

BMJ Open

Dynamic Automated External Defibrillator (AED) Registry: Rationale and Methods for Active Reporting of Surveillance of Cardiac Arrest in Community Settings

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2016-014902
Article Type:	Protocol
Date Submitted by the Author:	25-Oct-2016
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Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Epidemiology, Emergency medicine
Keywords:	STATISTICS & RESEARCH METHODS, PUBLIC HEALTH, Cardiac Epidemiology < CARDIOLOGY

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8 **Dynamic Automated External Defibrillator (AED) Registry: Rationale and**
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10 **Methods for Active Reporting of Surveillance of Cardiac Arrest in**
11 **Community Settings**
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22 Supported by 1U01FD004587-04 from the Food and Drug Administration, Silver Spring,
23 MD and ZOLL Medical Corporation, Chelmsford, MA.
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30 Word Count:
31 Abstract 298
32 Body, not including figure, table or references 3,874
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Abstract

Introduction Lay use of automated external defibrillators (AEDs) before the arrival of Emergency Medical Services (EMS) providers on scene increases survival after out-of-hospital cardiac arrest (OHCA). Large numbers of AEDs have been placed in public locations to improve this community response to cardiac arrest. These devices may be forgotten, moved or may not be ready for use when needed. We describe a novel approach to AED surveillance that tracks these devices through time and space to improve public health.

Methods and Analysis Included AEDs are installed in public locations for use by laypersons to treat patients with OHCA before the arrival of EMS providers on scene. Included cases of OHCA are patients evaluated by organized EMS personnel and receive attempts at external defibrillation by any provider, or receive chest compressions by organized EMS personnel.

Recruitment is ongoing. AEDs are found primarily by using crowdsourcing methods. Then each AED is tagged with a label which is a unique two-dimensional (2D) matrix code; the 2D matrix code is recorded as well as the location and status of the AED by using a smartphone; these elements are automatically passed via the internet to a secure and confidential database in real time. Initially and whenever the 2D matrix code is rescanned are non-clinical or clinical use of an AED, the user is queried to answer a finite set of questions about the status of the device. The primary outcome of any clinical use of an AED is survival to discharge. Results are summarized descriptively.

Ethics and Dissemination These activities are conducted under a grant of authority for public health surveillance from the Food and Drug Administration as allowed by the Health Insurance Portability and Accountability Act (HIPAA). Results are provided periodically to participating sites and sponsors so as to improve public health.

Strengths and Limitations of This Study

- Simple, sustainable and scalable registry of automated external defibrillators and cases of out-of-hospital cardiac arrest.
- Functions under a grant of authority for public health surveillance
- Framework for embedded prospective research evaluations.
- Small footprint at present.
- Can not apply crowdsourcing in every urban and rural community.

Introduction

Out of hospital cardiac arrest (OHCA) is defined as a sudden and unexpected pulseless condition attributable to cessation of cardiac mechanical activity.⁽¹⁾ Cardiac arrest has multiple etiologies, and the etiology of arrest influences treatment decisions. Underlying mechanisms for non-traumatic cardiac arrest are crudely categorized as a) conductive abnormalities of the myocardium leading to arrhythmias, b) chronically weakened myocardium leading to end-stage pump failure, and c) acute occlusion of a coronary artery leading to myocardial infarction. Of these mechanisms of OHCA, resuscitation is generally most successful for isolated conductive abnormalities or for acute coronary thrombosis that is treated rapidly. Acute occlusion is most common among patients with a first recorded rhythm of ventricular fibrillation (VF), which hereafter includes pulseless ventricular tachycardia as well as rhythms interpreted as shockable by an automated external defibrillator (AED). Recognition⁽²⁾ and successful treatment of VF is highly time-dependent.⁽³⁾ AEDs are medical devices (MDs) intended to simplify and improve treatment of OHCA. The timely use of AEDs by laypersons in conjunction with cardiopulmonary resuscitation (CPR including manual chest compressions with or without ventilation) is the only field intervention that has been shown to significantly increase the number of individuals who survive to discharge after OHCA.⁽⁴⁾

Since the effectiveness of use of AEDs by laypersons was demonstrated more than a decade ago, more than 2.4 million AEDs have been sold for use by laypersons in the United States.⁽⁵⁾ As more of these MDs are placed in the community, the FDA has received reports of potential adverse events associated with them. Since the overall number of AEDs installed is not public information and it is difficult to track individual AEDs through time and space, agency staff have experienced challenges in trying to interpret these

