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Rationale and design of the Lowlands Saves Lives trial: a randomised trial to compare CPR quality and long-term attitude towards CPR performance between face-to-face and virtual reality training with the Lifesaver VR app

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ABSTRACT

Introduction Layperson cardiopulmonary resuscitation (CPR) is a key aspect in the chain of survival after cardiac arrest. New, low-cost, easily accessible training methods such as virtual reality (VR) training with a smartphone application may reach broader populations, but data on CPR performance are scarce.

Methods and analysis The Lowlands Saves Lives trial is a prospective randomised open-blinded end-point evaluation study, comparing two 20 min CPR training protocols: standardised, certified instructor-led face-to-face training complying with current education guidelines (using Laerdal Little Anne manikins), and VR training, using the UK Resuscitation Council endorsed Lifesaver VR app. In the latter, chest compressions are practiced on a pillow. During VR training, participants learn to resuscitate by completing a filmed CPR scenario while wearing VR goggles and headphones. Eligible for inclusion are adult attendees of Lowlands Science, a specific section of the 3-day Lowlands music festival (50 000 attendees), dedicated exclusively to science. Following the training, all participants will perform a CPR test on a Laerdal Resusci Anne QCPR manikin. Primary outcome measures are depth and rate of chest compressions, measured using CPR manikins. The key secondary outcome is overall CPR performance, with real-time examination (blinded for study group) of all items of a European Resuscitation Council endorsed checklist, and evaluation of a sample of videotaped CPR tests by a blinded event committee.

Given the unique setting of a festival, the primary additional analysis will address the impact of alcohol levels on CPR quality parameters and overall performance. Follow-up questionnaires will evaluate the attitude towards performing CPR. This unique study may provide important insights into innovative CPR training methods, factors that impact CPR performance and the impact on long-term attitude towards resuscitation.

Ethics and dissemination This study received approval from the research ethics committee of the Radboudumc. All participants will provide written informed consent. The results of this study will be published in peer-reviewed journals and presented at (inter)national conferences.

Strengths and limitations of this study

► The Lowlands Saves Lives trial uses a unique real-world study setting of a Dutch music festival, and is the first randomised trial to compare cardiopulmonary resuscitation (CPR) quality between certified instructor-led face-to-face training and Lifesaver virtual reality training.

► We will assess clinically relevant CPR quality and performance measures, obtained using objective measurements from CPR manikins and assessors blinded for the intervention, and follow-up will be collected on attitude towards CPR and influencing factors.

► Due to the nature of the intervention, participant blinding is not possible.

► The festival setting allows for a unique and relevant prespecified study question, and there will be stratification according to alcohol levels to assess its impact on CPR quality and overall performance.

► The results of our study will provide important insights into the efficacy of innovative CPR training methods which may help to improve CPR skills of layperson rescuers, with the ultimate goal of improving outcomes after cardiac arrest.
It is therefore essential to create awareness, willingness and capability of lay-volunteers to perform CPR. In this context, leading authorities have identified research on education as one of the top priorities for cardiac arrest research. Current guidelines state that high-level scientific evidence on the optimal CPR training method is scarce. Face-to-face CPR training has long been the gold standard, but new technologies have evolved that may hold potential to reach broader populations and provide quick, easily accessible CPR training that can be performed at home at low costs.

One of these novel training methods is virtual reality (VR), a modality with promising potential according to a recent survey among resuscitation experts. The Lifesaver VR app provides an engaging learning experience, through participation in a filmed CPR scenario. This application is endorsed by the UK Resuscitation Council and can be installed for free on smartphones. Apart from improving laypersons’ skills, better insight into the attitude towards CPR and factors that may influence the decision to start may affect future bystander CPR rates. Aspects like fear to do harm, having no experience or uncertainty about the impact of recent alcohol levels on CPR performance are everyday issues.

