## 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

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| **TITLE (PROVISIONAL)** | Development of unmanned aerial vehicle (UAV) networks delivering early defibrillation for out-of-hospital-cardiac-arrests (OHCA) in areas lacking timely access to emergency medical services (EMS) in Germany – A comparative economic study |
| **AUTHORS** | Bauer, Jan; Moormann, Dieter; Strametz, Reinhard; Groneberg, David |

## VERSION 1 – REVIEW

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| **REVIEWER** | Andreas Claesson<br>Centre for resuscitation science, Karolinska Institutet Stockholm, Sweden |
| **REVIEW RETURNED** | 15-Sep-2020 |

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| **GENERAL COMMENTS** | Comments<br><br>Lines 77-83: Please clarify if these data are national and give 30day survival if possible.<br><br>Line 92-93: Authors state a mean EMS response time of just below 7 minutes in Germany as a whole. Is this only the driving time? Please clarify Please as well clarify your definition of EMS. Is this ambulance only, does it include first responders i.e. fire and/or police? A section in methods describing the EMS system would be of interest to the reader.<br><br>Line 93-94: Please clarify how the mean time from emergency call to defibrillation can be 18 minutes if the EMS response time ( time from pic-up at EMCC to defibrillation?) is a mean of 7. Or, are these cases just rural areas? Onsite defibrillation only? Are onsite defibrillation cases included or not? What about first responder defibrillation?<br><br>Line 111: Why only rural areas? There must be cases of OHCA occurring in semi-urban or urban areas with a EMS response time of > 10 minutes?<br><br>Line 117: Thinly populated I subjective, please give another more precise measure such as individuals/km2.<br><br>Line 132: Does the term "rural" properly fit OHCA cases where the driving time is 7 minutes? |

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| | Line 144-146: Evenly distribution of OHCA in the demand area is not representative for reality, in fact there is a very un-even distribution of OHCA cases. Using this methodology for modelling It is likely that the incidence of OHCA will be biased and will differ heavily thus in reality decreasing the proportion of OHCA available for drone-intervention. EMS-stations are probably geographically positioned based upon historical data and population density. Authors most probably heavily over-estimates the coverage and the effect of the network.<br>GPS-data from historical OHCA could better serve as a base to predict drone locations and reach.<br><br>Line 150: Please reflect on why 80%, 90% and 100% coverage was chosen. It does not seem feasible to deploy thousands of drones in a close future, which areas are most interesting?<br><br>Line 154: Please clarify how you see delivery is made, is time measured from "take off" or when requesting airspace from CTR? Is time stopped when the UAV lands?<br><br>Line 155: Please explain why the time for a bystander to pic up an AED from an UAV outside a house (2 min) and then back to victim should be shorter than EMS personnel arriving outside a house (3 min) and reaching the victim? Attaching an AED might take longer time for someone not familiar.<br><br>Line 159: In how large proportion of cases are there >1 bystander onsite? If alone, interruptions in CPR will be introduced when picking up the AED. Do you see any ethical problems here? Could the UAV be deployed to OHCA cases with single bystanders?<br><br>Line 178: What does reference 7 state in the context of UAVs? Agerskovs publication is not on UAVs. Assumptions made – please add reference to these costs.<br><br>Line 266-267: 100% coverage does not equal 100% deployment of drones. Weather; rain, wind, temperatures, conflict in airspace,maintenance, no-fly zones, no-fly objects etc will prohibit flights thus decreasing the real proportion of delivered AEDs, please reflect on these real life clinical problems. |

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| **REVIEWER** | Daniel Ślęzak<br>Gdański Uniwersytet Medyczny - Polska<br>Medical University of Gdańsk – Poland |
| **REVIEW RETURNED** | 24-Sep-2020 |

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| **GENERAL COMMENTS** | The authors raised a very important aspect of AED. The use of AED should be promoted everywhere. Bringing the AED to the scene should be unhindered. Development of unmanned aerial vehicle (UAV) networks delivering early defibrillation for out-of-hospital-cardiac-arrests (OHCA) in |

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| | areas lacking timely access to emergency medical services (EMS) should be supported by each country.<br>The authors presented the state of Germany. It would be worth checking what the situation is in other countries. |