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5 reports. As well, each major manufacturer of AEDs in the United States has recalled their devices to address one or more potential
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7 safety issues over the past five years. These facts were referenced in the proceedings surrounding reclassification of AEDs to require
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9 premarket approval applications which are reserved for high-risk MDs. ⁽⁶⁾ During these proceedings, and subsequent comments, a
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11 need for a more comprehensive surveillance system was identified.⁽⁷⁾ Specifically, FDA’s advisory panel recommended “Registry
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13 information should be established to collect more data. An active reporting registry would help with recalls and would help to
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15 maintain the quality and confidence of the data collected. Sold devices could be tracked prospectively, and long term device
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17 performance would be captured.”
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20 In this paper we describe the rationale for and design of an ongoing dynamic registry for surveillance of AED location and use.
21
22 This registry has been created through a partnership of academics, FDA, key stakeholders and manufacturers of AEDs. The long-term
23
24 goals of the registry are to provide reliable, valid and sustainable post-market surveillance of AEDs; to provide important and timely
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26 information to patients, providers and the public to improve MD device development including the quality of AEDs and the quality of
27
28 care for patients with OHCA; and to provide a framework for prospective embedded studies of the effectiveness of next-generation
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30 AEDs. The Dynamic AED Registry represents a novel approach to AED surveillance, leverages a clinical registry infrastructure, and
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32 can be applied to other MDs that are mobile in time and space.
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34 35 **Methods and Analysis**

36 37 ***Study Populations***

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39 Included AEDs are those:
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- 5 a) Pre-existing in community settings and
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- 7 i. Identified by crowdsourcing techniques, or
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- 9 ii. Identified by manufacturer or distributor.
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- 11 b) Newly installed in community setting:
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- 13 i. Identified by owner during at time of installation, or
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- 15 ii. Identified by manufacturer at time of sale.
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17 Included patients are those treated for OHCA:

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- 20 a) Evaluated by organized EMS personnel and receive attempts at external defibrillation (by lay, police or EMS), or
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- 22 b) Receive chest compressions by organized EMS personnel.
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24 Although a minority of patients with OHCA have an AED applied by a layperson
25 before the arrival of EMS providers on scene,^{p 339 of (8)} we monitor all cases of EMS-treated cardiac arrest in participating communities
26 to obtain complete case finding. Monitoring the outcome of every AED use is necessary to identify those uses that may have caused or
27 contributed to survival or death (21CFR803), since the majority of patients treated for OHCA die.
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32 To date, studies reported from smaller selective registries were difficult to interpret because of potential selection bias and
33 lack of knowledge of the overall population. This potential selection bias should be mitigated as the Dynamic AED Registry evolves
34 over time to include a high percentage of treated patients in the United States.
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5 Several strategies are used to achieve a high rate of enrollment in the Dynamic AED Registry. AEDs pre-existing in
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7 community settings will be identified by using social media techniques and other methods. In addition to collating information about
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9 AEDs by using periodic scavenger hunts, we collate information about individual AEDs reported by laypersons who registered online,
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11 then used their smartphone.(<https://heartmap.uwctc.org/> accessed on May 25, 2016) Individual device identifiers are provided by the
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13 investigators to owners or responsible individuals of these AEDs, with information about the purpose and methods of AED
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15 surveillance, as well as instructions on where to apply the identifier to the AED and how to register the AED in the dynamic registry
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17 by scanning the identifier. A series of individual identifiers are provided to each sponsoring manufacturer for inclusion with the
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19 product registration materials provided with AEDs newly sold for use in community settings. As well, organizations that provide
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21 physician oversight and AED readiness services encourage client participation by placing an individual identifier on each AED under
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23 their supervision then scanning the identifier to record information about the location of the device in our secure database. With
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25 permission of the client, this information is shared with the relevant EMS dispatch center so as to improve the community response
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27 to OHCA for the client's staff and customers. The lightweight and portability of AEDs makes them easily movable. If the AED is
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29 moved later and then the identifier is rescanned, we provide information about the new location of the device to the oversight
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31 organization so that they know where the client's AEDs are at all times.
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35 Participating EMS agencies are recruited as interest and resources allow. At present, this includes a mix of EMS agencies that
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37 participated in the Resuscitation Outcomes Consortium (funded by the National Institutes of Health, American Heart Association
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39 and other agencies), are participating in the Mission:Lifeline Cardiac Resuscitation program (funded by American Heart Association)
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5 or are associated with a dispatch center using software to enable faster lifesaving AED response within the community (PulsePoint
6 Responder, PulsePoint Foundation, San Ramon, CA). Importantly, it is anticipated that this will expand over time to include as many
7 EMS agencies as possible throughout the United States. Furthermore, EMS agencies or receiving hospitals may enroll patients to
8 provide a site-specific analysis of their program as well as to benchmark the process and outcome of care compared to other
9 participant's experience.
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15 **Data Acquisition**

