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**Research Article** 

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# Comparison of Augmented Reality-assisted and Instructor-assisted Cardiopulmonary Resuscitation: A Simulated Randomized Controlled Pilot Trial

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#### **KEYWORDS**

Augment Reality (AR);<br/>Cardiopulmonary<br/>Resuscitation (CPR);<br/>Bystander CPR;<br/>CPR training;<br/>Nursing educationBackground: A trained I<br/>arrest. Augmented Reali-<br/>self-training especially d<br/>Methods: A prospective<br/>was developed and 28 p<br/>assisted group. Acceptab<br/>and accuracy were measu<br/>Results: The mean score<br/>real-time AR-assisted CPR<br/>(95% CI: -0.18-0.53) cm<br/>to instructor training, th<br/>compression depth, rate<br/>Conclusion: We found th<br/>CPR and self-training CPR<br/>Cite this article:<br/>Hou, L., Dong, X., Li, K., M<br/>and Instructor-assisted C

Abstract

**Background:** A trained lay rescuer is the most important determinant of survival from sudden cardiac arrest. Augmented Reality (AR) device may represent a powerful instrument for CPR assistance and self-training especially during the COVID-19 pandemic.

**Methods:** A prospective, parallel, 1:1 pilot randomized clinical trial was designed. An AR CPR app was developed and 28 participants were randomly allocated into AR-assisted group and instructor-assisted group. Acceptability, usability, and mean per minute/per cycle chest compression depth, rate and accuracy were measured.

**Results:** The mean scores for acceptability and usability were all rated good in each group. Comparing real-time AR-assisted CPR to instructor-assisted CPR, the mean difference of compression depth was 0.18 (95% CI: -0.18-0.53) cm and rate was -1.58 (95% CI: -6.11-2.95) min-1. Comparing AR self-training to instructor training, the AR group was not significantly different between two groups regarding both compression depth, rate and accuracy (p > .05).

**Conclusion:** We found that the AR CPR app was an acceptable and usable tool both in real-time-assisted CPR and self-training CPR.

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# Introduction

Sudden cardiac death occurs in up to 550,000 people every year in China, the highest level globally (Xu, Zhang, & Chen, 2017). Performing chest compression to the correct depth and rate during cardiopulmonary resuscitation (CPR) is crucial for survival after cardiac arrest (Meaney et al., 2013; Talikowska, Tohira, & Finn, 2015). In recent

#### **Key Points**

- A valid augmented reality assisted CPR application using Hololens2 that could guide the users stepby-step to correct compression in realtime was developed in this study.
- It is suggested that Augment Reality device may be acceptable and useful option for CPR self-training during the periods of Covid-19 pandemic.
- Augmented reality assisted CPR application could increase the proportion of participants who met the guidelines for quality CPR over time.

years, China has been working to promote CPR public training (People.cn, 2016). However, with a very large population in China, the training and implementation rates of bystander CPR are still far behind that of developed countries (Ge et al., 2015; Girotra et al., 2016; Hawkes et al., 2016). There are currently two significant challenges with CPR during outof-hospital cardiac arrest (OHCA). The first is to improve the willingness and engagement of the general public with CPR in cardiac arrest, and the second is to increase the quality of CPR performance.

The American Heart Association (AHA) has

called for innovative strategies to increase public CPR training rates (Rumsfeld et al., 2016). Innovative strategies and emerging technology provide a new model for CPR learning, offering better knowledge and patient outcomes (Cook et al., 2011). One such technology is augmented reality (AR), which involves overlaying an interactive, digital layer of information on top of the physical environment (Barsom, Graafland, & Schijven, 2016). This could make learning faster, more efficient, and more engaging (Geroimenko, 2020). Owing to the advantages that AR technology offers, several programs using available devices such as Google Glass and Microsoft Hololens2 have been successfully implemented in the field of CPR, and demonstrate its feasibility and usability (Balian, McGovern, Abella, Blewer, & Leary, 2019; Ingrassia et al., 2020; Siebert et al., 2017). Furthermore, AR devices for self-training could reduce the need for group training, which is difficult to conduct in the context of the ongoing COVID-19 pandemic.

