of the results). The text has been amended to make this clearer:

"Assess the match rate of combinations of OHCAO patient demographic variables in the sample (NHS number, surname, forename, date of birth (DOB), and home postcode) for linking to the NHS PDS database through NHS Digital list cleaning"

Comment: Page 6, line 19: Validation "was"….

Response: Thank you. We have corrected the text.

Comment: Page 7, line 33: How is this date of death/discharge collected in the OHCAO? I would like to see greater explanation of data collection methods in the OHCAO.

Response: Date of death/discharge is collected by the ambulance services. The ambulance service can confirm the date of death if the patient is not transferred to hospital alive. Where the patient is transferred to hospital the ambulance service follows up with the hospital directly (if a data sharing agreement is in place) to confirm survival to discharge status – this may also include a date of death/discharge. A better explanation is given on OHCAO data collection methods under 'OHCAO project data collection':

"Core and supplemental Utstein variables were collected encompassing demographic, system, process and outcome data.16 Each ambulance service has their own methods for OHCA case ascertainment e.g. electronic searches of patient report form databases for diagnostic codes indicating cardiac arrest. A trained member of the ambulance service clinical audit team entered eligible cases into a cardiac arrest database, followed by data cleaning and verification processes. Survival to hospital discharge data was collected directly from hospitals by the clinical audit team if data sharing protocols were in place. Each ambulance service uploaded their data via a secure server to the OHCAO registry which is stored at the University of Warwick."

Comment: Page 8, line 12: Should "ROSC at anytime" actually be "ROSC in the prehospital setting"?

Response: Based on other reviewer comments this paragraph has been removed as we agree with another reviewer that table 5 does not enhance the paper.

Comment: Page 8, line 23: Place the last sentence of this paragraph earlier to explain why you are comparing these three groups.

Response: Based on other reviewer comments this paragraph has been removed as we agree with another reviewer that table 5 does not enhance the paper.

Comment: Page 9, line 55: Just to confirm – there were no errors with the originally recorded NHS number? Ie. These were all correct linkages?

Response: No – out of 989 NHS numbers in the sample there were 14 (1.4%) NHS numbers where the NHS number received back from NHS digital differed slightly (i.e. the OHCAO NHS number was corrected). Of these, 11 also had OHCAO surname+forename+DOB+postcode and 3 also had OHCAO surname+forename+DOB.

Text has been added stating that:
"A further strength is that NHS Digital used both deterministic and probabilistic data linkage methods; they have different strengths and utilising both methods may enhance linkage performance.37 Deterministic linkage methods have greater specificity but require exact matches between records, whilst probabilistic data linkage has greater sensitivity, working better with poorer quality data as it allows imperfect matches between records.27 For example, the returned demographic data for the linked cases showed that 14 OHCAO cases with between 4 and 5 data points were linked despite having an erroneous NHS number. This allowed correction of the inaccurate NHS number in the OHCAO sample."

Comment: Page 17, line 40: This last sentence does not make sense. Additionally, how does having the postcode assist in the determination of arrests that occur at home vs those in public places? It may aid in determining whether an arrest occurs outside of the primary residence, but it may still occur in a 'home'.

Response: Thank you, we agree. The paragraph has been amended to explain better the potential benefit of receiving further postcodes and now states:
“NHS Digital also provided postcodes for a further 942 (30.2%) cases, which increases the potential to examine the influence of neighbourhood characteristics, such as population density and social deprivation, on OHCA incidence, whether an event is witnessed, and if they receive bystander CPR.35,36”

Going forwards the OHCAO project is looking to collect additional location data based on the Ustein definitions so we can examine better the effect of an OHCA occurring in the home vs in a public place.

Comment: Discussion: I’d like to see some additional commentary around the reliance of data capture in the prehospital setting with respect to the linkage methods outlined in this study. The only way that these linkage methods will improve is through improved data capture in the prehospital setting (and there are obvious challenges with this).

Response: We have added some text in the discussion under limitations which states:

“This study had several limitations. Firstly, only 868 (27.8%) cases had all 5 OHCAO data points, whilst 178 (5.7%) cases had missing data for all OHCAO data points. Missing data is an issue in OHCA registries,32 and improved data linkage in the OHCAO project is reliant on improved data capture of patient demographic data by ambulance services. Whilst NHS numbers were provided for only 989 (31.7%) OHCAO cases, one ambulance service provided NHS numbers for 100% of their cases. This suggests potential for the OHCAO project to work with ambulance services to increase provision of patient demographic data to improve data linkage.”

Please also note that the following further additions have been made to the manuscript:

• In the methods section under ‘OHCAO data linkage to ONS mortality data’, text has been added to briefly explain deterministic and probabilistic data linkage methods.

• In the results section, data reported under ‘Accuracy of OHCAO date of death data’ has been corrected following a review of the data. The main correction is the number of cases where a date of death was provided by the ambulance service but was not confirmed by a corresponding ONS date of death was 7 (0.6%) rather than 64 (5.4%). The text has also been amended in the discussion section to reflect this correction.

The table reporting this data has been added under the text (Table 5: Comparison of date of death confirmed by OHCAO and ONS data). This table was previously in the supplementary material but has been added to the main manuscript following deletion of ‘Table 5: Comparison of matched and unmatched OHCA case characteristics by outcome group’.

Table 5 has had an extra column added to account for unmatched cases where ‘ONS confirmed survival status’ is ‘no’ i.e. ONS mortality data could not confirm survival status if the cases was not linked.