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| **REVIEWER** | Mathias Ströhle<br>Trauma Critical Care Division<br>Dept. for Anesthesia and Critical Care Medicine<br>Medical University Innsbruck<br>Austria |
| **REVIEW RETURNED** | 24-Sep-2020 |

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| **GENERAL COMMENTS** | General comments to the editor:<br><br>Dear Editor,<br>Thank you for giving the opportunity to review this manuscript.<br><br>The manuscript "Development of unmanned aerial vehicle (UAV) networks delivering early defibrillation for out-of-hospital-cardiac- arrests (OHCA) in areas lacking timely access to emergency medical services (EMS) in Germany – A comparative economic study." The Study of Bauer et al. is focusing on an interesting part in OHCA treatment. They are calculating the potential costs to implement a nationwide 80 to 100% coverage of AEDs with the help of UAVs. The study is well performed and is focusing on the problem to implement AEDs in BLS CPR within the shortest time possible.<br>Some things are impossible to prove like the statistical methods which have been used. Firstly, (luckily) due to unavailability of data. Secondly because the method is only explained by using a reference. Thirdly this reference is inaccessible.<br>One major concern is the calculation of the UAV accessible radius within 5 minutes and other timespans. These calculations look more like pure laboratory data and not real-life data. This could potentially change the outcome.<br>The rest of the data are presented in a clear manner, easy to read and understand.<br>The authors seem to know the studies necessary to discuss advantages but also limitations of UAVs especially under the circumstances of CPR.<br>The work is performed in good quality and might therefore be suitable for publication.<br><br>Best regards<br><br><br><br>General Comments:<br><br>Dear Authors,<br>Your study is focusing on an interesting part in OHCA treatment. As you are calculating the potential costs to |

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| | implement a nationwide 80 to 100% coverage of AEDs with the help of UAVs. Though your study is well performed and is focusing on the problem to implement AEDs in BLS CPR within the shortest time possible, there are some major issues regarding your manuscript.<br><br>Some things are impossible to prove like the statistical methods which have been used as they are almost not described.<br><br>Time periods used are hard to understand (e.g. Line 115 – are the laypersons faster in running than paramedics – you assume that they grab unknown equipment out of a garden, street… etc. in a faster time than paramedics their well-known material). You refer on the 94 seconds of Sanfridsson in SJTREM. You should explain why you believe that Toronto Regional RescuNET (58 Inhabitants/km2 up to 4334 Inhabitants/km2) compared to Germanies UAV area (41 Inhabitants/km2) is comparable when comparing accessing times and why not only taking the same timespan for EMS and lay rescuers. Your timespans are "multinational time periods" out of different works, probably reflecting characteristics of the systems and urban/rural settings of different locations.<br><br>Line 160 – the radius which was calculated with 8,33km is without starting and landing? Which time is realistic especially for landing procedure? Studies like Boutillier, assume that starting and landing needs about 10 seconds (this would result in a radius reduction of about 500 meters (6%).<br>My personal opinion is that the calculation of the radius in relation to the necessary time to achieve (10 minutes) is too optimistic. For example: If there is a slight breeze of wind (4 bft = 28km/h = 10-15 kt – even too lose to lift a kitesurf kite) this would reduce the real speed over ground to 72km/h and therefore reduce the calculated diameter to 6km. Not to think about northern sea shore winds or alpine "Föhn" winds as common in southern Bavaria. Was there a calculation for nighttime or situations with limitations of flight (fog…)? Are there limitations for UAVs? These time and radius diameter calculations under laboratory conditions are potentially dangerous and a major issue as they could change the whole calculation!<br><br>Wouldn't police, fire rescue laypersons using an AED reduce much of the costs as they cover additional landscape area? Is this not a big part of available laypersons using AEDs, especially in rural area to achieve the AED time within 10 minutes?<br><br>Though you mentioned in the manuscript that you decided against QALY which is understandable - REF 18 is also focusing on HR-QOL (Quality of life) – wouldn't it be of interest to give a lookout on the estimated additionally generated cost for those rescued like for PTCA (ICER). |

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| | Would it be possible to estimate additionally generated CPC 3 and 4 Patients?<br><br>Specific Comments:<br><br>- Reference 15 - link does not work<br><br>- Line 107 – Such an application … this sentence is awkward to read. …has already been studies???<br><br>- Spatial demand used was not approvable nor explained how it works.<br><br>- No Statement on ethical approvement or not can be found. |

## VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comments to the Author
Comments

Lines 77-83: Please clarify if these data are national and give 30day survival if possible.

