

### PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Benefits of adding a physician-staffed ambulance to bystander witnessed out-of-hospital cardiac arrest. A Community-Based Observational Study in Niigata, Japan
<b>AUTHORS</b>	Sato, Nobuhiro; Matsuyama, Tasuku; Akazawa, Kouhei; Nakazawa, Kyoko; Hirose, Yasuo

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Mohamud Daya Oregon Health & Science University
<b>REVIEW RETURNED</b>	06-Aug-2019

<b>GENERAL COMMENTS</b>	<p>Interesting paper that looks at benefits from having a physician staffed vehicle respond to OHCA calls. The analysis is restricted to bystander witnessed cardiac arrests which is helpful since this group has the highest survival rate. It would be helpful to know if the physician vehicle is available 24-7 why it was not dispatched on the 757 cases where only an EMS staffed vehicle was sent. (perhaps as a supplemental table if this info is available) It is also not clear if you send both a physician staffed and EMS staffed vehicles to OHCA calls or do that based on availability. Please clarify the response determinants in a flow chart if possible. You also noted that these were presumed medical OHCA at times and at other times state that the cause was cardiac. Please try to use the word presumed throughout. You also use word cardiac but do not define how this was determined or defined since it's accuracy is questionable based on some studies. Please see my additional comments in the attachment, This work is challenging many of our normal assumptions as to what works and what does not. It is also important to note however that in countries like the US and Canada, survival rates higher than Nigate are reported with EMS only responses sine the paramedics and EMT;s are allowed to do much more than in Japan. So perhaps it is not that physician staffing is better, but that the better outcome is related to the quality of care provided by EMS only units.</p> <p>Line 27: 800, 000          Line 28: bystander witnessed          Line 29: presumed medical etiology          Line 46: are needed in Nigata (since that is where the study was done)          Line 57: consider adding physician as another keyword          Line 77: my understanding is that they are allowed to intubate the teaches as well as give adrenaline but only after calling a physician...this creates an added delay for EMS drive care.          Please clarify.</p>
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	<p>Line 85: not sure what EMSs is referring to...please spell this out once before abbreviating</p> <p>Line 92: bystander-witnessed</p> <p>Line 109: not sure when you have to comment on “not allowed prehospital TOR”. Please clarify?</p> <p>Line 110: what is the 2-tier? Fire FR with EMS as the 2nd tier (regular units or MD staffed?)</p> <p>Line 123: bystander witnessed events only or all witnessed cases?</p> <p>Line 156: how was cardiac vs. noncardiac determined? Has this process been validated? Or are these presumed cardiac vs. non-cardiac, what is the difference between presumed medical vs. presumed cardiac?</p> <p>Line 159: this is traditionally referred to as scene time, in EMS we speak of response, scene and transport times</p> <p>Line 178: a greater number of victims had received dispatch CPR instructions</p> <p>Table 1: line 37 – the overall time on scene seems similar but transport time is different. Do you have any idea why this may be? Did physician staffed cases go mainly to one hospital or both hospitals?</p> <p>Tables: suggest you bold the p values that are statistically significant to make it easier to read</p> <p>Table 3: interesting to see that bystander CPR does not affect outcome and that only age and initial rhythm are predictive in your MV model, any ideas why this may be the case since bystander CPR is supposed to double survival rates based on historical data.</p> <p>Line 226: This seems very to a bit of a stretch that physicians can provide better quality chest compressions than EMS. If physician staffed ambulances used a stay and play approach then this should be reflected in longer scene times for this group which is not the case.</p> <p>Line 244 – I am not sure that I agree with ethical concerns, the baseline differences between groups suggest that the findings you see may all be related to an unmeasured confounder. Given the expense of a physician staffed unit, a RCT would seem reasonable to see if it is worth the ROI.</p> <p>Line 264 – not sure you can say selection bias was minimized given that you only looked at a small portion of the OHCA in your community (bystander witnessed cases)</p> <p>Your small sample size is also an important limitation to mention,</p> <p>Line 270 – in Nigata</p>
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<b>REVIEWER</b>	Søren Mikkelsen, Professor, Consultant, MD, PhD The Prehospital Research Unit, Region of Southern Denmark Odense University Hospital DK 5000 Odense C Denmark
<b>REVIEW RETURNED</b>	18-Aug-2019

<b>GENERAL COMMENTS</b>	<p>Comments regarding the manuscript “The Efficacy of Physician-Staffed Ambulance Services for Out-of-Hospital Cardiac Arrest: A Community-Based Observational Study” by Sato et al.</p> <p>Thank You for the opportunity to assess this interesting manuscript.</p> <p>The paper reports a register based study in which the authors study aimed to assess the effectiveness of physician-staffed ambulance services by comparing survival following patients with cardiac arrest treated by a prehospital physician with patients with</p>
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	<p>cardiac arrest treated without the presence of a physician – that is - standard emergency medical care.</p> <p>The authors report that among adults with out-of-hospital cardiac arrest, physician-staffed ambulance services were associated with significantly greater favourable neurological outcomes than when only standard emergency medical services were employed.</p> <p>The authors report that strengths of the study include the use of a population-based registry and a well-established ambulance service.</p> <p>One reported weakness of the study is the lack of adjustments concerning in-hospital or post-resuscitation care.</p> <p>The authors applied logistical regression analysis taking the following variables into consideration:  Age dichotomised into (18–74 years, ≥75 years), sex (male, female), cause of cardiac arrest (cardiac, noncardiac), first documented rhythm (shockable or non-shockable), use of public-access automated external defibrillator, presence of bystander-initiated CPR. Furthermore, treatments administered was included into the analysis: Intravenous fluids and adrenaline administration and/or advanced airway management. Finally, the EMS time spent at the scene was incorporated into the analysis</p> <p>The authors did not consider pre-existing illness in the patients. Response time (reported as “Time from call to contact with patient by EMS) was registered but apparently had not been entered into the analysis.</p> <p>Results:  The authors report that the presence of a physician-manned ambulance was associated with significantly greater neurological outcome than the presence of standard care EMS.</p> <p>General comments:  The results are obtained in a population that is serviced by two tertiary care hospitals. One must assume that there is no difference in the post-resuscitation care in these two hospitals. Otherwise it must be considered a major methodological weakness that no post-resuscitation care markers are included in the regression analysis.</p> <p>The authors should comment on that.  Apparently, the two groups differed: The patients in whom there was a physician involved were younger, a greater number of dispatcher instructions had been provided, more patients had a shockable rhythm at first rhythm check, more patients received adrenaline administration, and the time from departure from the scene to the hospital was longer. This reviewer fully appreciate that adjustments have been made. However, the paper would benefit from some form of comments regarding the apparent difference between the two groups. Who decides when to dispatch the whole set of prehospital providers? Is that decision influenced by something that might skew the population (it certainly appears so). I am not quite convinced that the authors are absolutely correct when they state that selection bias was minimised (Page 17, line 264). Can the authors insert some comments regarding this question?</p> <p>The influence of response time of the ordinary EMS on survival following cardiac arrest is probably relevant.  It is possible that the response time of a rapid response unit manned by a physician and dispatched together with an ordinary ambulance has no influence on mortality (Mikkelsen s, et al BMJ Open 2017;7:e014383.) I still find it peculiar why response time has not been included in the analyses. As it appears from studying</p>
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	<p>Table 1, there is indeed a difference in response times between the two groups. I feel that including response times as a variable would have been more relevant than including on-scene time as variable. On-scene time and some of the other variables analysed seems to me to be interdependable: For example has intubation of the patient previously been shown to prolong on-scene time. (Intubation of the patient prolongs the on-scene tim (Fok PT, et al. Prehosp Disaster Med. 2019 Jun;34(3):317-321. doi: 10.1017/S1049023X19004394.)</p> <p>Specific comments:</p> <p>A possible error occurs in page 3, line 49. Apparently a denominator is missing. Is this “the first”, “the second” or “the third” study or is it “a” study? It is not “the” study...</p> <p>I fail to understand the meaning of the sentence on page 6, lines 108-110: “bystander-witnessed shockable-rhythm cardiac arrest in Niigata City was 32.4%, which was higher than the national rate of 20.8%, although EMS personnel in Japan are not legally permitted to terminate resuscitation.” What are the authors trying to convey with this sentence?</p> <p>There is another sentence that to this reviewer, at least, requires some clarification: page 17, lines 259 to 261: “...excluded OHCA occurring in long-term care facilities where physician-staffed ambulances are frequently cancelled because of the low probability of a favourable outcome.” Does this imply that EMS personnel routinely may cancel the physician if the EMT considers a case a “low reward-case”? If this is the case, this procedure surely must influence the results warranting a comment. There already seems to be a difference between the two groups as the patients in the physician-treated group are younger and to a greater extent display shockable rhythm. This undoubtedly influences the results. If termination or resuscitation attempts takes place</p> <p>Conclusion:</p> <p>This is an interesting work which has some flaws: Although the authors perform a logistical regression analysis adjusting for several factors, to this reviewer it seems that the two populations compared are far from identical. This jeopardises the conclusions. Furthermore, some interesting elements are not included as variables: Pre-existing illness would have been very interesting to have entered into the analysis, either in the form of a comorbidity score or, at least, by addressing the potential for pre-existing known cardiac illness.</p>
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### VERSION 1 – AUTHOR RESPONSE

