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Simulation and education

A machine learning based model for Out of Hospital cardiac arrest outcome classification and sensitivity analysis

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Abstract

Background: Out-of-hospital cardiac arrest (OHCA) affects nearly 400,000 people each year in the United States of which only 10% survive. Using data from the Cardiac Arrest Registry to Enhance Survival (CARES), and machine learning (ML) techniques, we developed a model of neurological outcome prediction for OHCA in Chicago, Illinois.

Methods: Rescue workflow data of 2639 patients with witnessed OHCA were retrieved from Chicago's CARES. An Embedded Fully Convolutional Network (EFCN) classification model was selected to predict the patient outcome (survival with good neurological outcomes or not) based on 27 input features with the objective of maximizing the average class sensitivity. Using this model, sensitivity analysis of intervention variables such as bystander cardiopulmonary resuscitation (CPR), targeted temperature management, and coronary angiography was conducted.

Results: The EFCN classification model has an average class sensitivity of 0.825. Sensitivity analysis of patient outcome shows that an additional 33 patients would have survived with good neurological outcome if they had received lay person CPR in addition to CPR by emergency medical services and 88 additional patients would have survived if they had received the coronary angiography intervention.

Conclusions: ML modeling of the complex Chicago OHCA rescue system can predict neurologic outcomes with a reasonable level of accuracy and can be used to support intervention decisions such as CPR or coronary angiography. The discriminative ability of this ML model requires validation in external cohorts to establish generalizability.

Keywords: Out of hospital cardiac arrest, Neurological outcome, Machine learning

Introduction

Out-of-hospital cardiac arrest (OHCA), also known as sudden cardiac arrest, is defined as a cessation of cardiac mechanical activity that occurs outside of the hospital setting and is confirmed by the absence of signs of circulation.[1] This disease affects nearly 400,000 people each year in the United States of which only 10 percent survive.[2] The burden of premature death for men (2.04 million years of potential life lost) and women (1.29 million years of potential life lost) is greater for OHCA than for all individual cancers and most other leading causes of death.[3] In many cases, OHCA is the patient's first and only symptom of cardiovascular disease.[4] The sudden, unexpected nature and high incidence of OHCA, combined with the low rates of successful

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resuscitation, make this disease a critical public health issue in need of solutions.

Cardiac arrest survival is dependent on time-sensitive actions requiring an immediate and coordinated response from bystanders, emergency dispatch (i.e., 911 in the United States) call takers, first responders, emergency medical services (EMS) personnel, and hospital healthcare providers. Survival outcomes can improve by establishing integrated cardiac resuscitation systems of care, measurement systems, and strategies for ensuring proper implementation of evidence-based interventions by bystanders, EMS, and hospital personnel.[5] Critical "links" of intervention in the "chain of survival" for OHCA outcomes include: witnessed arrest; bystander cardiopulmonary resuscitation (CPR); public access defibrillation; telecommunicator assisted CPR; shorter EMS response interval; first shockable rhythm; the quality of CPR; return of spontaneous circulation (ROSC) in the field; and post-resuscitation care.[6] Identification of sensitive points within the continuum of care can direct research priorities to improve survival outcomes.

Machine learning (ML) techniques are used by large companies such as Google, Netflix, and Amazon to improve predictions of human behavior. For example, picking a movie no longer requires getting advice from friends or reading reviews from critics and instead streaming media sites deliver personalized recommendations directly to your nearest screen.[7] Although pervasive in the business world, ML has only recently begun to influence clinical research and practice. One such example is the use of ML for warfarin dosing.[8] The resuscitation community would benefit from implementing ML methods for prediction of OHCA survival outcomes. While traditional statistical methods, such as logistic regression, are the standard for investigating patient and treatment intervention and their association with outcomes, studies have suggested that ML methods can be more accurate across a wide variety of clinical settings.[9–11] ML models can serve as virtual laboratories for examining the interaction of treatment strategies and interventions under different patient and system of car circumstances that may be otherwise costly, time consuming, or even unethical to manipulate in the real world.[12,13] ML models, thus, can help inform strategic allocation of resources and research priorities[14,15] and can be used to develop clinical decision support tools to select patients who are most likely to benefit from specific interventions.[16,17]

The objective of this study is to develop a machine learning model to predict a patient's Cerebral Performance Category (CPC)[18] score given a set of intervention and intermediate outcomes during a cardiac arrest event. The proposed ML model can provide metrics based on groups of patients to assist decision making in the management of OHCA. Fig. 1 illustrates the information collection pipeline that will be further discussed in the data collection section. All the information listed in Fig. 1 was used in the creation of the ML model.