**Response:**
We were not able to provide the 30day survival rate for these data. However, we were able to include the survival to discharge rate. Therefore, we included the following statement:

"The incidence of OHCA in Germany in 2018 was 121 per 100,000 citizens with a survival to discharge rate of 13.2%, based on representative data taken from 31 emergency medical services [1]"

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Line 92-93: Authors state a mean EMS response time of just below 7 minutes in Germany as a whole. Is this only the driving time?

**Response:**
This is the time from the emergency phone call to the arrival at the scene. We changed the sentence as follows:

"In Germany, the mean time from emergency call to arrival at the scene of EMS was 6 minutes and 54 seconds in 2018.[1]"

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Please clarify Please as well clarify your definition of EMS. Is this ambulance only, does it include first responders i.e. fire and/or police? A section in methods describing the EMS system would be of interest to the reader.

**Response:**
EMS only includes ambulance vehicles without police or fire vehicles, even though many EMS are located at fire departments. We included the following sentence to clarify this:

"EMS in Germany are represented by ambulance vehicles and/or emergency physician vehicles"

Describing the EMS system in Germany would be beyond the extent of this paper. Therefore, we did not include a comprehensive overview and we hope the reviewer can follow this argument.

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Line 93-94: Please clarify how the mean time from emergency call to defibrillation can be 18 minutes if the EMS response time (time from pic-up at EMCC to defibrillation?) is a mean of 7. Or, are these cases just rural areas? Onsite defibrillation only? Are onsite defibrillation cases included or not? What about first responder defibrillation?

**Response:**
The mean times are taken from the German Resuscitation Registry on OHCA in Germany as of 2018. The 18 Minutes represent the documented time from emergency phone call to first defibrillation by EMS with ventricular tachycardia or ventricular fibrillation. Possible lay defibrillation with AED was not considered. We agree that a difference of 11 minutes between the arrival at the scene and the first defibrillation seems longer that it should be. The difference may be explained by difficulties reaching the patient, bearing in mind that the majority of OHCA occur at home. Also, the documented time may not represent the exact time (documentation error). However, we are not able to provide more insight as to why there is a mean gap of 11 minutes in 2018 between arrival at the scene and first defibrillation since we do not have the raw data (maybe there were outliers heavily increasing the mean time). Therefore, we cannot provide more evidence to better explain this issue. We hope the explanation given here addresses the issue raised by the reviewer. Additionally, we included the following paragraph:

"The large mean time gap between arrival at the scene and first defibrillation in 2018 may be due to difficulties reaching the patient, documentation error or few outliers."

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Line 111: Why only rural areas? There must be cases of OHCA occurring in semi-urban or urban areas with a EMS response time of > 10 minutes?

**Response:**
We agree with the reviewer that there will be urban areas with a EMS response time of >10 minutes. However, we focused on rural areas since the potential benefit of UAV in rural areas was deemed to be higher compared to urban areas, where the availability and accessibility of EMS is higher leading to better outcomes in OHCA settings. This association with outcome was shown in a recent study: "We found a significantly higher probability for survival to hospital admission (OR: 1.84, 95% CI 1.43-2.36, p < 0.001), to hospital discharge (OR: 1.51, 95% CI 1.08-2.11, p = 0.017), and at 1 year (OR: 1.58, 95% CI 1.11-2.26, p = 0.012) in the urban group versus the rural group" (Mathiesen WT, Bjørshol CA, Kvaløy JT, et al. Effects of modifiable prehospital factors on survival after out-of-hospital cardiac arrest in rural versus urban areas. Crit Care 2018;22:99)

We added the following paragraph in the introduction to explain our choice of study area:

"In this study we will focus on rural areas, since the potential benefit of UAV in rural areas was deemed to be higher compared to urban areas, where the availability and accessibility of EMS is higher with better outcomes in OHCA settings.[12]"

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Line 117: Thinly populated I subjective, please give another more precise measure such as individuals/km2.