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18 EMS providers and personnel responsible for maintenance of AEDs are encouraged to scan the individual identifier after each
19 AED use. Upon scanning of a UDI, the date, time and location of use are automatically identified, recorded and transmitted to the
20 dynamic registry. As well, users are asked to respond to a finite set of queries confirming the location of the AED as well as describing
21 the reason for its use. In the event of a clinical use, EMS providers who scan the individual identifier are queried about the patient's
22 intended hospital destination to facilitate subsequent tracking of patient vital status at hospital discharge. After the event, EMS
23 providers are queried about a finite set of patient and EMS factors to facilitate adjustment of outcomes for case-mix as well as
24 assessment of rates of potential adverse events in a manner consistent with the Utstein template for reporting of outcomes after
25 OHCA.⁽⁹⁾ As well, investigators ascertain the subject's vital status at discharge from the receiving hospital. Anonymized quarterly
26 reports are provided to participating EMS systems, which describe the process and outcome of care for patients with OHCA as an
27 incentive to facilitate continued surveillance of AEDs, their use, and factors that contribute to positive clinical outcomes. The quality
28 of the data included in the registry is monitored and improved by using regular data quality checks and audits.
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Data Elements

Baseline characteristics, covariates and outcomes included in the registry were developed and implemented by consensus of the executive committee. In doing so, emphasis was placed on developing a finite set of key variables so as to ensure that the registry was simple, sustainable and scalable. These can be revised periodically as required.

Data Quality Control

The Dynamic AED Registry uses multiple mechanisms to ensure data completeness and accuracy (Table 1). Monitoring and auditing use standardized data quality checks. Events are adjudicated as required for pre-specified events.

Reporting

The Dynamic AED Registry provides feedback to participating sites including periodic quality benchmarking. Participants have access to a repository of their own data and tools to evaluate their local practice and conduct user-specified local data queries. This is especially valuable for communities that alert lay responders to the need for bystander CPR and AED need through dispatch-identified OHCA. Data are also provided to FDA to address specific surveillance questions.

Innovative Methods

The Dynamic AED Registry uses multiple innovative methods to enhance surveillance of AEDs.

a) Crowdsourcing

We have adapted crowdsourcing methods to find AEDs installed in public locations for use by laypersons in major metropolitan areas that are participating in the Dynamic AED Registry. Merchant pioneered use of crowdsourcing to identify AEDs

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5 installed in community settings.⁽¹⁰⁾ According to these methods, help is solicited for tasks usually performed by particular individuals
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7 from an undefined large group (i.e. a crowd). Since the task is offered to a large group with diverse backgrounds, it has the potential
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9 to attract individuals who are interested in the problem, likely to finish the task, and likely to contribute innovative ideas. Based on
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11 methods developed by the Defense Advanced Research Projects Agency (DARPA),⁽¹¹⁾ adults were invited to identify AEDs installed in
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13 community settings in Philadelphia County, PA. According to state law, AEDs installed in community settings in Philadelphia County,
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15 PA should be registered with the local EMS authority. Before the contest began, 57 devices were registered with Philadelphia EMS.
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17 Monetary prizes were awarded to those individuals or teams who reported the most AEDs as well as to those who were first to report
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19 any of 200 preselected AEDs. During the contest, 313 individuals and teams identified 852 unique AEDs in 528 locations. These
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21 locations were in 94% of eligible census tracts and included a mix of public (59%) and private (41%) locations. 50% of AEDs were
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23 identified as non-functional or having unknown functional status. The investigators concluded that crowdsourcing is a feasible
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25 approach for identifying AEDs installed in community settings in a large urban city.
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28 **b) Able to Track Individual Medical Devices**

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30 We have pioneered the use of an individual identifier to track AEDs or other MDs through time and space in community
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32 settings. According to this method, each AED is tagged with a label which consists of a unique two-dimensional (2D) matrix code (QR
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34 code, Denso Wave Inc., Chita-gun, Japan); then the QR code or 2D matrix code is recorded as well as the location and status of the
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36 AED by using open-source software native to any contemporary smartphone (e.g. Google Goggles, Google Inc., Mountain View, CA);
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38 and finally these elements are automatically passed via the internet to a secure and confidential database in real time (Provisional
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5 Patent # 61/498,424, Figure 1). The user is queried to answer a finite set of questions when the smartphone is connected to the
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7 database. If the device has a clinical use, these queries include verification of the intended receiving hospital to facilitate longitudinal
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9 follow-up of patient outcome to hospital discharge.