Methods

This study aims to predict the neurological outcome of a patient given demographic variables, OHCA characteristics, and interventions delivered by bystanders, first responders and EMS, and in the hospital. This study was approved by the Office for the Protection of Research Subjects of the University of Illinois at Chicago.

Study setting

Approximately three million people live in the City of Chicago, the third largest city in the United States.[19] The Chicago Fire Department is the largest provider agency in the Chicago EMS System and provides the exclusive emergency response for all 911 calls in the City of

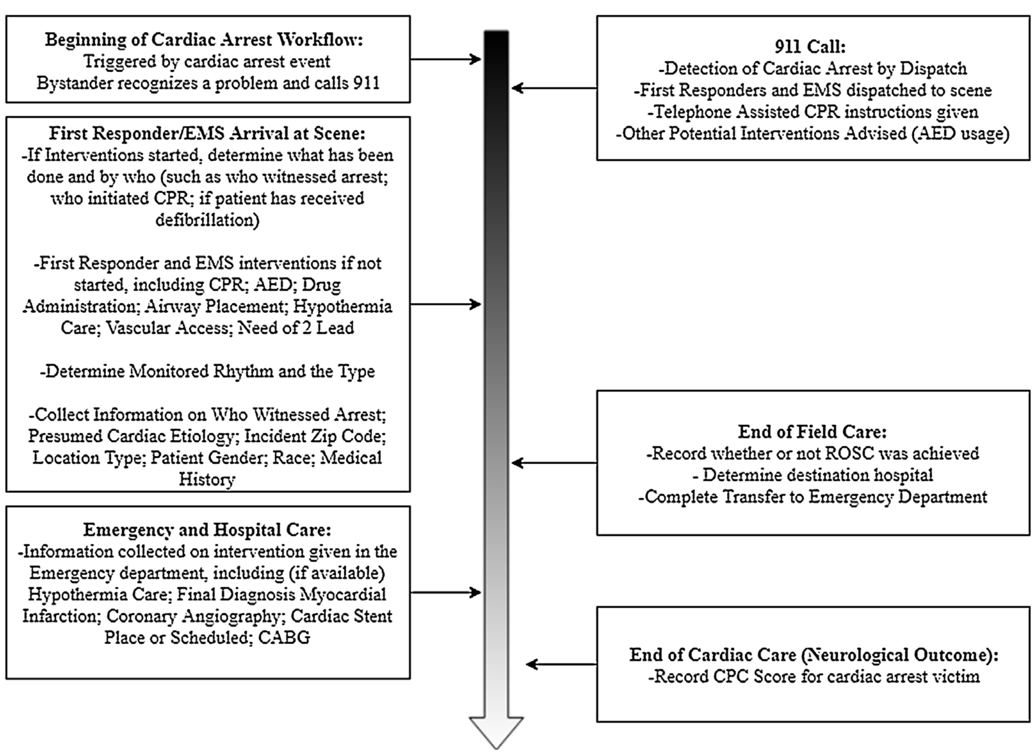

Fig. 1 – Chicago CARES Relevant Data Collection Flow.

Chicago.[20] Also, the Chicago Fire Department treats over 3000 patients of OHCA every year. Emergency calls for OHCA identified at the point of emergency medical dispatch result in the tiered response of a 4-person basic or advanced life support fire suppression company, a 2-person advanced life support transport ambulance, and a paramedic field chief. The Chicago EMS system has 33 receiving hospitals; 24 are ST-elevation myocardial infarction Receiving Centers with 24/7 interventional cardiology and targeted temperature management (TTM) capabilities.

Data collection

This study utilizes data reported by the city of Chicago to the Cardiac Arrest Registry to Enhance Survival (CARES)[21]: a multicenter registry coordinated by the Centers for Disease Control and Prevention and Emory University. The CARES registry is the largest cardiac arrest data source in the United States.[22] This registry incorporates data on non-traumatic cardiac arrests involving persons who received resuscitative efforts by EMS providers, including CPR or defibrillation. Participating sites collect data from three sources that define the continuum of emergency cardiac care: 911 dispatch centers, EMS providers, and receiving hospitals.