Response to Reviewer 1:

Interesting paper that looks at benefits from having a physician staffed vehicle respond to OHCA calls. The analysis is restricted to bystander witnessed cardiac arrests which is helpful since this group has the highest survival rate.

Thank you for your thorough reviews and suggestions. Our responses to your queries follow.

It would be helpful to know if the physician vehicle is available 24-7 why it was not dispatched on the 757 cases where only an EMS staffed vehicle was sent. (perhaps as a supplemental table if this info is available).

Unfortunately, we didn't know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases. The physician-staffed ambulance service is available all day when a dispatch centre receives an emergency call which is indicated for activating the physician-staffed ambulance service are as follows: bystander witnessed cardiac arrest, severe trauma, stroke, acute coronary syndrome, anaphylactic shock, or a mass casualty incident. However, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy. In addition, a physician-staffed ambulance service cannot be activated if it is being used to treat another patient, if it has been dispatched and is en route to another patient, or if the emergency call has not been recognised by a dispatch centre as a situation conforming to protocol. In these cases, only regular EMS is dispatched on the scene. Furthermore, in the case an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel when the ELSTs consider the low probability of favorable outcome. Therefore, we excluded OHCA's witnessed in long-term care facilities because they may have lower probability of favorable outcome and the dispatch of the physician vehicle for them was often canceled. Again, we did not catch up the exact reason for the undischarged cases. We agree with the Reviewer's comment, and we consider that selection bias might exist. We also consider that observational studies cannot avoid such selection bias, but we believe our findings provide important suggestions to perform randomized controlled trial in the future, which will reveal the actual impact of physician-staffed ambulance service.

Therefore, we have added the information and revised the sentences in the Method and Discussion as follows (Page 6 Line 119-122, Page 7 Line 142-145, Page 16-17 Line 262-280, Page 17 Line 290); "In addition, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy." "In the case an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel when the ELSTs don't need physician on the scene, e.g. the ELSTs consider the low probability of favorable outcome." "Apparently, the patients who did and did not have prehospital physician involvement differed in our study. Unfortunately, we didn't know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases. The physician-staffed ambulance service is available all day when a dispatch centre receives an emergency call which is indicated for activating the physician-staffed ambulance service are as follows: bystander witnessed cardiac arrest, severe trauma, stroke, acute coronary syndrome, anaphylactic shock, or a mass casualty incident. However, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy. In addition, a physician-staffed ambulance service cannot be activated if it is being used to treat another patient, if it has been dispatched and is en route to another patient, or if the emergency call has not been recognised by a dispatch centre as a situation conforming to protocol. In these cases, only regular EMS is dispatched on the scene. Furthermore, in the case an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel when the ELSTs consider the low probability of favorable outcome. Therefore, selection bias might exist. We also consider that observational studies cannot avoid such selection bias, but we believe our findings provide important suggestions to perform a randomized controlled trial in the future, which will reveal the actual impact of physician-staffed ambulance service." "Selection bias as mentioned above might exist."

It is also not clear if you send both a physician staffed and EMS staffed vehicles to OHCA calls or do that based on availability. Please clarify the response determinants in a flow chart if possible.

As mentioned above, unfortunately, we didn't know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases. Once a dispatch centre receives an emergency call, EMS personnel request both a physician-staffed ambulance from an emergency medical centre in Niigata City General Hospital and an ambulance from the nearest emergency medical centre if the patient is suspected to have bystander witnessed cardiac arrest, severe trauma, stroke, acute coronary syndrome, anaphylactic shock, or a mass casualty incident. However, a physician-staffed ambulance service cannot be activated if it is being used to treat another patient, if it has been dispatched and is en route to another patient, if the emergency call has not been recognised by a dispatch centre as a situation conforming to protocol, or if emergency department or intensive care unit is busy because a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital.

Therefore, we have added this information to the Method (Page 6 Line 119-122) and revised the Discussion as follows (Page 16-17 Line 262-280); "In addition, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy." "Apparently, the patients who did and did not have prehospital physician involvement differed in our study. Unfortunately, we didn't know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases. The physician-staffed ambulance service is available all day when a dispatch centre receives an emergency call which is indicated for activating the physician-staffed ambulance service are as follows: bystander witnessed cardiac arrest, severe trauma, stroke, acute coronary syndrome, anaphylactic shock, or a mass casualty incident. However, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy. In addition, a physician-staffed ambulance service cannot be activated if it is being used to treat another patient, if it has been dispatched and is en route to another patient, or if the emergency call has not been recognised by a dispatch centre as a situation conforming to protocol. In these cases, only regular EMS is dispatched on the scene. Furthermore, in the case an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel when the ELSTs consider the low probability of favorable outcome. Therefore, selection bias might exist. We also consider that observational studies cannot avoid such selection bias, but we believe our findings provide important suggestions to perform randomized controlled trial in the future, which will reveal the actual impact of physician-staffed ambulance service."

You also noted that these were presumed medical OHCA at times and at other times state that the cause was cardiac. Please try to use the word presumed throughout.

As suggested, we have used the word presumed (Page 5 Line 96, Page 9 Line 190, Figure 1).