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11 This device identifier complement's the FDA's Global Use Device Identification Database (GUDID) initiative.⁽¹²⁾ This
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13 establishes that: a unique device identifier number is assigned by the device manufacturer to each version or model of a device. This
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15 identifier is both in human-readable format and in machine-readable format. It is intended to contain information about the type of
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17 device as well as information about its manufacture. The primary difference is that GUDID does not require or enable tracking of the
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19 location of a device through time and space.

20 21 **Sample Size and Analysis**

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23 Enrollment of AEDs and patients with OHCA are ongoing. The primary analysis will be descriptive. If 95% of AEDs are ready
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25 for use, enrollment of 10,000 AEDs annually will yield precision (measured as half of the 95% confidence interval) of 0.4% in the
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27 estimate of readiness for use. If 10% of patients treated for OHCA survive to discharge, enrollment of 2500 patients annually will
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29 yield precision of 1.9% in the estimate of survival to discharge.

30 31 **Ethics and Dissemination**

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33 The Dynamic AED Registry is the first registry to be conducted under a grant of authority for public health surveillance from
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35 FDA. As such, these activities have been determined by multiple institutional review boards (IRBs) to not be subject to human
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37 subjects' regulations and to exercise the public health exception within the Health Insurance Portability and Accountability Act
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(HIPAA, 45 CFR 164.512(b)). These methods are adaptable to public health surveillance of other MDs.

Discussion

Lay use of AEDs before the arrival of EMS providers on scene increases survival after OHCA.⁽⁴⁾ Large numbers of AEDs have been placed in public locations to improve the community response to cardiac arrest.⁽⁵⁾ It is sometimes difficult to determine whether these devices are maintained in a state of readiness for use or whether they functioned as intended when applied to someone in presumed cardiac arrest. Importantly, there is no widely-deployed method of tracking their location and use in community settings. We describe the implementation and maintenance of a dynamic registry for surveillance of AEDs through time and space.

The Dynamic AED Registry has several strengths. By design, it is simple, sustainable and scalable. Since the registry functions under a grant of authority for public health surveillance, the base surveillance and quality improvement functionality is not subject to human subjects' research regulations and is exempted from HIPAA. Data collected for public health surveillance can, subject to appropriate permissions, can be used to improve the process and outcome of care for patients with OHCA in participating communities. Like other registries, it can also be used as a framework for embedded prospective research evaluations of existing or next-generation defibrillators, as well as other interventions intended to improve outcomes after OHCA. What does the Dynamic AED Registry offer over other registries? It tracks the location and use of individual AEDs in diverse communities. This identifies the specific AED used, allowing verification of the diagnostic algorithm in no-shock advised cases. It supports passive reporting of potential AED failure that is supposed to occur. AED manufacturers have recognized the value of and subsequently invested in the Dynamic AED Registry to provide ongoing safety and effectiveness data, which can be useful as real-world evidence to

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5 support regulatory decisions for AEDs. Recognizing that data collated in different resuscitation registries may not be comparable, the
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7 academic leadership of the Dynamic AED Registry is working with leaders of other resuscitation-related registries to encourage
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9 harmonization of data elements, quality control techniques, outcomes and adverse event classification.
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11 This registry has some limitations. At present, it has a small footprint. But this is expected to grow over time. Although
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13 crowdsourcing methods are used to identify AEDs that were placed in public locations, it is not feasible to apply crowdsourcing in
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15 every urban and rural community. Instead, the registry is evolving to include prospective tagging of AEDs as they are placed in public
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17 locations. The distribution of AEDs by geography may be non-random (i.e., one manufacturer may have more devices placed in a
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19 given community than another). Since geographic region is a strong predictor of outcome after OHCA,⁽⁴⁸⁾ comparison of outcomes by
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21 different manufacturers needs to account for differences in geography.
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24 The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) of the United States is
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26 responsible for regulating firms who manufacture, distribute, or import MDs sold in the United States. MDs are instruments or
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28 related articles which are intended for use in the diagnosis or treatment of disease, are applied externally or internally to patients to
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30 affect the structure or function of their body, and do not achieve their purpose through chemical action or metabolism.⁽¹³⁾ FDA relies
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32 on registries for post-market surveillance of MDs to ensure their safety and efficacy. Congress has directed the agency to implement
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34 an active system capable of identifying safety issues and communicating them in a timely manner to patients, providers and the
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36 public.⁽¹⁴⁾ Policy makers have suggested that increased surveillance of MDs is necessary to enhance and maintain patient safety.⁽¹⁵⁾
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38 The Institute of Medicine made recommendations about how to improve the approval process and post-market surveillance of
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5 MDs.⁽¹⁶⁾ As well, the Institute of Medicine made recommendations about how to improve outcomes after OHCA that included the
6 establishment and maintenance of a sustainable method of national surveillance of the process and outcome of care of all patients
7 with OHCA.⁽²¹⁾ Experts have recommended post-market surveillance of any defibrillator introduced for in-hospital, emergency
8 medical services, or public access defibrillation.⁽²²⁾