To shorten the rescue starting time before the arrival of the ambulance and increase CPR quality, dispatcher-

assisted CPR during OHCA is the most common method used by bystanders and has a survival rate of 8.6%-13% (Chang et al., 2018; Riva et al., 2020). With the development of technology, studies revealed that videoassisted CPR offers a more accurate chest compression rate and depth compared to voice-assisted CPR (Lin et al., 2018; Yang et al., 2008). Moreover, some real-time feedback devices are effective in improving CPR performance (Anderson, Sebaldt, Lin, & Cheng, 2019; S.-A. Wang, Su, Fan, Hou, & Chen, 2020). As an emerging technology, AR can provide visual and real-time feedback to increase CPR quality.

In this study, we investigated the use of an AR CPR app we developed for CPR assistance and training. We aimed to evaluate the feasibility of real-time AR-assisted bystander CPR during simulated OHCA and self-training CPR by AR CPR app.

# Materials and Methods

#### Study Design

This pilot was a prospective, parallel, 1:1 randomized clinical trial following the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline. Ethical approval was received from the Peking University Biomedical Ethics Committee (IRB00001052-21035) in April 2021. All participants could withdraw from the study at any time and the data were confidential, anonymous, and used for research purposes only. Written informed consent was obtained from all participants.

#### Participants

Convenience sampling was used to recruit participants via social media advertisements in August 2021 in Beijing. The inclusion criteria were as follows: (1) over 18 years old; (2) had not undergone CPR training in the past two years; and (3) voluntary participation. The exclusion criteria were: (1) unable to participate in the study safely due to serious cardiovascular disease or neurological dysfunction, or unable to participate in physical education classes due to physical reasons; and (2) episodes of severe dizziness, nausea, or headache while watching 3D movies or using AR/VR devices.

Participants were enrolled according to the criteria and randomized to either the instructor-assisted group or the AR-assisted group. This study was conducted in the Simulation Teaching Center of Peking University School of Nursing.

#### Randomization

Randomization was conducted by an independent researcher using the random number function in Excel to



Figure 1 The holograms of the AR CPR app using HoloLens2: (a) a simulated subway station scenario with cardiac arrest; (b) chest compression and posture guidance (third-person perspective); (c) breathing guidance (first-person perspective); (d) real time feedback of compression depth and rate (first-person perspective).

generate a randomization sequence. The independent researcher obtained participants' random numbers and group allocation by opening opaque envelopes. Another researcher assigned the participant to interventions. Owing to the informed consent of the intervention of each group, participants were not blinded.

### Interventions

#### Development Of the AR CPR App

The immersive, multi-sensory AR CPR app used HoloLens 2 (Microsoft, Redmond, Washington, USA), a head-mounted wearable device, and was developed jointly by Peking University School of Nursing and Chengdu Techman Software Co., Ltd (Chengdu, China). Based on the current AHA CPR guidelines and under the supervision of the AHA Basic Life Support course director, the contents were adaptive to several scenarios, such as subway stations, public parks, or empty streets. All participants in this study performed CPR in a simulated subway station scenario with a middle-aged man who suddenly had a cardiac arrest, as represented by a via Little Anne manikin (Laerdal Medical, Norway). Participants could check for responsiveness, call for emergency medical assistance, perform CPR and rescue breathing (this aspect can be omitted) and use an automated external defibrillator (Laerdal AED trainer 2), guided by the AR CPR app (Figure 1). Most significantly, holographic real-time feedback was given on the compression depth, rate, and time in the view of HoloLens 2. Audio feedback was also provided to rectify incorrect compression.

#### Prebriefing

The steps of simulation-based intervention in this study was on the basis of simulation-based education (SBE), which was consistent with the published international simulation standards of best practice related to simulation design (INACSL Standards Committee, 2016a). In the phase of prebriefing, since most participants had never used AR devices, a Hololens2 introduction was provided and the "Tips" app was used in Hololens2 to practice and master how to use the device for both groups. The scene was set in a simulated subway station with a man in cardiac arrest, with logistics of the facility, safety, and building layout explained at the start of the intervention. Furthermore, the planned outline and objectives of the simulation-based intervention was described for all of the participants.