**Response:**

In this case we have to disagree with the reviewer: “thinly populated according to the degree of urbanization defined by EUROSTAT” is not subjective but follows a commonly used objective classification of urbanisation: “The Degree of urbanisation (DEGURBA) is a classification that indicates the character of an area. Based on the share of local population living in urban clusters and in urban centres, it classifies local administrative units level 2 (LAU2) into three types of area: thinly populated area (rural area); intermediate density area (towns and suburbs/small urban area), and densely populated area (cities/large urban area).”( https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Degree_of_urbanisation_classification_-_2011_revision)

We included the acronym “DEGURBA” to emphasize that this classification is a commonly used measure of urbanization. Additionally, we changed the sentence as follows:

“…area classified as ‘thinly populated area’ according to the degree of urbanization (DEGURBA) as of 2018 defined by EUROSTAT based on the share of local population living in urban clusters and in urban centers [13]…”

Line 132: Does the term “rural” properly fit OHCA cases where the driving time is 7 minutes?

**Response:**
The term “rural” is used for the classification of an area based on population density (see above DEGURBA). EMS locations are also present in rural areas (“thinly populated areas” see above). Therefore, the area surrounding these EMS locations will both be classified as “thinly populated” and provide a response times of <7 minutes in the case of a catchment area of 7 minutes). In other words, the definition of “thinly populated” (rural) is independent of the EMS response time. We hope we have clarified this issue with this explanation.

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Line 144-146: Evenly distribution of OHCA in the demand area is not representative for reality, in fact there is a very un-even distribution of OHCA cases. Using this methodology for modelling It is likely that the incidence of OHCA will be biased and will differ heavily thus in reality decreasing the proportion of OHCA available for drone-intervention. EMS-stations are probably geographically positioned based upon historical data and population density. Authors most probably heavily over-estimates the coverage and the effect of the network. GPS-data from historical OHCA could better serve as a base to predict drone locations and reach.

**Response:**
We fully agree with the reviewer. Our first approach was to use GPS-data from historical data from the German Resuscitation Registry. Unfortunately, the German Resuscitation Registry was not able to provide the data due to data protection concerns. Furthermore, no other data source could be identified that could provide these data. Due to the lack of data we applied the approach described in the manuscript knowing the limitations of this approach. In order to address the limitations raised by the reviewer we included the following statement in the discussion:

“It must be noted that we assumed evenly distributed incidence of OHCA among the grid cells within a municipality. This leads to possible overestimation of UAV coverage since, in reality, the incidence of OHCA is unevenly distributed within a municipality or even within the grid cells. This bias was introduced due to a lack of data providing the exact location of historical OHCA in a municipality.”

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Line 150: Please reflect on why 80%, 90% and 100% coverage was chosen. It does not seem feasible to deploy thousands of drones in a close future, which areas are most interesting?

**Response:**

We chose our study area with the aim to identify the most interesting areas by applying the two inclusion criteria described in the manuscript. Only within these areas a coverage of 80, 90 and 100% was chosen. These percentages were chosen to guarantee equal access to defibrillation within the study area even if such coverages may not be the primary goal by a health policy addressing this issue. However, if UAV are deemed to be cost-effective, such coverages are likely to be the goal on the long run, in order to provide equal access within an area. We included the following paragraph in the method section to further elaborate on this issue:

“These percentages were chosen to guarantee equal access to defibrillation within the study area even if such coverages may not be the primary goal by a health policy addressing this issue. However, if UAV are deemed to be cost-effective, such coverages are likely to be the goal on the long run, to provide equal access within an area.”

Line 154: Please clarify how you see delivery is made, is time measured from “take off” or when requesting airspace from CTR? Is time stopped when the UAV lands?

**Respond:**
Time is measured from the take off to the arrival at the scene. We included the following clarification in the method section:

“2. UAV flying time between take off and arrival at the scene: depending on location of OHCA”

The delivery of the AED by the UAV is assumed to be made by drop-off. We included a respective statement:

“The delivery of the AED by the UAV is assumed to be made by drop-off”

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Line 155: Please explain why the time for a bystander to pic up an AED from an UAV outside a house (2 min) and then back to victim should be shorter than EMS personnel arriving outside a house (3 min) and reaching the victim? Attaching an AED might take longer time for someone not familiar.