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13 Our registry can be placed in the context of FDA's evolving medical device regulatory process (Table 2) as well as in the
14 context of other resuscitation-related registries. It is a next-generation registry implemented with the multiple purposes of
15 surveillance of MDs as well as measurement and improvement of the process and outcome of care for patients in real-world settings,
16 as well as serving as a framework for embedded studies of the effectiveness of defibrillator as well as other interventions in patients
17 with OHCA. The Dynamic AED Registry is designed to evolve into a comprehensive but scalable and sustainable national registry in
18 the United States. Multiple other resuscitation-related registries exist in the United States and the rest of the world that seek to
19 characterize the process and outcome of care related to OHCA.⁽²³⁾ However, to the best of our knowledge, none are capable of tracking
20 clinical and non-clinical use of individual AEDs including vital status at hospital discharge. As well, some have experienced
21 challenges related to sustainability.

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33 Multiple other registries exist that describe the process and outcome of care for patients with OHCA. In the United States, the
34 Resuscitation Outcomes Consortium Cardiac Arrest Registry enrolled such patients in geographic sites that were selected by a
35 competitive process to participate in a clinical research network.⁽²⁴⁾ This registry included all patients with non-traumatic OHCA
36 assessed or treated by participating EMS providers. Data reported by participating EMS agencies was routinely screened for missing
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5 cases by comparing the observed number of cases in any month to the expected number for that agency as estimated by averaging the
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7 observed cases over a 12-month period. As a consequence of this, the incidence of EMS-treated OHCA enrolled in this registry
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9 increased by 25% over time.^(25, 26) The registry used multiple methods to monitor and improve data quality and completeness. It was
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11 intended to facilitate case identification and data collection for ROC intervention trials so it used more than 200 variables to
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13 characterize each enrolled episode. The registry informed the design and implementation of multiple pragmatic trials in patients
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15 with OHCA,⁽²⁷⁻³¹⁾ and secondary analyses about the association between patient and treatment characteristics.^(25, 32-40) Although
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17 funding to support data collection in US ROC sites has ceased, most US sites are continuing to enroll cases in this registry during
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19 ROC's current no-cost extension phase. We adapted and extended the ROC registry as a simple, sustainable, registry focused on
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21 tracking the process and outcome of care associated with use of AEDs.
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25 The Cardiac Arrest Registry to Enhance Survival (CARES) Registry initially focused on enrollment of cardiac arrest of
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27 presumed cardiac etiology, but has broadened its inclusion criteria to include cardiac arrest of any etiology.⁽⁴¹⁾ Since there is at least a
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29 two-fold variation in the reported proportion of cardiac arrests that are of non-cardiac etiology,^(42, 43) assessments of the effectiveness
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31 of interventions for OHCA that include only cases with presumed cardiac etiology may be susceptible to selection bias. Reports from
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33 CARES emphasize survival among patients with witnessed VF rather than among all treated patients. Importantly, the likelihood that
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35 an initial rhythm will be VF depends in part on the time of rhythm assessment.⁽²⁾ A consequence of emphasizing survival in this
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37 subpopulation rather than all patients treated for OHCA is that assessments of the effect of interventions intended to improve
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39 survival (e.g. AEDs) may be susceptible to bias or confounding. CARES reports that 32 states contribute data to it, but the catchment
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5 population within each ranges from 50 to 100 percent.⁽⁴⁴⁾ As well, multiple EMS agencies that participate in CARES report that 100%
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7 of their cases received bystander CPR and 100% survived to discharge, which suggests that they may be missing cases that did not
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9 receive bystander CPR (and did not have a good outcome).^{p 16, 17 in (44)} Collectively, these observations suggest that the external validity
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11 of CARES data may require further assessment. CARES was initially funded by the Centers for Disease Control. It is currently funded
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13 by the American Heart Association and Medtronic Foundation, as well as a subscription-based funding model.
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16 The National Emergency Medical Services Information System (NEMSIS) is an electronic documentation system that is
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18 intended for use in every local EMS system.⁽⁴⁵⁾ Local data are collated by each state or territory, then contributed to a national data
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20 warehouse. Over 90% of states and territories have a NEMSIS-compliant system.⁽⁴⁶⁾ Challenges to use of NEMSIS for public health
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22 surveillance of AEDs include that many states are working to revise data elements, improve data capture and ensure compliance with
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24 the latest NEMSIS data standard. Another challenge is that historically NEMSIS has had limited hospital outcome data. NEMSIS is
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26 supported by state public health departments.
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29 The PulsePoint program (PulsePoint Foundation, San Ramon, CA) links information about AED locations (as opposed to
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31 individual AEDs) to dispatch software used by Public Safety Answering Points to improve the community response to OHCA. The
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33 Dynamic AED Registry provides location information to PulsePoint to supplement and periodically update their location information.
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35 When a dispatcher identifies that someone has had OHCA in a community that is participating in the PulsePoint program, citizens
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37 who have previously downloaded a location-aware application to their smartphone are alerted to the event if they are close to the
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39 patient. They can then respond to provide CPR and use a nearby AED before the arrival of EMS providers on scene. PulsePoint does
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5 not routinely collate outcome on patients with OHCA for whom citizens are activated. As of May 25, 2016, the PulsePoint program
6 has been adopted by more than 1,600 EMS agencies that are primarily based in the United States.⁽⁴⁷⁾ PulsePoint is supported by a
7 subscription-based funding model.
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11 Lay use of AEDs before the arrival of EMS providers on scene increases survival after OHCA. Large numbers of AEDs have
12 been placed in public locations to improve the community response to cardiac arrest. These devices may be moved or may not be
13 ready for use when needed. Our dynamic AED registry surveys the location of AEDs dynamically through time and space so as to
14 improve the community response to and outcome of OHCA.
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20 21 22 **Contributorship Statement**