The Chicago Fire Department EMS treated 7765 persons with non-traumatic cardiac arrests from September 1st, 2013 through December 31st, 2016. Because unwitnessed cardiac arrests generally have a poor prognosis (e.g. death),[7,23] our analysis focused on 2639 witnessed cardiac arrest events (see Fig. S1. and Table S1). The original data source contains the information required by the CARES platform.[21] The information used for modeling includes the following 27 features (see Table S2 for details regarding feature reduction and feature values). The 27 features used for modeling are all categorical. In order to use categorical features, they must be encoded. Encoding transforms a single value to a binary representation of that value and the possible values a feature could take. Since our processed data set can still have missing values, these values are considered when encoding. For example, Coronary Angiography can be Yes, No, Unknown, Missing where the encoding for the value No is [0,1,0,0].

The primary outcome of interest was neurologic outcome. CARES documents neurologic function from the hospital record measured by the cerebral performance category (CPC) score.[24] A CPC score of 1 denotes a patient with mild or no neurological disability, 2 reflects moderate neurological disability, 3 indicates severe neurological disability, 4 is assigned to patients in a persistent coma or vegetative state, and 5 indicates death. For the purpose of this study, neurologic outcome was modified to a binary classification based on CPC score: Class 0 consists of individuals who survived with good neurological outcomes (CPC1/2) and Class 1 consists of both patients with poor neurological outcomes (defined as CPC3/4/5).

Machine learning modeling

To predict the neurological outcome of patients who had a witnessed OHCA, we train a machine learning model using a subset of the available data. We then evaluate the performance of the developed model on the remaining part of the available data, i.e. the data not used in the training phase. Out of 2639 witnessed OHCA cases, 250 belong to Class 0 (good neurologic outcome) and 2389 belong to Class 1 (poor neurologic outcome). We randomly split the 2639 witnessed OHCA cases into three datasets for analysis. The first dataset consisted of 1584 events (60% of full data) and functioned as the training set; this was used to construct the ML model. The second dataset consisted of 395 events (15% of full data) and functioned as the validation set, used to validate the ML model emerging from the training set. The remaining dataset consisted of 660 events (remaining 25% of full data) and functioned as the test set, and it was used to evaluate the model. These features were used to predict the outcome of the OHCA event, CPC score. Out of 250 individuals in Class 0, 182 were assigned to the training and validation sets, and 68 were assigned to the test set. The remaining 2389 individuals are in Class 1, 1797 were assigned to the training and validation sets, and 592 were assigned to the test set.

We compared several ML models for the prediction problem stated in our study including Decision Tree,[25] Random Forest,[26] K-Nearest Neighbors,[27] XGBoost,[28] LightGBM,[29] and Neural Networks. Each model was constructed using the training set and is iteratively improved using the validation set. The model that yields the best sensitivity on the validation data was selected and its final sensitivity was evaluated using the test data.

For the neural network model, we propose an Embedded Fully Convolutional Network (EFCN) model inspired by fully convolutional blocks commonly used in various time series classification[30] and image classification applications.[31,32] Fig. 2 illustrates the EFCN model architecture. The EFCN model comprises of multiple entity embeddings[33] followed by a fully convolutional feature extractor. The fully convolutional feature extractor contains three convolutional

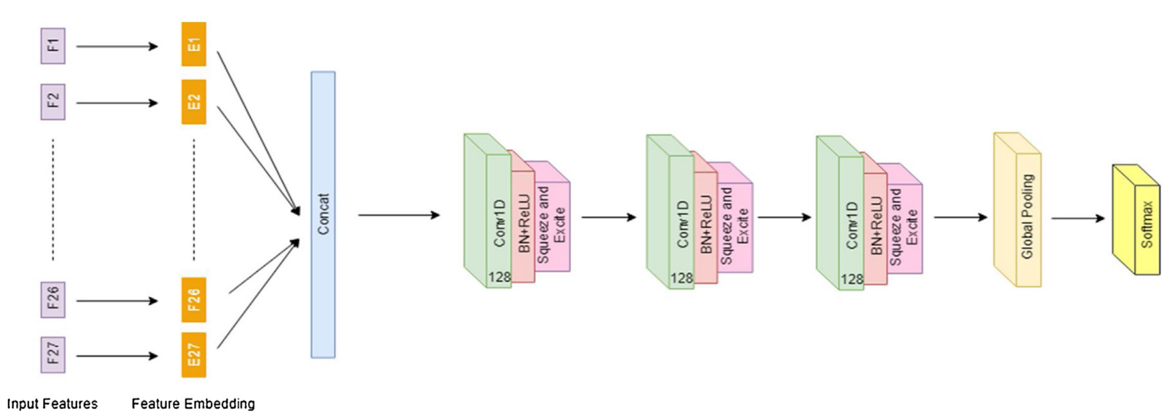

Fig. 2 – Embedded Fully Convolutional Network Architecture.