#### Simulation

In the AR-assisted group, participants were asked to try their best to perform a continuously Hololens-assisted hands-only CPR to simulate an OHCA. During this phase, the scenario last approximately 10 minutes. Participants could stop chest compressions at any time if they were

Phases Of the Simulation-Based Intervention	Content		
	AR-Assisted Group	Instructor-Assisted Group	
Prebriefing	Introduction and practice	Introduction and practice	10min
Simulation	Continuously real-time AR-assisted CPR with data collection	Continuously real-time supervisor-assisted CPR with data collection	10min
Debriefing	Self-training by AR CPR app	Skills training by instructor	15min
	CPR Skills evaluation	CPR Skills evaluation	2min
	Learner feedback	Continuously real-time AR-assisted CPR and learner feedback	10min

unable to continue. In the instructor-assisted group, participants were asked to perform a continuously 10-min of instructor-assisted CPR in the same scenario. The instructor, trained in AHA Basic Life Support, orally guided the participants step by step according to the standardized instruction for out-of-hospital hand-only CPR, which simulated dispatcher-assisted CPR (X. Wang, 2017).

#### Debriefing

Debriefing was conducted immediately after the scenario following the INACSL standards of best practice for debriefing (INACSL Standards Committee, 2016b). Plus Delta  $(+/\Delta)$  debriefing method was used in this study. A plus sign is used to identify positive actions such as mastering this step of CPR and delta means this step could be done better (Jeffries, 2020). In the AR-assisted group, participants underwent 15-minutes self-training CPR by Hololens2. They could practice steps of self-training CPR repeatedly according to the Plus Delta debriefing, using a guide of an immersive multi-sensory AR CPR app. After that, CPR skill check without an assistant was subsequently performed and the acceptability and usability evaluation questionnaires were completed. In the instructor-assisted group, a 15-minutes instructor-assisted CPR training session and a 2-min CPR skill check without assistance were completed. Afterwards, to compensate the participants in this group, the same interventions, including the 10-min HoloLens CPR self-training was offered to this group based on participants' willingness after their assessments. Finally, the acceptability and usability evaluation questionnaires were completed. Table 1 shows the intervention details of the two groups.

#### **Outcomes**

The Unified Theory of Acceptance and Use of Technology (UTAUT) questionnaire was used to measure the acceptability of the AR environment (details in Supplementary table S1). From this, 21 items were selected because dimensions of price value and habit were not applicable (Venkatesh, Thong, & Xu, 2012). Dimensions of performance expectancy, effort expectancy, social influence, facilitating condition, hedonic motivation, and behavioral intention were included in this study. Cronbach's alphas were from 0.854 to 0.992 for each of its dimensions and for the total scale. A score was calculated for each dimension by a seven-point Likert scale ranging from one (totally disagree) to seven (totally agree), and a higher score means better acceptability. Based on the UTAUT model, age, gender, and experience would affect the attitude towards the AR device so these were all collected at baseline.

Based on the simulator sickness questionnaire (Cybulski, Rzeźniczek, & Bilski, 2020; Kennedy, Lane, Berbaum, & Lilienthal, 1993), the usability was measured by a five-item sickness questionnaire including "I felt nervous, anxious, depressed or irritable", "I felt sick in my stomach", "I felt unable to concentrate", "I felt eye strain or blurred vision" and "I felt dizzy or headache" with a seven-point scale from one (totally disagree) to seven (totally agree). The lower the sickness score, the higher the usability. The reliability of the sickness questionnaire was satisfactory with a Cronbach's alpha value of 0.828.

Real-time feedback compression rate and depth data were collected by Palm CPR<sup>TM</sup> (Sunlife Science, China, http://www.sunlifescience.com/en/PalmCPR\_en.htm), which could match up with using in manikins. Moreover, CPR statistics for PC software was developed jointly by Peking University School of Nursing and Chengdu Techman Software Co., Ltd (Chengdu, China), which could calculate and output the compression feedback data in the stages of real-time-assisted skills and skills check via a Bluetooth connection to Palm CPR<sup>TM</sup>.

CPR quality was measured in the pilot, expressed as mean, per minute mean, per cycle (across 30 chest compressions) mean depth (cm) and rate (minute-1) of chest compressions. Evidence suggests that these have a strong association with patient outcomes (Considine et al., 2020). In addition, we calculated every participant's compression accuracy and the proportion of participants within the guideline rate of 100 minute-1 to 120 minute-1 and depth

of 5 cm to 6 cm (Soar et al., 2020; Soar et al., 2019). All of these data were calculated and output by CPR statistics for PC software (Techman Software Co., Ltd, Chengdu).

#### **Statistical Analysis**

Based on rationale about feasibility and precision about the mean and variance, a sample size of 12 per group was recommended in a parallel-group pilot trial (Julious, 2005). Considering the 10% dropout rate, the sample size was further increased to 14 per group.