You also use word cardiac but do not define how this was determined or defined since it's accuracy is questionable based on some studies.

We appreciate this helpful suggestion. Based on the international Utstein Style, an arrest was presumed to be of cardiac origin unless it was caused by cerebrovascular diseases, respiratory diseases, malignant tumours, external causes such as trauma, drowning, drug overdose, asphyxia, or any other non-cardiac causes. Diagnoses were made by the overseeing physician in collaboration with the EMS rescuers.

As suggested, we have clarified this definition and added the reference in the Methods as follows (Page 5 Line 97-101). “Based on the international Utstein Style, an arrest was presumed to be of cardiac origin unless it was caused by cerebrovascular diseases, respiratory diseases, malignant tumours, external causes such as trauma, drowning, drug overdose, asphyxia, or any other non-cardiac causes<sup>16</sup>. Diagnoses were made by the overseeing physician in collaboration with the EMS rescuers.”

We added the following new citations;

16. Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). *Circulation* 2004;110:3385-97.

Please see my additional comments in the attachment, This work is challenging many of our normal assumptions as to what works and what does not. It is also important to note however that in countries like the US and Canada, survival rates higher than Nigate are reported with EMS only responses since the paramedics and EMT;s are allowed to do much more than in Japan. So perhaps it is not that physician staffing is better, but that the better outcome is related to the quality of care provided by EMS only units.

We agree with the reviewer’s comment. As pointed, we have added this issue to the Discussion as follows (Page 16 Line 252-253); “Therefore, extending the procedure by ELSTs might also be a solution as the paramedics in countries like the United States or Canada are allowed.”

Line 27: 800, 000

We thank the reviewer for the careful review. We corrected the typo (Page 2 Line 27).

Line 28: bystander witnessed

We have added the word (Page 2 Line 28).

Line 29: presumed medical etiology

We have corrected the word (Page 2 Line 29).

Line 46: are needed in Nigata (since that is where the study was done)

We have removed this sentence because we revised the Discussion and the Conclusion.

Line 57: consider adding physician as another keyword

As suggested, we have added physician as another keyword (Page 3 Line 61).

Line 77: my understanding is that they are allowed to intubate the teaches as well as give adrenaline but only after calling a physician...this creates an added delay for EMS drive care. Please clarify.

We agree the reviewer’s comment. In our study, there was a significant decrease in the time from the call to adrenaline administration in patients with prehospital physician involvement compared with patients without prehospital physician involvement. The delay might influence to the outcome.

Therefore, we have added this information to the Methods and Discussion as follows (Page 7 Line 135-136 and Page 15-16 Line 250-252); “ELSTs are allowed to use advanced airways, intravenous line, and adrenaline administration only after calling a physician.” “Furthermore, ELSTs are allowed to administer adrenaline and intravenous fluid as well as intubate only after calling a physician, which might create an added delay for EMS drive care.

Line 85: not sure what EMSs is referring to...please spell this out once before abbreviating

As shown in the Introduction (Page 4, Line 66-67), EMSs is referring to emergency medical services.

Line 92: bystander-witnessed

We have corrected the word (Page 5 Line 95).

Line 109: not sure when you have to comment on “not allowed prehospital TOR”. Please clarify?

We have removed this sentence because it is not informative.

Line 110: what is the 2-tier? Fire FR with EMS as the 2<sup>nd</sup> tier (regular units or MD staffed?)

It is a physician-staffed ambulance as the 2<sup>nd</sup> tier only when it is indicated for the protocol of physician-staffed ambulance service.

We have added this information as follows (Page 6 Line 114-115); “only when it is indicated for the protocol of physician-staffed ambulance service”

Line 123: bystander witnessed events only or all witnessed cases?

We appreciate these helpful suggestions. They are bystander witnessed events.

We added bystander (Page 7 Line 137).

Line 156: how was cardiac vs. noncardiac determined? Has this process been validated? Or are these presumed cardiac vs. non-cardiac, what is the difference between presumed medical vs. presumed cardiac?

We thank the reviewer for these insightful comments. As mentioned above, based on the international Utstein Style, an arrest was presumed to be of cardiac origin unless it was caused by cerebrovascular diseases, respiratory diseases, malignant tumours, external causes such as trauma, drowning, drug overdose, asphyxia, or any other non-cardiac causes<sup>1</sup>. Diagnoses were made by the overseeing physician in collaboration with the EMS rescuers. Presumed medical includes presumed cardiac, cerebrovascular diseases, respiratory diseases, malignant tumours and unknown other medical cause. This is also based on the international Utstein Style.

Therefore, we have added this information to the Method as follows (Page 5 Line 97-101); “Based on the international Utstein Style, an arrest was presumed to be of cardiac origin unless it was caused by cerebrovascular diseases, respiratory diseases, malignant tumours, external causes such as trauma, drowning, drug overdose, asphyxia, or any other non-cardiac causes.<sup>16</sup> Diagnoses were made by the overseeing physician in collaboration with the EMS rescuers.”

Line 159: this is traditionally referred to as scene time, in EMS we speak of response, scene and transport times

We thank the reviewer for the careful review. We have carefully reviewed the manuscript, and corrected the words.



Line 178: a greater number of victims had received dispatch CPR instructions

We thank the reviewer for the careful review. We corrected the sentence (Page 9 Line 198).

Table 1: line 37 – the overall time on scene seems similar but transport time is different. Do you have any idea why this may be? Did physician staffed cases go mainly to one hospital or both hospitals?

We agree with the reviewer's comment. As pointed, physician staffed cases go mainly to both tertiary care centers even if it is long distance, therefore we speculate that transport time is different.

Tables: suggest you bold the p values that are statistically significant to make it easier to read

As suggested, we have bolded the p values that are statistically significant (Table 1, Table 2, Table 4).

Table 3: interesting to see that bystander CPR does not affect outcome and that only age and initial rhythm are predictive in your MV model, any ideas why this may be the case since bystander CPR is supposed to double survival rates based on historical data.

As pointed, adjusted odds ratio of bystander CPR was 1.41 (95% confidence interval 0.69-2.87) and was not statistically significant. However, it might be caused by smaller sample size because the 95% confidence interval was wide and the result was not different from nation-wide registry of OHCA based on the standardized Utstein style in Japan (adjusted odds ratio 1.25 and 95% confidence interval 1.08-1.44).<sup>1</sup> In addition, the study among shockable OHCA patients in the United States showed that adjusted odds ratio of bystander CPR was 1.76 (95% confidence interval 1.55-2.01),<sup>2</sup> and other study in the United States showed not statistically significance of bystander CPR (adjusted odds ratio 1.09 and 95% confidence interval 0.57-2.10)<sup>3</sup>. Therefore, we suppose that odds ratio is similar to previous studies.

#### Reference;

1 Iwami T, Kitamura T, Kiyohara K, Kawamura T. Dissemination of Chest Compression-Only Cardiopulmonary Resuscitation and Survival After Out-of-Hospital Cardiac Arrest. *Circulation* 2015;132:415-22.

2 Weisfeldt ML, Everson-Stewart S, Sitlani C, et al. Ventricular tachyarrhythmias after cardiac arrest in public versus at home. *N Engl J Med* 2011;364:313-21.