23
24 GN and RM contributed to the study conception and design. MD, SY, DS, TV and RM contributed to acquisition of data. GN, JBE,
25 MD, SY, DS, TV and RM participated in drafting the article, revising it for critically important intellectual content and gave final
26 approval of the submitted version.
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30 31 32 **Funding Statement**

33
34 This work is supported by 1U01FD004587-04 from the Food and Drug Administration, Silver Spring, MD and ZOLL Medical
35 Corporation, Chelmsford, MA.
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Competing Interests

The Dynamic AED Registry is funded by the Food and Drug Administration, Silver Spring, MD and ZOLL Medical Corporation, Chelmsford, MA. No other competing interests are declared.

Figure 1: Use of Unique Device Identifier for AED Surveillance



Table 1: Techniques for Optimizing Data Quality Control

	Applied to all Dynamic AED Registry Data	Applied to Post- Approval Studies
Site training and support from Registry staff for queries	Yes	Yes
Data cleaning: data integrity checks utilizing range validation and other measures	Yes	Yes
Audit portion of data	Yes	Yes
Collection of source documents and verification of pre-specified key events	No	Yes
Adjudication of selected outcomes	Yes	Yes
Potential adverse events	No shock advised by AED but first EMS rhythm shockable	Yes

Table 2: Dynamic AED Registry in Context of FDA Approval Process for Medical Devices

	Premarket		Hybrid	Post-market		
			Dynamic AED Registry			
	Phase I	Phase 2	Phase 3	Post-Approval	Post-market	Clinical Registry
Aim	Safety	Efficacy	Safety, Efficacy and Effectiveness		Effectiveness	
Inclusion criteria	Restrictive		Either	Broad		
Intervention	Tight protocol		Either	Implemented in usual clinical practice		
Cointervention	Based on protocols for many aspects of care		Either	Based on local practice; monitored but minimal control		
Adherence to protocol	Required		Either	Expected and considered in sample size and analysis plan		
Events	Related to biologic effect (e.g. conversion out of shockable rhythm)		Either		Related to patient outcome (e.g. survival)	
Analysis	Treatment received		Both	Intention to treat		
Sample size	Usually < 1,000		Either		Usually > 1,000	
Data Burden	Large		Core supplemented by study-specific	Minimal and simple core		
Study Management	Significant interventions and support from research staff		Minimal support and interventions from research team			

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BMJ Open

Public Health Surveillance of Automated External Defibrillators in Community Settings: The Dynamic Automated External Defibrillator (AED) Registry Study Protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2016-014902.R1
Article Type:	Protocol
Date Submitted by the Author:	10-Jan-2017
Complete List of Authors:	Elrod, JoAnn; University of Washington Merchant, Raina; Penn Medicine Social Media and Health Innovation Lab Daya, Mo; Oregon Health and Science University, Emergency Medicine Youngquist, Scott; University of Utah School of Medicine, Emergency Medicine; Salt Lake City Fire Department Salcido, David; University of Pittsburgh, Emergency Medicine Valenzuela, Terence; University of Arizona College of Medicine, Emergency Medicine; Tucson Fire Department Nichol, Graham; University of Washington, ; University of Washington
Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Epidemiology, Emergency medicine, Cardiovascular medicine
Keywords:	STATISTICS & RESEARCH METHODS, PUBLIC HEALTH, Cardiac Epidemiology < CARDIOLOGY