**Response:**
The definition of the time intervals differed between EMS and UAV. The total time from arrival at scene to defibrillation is identical (4 minutes) for both EMS (3+1) and UAV (2+2). These time intervals consider the issue raised by the reviewer since for EMS, the time between arrival at patient side and first defibrillation was considered to be 1 minute whereas for UAV the time interval was 2 minutes. On the other side, EMS may take longer to arrive at the patient side since the ambulance vehicle has to be stopped at a car accessible road, the equipment has to be grabbed and the patient has to searched for whereas the UAV may drop the AED directly in front of the patient’s house and the bystander exactly knows where the patient is located. This is why the time between arrival at scene and arrival at patient side for EMS was 3 minutes whereas for UAV was 2 minutes. We changed the terminology of the time intervals to make this clearer:

EMS

“For EMS, the following time intervals were used (rounded to minutes):

1. Dispatch time between emergency phone call arrival and dispatch: 1 minute [14]
2. Driving time: depending on location of OHCA
3. Time between arrival at scene and arrival at patient side: 3 minutes [14]
4. Time between arrival at patient side and first defibrillation: 1 minute [15]”

UAV

“The following time intervals were used (rounded to minutes):[14,18]

1. Dispatch time between emergency phone call and dispatch: 1 minute
2. UAV flying time between take off and arrival at the scene: depending on location of OHCA
3. Time between arrival at scene, retrieving AED and delivery to patient side: 2 minutes
4. Time between arrival at patient side and first defibrillation: 2 minutes"

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Line 159: In how large proportion of cases are there >1 bystander onsite? If alone, interruptions in CPR will be introduced when picking up the AED. Do you see any ethical problems here? Could the UAV be deployed to OHCA cases with single bystanders?

**Response:**
We cannot provide data on the proportion of dual bystander situations. However, we already addressed this issue in the discussion section but also further expanded it:
"Furthermore, retrieving an AED in a single bystander OHCA situation would require an interruption of CPR: the median hands-off time in a simulation was reported to be 94 seconds.[19] Since continued CPR is the mainstay of any effort made by lay bystanders, CPR must be continued until a dual bystander situation develops where one bystander can proceed with CPR while the other one retrieves the AED. This issue, however, also applies to publicly accessible AED in a single bystander situation."

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Line 178: What does reference 7 state in the context of UAVs? Agerskovs publication is not on UAVs. Assumptions made – please add reference to these costs.

**Response:**
We thank the reviewer for this comment. This reference was put there by mistake. The maintenance costs were taken from the source already stated in the manuscript: Bogle BM, Rosamond WD, Snyder KT, *et al.* The Case for Drone-assisted Emergency Response to Cardiac Arrest. *N C Med J* 2019;**80**:204–12.
We removed the reference.

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Line 266-267: 100% coverage does not equal 100% deployment of drones. Weather; rain, wind, temperatures, conflict in airspace,maintenance, no-fly zones, no-fly objects etc will prohibit flights thus decreasing the real proportion of delivered AEDs, please reflect on these real life clinical problems.

**Response:**
We expanded the following paragraph in the discussion section to reflect the issue raised by the reviewer (see also comment Reviewer 3):

"Finally, it should be noted that the most frequent barriers regarding the application of UAV in the above-described scenarios were legal restrictions and technical problems. Such restrictions represent not only barriers regarding the implementation but also the utilization of UAV in such a setting: legal issues (e.g. conflicts in airspace or no-fly zones) and technical issues (e.g. weather conditions or maintenance) may prohibit or hinder the UAV utilization. From a legal point of view, UAV must be provided an automatic launch license in case of an OHCA, otherwise obtaining a separate launch license would exceed both the relevant time frames and the costs. Therefore, a future implementation must be accompanied by both legal and technical aspects. Having this said, the results of this study demonstrate potential benefits of AED equipped UAV in a best-case scenario with optimal circumstances."

Reviewer: 2

Comments to the Author
The authors raised a very important aspect of AED. The use of AED should be promoted everywhere. Bringing the AED to the scene should be unhindered. Development of unmanned aerial vehicle (UAV) networks delivering early defibrillation for out-of-hospital-cardiac-arrests (OHCA) in areas lacking timely access to emergency medical services (EMS) should be supported by each country.
The authors presented the state of Germany. It would be worth checking what the situation is in other countries.