3 Ewy GA, Bobrow BJ, Chikani V, et al. The time dependent association of adrenaline administration and survival from out-of-hospital cardiac arrest. *Resuscitation* 2015;96:180-5.

Line 226: This seems very to a bit of a stretch that physicians can provide better quality chest compressions than EMS. If physician staffed ambulances used a stay and play approach then this should be reflected in longer scene times for this group which is not the case.

We agree with the reviewer's comment. We have removed this sentence from the discussion.

Line 244 – I am not sure that I agree with ethical concerns, the baseline differences between groups suggest that the findings you see may all be related to an unmeasured confounder. Given the expense of a physician staffed unit, a RCT would seem reasonable to see if it is worth the ROI.

We agree with the reviewer's comment. As mentioned above, selection bias might exist. Therefore, randomized controlled study is reasonable to adjust the baseline differences between groups and unmeasured confounder, and we have changed the Discussion as follows (Page 17 Line 278-280,

Page 18 Line 299); “ We also consider that observational studies cannot avoid such selection bias, but we believe our findings provide important suggestions to perform randomized controlled trial in the future, which will reveal the actual impact of physician-staffed ambulance service.” “a randomised controlled study would seem reasonable to adjust the baseline differences between groups and unmeasured confounder.”

Line 264 – not sure you can say selection bias was minimized given that you only looked at a small portion of the OHCA in your community (bystander witnessed cases)  
Your small sample size is also an important limitation to mention,

We agree with the reviewer’s comment. As mentioned above, selection bias might exist. Sample size in our study is smaller than previous nation-wide studies. However, we consider that small sample size is not limitation because we showed the statistically significant difference regardless of its smaller sample size. Furthermore, we believe that our study in limited area which has standardized protocol in a small community and only skilled physician above a certain level can give us important information rather than nation-wide study which were wide variations in the protocol and the quality of physician was unknown.

Line 270 – in Nigata

We have removed this sentence because we revised the Discussion and the Conclusion.

Response to Reviewer 2:

Comments regarding the manuscript “The Efficacy of Physician-Staffed Ambulance Services for Out-of-Hospital Cardiac Arrest: A Community-Based Observational Study” by Sato et al.

Thank You for the opportunity to assess this interesting manuscript.

The paper reports a register based study in which the authors study aimed to assess the effectiveness of physician-staffed ambulance services by comparing survival following patients with cardiac arrest treated by a prehospital physician with patients with cardiac arrest treated without the presence of a physician – that is - standard emergency medical care.

The authors report that among adults with out-of-hospital cardiac arrest, physician-staffed ambulance services were associated with significantly greater favourable neurological outcomes than when only standard emergency medical services were employed.

The authors report that strengths of the study include the use of a population-based registry and a well-established ambulance service.

One reported weakness of the study is the lack of adjustments concerning in-hospital or post-resuscitation care.

The authors applied logistical regression analysis taking the following variables into consideration: Age dichotomised into (18–74 years, ≥75 years), sex (male, female), cause of cardiac arrest (cardiac, noncardiac), first documented rhythm (shockable or non-shockable), use of public-access automated external defibrillator, presence of bystander-initiated CPR. Furthermore, treatments administered was included into the analysis: Intravenous fluids and adrenaline administration and/or advanced airway management. Finally, the EMS time spent at the scene was incorporated into the analysis

The authors did not consider pre-existing illness in the patients. Response time (reported as “Time from call to contact with patient by EMS) was registered but apparently had not been entered into the analysis.

Results:

The authors report that the presence of a physician-manned ambulance was associated with significantly greater neurological outcome than the presence of standard care EMS.

Thank you for your thorough reviews and suggestions. Our responses to your queries follow.

General comments:

The results are obtained in a population that is serviced by two tertiary care hospitals. One must assume that there is no difference in the post-resuscitation care in these two hospitals. Otherwise it must be considered a major methodological weakness that no post-resuscitation care markers are included in the regression analysis.

We thank the reviewer for these insightful comments. Two tertiary care hospitals are certificated as critical care medical center (CCMC) in Japan. In order to be licensed as a CCMC, a hospital needs to have ≥20 beds and an intensive care unit for critically ill patients, and it should be able to provide highly specialised procedures such as extracorporeal membrane oxygenation (ECMO) or percutaneous coronary intervention, and target temperature management 24 hour a day. Therefore, these hospitals basically have the same quality in the post-resuscitation care. We have added this information in the Methods as follows (Page 6, Line 123-128); “Two tertiary care hospitals are certificated as critical care medical center (CCMC) in Japan. In order to be licensed as a CCMC, a hospital needs to have ≥20 beds and an intensive care unit for critically ill patients, and it should be able to provide highly specialised procedures such as extracorporeal membrane oxygenation (ECMO) or percutaneous coronary intervention, and target temperature management 24 hour a day.<sup>20</sup>”

We added the following new citations;

20 Matsuyama T, Kiyohara K, Kitamura T, et al. Hospital characteristics and favourable neurological outcome among patients with out-of-hospital cardiac arrest in Osaka, Japan. *Resuscitation* 2017;110:146-53.

The authors should comment on that.

Apparently, the two groups differed: The patients in whom there was a physician involved were younger, a greater number of dispatcher instructions had been provided, more patients had a shockable rhythm at first rhythm check, more patients received adrenaline administration, and the time from departure from the scene to the hospital was longer. This reviewer fully appreciate that adjustments have been made. However, the paper would benefit from some form of comments regarding the apparent difference between the two groups. Who decides when to dispatch the whole set of prehospital providers? Is that decision influenced by something that might skew the population (it certainly appears so). I am not quite convinced that the authors are absolutely correct when they state that selection bias was minimised (Page 17, line 264). Can the authors insert some comments regarding this question?

Thank you for your important suggestion. We agree with your comment and also consider that selection bias might exist. Unfortunately, we didn't know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases. The physician-staffed ambulance service is available all day when a dispatch centre receives an emergency call which is indicated for activating the physician-staffed ambulance service are as follows: bystander witnessed cardiac arrest, severe trauma, stroke, acute coronary syndrome, anaphylactic shock, or a mass casualty incident. However, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy. In addition, a physician-staffed ambulance service cannot be activated if it is being used to treat another patient, if it has been dispatched and is en route to another patient, or if the emergency call has not been recognised by a dispatch centre as a situation conforming to protocol. In these cases, only regular EMS is dispatched on the scene. Furthermore, in the case an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel when the ELSTs consider the low probability of favorable outcome. Therefore, we excluded OHcAs witnessed in long-term care facilities because they may have lower probability of favorable outcome and the dispatch of the physician vehicle for them was often canceled. Again, we did not catch up the exact reason for the undischatched cases. We agree with the Reviewer's comment, and we consider that selection bias might exist. We also consider that observational studies cannot avoid such selection bias, but we believe our findings provide important suggestions to perform RCT in the future, which will reveal the actual impact of physician-staffed ambulance service. Therefore, we have added the information and revised the sentences in the Method and Discussion as follows (Page 6 Line 119-122, Page 7 Line 142-145, Page 16-17 Line 262-280, Page 17 Line 290); "In addition, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy." "In the case an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel when the ELSTs don't need physician on the scene, e.g. the ELSTs consider the low probability of favorable outcome." "Apparently, the patients who did and did not have prehospital physician involvement differed in our study. Unfortunately, we didn't know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases. The physician-staffed ambulance service is available all day when a dispatch centre receives an emergency call which is indicated for activating the physician-staffed ambulance service are as follows: bystander witnessed cardiac arrest, severe trauma, stroke, acute coronary syndrome, anaphylactic shock, or a mass casualty incident. However, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy. In addition, a physician-staffed ambulance service cannot be activated if it is being used to treat

another patient, if it has been dispatched and is en route to another patient, or if the emergency call has not been recognised by a dispatch centre as a situation conforming to protocol. In these cases, only regular EMS is dispatched on the scene. Furthermore, in the case an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel when the ELSTs consider the low probability of favorable outcome. Therefore, selection bias might exist. We also consider that observational studies cannot avoid such selection bias, but we believe our findings provide important suggestions to perform randomized controlled trial in the future, which will reveal the actual impact of physician-staffed ambulance service.” “Selection bias as mentioned above might exist.”