Continuous data were reported by mean (SD) or median (interquartile ranges [IQR]) according to a normality distribution test and compared using a 2-sample t-test or Mann-Whitney U test, while categorical data were reported by numbers (%) using  $\chi^2$  or Fisher exact tests. For more efficient analysis, the data underwent multiple imputations for time series data methods to impute missing values where chest compressions were performed for less than ten minutes (Z. Zhang, 2016).

To compare quality of 10-min hands-only AR-assisted CPR to instructor-assisted CPR, a 2-sample t-test was used, and mean differences (95% CI) of compression depth, rate, and accuracy were reported. We also calculated the proportion of participants who could perform compressions within the guideline ranges during the ten minutes and first ten cycles in the two groups and compared the difference using a  $\chi^2$  test. To compare the CPR quality of self-training by AR and instructor training, a 2-sample ttest was used, and mean differences (95% CI) were reported for chest compression depth, rate, and accuracy. Moreover, mean compression depth and rate in the two groups were reported and the proportion of participants within the guideline was compared by  $\chi^2$  tests to analyze the effectiveness of different training methods. Data were recorded using Microsoft Excel 2019 software after double-checking. Data analysis and presentation were performed using R v. 3.6.0 (https://www.r-project.org/) and GraphPad Prism 9 (GraphPad software, California). p < p.05 was statistically significant.

# Results

Overall, 28 participants were enrolled in this pilot RCT with 14 in each group. Of these, one participant withdrew after randomization because of physical discomfort and the others performed CPR for more than five minutes. A final total of 14 participants in the AR-assisted group and 13 in the instructor-assisted group were analyzed (Figure 2). Two participants (14.29%) in AR-assisted group and three (23.08%) in instructor-assisted group performed less than 10-minute continuously CPR because of exhaustion but all the participants performed more than five minutes.

Of the 27 participants, 92.59% were women. The average age was 24.19  $\pm$  3.14 years and BMI was 20.52  $\pm$ 

3.41 kg/m2. Details and differences of participants' characteristics in two groups were present in Table 2. There were no significant differences between the two groups in terms of baseline.

The acceptability was rated as good by both groups, and the mean score of each dimension scored above 4 and is shown in Figure 3. There was no significant difference between the two groups at each dimension. We also analyzed the correlation between age and acceptability, no significant correlation was observed.

The results of the sickness questionnaire show good usability in that the highest median (IQR) score was 3 (2-4.25) for "I felt nervous, anxious, depressed or irritable" in the AR group, and 3 (1.5-5) in the instructor group (p = .751). Other items were all scored <3 and showed no significant difference between the two groups.

For the quality of 10-minute hands-only continuously CPR, the mean (SD) chest compression depth in the ARassisted group was 5.05 (0.34) cm compared to 4.87 (0.54) cm in the instructor-assisted group (p = .317). The mean difference of compression depth was 0.18 (95% CI: -0.18-0.53) cm. The mean (SD) chest compression rate in the AR group was 109.07 (6.10) min-1 compared to 110.65 (5.25) minute-1 in the instructor group (p = .479). The mean difference of compression rate was -1.58 (95% CI: -6.11-2.95) minute-1. The mean (SD) rate of compression accuracy was 76.79 (15.65) % in the AR group compared to 70.70 (30.63) % in the instructor group (p = .528). The rate difference of compression accuracy was 6.09 (95% CI: -13.83-26.02).

More than 60% of participants in the AR group and more than 50% of participants in the instructor group could perform compressions to the guideline-endorsed depth over five minutes. To further present the learning trajectory of the two groups, we analyzed the first ten cycles of compression depth and found no significant difference in any cycle between the two groups (p > .05). After three minutes, more than 80% of participants in the AR group and 75% in the instructor group could still perform compressions at the guideline-endorsed rate. Furthermore, there was no significant difference in compression rate in any cycle in either group (p > .05; Supplementary figure S1).

After brief training, for the skills check, the mean (SD) compression depth in the AR group was 5.59 (0.65) cm compared with 5.42 (0.66) cm in the instructor group (p = .499). The mean difference of compression depth between the two groups was 0.17 (95% CI: -0.35-0.69) cm. The mean (SD) compression rate was 108.95 (3.91) min-1 in the AR group and 111.06 (4.77) min-1 in the instructor group (p = .219). The mean difference of compression rate was -2.11 (95% CI: -5.56-1.33) minute-1. In addition, the rate difference of compression accuracy between the two groups was 2.93 (95% CI: -8.23-14.09) with a *p*-value of .499. The proportion of participants that met the guideline compression depth was 64.29% in the AR self-training group compared with 76.92% in the instruc-





Figure 2 CONSORT Flow diagram.