layers of filter size 128, succeeded by three batch normalization layers, and three squeeze-and-excite layers.[34] EFCN uses a focal loss[35] due to the imbalance of each class.

Sensitivity analysis

To perform sensitivity analysis, the value of a certain intervention feature (such as bystander-CPR) is changed for patients in the test set who received that intervention. All other feature values remain the same for these patients. Using the ML model, the value of the class label (Class 0 or Class 1) is recalculated for each of these patients. A change in the expected class label shows the effect of an individual intervention on the patient's survival.

Results

The test set consists of 660 cardiac arrest patients. Of these 660 instances, 68 belong to Class 0 and 592 belong to Class 1. Given the class imbalance of the problem, an evaluation of sensitivity[36] is a good metric for model selection. Eq. (1) provides the formula required to calculate the sensitivity for each class.

Table 1 provides the average sensitivity and key parameters for each examined model. The six tested models have sensitivity values between 0.5 and 0.825. An average recall rate of 0.5 achieved by the K-Nearest Neighbor method suggests that the model classifies all patients as one class (Class 1). EFCN achieves an average sensitivity of 0.825 where the rate is the unweighted average of both class sensitivities. Table 2 provides a confusion matrix for the results of the EFCN model. Eq. (2) shows the details of the sensitivity calculations for the EFCN model based on the results from Table 2.

$$\text{Sensitivity} = \text{True Positives}/(\text{True Positives} + \text{False Negatives}) \tag{1}$$

$$\text{Sensitivity (EFCN)} = 0.5(51/(51+17)) + 0.5(531/(531+61)) \tag{2}$$

The EFCN model was then used to conduct a sensitivity analysis for bystander CPR, targeted temperature management, and coronary angiography. Table 3 illustrates the results of sensitivity analysis on CPR initiation. CPR sensitivity analysis shows a drastic increase in expected survival when bystander CPR is given. When shifting the initiation of CPR from EMS to Lay Person (LP) care, the ML model predicts 36(3 + 33) patients will survive as Class 0. Additionally, when patients go from receiving first responder (FR) to LP care, the ML model predicts 27(26 + 1) patients will survive as Class 0.

The in hospital analysis is performed on the 292 individuals from the testing set that survived to the hospital inpatient stage in the cardiac arrest workflow. For in hospital care, the analysis is done on TTM and coronary angiography. Table 4 illustrates the results of such sensitivity analysis. Most patients are unaffected by a change in the specified interventions. This includes 273 patients for TTM and 180 patients for coronary angiography. The analysis shows that 99(88 + 11) patients were not given a coronary angiography and the model results suggest that this intervention would have resulted in these patients belonging to Class 0. Sensitivity analysis also shows how patients are affected when an intervention is not performed. The analysis shows that 19(12 + 7) patients for TTM and 13(9 + 4) patients for coronary angiography would not have survived if each intervention was not given.

Table 1 – Model evaluations.

Model	Key model parameters	Sensitivity
Decision tree	Min samples split = 2 Min Samples leaf=1	0.7
Random forest	Number estimators = 1000 Max depth = 7	0.68
K nearest neighbor	K = 7	0.5
XGBoost	Gamma = 1.5 Max depth = 5 Min child weight = 5 Number estimators = 500	0.7
LightGBM	Colsample bytree = 0.65 Learning rate = 0.01 Number estimators = 100 Number leaves = 16	0.675
EFCN	Explained in Fig. 2	**0.825**

Table 2 – Confusion matrix of EFCN results.