**Response:**
We thank the reviewer for this review. To the knowledge of the authors there is no country that has implemented UAV delivering AED within the standard care. All implementation efforts have been of an experimental nature. This has also been stated by a recent review stating, "Despite their effectiveness, their [UAV] use in OHCA has not yet become common
practice" (Mermiri MI, Mavrovounis GA, Pantazopoulos IN. Drones for Automated External Defibrillator Delivery: Where Do We Stand? J Emerg Med 2020;59:660–7)

Regarding the implementation, there are numerous studies that have addressed this issue in different countries (e.g. Netherlands or Sweden or Canada). We added the following paragraph to outline the situation in other countries:

"However, so far, AED equipped UAV have not been implemented within common practice but are the focus of many national studies (e.g. Sweden or Canada).[28,33,42]"

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Reviewer: 3

Comments to the Author

General Comments:

Dear Authors,
Your study is focusing on an interesting part in OHCA treatment. As you are calculating the potential costs to implement a nationwide 80 to 100% coverage of AEDs with the help of UAVs. Though your study is well performed and is focusing on the problem to implement AEDs in BLS CPR within the shortest time possible, there are some major issues regarding your manuscript.

Some things are impossible to prove like the statistical methods which have been used as they are almost not described.

**Response:**
We included the following paragraph in the method section to describe the statistical methods used by the location-allocation solver:

"The location-allocation solver uses Hillsman editing to generate a set of semi randomized solutions. Then a vertex substitution heuristic is applied to refine the solutions. Finally, the solutions are combined by a metaheuristic to return near-optimal results.[20]"

Time periods used are hard to understand (e.g. Line 115 – are the laypersons faster in running than paramedics – you assume that they grab unknown equipment out of a garden, street… etc. in a faster time than paramedics their well-known material). You refer on the 94 seconds of Sanfridsson in SJTREM. You should explain why you believe that Toronto Regional RescuNET (58 Inhabitants/km2 up to 4334 Inhabitants/km2) compared to Germanies UAV area (41 Inhabitants/km2) is comparable when comparing accessing times and why not only taking the same timespan for EMS and lay rescuers. Your timespans are "multinational time periods" out of different works, probably reflecting characteristics of the systems and urban/rural settings of different locations.

**Response:**
We agree with the reviewer that the time spans are taken from different works with probably differing circumstances. However, there are no studies that address the specific time spans in Germany for the case of AED equipped UAV. We tried to adhere to known time spans rather than arbitrarily choosing Germany specific time spans. We are aware of the limitation applying time spans from other countries. We added the following paragraph in the discussion section to address this issue:

"It must also be noticed that the time frames used, have been adopted from international studies that may not reflect Germany specific time frames."

In addition, we tried to clarify the definitions of the time spans to facilitate their understanding (see also comment from reviewer 1). The definition of the time interval differed between EMS and UAV. The total time from arrival at scene to defibrillation is identical (4 minutes) for both EMS (3+1) and UAV (2+2). These time intervals consider the issue raised by the reviewer since for EMS, the time between arrival at patient side and first defibrillation was considered to be 1 minute whereas for UAV the time interval was 2 minutes. On the other side, EMS may take longer to arrive at the patient side since the ambulance vehicle has to be stopped at a car accessible road, the equipment has to be grabbed and the patient has to searched for whereas the UAV may drop the AED directly in front of the patient's house and the bystander exactly knows where the patient is located. This is why the time between arrival at scene and arrival at patient side for EMS was 3 minutes whereas for UAV was 2 minutes. We changed the terminology of the time intervals to make this clearer:

EMS

"For EMS, the following time intervals were used (rounded to minutes):

5. Dispatch time between 112 call arrival and dispatch: 1 minute [14]
6. Driving time: depending on location of OHCA
7. Time between arrival at scene and arrival at patient side: 3 minutes [14]
8. Time between arrival at patient side and first defibrillation: 1 minute [15]"

UAV

"The following time intervals were used (rounded to minutes):[14,18]

5. Dispatch time between emergency call and dispatch: 1 minute
6. UAV flying time between take off and arrival at the scene: depending on location of OHCA
7. Time between arrival at scene, retrieving AED and delivery to patient side: 2 minutes
8. Time between arrival at patient side and first defibrillation: 2 minutes"

We hope we have addressed the issue raised by the reviewer.