• In the discussion the text has been expanded to note the potential for utilising data linkage to follow OHCA patients longitudinally or to investigate post-resuscitation care via linkage to existing routinely collected hospital data sources (such as HES and ICNARC)

• In the discussion the text has been expanded to note the strengths of this study (in addition to the addition of a limitations section).

• The manuscript has also undergone a further general edit to reduce the word count to <4000 words.

VERSION 2 – REVIEW

REVIEWER	Siobhán Masterson Discipline of General Practice School of Medicine National University of Ireland Galway Ireland None declared but just to note that I am a colleague of Prof. Perkins and Mr. Booth on the EuReCa project
REVIEW RETURNED	08-Aug-2017

GENERAL COMMENTS	Thank you for comprehensively addressing my comments. My primary concern was whether absence from the UK ONS is absolute confirmation that a person is still alive after 30 days. You have provided a lot of evidence for the comprehensiveness of the UK ONS, but I still think that it is not possible to state that it is 100% comprehensive, even after 13 months. I may be underestimating the ONS, but from my understanding of your explanation, it is plausible that a death may not be registered. With this in mind, I suggest you consider mentioning this issue in your limitations section. You also highlight the Danish scenario where 100% of OHCA patients can be linked due to 100% provision of a patient identifier, and the value of unique identifiers in data linkage. I fully agree with this. I am not sure however, that all unique identifiers are equally 'powerful'. I would suggest the Danish identifier and UK NHS identifier are not quite the same, as the Danish identifier is a universal number, used for banking, social services etc. It MAY be appropriate to highlight this, as I suspect that the Scandinavian universal number system is more established and embedded than the UK system. I may be underestimating the 'reach' of the UK NHS identifier, and am very happy to stand corrected on this observation.

REVIEWER	Jan Wnent,MD University Medical Center Schleswig-Holstein, Institute for Emergency Medicine, Kiel, Germany
REVIEW RETURNED	23-Aug-2017

GENERAL COMMENTS	Dear colleagues, thank you very much for your work. I find all my comments addresed and have no further amendments.

REVIEWER	Ben Beck Monash University, Australia
REVIEW RETURNED	16-Aug-2017

GENERAL COMMENTS	Authors, thank you for your detailed responses to all reviewers. I am happy to now recommend this manuscript for publication.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Siobhán Masterson

Please leave your comments for the authors below

Comment:Thank you for comprehensively addressing my comments. My primary concern was whether absence from the UK ONS is absolute confirmation that a person is still alive after 30 days. You have provided a lot of evidence for the comprehensiveness of the UK ONS, but I still think that it is not possible to state that it is 100% comprehensive, even after 13 months. I may be underestimating the ONS, but from my understanding of your explanation, it is plausible that a death may not be registered. With this in mind, I suggest you consider mentioning this issue in your limitations section.

Response: Thank you. We have moved the text from after "Finally, successful data linkage enabled access to high quality national date of death data from ONS that is subject to rigorous data quality and validation processes.28" on page 16/17, and have moved this to the limitations section. This text in the limitations section now states:

"Thirdly, where no date of death was provided, cases were categorised as alive. However, absence of recorded death may mean registration of death has been delayed e.g. due to a coroner's inquest. Although it should also be noted that NHS Digital did not commence data linkage until >12 months (March 2016) after the date (31st January 2015) where 30-day survival could be calculated for patients in the sample suffering an OHCA on 31st December 2014. ONS data for 2014-2015 shows that only 6.1% of deaths in England and Wales required a coroner's inquest28 and the average time of an inquest was 24 weeks.39,40 Furthermore, ONS data from 2011 reports that overall 94% of deaths were registered within one month.29"

Comment: You also highlight the Danish scenario where 100% of OHCA patients can be linked due to 100% provision of a patient identifier, and the value of unique identifiers in data linkage. I fully agree with this. I am not sure however, that all unique identifiers are equally 'powerful'. I would suggest the Danish identifier and UK NHS identifier are not quite the same, as the Danish identifier is a universal number, used for banking, social services etc. It MAY be appropriate to highlight this, as I suspect that the Scandinavian universal number system is more established and embedded than the UK system. I may be underestimating the 'reach' of the UK NHS identifier, and am very happy to stand corrected on this observation.

Response: Thank you. We do agree that there is a difference between the Danish Civil Registration Number and the England and Wales NHS number in terms of their universal role in society. However, the NHS number should be fairly universal as it has been allocated to:
• Anyone who is, or has ever been, registered with a GP practice in England, Wales or the Isle of Man
• Anyone born in England, Wales or the Isle of Man since October 2002
• Additionally, anyone who has received NHS treatment in England, Wales or the Isle of Man is likely to have an NHS number.
As such, there should be very few people without an NHS number.
However, the point is more that both are unique patient identifiers and the Danish example shows that a unique patient identifier, if 100% available, can result in 100% data linkage. Our study also indicates that the NHS number (as a unique patient identifier) results in successful data linkage. The main difference in our study being the much more limited availability of the NHS number to the EMS in the pre-hospital setting, although this issue is also discussed in the study limitations section. As such, we have made no further changes to this paragraph.

VERSION 3 – REVIEW

REVIEWER	Siobhan Masterson Discipline of General Practice National University of Ireland Galway Ireland None declared but just to note that I am a colleague of Prof. Perkins and Mr. Booth on the EuReCa project
REVIEW RETURNED	14-Sep-2017

GENERAL COMMENTS	Thank you, you have sufficiently addressed my final comments