The influence of response time of the ordinary EMS on survival following cardiac arrest is probably relevant.

It is possible that the response time of a rapid response unit manned by a physician and dispatched together with an ordinary ambulance has no influence on mortality (Mikkelsen s, et al BMJ Open 2017;7:e014383.) I still find it peculiar why response time has not been included in the analyses. As it appears from studying Table 1, there is indeed a difference in response times between the two groups. I feel that including response times as a variable would have been more relevant than including on-scene time as variable.

We appreciate your suggestions. As suggested, we have entered response time as variables into the analysis. We demonstrated basically the same result as prior one. Therefore, we have revised the sentences in the Method and Results as follows (Page 8 Line 172-176 and Page 11 Line 205-207); “Potential confounding factors based on biological plausibility and previous studies were included in the multivariable analysis.<sup>21 22</sup> These variables included age (18–74 years, ≥75 years), sex (male, female), cause of cardiac arrest (cardiac, noncardiac), first documented rhythm (shockable [ventricular fibrillation or ventricular tachycardia], non-shockable), public-access automated external defibrillator use (yes, no), bystander-initiated CPR (yes, no), response time, intravenous fluids and adrenaline administration (yes, no), and advanced airway management (yes, no).” “Overall, 20.7% of the OHCA patients with physician involvement and 10.4% of the OHCA patients without physician involvement were alive after 1 month with a favourable neurological outcome (OR = 2.25, 95% CI: 1.39–3.62; adjusted OR = 3.44, 95% CI: 1.64–7.23).”

We added the following new citations;

22 Mikkelsen S, Lossius HM, Toft P, Lassen AT. Characteristics and prognoses of patients treated by an anaesthesiologist-manned prehospital emergency care unit. A retrospective cohort study. BMJ Open 2017;7:e014383.

Table 3. Multivariable associations of prehospital predictors with outcomes

	ROSC prior to hospital arrival	1-month survival rate	Neurologically favourable outcome
	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
<b>Primary exposure</b>			
Presence of physician	2.69 (1.73-4.19)	2.60 (1.41-4.78)	3.44 (1.64-7.23)
Absence of physician	1 (reference)	1 (reference)	1 (reference)
<b>Covariates</b>			

Age	2.03 (1.39-2.97)	2.90 (1.68-5.01)	5.70 (2.81-11.58)
Sex	1.03 (0.70-1.52)	0.79 (0.46-1.39)	0.70 (0.36-1.38)
Dispatcher instruction	1.34 (0.88-2.05)	0.93 (0.52-1.65)	0.87 (0.44-1.73)
Bystander CPR	0.67 (0.43-1.02)	1.28 (0.71-2.31)	1.41 (0.69-2.87)
Bystander AED	1.72 (0.67-4.44)	2.12 (0.66-6.85)	2.80 (0.78-10.02)
Cardiac origin	1.07 (0.71-1.60)	4.73 (2.28-9.81)	4.87 (2.00-11.86)
Shockable rhythm	3.94 (2.53-6.13)	8.39 (4.69-15.00)	7.87 (3.82-16.21)
Response time	0.93 (0.88-0.99)	0.93 (0.86-1.01)	0.95 (0.87-1.04)
Intravenous fluids	1.30 (0.80-2.12)	1.07 (0.56-2.03)	0.76 (0.36-1.60)
Adrenaline administration	0.53 (0.34-0.83)	0.18 (0.09-0.33)	0.08 (0.04-0.17)
Advanced airway management	0.38 (0.19-0.74)	0.12 (0.05-0.28)	0.09 (0.04-0.24)

AED, automated external defibrillator; CI, confidence interval; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; OR, odds ratio; ROSC, return of spontaneous circulation.

Table 4. Stratified analyses for outcomes according to first documented rhythm, adrenaline administration, and advanced airway management

Stratification	Neurologically favourable outcome			P for interaction
	%	Adjusted OR		
		(95% CI)		
First documented rhythm				0.159
Shockable				
Physician present	23/51	45.1	4.09 (1.57-10.64) †	
Physician absent	54/154	35.1	Reference	
Non-Shockable				
Physician present	5/84	6.0	3.16 (0.86-11.68) †	
Physician absent	25/603	4.1	Reference	
Adrenaline administration				0.001
Yes				
Physician present	13/107	12.1	3.41 (1.31-8.89) ‡	
Physician absent	12/436	2.8	Reference	
No				
Physician present	15/28	53.6	2.77 (0.73-10.52) ‡	
Physician absent	67/321	20.9	Reference	
Advanced airway management				0.378
Yes				
Physician present	23/128	18.0	3.25 (1.49-7.06) §	
Physician absent	55/709	7.8	Reference	
No				
Physician present	5/7	71.4	Not analysed	

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CI, confidence interval; OR, odds ratio.

† Adjusted for age, sex, cause of cardiac arrest, public-access AED use, bystander-initiated CPR, response time, intravenous fluids, adrenaline administration, and advanced airway management.

‡ Adjusted for age, sex, cause of cardiac arrest, first documented rhythm, public-access AED use, bystander-initiated CPR, response time, intravenous fluids, and advanced airway management.

§ Adjusted for age, sex, cause of cardiac arrest, first documented rhythm, public-access AED use, bystander-initiated CPR, response time, intravenous fluids, and adrenaline administration.

On-scene time and some of the other variables analysed seems to me to be interdependable: For example has intubation of the patient previously been shown to prolong on-scene time. (Intubation of the patient prolongs the on-scene tim (Fok PT, et al. Prehosp Disaster Med. 2019 Jun;34(3):317-321. doi: 10.1017/S1049023X19004394.)

As suggested, we have excluded the scene time as variables because we agree that it is interdependent with advanced airway management, intravenous line and adrenaline administration.

Specific comments:

A possible error occurs in page 3, line 49. Apparently a denominator is missing. Is this “the first”, “the second” or “the third” study or is it “a” study? It is not “the” study...

We thank the reviewer for the careful review. We have corrected the typo (Page 3 Line 48).

I fail to understand the meaning of the sentence on page 6, lines 108-110: “bystander-witnessed shockable-rhythm cardiac arrest in Niigata City was 32.4%, which was higher than the national rate of 20.8%, although EMS personnel in Japan are not legally permitted to terminate resuscitation.” What are the authors trying to convey with this sentence?