The Lowlands Saves Lives trial is a randomised controlled trial comparing CPR quality and long-term attitude towards CPR between face-to-face and Lifesaver VR app CPR training. It will be conducted in the unique setting of a 3-day Dutch music festival (50 000 attendees), which will provide a real-world sample of young and outgoing participants. Furthermore, this setting will allow for unique additional analyses, such as the impact of alcohol use and previous CPR training on CPR performance.

**METHODS AND ANALYSIS**

We followed the SPIRIT guidelines in the design of our study protocol.

**Aim of the study**

The primary aim of this study is to compare CPR quality between face-to-face CPR training and training using the Lifesaver VR app.

**Hypothesis**

Our hypothesis is that training with the Lifesaver VR app will result in CPR quality that is non Inferior to CPR quality achieved by face-to-face training.

**Setting**

The present study will be performed during the Lowlands festival (16–18 August 2019). This is an annual music festival in the Netherlands with over 50 000 attendees. This project of the department of Cardiology, Radboudumc, Nijmegen, The Netherlands, was selected by a jury to be conducted during Lowlands Science, a section of the festival dedicated exclusively to performing scientific research.

**Overview of the study design**

The Lowlands Saves Lives trial is a national, prospective randomised open-blinded end-point evaluation (PROBE) study. The study flow chart is depicted in figure 1. Participants will be randomly allocated (1:1) to either certified instructor-led, face-to-face training or VR training with the Lifesaver VR app. As the study will be performed during a musical festival where alcohol consumption is common, and alcohol consumption may impact CPR performance, we will perform an alcohol breathalyser test in all participants. In case of an alcohol level ≥0.5‰ (the Dutch legal driving limit), participants will perform a tandem gait test. Participants not able to complete this test will not be randomised and excluded from the study. Randomisation will be stratified according to alcohol level.

Directly following the training, all participants will complete a CPR skill test, which will take place in a separate room, with an assessor blinded for the study group. Participants will demonstrate acquired basic life support (BLS) and automated external defibrillator (AED) skills during a specifically designed CPR scenario. We will use a certified CPR training manikin to objectively measure chest compression depth and rate (and other parameters, such as flow fraction, leaning, etc.). Furthermore, overall CPR performance will be scored with use of a European Resuscitation Council endorsed checklist, with items that focus on the required steps for performing adequate CPR and AED use (online supplementary 1).
Inclusion and exclusion criteria of the Lowlands Saves Lives trial

| Inclusion criteria                                                                 |
| ----------------------------------------------------------------------------------- |
| Adult (≥18 years) Lowlands attendees.                                               |
| Provide informed consent.                                                           |

| Exclusion criteria                                                                 |
| ----------------------------------------------------------------------------------- |
| Alcohol level ≥0.5‰ and not able to complete tandem gait test.                     |
| For any reason not being able to partake in the face-to-face or VR app training   |
| For any reason not being able to perform the CPR test on the CPR manikin           |

Inclusion and exclusion criteria of the Lowlands Saves Lives trial. CPR, Cardiopulmonary resuscitation; VR, virtual reality.

Participants

Adult (≥18 years) attendees of Lowlands Science, a specific section of the Lowlands music festival, dedicated exclusively to scientific research. Further inclusion and exclusion criteria are shown in Table 1. Inclusion of participants with previous CPR training (CPR course ≤2 years) is capped at 20% of the total inclusions. Consent to participation includes an alcohol breathalyser test in all participants (AlcoTrue P, Bluepoint Medical, Selmsdorf, Germany). In addition, video recording of the final CPR skill assessment will be performed on an individual basis, in the subset of participants who provide consent.

The study will be performed during the entire duration of the festival, which is three full days and inclusion will continue until the end of the festival. Our estimated maximum educational capacity is 480 participants.

Randomisation and data management

Participants will be randomly allocated (1:1) to either of both training methods using the online Castor Electronic Data Capture (Castor EDC) system. We will use a random block randomisation algorithm and stratify randomisation according to alcohol level, using a binary cutoff value of <0.5 vs ≥0.5‰. Castor EDC will also be used for data management. Castor EDC data will be exported for analysis.