Line 160 – the radius which was calculated with 8,33km is without starting and landing? Which time is realistic especially for landing procedure? Studies like Boutillier, assume that starting and landing needs about 10 seconds (this would result in a radius reduction of about 500 meters (6%).
My personal opinion is that the calculation of the radius in relation to the necessary time to achieve (10 minutes) is too optimistic. For example: If there is a slight breeze of wind (4 bft = 28km/h = 10-15 kt – even too lose to lift a kitesurf kite) this would reduce the real speed over ground to 72km/h and therefore reduce the calculated diameter to 6km. Not to think about northern sea shore winds or alpine "Föhn" winds as common in southern Bavaria. Was there a calculation for nighttime or situations with limitations of flight

(fog…)? Are there limitations for UAVs? These time and radius diameter calculations under laboratory conditions are potentially dangerous and a major issue as they could change the whole calculation!

**Response:**
We agree with the reviewer that real life scenarios may hinder the UAV to deliver the AED with the time frames used in this study. This issue was also raised by reviewer 1. We included the following paragraph in the discussion section to address these limitations:

"Finally, it should be noted that the most frequent barriers regarding the application of UAV in the above-described scenarios were legal restrictions and technical problems. Such restrictions represent not only barriers regarding the implementation but also the utilization of UAV in such a setting: legal issues (e.g. conflicts in airspace or no-fly zones) and technical issues (e.g. weather conditions or maintenance) may prohibit or hinder the UAV utilization. From a legal point of view, UAV must be provided an automatic launch license in case of an OHCA, otherwise obtaining a separate launch license would exceed both the relevant time frames and the costs. Therefore, a future implementation must be accompanied by both legal and technical aspects. Having this said, the results of this study demonstrate potential benefits of AED equipped UAV in a best-case scenario with optimal circumstances."

Regarding the time needed for starting and landing. We were aware of the time needed for starting and landing used by Boutillier et al. (10 seconds). The maximum flight time of 5 minutes used in our study did not include the 10 seconds needed for starting and landing. We wanted the 5 Minutes (8.33km) to be the exactly the value of the catchment that is used for the calculation within the analysis. Still within our time frame concept, the time needed for starting and landing was theoretically included within the adjacent time frames (Number 1 (starting) and 3 (landing)). Since the time frames used were also rounded to minutes, we accepted to introduce inaccuracy to a certain extent. However, we still think that the time frames used are justifiable without claiming to be 100% accurate. We hope that we have addressed the issues accordingly.

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Wouldn't police, fire rescue laypersons using an AED reduce much of the costs as they cover additional landscape area? Is this not a big part of available laypersons using AEDs, especially in rural area to achieve the AED time within 10 minutes?

**Response:**
Theoretically police and fire fighters could be additionally dispatched in OHCA settings, where the response time of EMS would be too long. However, this is not standard care in Germany but happens occasionally if police or fire fighters are also dispatched for a different reason (e.g. house fire with a person having a OHCA or criminal act leading to an OHCA). Including police and fire fighters within the rescue chain of a "regular" OHCA would require specific regulations that address the legal, technical and personal aspects in Germany. To the best knowledge of the authors there is no political intention to regularly include other professions than EMS in the emergency care in an OHCA setting in Germany. Even though this topic (including other professions than EMS in the emergency care) is interesting, we think it would be beyond the scope of the manuscript. However, we added a paragraph addressing this issue in the discussion section:

"However, so far, AED equipped UAV have not been implemented within common practice but are the focus of many national studies (e.g. Sweden or Canada).[28,33,42] Theoretically, police officers and firefighters could be additionally dispatched instead of an UAV to reduce the time-to-defibrillation in OHCA settings, where the response time of EMS would be too long. However, this is not standard care in Germany but happens occasionally if police or fire fighters have been dispatched for a different reason (e.g. house fire or a possible crime). Including police and fire fighters within the rescue chain of a "regular" OHCA would require specific regulations that address the legal, technical, and personal aspects in Germany. In other countries such dual dispatch systems have already been studied or even implemented on regional level showing a moderate, but significant increase in the 30-day survival of OHCA cases.[43] However, further studies are needed to address these issues more deeply."

We hope that giving this explanation we have addressed the issue raised by the reviewer.