As suggested, we have removed this sentence because it is not informative.

There is another sentence that to this reviewer, at least, requires some clarification: page 17, lines 259 to 261: “...excluded OHCA occurring in long-term care facilities where physician-staffed ambulances are frequently cancelled because of the low probability of a favourable outcome.” Does this imply that EMS personnel routinely may cancel the physician if the EMT considers a case a “low reward-case”? If this is the case, this procedure surely must influence the results warranting a comment. There already seems to be a difference between the two groups as the patients in the physician-treated group are younger and to a greater extent display shockable rhythm. This undoubtedly influences the results. If termination or resuscitation attempts takes place

As mentioned above, there are several reasons for the undischarged cases. In particular, in the cases an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel while physician-staffed ambulance arrives first on the scene. Unfortunately, we did not measure the proportion of the cancellation.

Therefore, we have acknowledged this important limitation and added the new paragraph to the Discussion section as follows (Page 17 Line 262-280); “Apparently, the patients who did and did not have prehospital physician involvement differed in our study. Unfortunately, we didn’t know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases. The physician-staffed ambulance service is available all day when a dispatch centre receives an emergency call which is indicated for activating the physician-staffed ambulance service are as follows: bystander witnessed cardiac arrest, severe trauma, stroke, acute coronary syndrome, anaphylactic shock, or a mass casualty incident. However, a physician who is in charge of physician vehicle works concurrently in emergency department or intensive care unit in our hospital because we have a few emergency physicians and intensivists. Therefore, a physician-staffed ambulance service cannot be activated if emergency department or intensive care unit is busy. In addition, a physician-staffed ambulance service cannot be activated if it is being used to treat another patient, if it has been dispatched and is en route to another patient, or if the emergency call has not been recognised by a dispatch centre as a situation conforming to protocol. In these cases, only regular EMS is dispatched on the scene. Furthermore, in the case an ambulance arrives first on the scene, physician-staffed ambulance is sometimes cancelled by the ambulance personnel when the ELSTs consider the low probability of favorable outcome. Therefore, selection bias might exist. We also consider that observational studies cannot avoid such selection bias, but we believe our findings provide important suggestions to perform a randomized controlled trial in the future, which will reveal the actual impact of physician-staffed ambulance service.”

**Conclusion:**

This is an interesting work which has some flaws: Although the authors perform a logistical regression analysis adjusting for several factors, to this reviewer it seems that the two populations compared are far from identical. This jeopardises the conclusions.

We thank the reviewer for these insightful comments. We have changed the Conclusion as follows (Page 18 Line 304-305); “Further prospective researches such as a randomized controlled trial will be warranted.”

Furthermore, some interesting elements are not included as variables: Pre-existing illness would have been very interesting to have entered into the analysis, either in the form of a comorbidity score or, at least, by addressing the potential for pre-existing known cardiac illness.

Unfortunately, we did not measure pre-existing illness. In the Limitation section, we have acknowledged this issue as follows (Page 17 Line 286-287); “this study could not adjust baseline characteristics such as pre-existing illness, which might affect the outcome of OHCA.”

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Mohamud Daya Oregon Health & Science University Portland, Oregon, USA
<b>REVIEW RETURNED</b>	21-Sep-2019

<b>GENERAL COMMENTS</b>	Thank you for addressing some of the concerns raised by the first review. In reading the latest version of the manuscript, you are looking at the value added of dispatching a physician staffed ambulance in addition to a conventional response to bystander witnessed OHCA in Nigata city. Since the dual response is only sent on selected calls, is it fair to say that what you are really studying is the benefits of having a physician staffed unit in addition to a regular unit on scene. if this is correct, then you have
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	<p>as many as 7 individuals compared to 3 individuals on a bystander witnessed OHCA based on the response generated. A prior observational study from ROC has shown that having 5 or more scene personnel was associated with better outcomes likely due to better CPR quality and more timely interventions such as administration of adrenaline and earlier vascular access.</p> <p>It is also helpful to have each table on a separate page rather than within the context of the manuscript.</p> <p>You noted a difference in the time to epinephrine administration but did not adjust for that in the MV analysis. Please elaborate on this decision.</p> <p>Your definitions of presumed medical origin and presumed cardiac vs. non-cardiac is confusing. You also use these terms at times interchangeably in the manuscript. Its best to define this clearly and then remain consistent.</p> <p>You might consider changing the title "benefits of a adding a physician staffed ambulance to bystander witnessed OHCA in Nigata Clty"</p> <p>Line 90 - I would note in the introduction that ELSTs can administer adrenaline but require OLMC to do so</p> <p>Line 107-115 - very confusing to follow, recommend you define his as either presumed cardiac vs. non-cardiac which is what is done conventionally and not presumed medical...EMS providers can only act off what information is readily available to them (drowning, drug OD, strangulation, trauma ...all of which are more clearly obvious on scene)</p> <p>Line 152 - this is confusing, your methods suggest that dispatchers send a regular ambulance and a physician staffed ambulance per protocol. Is so why do EMS personnel have to request anything?</p> <p>The major flaw in this study is that you are not comparing apples to apples. Given that the first arriving ambulance can cancel the physician ambulance, strong selection bias is present. Do you know how often this happened? Is it possible to obtain this via review of dispatch recordings.</p> <p>Line 283-290. There is a fair amount of redundant material in this part of the discussion that comes from your methods. I would consider removing this. Its clear that you have selection bias and hence your findings need to be reported and interpreted with that in mind.</p> <p>A RCT would be of value but only if you were able to remove some of the other differences such as number of personnel on scene, time to epi administration, ability to establish IO access. etc. The cost and availability of the physician ambulance vehicle is also something that needs to be discussed briefly.</p> <p>Your findings support the Franco-German model of EMS where physician response is common but due to the selection biases present does not refute the North American Model of EMS where teams of more highly trained EMS personnel form the primary</p>
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	<p>resuscitation team. In addition, the number of personnel present could also be influencing your findings.</p> <p>Your findings are worthwhile reporting but its important that the limitations be clearly communicated. Depending on cost, availability etc., the addition of a physician staffed ambulance may be valuable for some communities.</p>
<b>REVIEWER</b>	Søren Mikkelsen, Professor, Consultant, MD, PhD The Prehospital Research Unit, Region of Southern Denmark Odense University Hospital DK 5000 Odense C Denmark
<b>REVIEW RETURNED</b>	26-Sep-2019
<b>GENERAL COMMENTS</b>	The manuscript has been improved considerably and now appears more balanced than the first vesrion did.

### VERSION 2 – AUTHOR RESPONSE

Response to Reviewer 1:

Thank you for addressing some of the concerns raised by the first review.

Thank you for your thorough reviews and suggestions. Our responses to your queries follow.

In reading the latest version of the manuscript, you are looking at the value added of dispatching a physician staffed ambulance in addition to a conventional response to bystander witnessed OHCA in Nigata city. Since the dual response is only sent on selected calls, is it fair to say that what you are really studying is the benefits of having a physician staffed unit in addition to a regular unit on scene. if this is correct, then you have as many as 7 individuals compared to 3 individuals on a bystander witnessed OHCA based on the response generated. A prior observational study from ROC has shown that having 5 or more scene personnel was associated with better outcomes likely due to better CPR quality and more timely interventions such as administration of adrenaline and earlier vascular access.