Interventions

Face-to-face training: The training will comprise a 20 min CPR training by an instructor certified by the Dutch Resuscitation Council, who is not part of the study team and not an employee of the Radboudumc, Nijmegen, The Netherlands. The training protocol is standardised and was designed under supervision of our national BLS course director (HW). The ratio of instructors to participants is 1:5. Chest compressions and ventilations will be taught using certified CPR manikins (Little Anne, Laerdal Medical, Stavanger, Norway). These manikins will provide auditory feedback on compression depth. There will be enough manikins for each participant to have their own, but practicing CPR skills will be done in pairs of two participants. AED use will be demonstrated and practiced with use of Zoll training AEDs (Zoll AED Trainer 3, Zoll Medical, Chelmsford, USA).

In line with the recommendations of the European CPR education guidelines, we incorporated the following core elements into the training: willingness to start CPR, recognition of unconsciousness, good-quality chest compressions and feedback during the training. We will also focus on creating awareness for AED use and benefit, and provide education on common myths on CPR (eg, the belief that it may cause harm).

Lifesaver VR training: Lifesaver VR is an innovative, immersive and interactive game that can be installed for free on smartphones (https://lifesavervr.org/). During VR training, participants learn to resuscitate by completing a filmed CPR scenario while wearing VR goggles and headphones. The completion of this scenario will take approximately 20 min. The novel ‘game-in-film’ format provides an engaging learning experience with a real-life CPR scenario. Users become actively involved with the resuscitation of a victim of cardiac arrest and simulate cardiac compressions by performing compressions on a pillow. The app provides feedback on compression speed, and instructions on compression depth. It also teaches skills needed for adequate AED use. If a wrong decision is made, the user sees the impact but is then able to rewind and make the correct decision. The recently added VR feature allows the users to experience the resuscitation scenario in VR, using VR goggles, further enhancing the experience. For this training, we will use Samsung S7 smartphones (Samsung, Seoul, South Korea), in combination with Zeiss VR One Plus VR goggles (Carl Zeiss, Oberkochen, Germany) and headphones. Lifesaver VR endorsed by the UK Resuscitation Council has been developed using charitable funds and does not generate financial revenues.

Outcome measures and other parameters

Outcome measures in this study are based on a consensus document describing the preferred outcomes for reporting on CPR quality and on current CPR guidelines.

The primary outcomes are the CPR quality parameters chest compression depth (mm) and compression rate (compressions per minute), assessed with the certified CPR manikins (Resusci Anne QCPR, Laerdal Medical, Stavanger, Norway).

The key secondary outcome measure is the overall CPR performance expressed as a real-time appointed score by examiners blinded for study group, using the European Resuscitation Council endorsed CPR checklist (online supplementary 1). Video recordings of CPR skill tests will be made of the subset of participants who provide consent for this additional study feature. A random sample of all video recordings will be reviewed by an external event committee, blinded for study group. In addition, we will
report on other, secondary CPR quality parameters such as flow fraction (percentage of time where compressions given) and proportions of chest compressions with full release (as a measure for leaning), assessed with registrations of the certified CPR manikin. Finally, we will calculate proportions of participants meeting guideline CPR quality criteria.10 26 27

Other study parameters: At baseline, all participants will complete a questionnaire after informed consent, with information on, for example, age, sex, weight, education level, previous CPR experience and previous CPR training (online supplementary 2).28 All relevant baseline variables will be reported and compared between both study groups. Follow-up questionnaires after 6 months will focus on attitude towards CPR and aspects that influence the decision to start CPR.19 20

Study organisation
Diagram B.V. (Zwolle, The Netherlands) will be responsible for data monitoring and the coordination of the video evaluations of a sample of CPR skill tests. All primary outcome measures will be monitored. Baselines and follow-up data will be monitored as well. The review of CPR skill videos will be conducted by an event committee of two experienced CPR instructors, blinded for study group.