Characteristics	Total $n = 27$	AR-assisted $n = 14$	Instructor-assisted $n = 13$	t/χ²	р
Age (mean $\pm$ SD)	$\textbf{24.19} \pm \textbf{3.14}$	24.79 ± 3.97	$\textbf{23.54} \pm \textbf{1.85}$	1.03	.31
BMI (mean $\pm$ SD)	$\textbf{20.52} \pm \textbf{3.41}$	$19.58\pm1.61$	$21.53 \pm 4.50$	-1.47	.16
Gender, n (%)					
male	2 (7.41)	1 (7.14)	1 (7.69)	0.003	.96
female	25 (92.59)	13 (92.86)	12 (92.31)		
Exercise time per week, n (%)					
≤ 3h	15 (55.56)	10 (71.43)	5 (38.46)	2.97	.09
> 3h	12 (44.44)	4 (28.57)	8 (61.54)		
Education level, n (%)					
Bachelor degree or below	5 (18.52)	3 (21.43)	2 (15.38)	0.16	.68
Postgraduate or above	22 (81.48)	11 (78.57)	11 (84.62)		
Are you medical related majors, n (%)					
Yes	17 (62.96)	10 (71.43)	7 (53.85)	0.90	.34
No	10 (37.04)	4 (28.57)	6 (46.15)		
From where, n (%)					
Rural area	14 (51.85)	7 (50)	7 (53.85)	0.04	.84
City	13 (48.15)	7 (50)	6 (46.15)		
Have you ever participated in CPR training, n (%)					
Yes	11 (40.74)	7 (50)	4 (30.77)	1.03	.31
No	16 (59.26)	7 (50)	9 (69.23)		

tor training group (p = .385). The proportion of participants that met the guideline compression rate was 92.86% in the AR self-training group compared with 100% in the instructor training group (p = .519; Figure 4).

# Discussion

In this pilot RCT, we found that participants had a good acceptance and rated the usability as good of real-time AR-

assisted CPR and AR self-training CPR. To our knowledge, this is the first study attempting to report the feasibility of real-time AR-assisted bystander CPR compared to realtime instructor-assisted bystander CPR, which simulated dispatcher-assisted CPR in OHCA. This study provides a novel method for future research into real-time guidance of out-of-hospital CPR and also provides valuable and feasible evidence for future development of brief self-training by AR to improve CPR training rate.



Figure 3 Acceptability score of each dimension by the two groups.



Figure 4 Comparison of the mean chest compression depth and rate of AR self-training to instructor training.

Dimensions of acceptability in this study all scored above the mid-point, suggesting that participants rated the AR CPR app as comfortable, helpful, easy to use, enjoyable and that they intend to use it in the future. Ingrassia et al. found similar results for a Holo-BLSD app that they developed for CPR training (Ingrassia et al., 2020). Another app allowing medical students to perform clinical skills training simulation through Google Glass was rated as valuable by the majority of students (Tully, Dameff, Kaib, & Moffitt, 2015). A further study on AR-projected internal anatomy also demonstrated the usability and feasibility of AR technology as a potentially important adjunct to simulated medical skills training (Rochlen, Levine, & Tait, 2017).

Unlike the UTAUT model, age had no effect on acceptability, which was congruent with other studies (Bracq et al., 2019; Sumak, Polancic, & Hericko, 2010). A larger sample size is required to identify the effect of other socio-demographic variables. Simulation sickness is a challenge and overall symptomology significantly increases with usage time, especially for VR devices (Pettijohn, Peltier, Lukos, Norris, & Biggs, 2020). However, unlike for other head-mounted displays, very low scores of distraction, dizziness, and eyestrain were observed in this study (Moro, Štromberga, Raikos, & Stirling, 2017; Tully et al., 2015).