We appreciate these helpful suggestions. As pointed, physician staffed ambulance is added to a conventional response to bystander witnessed OHCA in Niigata city. More personnel on-scene might be associated with improved survival of out-of-hospital cardiac arrest or favorable neurological outcome rather than presence of physician.

Therefore, we have added this issue to the Discussion as follows (Page 11-12, Line 234-242); “On the other hand, another reason is that more personnel on-scene might be associated with improved survival of out-of-hospital cardiac arrest or favorable neurological outcome rather than presence of physician. A prior observational study has shown that having 5 or more EMS personnel on-scene was associated with higher rate of survival to hospital discharge.<sup>27</sup> Another observational study in Japan also demonstrated that the three on-scene ELST group was associated with the improved favorable neurological outcome from OHCA compared with the one on-scene ELST group.<sup>28</sup> Therefore, more personnel on-scene might be more important than presence of prehospital physician in the current system.”

We added the following new citations;

27. Warren SA, Prince DK, Huszti E, et al. Volume versus outcome: More emergency medical services personnel on-scene and increased survival after out-of-hospital cardiac arrest. *Resuscitation* 2015;94:40-8.

28. Kajino K, Kitamura T, Iwami T, et al. Impact of the number of on-scene emergency life-saving technicians and outcomes from out-of-hospital cardiac arrest in Osaka City. *Resuscitation* 2014;85:59-64.

It is also helpful to have each table on a separate page rather than within the context of the manuscript.

As suggested, we have moved the tables on a separate page (Page 21-26).

You noted a difference in the time to epinephrine administration but did not adjust for that in the MV analysis. Please elaborate on this decision.

We appreciate your suggestions. As suggested, we have entered the time from call to epinephrine administration as variables into the stratified analysis according to adrenaline administration. We demonstrated basically the same result as prior one. On the other hand, we did not adjust for that in the multivariable analysis of the other analysis including main analysis because adrenaline was administered to only 60.9% of all patients.

Therefore, we have added this information in the Method and revised the table 4 as follows (Page 9, Line 177-178); “We entered the time from call to adrenaline administration as variables into the stratified analysis according to adrenaline administration.” and (Page 25-26);

Table 4. Stratified analyses for outcomes according to first documented rhythm, adrenaline administration, and advanced airway management

Stratification	Neurologically favourable outcome			P for interaction
	Adjusted OR		P for interaction	
	%	(95% CI)		
First documented rhythm				0.159
Shockable				
Physician present	23/51	45.1	4.09 (1.57-10.64) †	
Physician absent	54/154	35.1	Reference	
Non-Shockable				
Physician present	5/84	6.0	3.16 (0.86-11.68) †	
Physician absent	25/603	4.1	Reference	
Adrenaline administration				0.001
Yes				

Physician present	13/107	12.1	3.29 (1.21-8.94) †
Physician absent	12/436	2.8	Reference
No			
Physician present	15/28	53.6	2.77 (0.73-10.52) §
Physician absent	67/321	20.9	Reference
Advanced airway management			0.378
Yes			
Physician present	23/128	18.0	3.25 (1.49-7.06)
Physician absent	55/709	7.8	Reference
No			
Physician present	5/7	71.4	Not analysed
Physician absent	24/48	50.0	Reference

CI, confidence interval; OR, odds ratio.

† Adjusted for age, sex, cause of cardiac arrest, public-access AED use, bystander-initiated CPR, dispatcher instruction, response time, intravenous fluids, adrenaline administration, and advanced airway management.

‡ Adjusted for age, sex, cause of cardiac arrest, first documented rhythm, public-access AED use, bystander-initiated CPR, dispatcher instruction, response time, intravenous fluids, advanced airway management, and time from call to adrenaline

§ Adjusted for age, sex, cause of cardiac arrest, first documented rhythm, public-access AED use, bystander-initiated CPR, dispatcher instruction, response time, intravenous fluids, and advanced airway management.

|| Adjusted for age, sex, cause of cardiac arrest, first documented rhythm, public-access AED use, bystander-initiated CPR, dispatcher instruction, response time, intravenous fluids, and adrenaline administration.

Your definitions of presumed medical origin and presumed cardiac vs. non-cardiac is confusing. You also use these terms at times interchangeably in the manuscript. Its best to define this clearly and then remain consistent.

We appreciate this helpful suggestion. As suggested, we have clarified this definition and added the reference in the Methods as follows (Page 5, Line 93-97); “Based on the international Utstein Style, medical origin includes cases in which the cause of the cardiac arrest is presumed to be cardiac, other medical cause (e.g. anaphylaxis, asthma, gastrointestinal bleeding), and in which there is no obvious cause of the cardiac arrest.<sup>16</sup> Diagnoses were made by the overseeing physician in collaboration with the EMS rescuers.” In addition, to define this clearly and then remain consistent, we

revised the term “cardiac” only as an explanation of a covariate in multivariable logistic regression analysis (“cardiac” [Page 5, Line 94, Page 8, Line 168], “noncardiac” [Page 8, Line 168]) and the term “medical” which is subject of our study in the other part (“medical aetiology” [Page 2, Line 28], “medical origin” [Page 5, Line 93, Page 9, Line 187], “non-medical origin” [Page 5, Line 97])

We added the following new citations;

16. Perkins GD, Jacobs IG, Nadkarni VM, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein Resuscitation Registry Templates for Out-of-Hospital Cardiac Arrest: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. *Circulation* 2015;132:1286-300.

You might consider changing the title "benefits of adding a physician staffed ambulance to bystander witnessed OHCA in Niigata City"

As suggested, we revised the title of our manuscript “Benefits of adding a physician-staffed ambulance to bystander witnessed out-of-hospital cardiac arrest. A Community-Based Observational Study in Niigata, Japan”.

Line 90 - I would note in the introduction that ELSTs can administer adrenaline but require OLMC to do so

We have added that ELSTs require on-line medical control in the introduction (Page 4, Line 75-79); “Most EMSs in Japan were limited to providing advanced life support during the period between 2005 and 2010 because, since July 2004, specially trained emergency life-saving technicians (ELSTs) were permitted to insert tracheal tubes and since April 2006, they have been permitted to administer intravenous adrenaline under on-line medical control direction.”

Line 107-115 - very confusing to follow, recommend you define this as either presumed cardiac vs. non-cardiac which is what is done conventionally and not presumed medical...EMS providers can only act off what information is readily available to them (drowning, drug OD, strangulation, trauma ...all of which are more clearly obvious on scene)

We agree with the reviewer’s comment. We defined “medical origin” based on the international Utstein-style.<sup>16</sup> As you mentioned, EMS providers can only act off what information is readily available to them (drowning, drug overdose, strangulation, and trauma, all of which are more clearly obvious on scene). Diagnoses of cardiac or non-cardiac are made by overseeing physician in collaboration with the EMS providers. Therefore, we believe that medical origin is better as the participants in our study. As pointed, it was confusing, therefore we have clarified this definition and added the reference in the Methods as follows (Page 5, Line 93-97); “Based on the international Utstein Style, medical origin includes cases in which the cause of the cardiac arrest is presumed to be cardiac, other medical cause (e.g. anaphylaxis, asthma, gastrointestinal bleeding), and in which there is no obvious cause of the cardiac arrest.<sup>16</sup> Diagnoses were made by the overseeing physician in collaboration with the EMS rescuers.”