Prespecified additional analyses
Our primary additional analysis concerns the impact of alcohol on CPR quality parameters and overall performance. In this context, randomisation will be stratified according to alcohol levels.

The second additional analysis concerns the impact of previous CPR training on CPR quality and overall performance. To ensure that this project provides sufficient information on the efficacy of the two training methods for laypersons without CPR training, the number of participants with previous CPR training is capped at 20% of the total of randomisations. Moreover, sample size calculations for the primary study aim were performed to assess the required number of laypersons without CPR training, after which this total was multiplied by 1.25 to calculate the total number of participants.

Exploratory analyses
The following subgroups are prespecified for analysis of the respective outcome measures: men versus women, above versus below median age, above versus below median weight, with versus without previous CPR experience, above versus below median education level and healthcare providers versus no healthcare providers.

Follow-up assessment
All participants will be asked to provide additional consent for a follow-up questionnaire to be conducted 6 months after finalisation of the trial. This questionnaire will contain questions regarding attitude towards the trial and CPR in general, follow-up training and real-life resuscitation experience following participation in the trial.19 20 Data will be analysed in a similar way as the primary and secondary outcomes: between study groups, according to the prespecified subgroups and in exploratory analyses.

Statistical considerations
This study is designed to evaluate the hypothesis that VR training is non-inferior to instructor-led training. A recent review reported that the expected effect on compression depth of instructor-led training is about 5 mm, and that the average effect on compression rate is about 17 per minute.29 Data on expected differences in CPR performance in relation to alcohol level are unavailable, but to optimally address this question randomisation will be stratified by alcohol level. To ensure sufficient data on the efficacy of both training methods for laypersons without CPR training, we decided that sample size calculations for the primary outcome measure should allow for meaningful conclusions in this group of specific interest. Main outcomes of interest will be tested for non-inferiority. Other variables will be assessed for normal distribution and reported as means (SD) or medians (IQR), whichever is appropriate. Continuous data will be compared using a Student’s t-test or Mann-Whitney U test, whichever is appropriate. Categorical variables will be reported as numbers (%) and compared using $\chi^2$ or Fisher’s exact tests, whichever is appropriate. All baseline variables
(demographics, previous CPR experience) and outcome data (CPR rate and depth, CPR score, flow fraction, leaning, etc.) variables will also be compared between the two study groups using the abovementioned tests. In case of confounding variables, we will correct comparisons on the outcome measures between the study groups for these confounders using analysis of covariance. A p-value of <0.05 will be considered statistically significant. Analyses will be performed using SPSS V.25 (IBM Corp.).

**Sample size calculation**

The present study is designed as non-inferiority trial, where the null hypothesis is that VR training is inferior to face-to-face training. The non-inferiority margin for depth is set at 5 mm, with an expected SD of 10 mm. Based on these assumptions, an alpha of 5% and a power of 90%, we calculated that we need 69 participants per group.

As the inclusion of participants with previous CPR training is capped at 20%, at least 80% of the participants will have no prior CPR training. As we prespecified that sample size calculations should be based on this latter group, the total number per study group will therefore need to be 1.25*69=86. Assuming a dropout of 10%, we will aim to include 95 participants per group, that is, a total of 190 participants. This sample size will also provide sufficient power for a non-inferiority hypothesis testing for chest compression rate, given the SD of 20 per minute and average increase in chest compression rate of 17 per minute found in previous studies.

**Patient and public involvement**

No patients were involved in the design of this study protocol. However, we incorporated several elements into our training that were identified by laypersons as important factors for performing CPR and using an AED.

**ETHICS AND DISSEMINATION**

All participants will provide written informed consent before participating in the trial. The results of this study will be published in peer-reviewed journals and presented at national and international conferences.