Though you mentioned in the manuscript that you decided against QALY which is understandable - REF 18 is also focusing on HR-QOL (Quality of life) – wouldn't it be of interest to give a lookout on the estimated additionally generated cost for those rescued like for PTCA (ICER). Would it be possible to estimate additionally generated CPC 3 and 4 Patients?

**Response:**
We thank the reviewer for this comment. If we were to include the components mentioned by the reviewer (HR-QOL, additional costs by PTCA and generated CPC 3 and 4 Patients), we would introduce three more outcomes that would 1) need reliable data sources and 2) need to be sufficiently explained. The former is difficult to provide regarding HR-QOL, PTCA and CPC patients in OHCA cases in Germany. The latter would increase the extent of the manuscript beyond the journal's limitations. Even though we agree that these are interesting aspects within this topic, we 1) do not have all necessary data to give a sufficiently evidence-based estimate and 2) we think that this is beyond the scope of this manuscript. We still hope we have addressed this issue accordingly.

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Specific Comments:

- Reference 15 - link does not work

**Response:**
We checked the link and the link does work. Maybe the reviewer has not used the compete link. Here again is the same link as provided in the manuscript https://ec.europa.eu/eurostat/statistics-explained/index.php/Population_grids#Methodology

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- Line 107 – Such an application … this sentence is awkward to read. …has already been studies???

**Response:**
We changed the sentence as follows: "The feasibility of this concept has already been shown on a small scale.[11]"

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- Spatial demand used was not approvable nor explained how it works.

**Response:**
Unfortunately, the reviewer does not specify the issue with the spatial demand used in our study. In the paragraph "spatial demand" within the method section, we describe how the demand was derived and point out that the applied approach is in line with the "disaggregation methodology applied by the European Statistical Office". However, we did not expand on the disaggregation methodology itself since we thought this would be beyond the scope of this manuscript and rather "only" provided the literature. In order to address the reviewer comment we included a short explanation of the disaggregation method.

"This approach is in line with disaggregation methodology applied by the European Statistical Office.[17] The disaggregation methodology is used to produce grids in the absence of geocoded micro data."

Regarding the issue "approvable", we already provided the data source of the OHCA numbers (German Resuscitation Registry). What we did not provide was the data source used to adjust the OHCA cases on municipality level by gender and age. Therefore, we added the data source (Municipality Directory Information System of the Federal Statistical Office and statistical offices of the Länder). We also further expanded the respective paragraph in the method section to provide more information regarding the method as follows:

"For the analysis, spatial demand was defined as the estimated regional number of OHCA with shockable rhythm. The regional number of OHCA with shockable rhythm was derived from national data regarding OHCA cases as of 2018. These data and were estimated projected on municipality level and adjusted by gender (male/female) and age (<18 years, 18-80 years, >80 years) according to the respective proportion in OHCA cases (i.e. in municipalities with an older population, a higher OHCA incidence was estimated).[1,16] The estimated projected regional number of OHCA falling within the study area was then evenly distributed among the grid cells within the municipality. Since grid cells representing non-accessible and unincorporated areas were excluded, the remaining grid cells were clustered in residential areas within a municipality leading to higher OHCA incidence inhose areas compared to non-residential areas. This approach is in line with disaggregation methodology applied by the European Statistical Office.[17] The disaggregation methodology is used to produce grids in the absence of geocoded micro data."

We hope we have addressed this issue accordingly.

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- No Statement on ethical approvement or not can be found.

**Response:**
A statement has been included (see also comment by the editor)

## VERSION 2 – REVIEW

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| **REVIEWER** | Andreas Claesson<br>Centre for resuscitation science Karolinska institutet |
| **REVIEW RETURNED** | 12-Jan-2021 |

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| **GENERAL COMMENTS** | Thankyou for addressing all questions raised in a good way. I now find this paper acceptable for publication. |

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| **REVIEWER** | Mathias Ströhle<br>Anaesthesiology and Critical Care Medicine, Medical University of Innsbruck,<br>Innsbruck, Austria |
| **REVIEW RETURNED** | 08-Jan-2021 |

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|---|---|
| **GENERAL COMMENTS** | Thank you for your accurate revision of your manuscript. To my point of view this revision has answered all my questions in a sufficient manner. |