We added the following new citations;

16. Perkins GD, Jacobs IG, Nadkarni VM, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein Resuscitation Registry

Templates for Out-of-Hospital Cardiac Arrest: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. *Circulation* 2015;132:1286-300.

Line 152 - this is confusing, your methods suggest that dispatchers send a regular ambulance and a physician staffed ambulance per protocol. Is so why do EMS personnel have to request anything?

We thank the reviewer for the careful review. We have corrected the word as follows (Page 7, Line 134-137); "Once a dispatch centre receives an emergency call, dispatchers request both a physician-staffed ambulance from an emergency medical centre in Niigata City General Hospital and an ambulance from the nearest emergency medical centre if the patient is suspected to have one of the above emergencies."

The major flaw in this study is that you are not comparing apples to apples. Given that the first arriving ambulance can cancel the physician ambulance, strong selection bias is present. Do you know how often this happened? Is it possible to obtain this via review of dispatch recordings.

Unfortunately, we did not know the reason and the number which the first arriving ambulance canceled the physician ambulance. As pointed, we have added this issue to the Discussion as follows (Page 13, Line 262-264); "Unfortunately, we didn't know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases and the number which the first arriving ambulance canceled the physician ambulance."

Line 283-290. There is a fair amount of redundant material in this part of the discussion that comes from your methods. I would consider removing this. Its clear that you have selection bias and hence your findings need to be reported and interpreted with that in mind.

We agree with the reviewer's comment. Importantly, we did not know the reason and the number which the first arriving ambulance canceled the physician ambulance, therefore selection bias is present.

Therefore, we have removed the redundant material and revised the discussion as follows (Page 13, Line 262-273); "Apparently, the patients who did and did not have prehospital physician involvement differed in our study. Unfortunately, we didn't know the detailed reason why the physician-staffed ambulance was not dispatched on the 757 cases and the number which the first arriving ambulance canceled the physician ambulance. Therefore, selection bias might exist. We also consider that observational studies cannot avoid such selection bias, but we believe our findings provide important suggestions to perform a randomized controlled trial in the future, which will reveal the actual impact of physician-staffed ambulance service. On the other hand, the cost and availability of the physician ambulance vehicle would need to be considered if physician-staffed ambulance services were proved to be effective. It is impractical to dispatch physicians to all witnessed OHCA patients when considering limited cost and resource, therefore increase of EMS personnel on-scene or extending the procedure by ELSTs like the North America (e.g. administer intravenous adrenaline without on-line medical control direction or establish intraosseous access) might be a solution."

A RCT would be of value but only if you were able to remove some of the other differences such as number of personnel on scene, time to epi administration, ability to establish IO access. etc. The cost and availability of the physician ambulance vehicle is also something that needs to be discussed briefly.

We agree with the reviewer's comment. As pointed, the cost and availability of the physician ambulance vehicle would be needed to be considered if physician-staffed ambulance service was proved to be effective.

Therefore we have changed the discussion as follows (Page 13, Line 267-273, Page 14, Line 291-294); "On the other hand, the cost and availability of the physician ambulance vehicle would need to be considered if physician-staffed ambulance services were proved to be effective. It is impractical to dispatch physicians to all witnessed OHCA patients when considering limited cost and resource, therefore increase of EMS personnel on-scene or extending the procedure by ELSTs like the North America (e.g. administer intravenous adrenaline without on-line medical control direction or establish intraosseous access) might be a solution." "Furthermore, a randomized controlled study would seem reasonable to adjust the baseline differences between groups and unmeasured confounder if we are able to remove some of the other differences such as number of personnel on scene or ability to establish intraosseous access."

Your findings support the Franco-German model of EMS where physician response is common but due to the selection biases present does not refute the North American Model of EMS where teams of more highly trained EMS personnel form the primary resuscitation team. In addition, the number of personnel present could also be influencing your findings.

We thank the reviewer for these insightful comments. It is impractical to dispatch physicians to all witnessed OHCA patients when considering limited cost and resource, therefore increase of EMS personnel on-scene or expanding procedures EMS personnel are allowed to use (e.g. administer intravenous adrenaline without on-line medical control direction or establish intraosseous access) as the North America might be effective.

Therefore, we have added that the number of personnel present could be influencing our findings in the discussion as follows (Page 13, Line 267-273, Page 14, Line 291-294); "On the other hand, the cost and availability of the physician ambulance vehicle would need to be considered if physician-staffed ambulance services were proved to be effective. It is impractical to dispatch physicians to all witnessed OHCA patients when considering limited cost and resource, therefore increase of EMS personnel on-scene or extending the procedure by ELSTs like the North America (e.g. administer intravenous adrenaline without on-line medical control direction or establish intraosseous access) might be a solution." "Furthermore, a randomized controlled study would seem reasonable to adjust the baseline differences between groups and unmeasured confounder if we are able to remove some of the other differences such as number of personnel on scene or ability to establish intraosseous access."

Your findings are worthwhile reporting but its important that the limitations be clearly communicated. Depending on cost, availability etc., the addition of a physician staffed ambulance may be valuable for some communities.

We appreciate these helpful suggestions. We have communicated important limitations as clearly as possible. Increase of EMS personnel on-scene or extending the procedure by ELSTs (e.g. administer intravenous adrenaline without on-line medical control direction or establish intraosseous) as the paramedics in the North America are allowed is important, therefore we have added the comment.

Response to Reviewer 2:

The manuscript has been improved considerably and now appears more balanced than the first version did.

Thank you for your thorough reviews and comments.

**VERSION 3 – REVIEW**

<b>REVIEWER</b>	Mohamud Daya Department of Emergency Medicine Oregon Health & Science University Portland, Oregon, USA I am NIH and AHRQ funded researcher with interest in EMS including out-of-hospital cardiac arrest
<b>REVIEW RETURNED</b>	02-Nov-2019

<b>GENERAL COMMENTS</b>	<p>These authors have done an excellent job of integrating the prior reviews into the latest revision of the paper. The paper is more balanced in that it does not over-interpret their findings especially given the baseline differences in the characteristics of patients managed by the physician and EMS vs. EMS alone.</p> <p>Since the title includes the study location, I am comfortable with the conclusion as noted. One additional point to consider is that in some EMS systems, the stay and play approach to OHCA has resulted in better outcomes than the load and go especially since CPR quality has been shown to deteriorate in the back of a moving ambulance in the absence of mechanical CPR. The longer scene time when physicians are present may be a sign that the approach used when a physician is present is different than when they are not. Something else to factor when looking ahead to designing or conducting a randomized controlled trial.</p> <p>minor comments:</p> <p>line 277, the word Apparently suggests that this was a surprising finding but it is a very clear finding of the study. Consider replacing with the " The baseline characteristics of the patients....differed in our study "</p> <p>line 279: the number in which the ....</p>
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