Total population 660	Predicted class 0	Predicted class 1
Actual class 0	51	17
Actual class 1	61	531

Discussion

This study demonstrates the potential utility of a ML model for population based OHCA intervention decisions. We found that the EFCN model performed better than five other methods for predicting neurologic outcome after a witnessed OHCA. The ML model had a sensitivity of 0.825 in predicting neurological outcomes among patients with a witnessed OHCA. Moreover, the results of the sensitivity analysis for bystander CPR, coronary angiography, and TTM are consistent with observations from previous systematic reviews and meta-analysis.

ML models can be used as implementation strategies for building buy-in and prioritizing implementation actions of decision makers.[37,38] The results of this analysis can be used to help direct public health interventions, such as bystander preparedness and scale up of dispatch assisted CPR instructions. Future analysis using a more granular data set can be used to predict the effect of coronary angiography and TTM in patients with specific clinical features, including comorbid illnesses and EKG patterns, to help in deciding inclusion and exclusion for future clinical trials.

We identified two previous studies that utilized ML models to predict OHCA survival outcomes. One study employed six different machine learning techniques during intelligent analysis of the data on a smaller sample of 477 OHCAs from a database from Slovenia: Decision trees, k-nearest neighbors, Naïve Bayes, Neural Networks, Support Vector Machine and Random forests.[39] The study concluded that decision trees were the most appropriate ML technique for predicting return of spontaneous circulation in OHCA and for predicting OHCA survival. Our study cohort was larger (2639 patients) and likely represents a more ethnically diverse patient population. Another study of 39,566 OHCA cases from the Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database

Table 3 – Sensitivity analysis of CPR initiation.

Out of hospital			Transitions of predicted class output from EFCN			
Actual patient class	Intervention	Intervention transition	0->0	1->1	1->0	0->1
Patients that actually lived with CPC1/2 (Class 0)	CPR	EMS-> FR	22 [7.1]	9 [2.9]	0 [0]	0 [0]
	CPR	EMS-> LP	22 [7.1]	6 [1.9]	3 [1]	0 [0]
	CPR	FR-> LP	12 [4.9]	2 [0.8]	1 [0.4]	0 [0]
Patients that actually CPC3/4/5 (Class 1)	CPR	EMS-> FR	24 [7.8]	245 [79.3]	9 [2.9]	0 [0]
	CPR	EMS-> LP	24 [7.8]	221 [71.5]	33 [10.7]	0 [0]
	CPR	FR-> LP	20 [8.1]	186 [75.3]	26 [10.5]	0 [0]

Table is organized by the actual class label of patients (first column). All values represent transitions in types of CPR. The Intervention Transition column shows the change in intervention received. EMS->LP means that the patients initially received EMS CPR and now we evaluate what would have happened if they had received Lay Person CPR. The last four columns represent the change in class output from our EFCN model. For example, 1->0 means that the patient initially was classified as Class 1 and the change in intervention resulted in the patient being classified as Class 0. Each value has its proportional representation next to it in [#]. Each proportion is based on the Intervention Transition, where proportions in rows with EMS->FR sum to 100.

Table 4 – Sensitivity analysis of in hospital interventions.

In hospital			Transitions of predicted class Output from EFCN			
Actual patient class	Intervention	Intervention transition	0->0	1->1	1->0	0->1
Patients that actually lived with CPC1/2 (Class 0)	TTM	No -> Yes	10 [7.8]	0 [0]	0 [0]	0 [0]
	TTM	Yes -> No	32 [19.5]	11 [6.7]	0 [0]	7 [4.2]
	Coronary angiography	No -> Yes	20 [8.4]	6 [2.5]	11 [4.6]	0 [0]
	Coronary angiography	Yes -> No	27 [49.1]	0 [0]	0 [0]	4 [7.3]
Patients that actually CPC3/4/5 (Class 1)	TTM	No -> Yes	21 [16.4]	97 [75.8]	0 [0]	0 [0]
	TTM	Yes -> No	9 [5.5]	93 [56.7]	0 [0]	12 [7.3]
	Coronary angiography	No -> Yes	35 [14.8]	77 [32.5]	88 [37.1]	0 [0]
	Coronary angiography	Yes -> No	11 [20]	4 [7.3]	0 [0]	9 [16.4]

Table is organized by the actual class label of patients (first column). The Intervention column denoted which In Hospital intervention is being changed. The Intervention Transition column shows the change in intervention received. Where No->Yes means that the patients initially did not received this intervention and now we evaluate what would have happened if they had received the intervention. The last four columns represent the change in class output from our EFCN model. For example, 1->0 means that the patient initially was classified as Class 1 and the change in intervention resulted in the patient being classified as Class 0. Each value has its proportional representation next to it in [#]. Each proportion is based on the Intervention & Intervention Transition, where proportions in rows with TTM and No->Yes sum to 100.