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Manuscripts

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8 **Public Health Surveillance of Automated External Defibrillators in**
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10 **Community Settings: The Dynamic Automated External Defibrillator (AED)**
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12 **Registry Study Protocol**
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22 Supported by 1U01FD004587-04 from the Food and Drug Administration, Silver Spring,
23 MD and ZOLL Medical Corporation, Chelmsford, MA.
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30 Word Count:
31 Abstract 380
32 Body, not including figure, table or references 4,586
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3 **Introduction** Lay use of automated external defibrillators (AEDs) before the arrival of
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5 Emergency Medical Services (EMS) providers on scene increases survival after out-of-
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7 hospital cardiac arrest (OHCA). AEDs have been placed in public locations may be not
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9 ready for use when needed. We describe a protocol for AED surveillance that tracks these
10
11 devices through time and space to improve public health, and survival as well as
12
13 facilitate research.

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15 **Methods and Analysis** Included AEDs are installed in public locations for use by
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17 laypersons to treat patients with OHCA before the arrival of EMS providers on scene.
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19 Included cases of OHCA are patients evaluated by organized EMS personnel and treated
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21 for OHCA.
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25 Enrollment of 10,000 AEDs annually will yield precision of 0.4% in the estimate of
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27 readiness for use. Enrollment of 2,500 patients annually will yield precision of 1.9% in
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29 the estimate of survival to hospital discharge.
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32 Recruitment began on Mar 21, 2014 and is ongoing. AEDs are found by using multiple
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34 methods. Each AED is then tagged with a label which is a unique two-dimensional (2D)
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36 matrix code; the 2D matrix code is recorded and the location and status of the AED
37
38 tracked using a smartphone; these elements are automatically passed via the internet to
39
40 a secure and confidential database in real time. Whenever the 2D matrix code is
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42 rescanned for any non-clinical or clinical use of an AED, the user is queried to answer a
43
44 finite set of questions about the device status. The primary outcome of any clinical use of
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46 an AED is survival to hospital discharge. Results are summarized descriptively.
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49 **Ethics and Dissemination** These activities are conducted under a grant of authority
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51 for public health surveillance from the Food and Drug Administration. Results are
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53 provided periodically to participating sites and sponsors to improve public health and
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55 quality of care.
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For peer review only

Strengths and Limitations of This Study

- Simple, sustainable and scalable registry of automated external defibrillators and cases of out-of-hospital cardiac arrest.
- Individual consent not required under a grant of authority for public health surveillance
- Potential incomplete case finding (selection bias)

Introduction

Out-of-hospital cardiac arrest (OHCA) is defined as a sudden and unexpected pulseless condition attributable to cessation of cardiac mechanical activity.⁽¹⁾ Cardiac arrest has multiple etiologies, and the etiology of arrest influences treatment decisions. Underlying mechanisms for non-traumatic cardiac arrest are crudely categorized as a) conductive abnormalities of the myocardium leading to arrhythmias, b) chronically weakened myocardium leading to end-stage pump failure, and c) acute occlusion of a coronary artery leading to myocardial infarction. Of these mechanisms of OHCA, resuscitation is generally most successful for isolated conductive abnormalities or for acute coronary thrombosis that is treated rapidly. Acute occlusion is common among patients with a first recorded rhythm of ventricular fibrillation (VF), which hereafter includes pulseless ventricular tachycardia as well as rhythms interpreted as shockable by an automated external defibrillator (AED). Recognition⁽²⁾ and successful treatment of VF is highly time-dependent.⁽³⁾ AEDs are medical devices (MDs) intended to simplify and improve treatment of OHCA. The timely use of AEDs by laypersons in conjunction with cardiopulmonary resuscitation (CPR including manual chest compressions with or without ventilation) is the only field intervention that has been shown to significantly increase the number of individuals who survive to discharge after OHCA.⁽⁴⁾

Since the effectiveness of use of AEDs by laypersons was demonstrated more than a decade ago, more than 2.4 million AEDs have been sold for use by laypersons in the United States (US).⁽⁵⁾ As more of these AEDs are placed in the community, the Food and Drug Administration (FDA) has received reports of potential adverse events associated with them. Since the overall number of AEDs installed is not public information and it is difficult to track individual AEDs through time and space, agency staff have experienced challenges in trying to interpret these reports.⁽⁶⁾ As well, each major manufacturer of AEDs in the US has recalled their devices to address one or more