**DISCUSSION**

The Lowlands Saves Lives trial has been initiated as a project to reach a large group of citizens in a short period of time during a Dutch music festival and to stimulate awareness, willingness and capability of laypersons for CPR. Appreciating that in about 40% of the OHCA bystander CPR is not given, while early start of resuscitation is the key determinant of survival, we wanted to test the efficacy of two innovative training methods on CPR performance and attitude towards resuscitation. In the setting of a randomised trial with PROBE design, we will compare 20 min certified instructor-led face-to-face training with 20 min VR training using the Resuscitation Council endorsed Lifesaver VR app.

**Layperson CPR**

Appreciating that the vast majority of cardiac arrests occur at home, it is imperative to increase the rate of layperson-initiated CPR as this is expected to markedly improve survival chances. Several factors affect the decision to actually start CPR, varying from the fear to do harm, to perceived inability due to lack of training, or fear to be contaminated by providing mouth-to-mouth ventilations. A previous American Heart Association consensus document on CPR education stated that layperson training should focus on overcoming barriers to initiating CPR. It is therefore one of the key aspects during training, and the impact of both training methods on the attitude towards CPR will be subject of interest of the follow-up questionnaires.

Despite growing interest in CPR training, and the fact that several companies have appointed an in-house emergency service, the vast majority of citizens is not currently trained in CPR. European documentation on BLS training for instructors (Cosy) states that BLS courses should be at least 2 hours. In the Dutch setting, current conventional certified training programmes last about 4 hours, which may pose a logistic and sometimes financial burden to partake in these programmes.

Programmes with a lower threshold to participate, preferably of shorter duration, may reach a broader population. Previous work has shown that a 30 min training yields similar results as a conventional training. In addition, a modality that allows for easy, repetitive training may not only appeal to a larger target population, but it may also facilitate a more sustained CPR quality. Several studies have shown that short booster training improves CPR performance and the guidelines place increasing emphasis on high-frequency, short, booster training for certified BLS providers. This may facilitate improved skill retention, a major topic in current CPR (education) guidelines.

The accessibility of Lifesaver VR app, its low cost and the possibility to perform it at convenient moments, at home, could be advantageous and useful for laypersons who experience a threshold to participate in face-to-face training. However, information on CPR quality data is limited, and we are the first to assess the Lifesaver app in combination with a VR modality.

**Training methods and outcome measures**

We will compare 20 min face-to-face training by a certified BLS instructor with 20 min VR training using the Lifesaver app. The instructors will provide a standardised training, developed with our national course director BLS. Outcomes achieved with the Lifesaver VR app will be tested in the setting of a non-inferiority design.

Our primary outcomes are in concordance with current international CPR guidelines. Both chest compression depth and compression rate have repeatedly been associated with survival after cardiac arrest. Moreover, both outcome measures can be objectively assessed with the output of the certified manikins.
A recent review on the impact of training demonstrated that instructor-led training results in about 5 mm additional chest compression depth.\(^2\) This is what we defined as the non-inferiority margin for this primary outcome measure, with a required total of 190 participants. This total is also sufficient to address non-inferiority for the number of chest compressions per minute. As instructor-led training is reported to result in about an additional 17 compressions per minute, this was set as non-inferiority margin for this primary outcome measure.

The key secondary outcome measure is overall CPR performance. This is an integrative score, appointed real time, by an assessor blinded for study groups. It reflects the entire CPR process, including alerting the emergency telephone number 112 and the ability to use the AED, and the score will be assessed with use of a checklist endorsed by the European Resuscitation Council. In addition, a blinded event committee will review a sample of the CPR skill tests registered on video in participants who provided additional consent.

In addition, we prespecified important additional analyses and incorporated specific elements in the design of our study to ensure that these questions could be adequately addressed. First, the goal of recruiting more laypersons to perform CPR may result in situations where CPR is required while someone has consumed alcohol in a restaurant or bar, which is often a controversial issue in case medical help is required.\(^3\) The unique setting of a music festival provides a setting to further explore this issue. In this context, randomisation will be stratified according to alcohol level, including a group with a level higher or equal to, and lower than 0.5%, the Dutch legal driving limit.