used five ML approaches (Gradient Boosting Machine, Support Vector Classifier, Random Forest, Artificial Neural Network, and an ensemble to assist in identifying the physiologic features that most contributed to an individual patient's survival.[40] However, the study was limited by the absence of pre-hospital data and did not discriminate survival from neurologic outcomes. To our knowledge, this is the first study using ML models to predict OHCA survival outcomes in a United States population cohort and the first study ever published using ML models to predict functional neurologic outcomes post OHCA.

Limitations

In creating the ML model, the aim was to classify patients as Class 0 (CPC1/2) or Class 1 (CPC3/4/5). The ML model could have been developed based on other classifications of the patient outcomes. The patient outcomes could be considered in a way that Class 0 would be CPC1-4 and Class 1 would be CPC5. This classification of patient outcome was not considered for the following reasons. First, the EFCN model would only achieve an average sensitivity of 0.79 (lower than the current rate of 0.825) under this outcome classification scheme. In addition, mixing the patients with good and poor neurological outcomes into a single patient outcome class would reduce our ability to use sensitivity analysis to measure the impact of specific interventions on increasing the number of patients with good neurological outcomes.

Another way that the patient outcome classification could have been performed was to classify patients into three classes based on the three possible neurologic outcomes of CPC1/2, CPC3/4, and CPC5. This specific classification scheme was not selected due to the low number of patients in the CPC3/4 class (140). The accuracy of the ML model would have been significantly reduced due to this imbalance in the dataset with a had we selected such a classification scheme with three categories.

Our study utilized witnessed cardiac arrest in the city of Chicago. While this is a large data source, our study would benefit from more granular data. For example, comorbid illnesses, EKG patterns, and timing of coronary angiography are considered in clinical decision making and affect patient outcomes. Implicit selection bias may explain the model's prediction of the effectiveness of coronary angiography and TTM. Deep learning models thrive when trained on large amounts of data. Additionally, more data would make it possible to learn the dependencies of interventions in our analysis. Sensitivity analysis of CPR assumes interventions in the workflow are not affected by the change in CPR initiation. Learning dependencies of interventions would result in a more practical sensitivity analysis of interventions in the middle of the cardiac arrest workflow. Finally, the information utilized for modeling is limited due to recent changes in data collection policy. Data related to dispatch assisted CPR and timing information are excluded from our models because they are incomplete. As this data becomes available and reliable the EFCN model can be updated to incorporate this information.

Conclusion

A neural network ML model was developed for predicting the patient survival outcome based on the OHCA workflow attributes and interventions. The ML model has a sensitivity of 82.5% in predicting the patients with good neurological outcomes, and patients with poor neurological outcomes or death. The ML model was also used for the sensitivity analysis of patient outcome with respect to three different interventions of the person who performs the CPR, performing coronary angiography, and performing TTM.

Future directions

The ML model was developed based on OHCA data of 2639 patients from the Chicago CARES database. Several other databases of OHCA patients, such as the CARES data from other states, are available that can be used in future construction of an improved ML model. The data from all these databases can be fused into a single large database that will be used for the ML model development. The improved ML model is expected to have a better sensitivity as the patient sample size would be much larger than the 2639 patients used in the current study.

Another advantage of using a larger database is it will enable us to consider other patient outcome classification schemes. For example, one might be interested in classifying the patients into three classes: patients with good neurological outcome, patients with poor neurological outcomes, and the patients who die. Implementation of this classification scheme would only be possible if the database contains a larger number of patients with CPC1/2 and CPC3/4.

Conflict of interest statement

Marina Del Rios and Terry Vanden Hoek receive salary support from Medtronic Philanthropy's Heart Rescue Program for their role as physician leads of the Illinois Heart Rescue Project. The data coordinator for the Cardiac Arrest Registry to Enhance Survival for Chicago is also supported in part by a grant from Medtronic Philanthropy's Heart Rescue Program. Medtronic had no role in the study design; collection, data analysis and interpretation; writing of the manuscript; nor in the decision to submit for publication. The rest of the authors of this manuscript have no other relevant conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.03.012.

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