Early and high-quality bystander CPR is the most crucial way to survive OHCA (Dumas et al., 2013). In this pilot study, we present an AR-assisted bystander CPR tool with real-time guidance and feedback, which can guide the users step-by-step to correct compression in real-time. We hope that bystanders could quickly transform into "professionals" and perform high-quality CPR under the guidance of this AR tool. This pilot didn't find any significant different quality between bystander CPR assisted by this tool and simulated traditional dispatcher-assisted CPR. However, in the stage of continuously 10-minutes AR-assisted CPR, there was an increasing proportion of participants who met the guidelines for quality CPR over time, with more than 80% able to produce the guideline rate over three minutes and 60% who met the guideline depth over five minutes. Although males can achieve a greater compression depth (Finke et al., 2018; F.-l. Zhang, 2013), there was just one male in each group and therefore proportions of participants that adhered to the guideline depth may investigate in a future trial if more males are enrolled.

Nonetheless, increasing awareness and willingness to perform CPR are as important as the ability to do so in the out-of-hospital environment (Malta Hansen et al., 2017; Soar et al., 2020; Soar et al., 2019). This pilot RCT also compared self-training CPR by AR to instructor training CPR and did not find significant difference of compression rate and depth. However, based on previous research, the non-inferiority margin of compression depth was set to 0.5 cm and compression rate to  $17 \text{ min}^{-1}$  (Bylow et al., 2019; Riggs, Franklin, & Saylany, 2019; Stiell et al., 2014). According to this margin, compression depth and rate of AR self-training group in this pilot were not inferior to the instructor training group with mean difference of depth was 0.17 (95% CI: -0.35-0.69) cm and mean difference of rate was -2.11 (95% CI: -5.56-1.33) min<sup>-1</sup>. Further research could evaluate the non-inferiority of the two groups after calculating the adequate sample size. Moreover, more than three-fifths of participants met the guideline rate or depth in the AR group, which is superior to results found by a previous study into brief CPR training by VR app (Nas et al., 2020). This confirms the potential of brief selftraining CPR by AR. In addition, a recent research have shown that the difference of compression depth between VR CPR training group and traditional CPR training group was smaller in participants with previous CPR training and participants who were health care professionals (Nas et al., 2020). Our pilot study enrolled a number of participants who were studying medically related majors or have prior CPR training two years ago, however, this impact on the quality of CPR were not analyzed due to the small sample. In the future, a larger sample randomized control simulation trial with subgroup analysis should be conducted to explore the influence of characteristic variables on CPR quality.

The study may have important implications for bystander CPR and CPR training in China with a large population. Especially during the COVID-19 pandemic, the gathering of people should be reduced. This AR-assisted self-training CPR environment have great potential of assigning for public places in the future, allowing trainees to perform out of hospital CPR for cardiac arrest with realtime multi-sensory feedback. The trainees can also conduct self-training CPR to acquire skills and knowledge of CPR in their spare time. However, there are many challenges from the lab environment to the real world. One of the most important is the effectiveness of the AR on CPR training and on supporting bystander CPR in the out of hospital setting. These must be verified in different large population trials in the future. In addition, equipment and maintenance costs, the mastery of AR glasses and the public's acceptance and willingness for AR are also issues we need to consider.

The study has limitations, especially if regarded beyond the actual aim of a pilot study. The sample size in this study was small with just two males enrolled, therefore a calculated larger and more diverse sample size is needed to draw a clear conclusion. Furthermore, participants enrolled in this trial were from one region with a very high education level; researchers should recruit in multiple centers in the future.

# Conclusions

We found that an AR CPR app using Hololens2 was an acceptable and usable tool both in real-time assisted CPR and for self-training. Future studies warranted to explore the effectiveness of AR CPR app for real-time assisted CPR and for self-training.

# **Clinical Trial Registration**

https://www.chictr.org.cn/showprojen.aspx?proj=130736 (ID: ChiCTR2100049254)

#### Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of Peking University Biomedical Ethics Committee (IRB00001052-21035, approval in April 2021).

# **Informed Consent Statement**

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the participants for this paper.

# Data Availability Statement

The data presented in this study are available on request from the corresponding author.

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# **Declaration of Competing Interest**

The authors declare no conflict of interest.

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#### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ecns.2022.04. 004.

#### CRediT authorship contribution statement

Luoya Hou: Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft. Xu Dong: Investigation, Methodology, Validation, Writing – review & editing. Ke Li: Investigation, Supervision, Validation. Congying Yang: Investigation, Validation. Yang Yu: Data curation, Software. Xiaoyan Jin: Resources, Supervision, Writing – review & editing. Shaomei Shang: Conceptualization, Data curation, Funding acquisition, Project administration, Resources, Writing – review & editing.

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