Second, lack of CPR training is often mentioned as a reason not to perform CPR.\(^4\) Data on how much previous CPR training affects CPR quality and overall CPR performance are limited, and we therefore aim to objectify this issue. This may help to provide better quality evidence to address these concerns.

**Follow-up**

With use of follow-up questionnaires, we will gather and compare information on the attitude towards CPR between both training methods. In addition, we will try and identify factors that may influence the decision to initiate bystander CPR. The Lowlands Saves Lives trial not only focuses on the training itself, but also on an entire experience. In this context, banners will be displayed with links to the Dutch Heart Foundation (www.hartstichting.nl), providing additional information on resuscitation and on potential venues to follow endorsed BLS-AED courses.

**Implications**

In a setting of a renowned Dutch music festival with about 50,000 attendees, our study is expected to contribute to increased awareness for resuscitation, and may result in about 200–400 trained citizens. In addition, it will address a key topic in current resuscitation research, that is, the search towards an optimal CPR training method, and it will be the first to study the Lifesaver app with a VR modality.

Until now, the only data available for the Lifesaver app have been obtained in children, at that time without a VR feature. Results were promising, although compression depth seemed suboptimal. Whether this is related to the low body weight of the children, or a consequence of the training method is uncertain. The VR modality may enhance the experience, and mimicking a situation that is closer to the real-life setting may contribute to better results.

Globally, increasing the rate of bystander CPR is anticipated to be one of the key factors to improve survival after cardiac arrest. In the Netherlands, campaigns stress the importance to initiate CPR within 6 min of the arrest, given the much higher chances of survival within this interval. All efforts are made to create a national network that consists of citizens with an official BLS-AED certificate that subscribe to a national text message-based alert system combined with a registration system of AEDs.\(^4\) The goal is to achieve a coverage that ensures a 6 min response in all parts of the Netherlands. European guidelines also stress the importance of early bystander response.\(^10\)

**Potential limitations**

In the present study, no data will be available on CPR performance prior to the training. Second, due to the lack of follow-up skill testing no data are available on CPR skill retention. We will include a maximum of 20% of participants with previous CPR experience, which may impact the overall skill performance in both study groups. However, the group of participants without previous CPR training comprises a subgroup of special interest, and our target sample size allows for adequate statistical power to perform analyses on the primary outcome measure in these participants. Due to the specific study setting, our study sample may be unique when compared with other studies on this topic, which may limit generalisability of our results to, for example, elderly civilians.

**CONCLUSION**

The Lowlands Saves Lives trial will create awareness for the importance of bystander CPR, and aims to increase willingness and capability to participate in CPR. If an easily available low-cost app can result in similar CPR results as instructor-led training, this may be an important step towards reaching this goal.

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**Collaborators** Scientific committee: Lars Wik MD PhD (Oslo University Hospital, Oslo, Norway) and Giuseppe Ristagno MD PhD (Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan, Italy). Event committee: Reinier Waalewijn MD PhD (National course director advanced life support, Gelre Hospital, Apeldoorn, the Netherlands) and Wiebe de Vries PhD (University of Applied Sciences Leiden, Leiden, The Netherlands).
Contributors JN, JT, JLB, and MAB conceived the idea. JN, JT, RVG, NVr, JLB and MAB designed the study methodology. JN, PV and MAB designed the statistical analyses. JN, JT, JLB and MAB drafted the manuscript. PV, RVG, and NVr provided critical revisions and substantial intellectual input. All authors agreed with the final version of the manuscript. JN takes full responsibility for integrity of the presented content.

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Ethics approval The study will be conducted according to the principles of the Declaration of Helsinki and in accordance with the Medical Research Involving Human Subjects act. The research ethics committee of the Radboud University Medical Center has reviewed this study on the basis of the Dutch Code of conduct for health research, the Dutch Code of conduct for responsible use, the Dutch Personal Data Protection Act and the Medical Treatment Agreement Act. The ethics committee has passed a positive judgement on the study.

Provenance and peer review Not commissioned; externally peer reviewed.

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