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3 potential safety issues over the past five years. A need for a more comprehensive
4 surveillance system has been identified.⁽⁷⁾ Specifically, FDA's advisory panel
5 recommended "Registry information should be established to collect more data. An
6 active reporting registry would help with recalls and would help to maintain the quality
7 and confidence of the data collected. Sold devices could be tracked prospectively, and
8 long term device performance would be captured."
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16 In this paper we describe the rationale for and design of an ongoing dynamic
17 registry for surveillance of AED location and use. This registry has been created through
18 a partnership of academics, FDA, key stakeholders and manufacturers of AEDs. The
19 long-term goals of the registry are to provide reliable, valid and sustainable post-market
20 surveillance of AEDs; to provide important and timely information to patients, providers
21 and the public to improve MD device development including the quality of AEDs and the
22 quality of care for patients with OHCA; and to provide a framework for prospective
23 embedded studies of the effectiveness of next-generation AEDs. The Dynamic AED
24 Registry represents a novel approach to AED surveillance, leverages a clinical registry
25 infrastructure, and can be applied to other MDs that are mobile in time and space.
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37 **Methods and Analysis**

38 ***Study Populations***

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41 Included AEDs are those:

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44 a) Pre-existing in community settings and
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46 i. Identified by crowdsourcing techniques, or
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48 ii. Identified by manufacturer or distributor.
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50 b) Newly installed in community setting:
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52 i. Identified by owner during at time of installation, or
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54 ii. Identified by manufacturer at time of sale.
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57 Included patients are those treated for OHCA:
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- a) Evaluated by organized EMS personnel and receive attempts at external defibrillation (by lay, police or EMS), or
- b) Receive chest compressions by organized EMS personnel.

Although a minority of patients with OHCA have an AED applied by a layperson before the arrival of EMS providers on scene,^{p 339 of (8)} we monitor all cases of EMS-treated cardiac arrest in participating communities to obtain complete case finding. Monitoring the outcome of every AED use is necessary to identify those uses that may have caused or contributed to survival or death (21CFR803), since the majority of patients treated for OHCA die.

To date, studies reported from smaller selective registries were difficult to interpret because of potential selection bias and lack of knowledge of the overall population. This potential selection bias should be mitigated as the Dynamic AED Registry evolves over time to include a high percentage of treated patients in the US.

Several strategies are used to achieve a high rate of enrollment in the Dynamic AED Registry. Initially AEDs were enrolled by their identification in community settings by using crowdsourcing techniques.⁽⁹⁾ According to these methods, individuals or teams of volunteers register to participate in a scavenger hunt contest. Those who identify the most AEDs during the contest period receive a prize. As well, the first individual or team to report one of a finite number of pre-selected AED receive a prize.

Now, enrollment has been extended to include prospective registry of AEDs sold by a manufacturer for use by lay persons in public locations. We also collate information about individual AEDs reported by laypersons who have registered online and then used their smartphone.(<https://heartmap.uwctc.org/> accessed on May 25, 2016)

Individual device identifiers are provided by the investigators to owners or responsible individuals of these AEDs, with information about the purpose and methods of AED surveillance, as well as instructions on where to apply the identifier to the AED and how

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3 to register the AED in the dynamic registry by scanning the identifier. A series of
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5 individual identifiers are provided to each sponsoring manufacturer for inclusion with
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7 the product registration materials provided with AEDs newly sold for use in community
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9 settings.
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11 Organizations that provide physician oversight and AED readiness services
12 encourage client participation by placing an individual identifier on each AED under
13 their supervision then scanning the identifier to record information about the location of
14 the device in our secure database. With permission of the client, this information is
15 shared with the relevant EMS dispatch center so as to improve the community response
16 to OHCA for the client's staff and customers. The lightweight and portability of AEDs
17 makes them easily movable. If the AED is moved later and then the identifier is
18 rescanned, we provide information about the updated location of the device to the
19 oversight organization so that the location of the AED is known at all times.
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31 Participating EMS agencies are recruited as interest and resources allow. Initially,
32 this included a mix of EMS agencies that participated in the Resuscitation Outcomes
33 Consortium (funded by the National Institutes of Health, American Heart Association
34 and other agencies), are participating in the Mission:Lifeline Cardiac Resuscitation
35 program (funded by American Heart Association) or associated with a dispatch center
36 using software to enable faster lifesaving AED response within the community
37 (PulsePoint Responder, PulsePoint Foundation, San Ramon, CA). These vanguard sites
38 included Philadelphia, PA, Pittsburgh, PA, Portland, OR, Salt Lake City, UT, Seattle, WA,
39 and Tucson, AZ. We expect that participation will expand over time to include as many
40 EMS agencies as possible throughout the US. Furthermore, EMS agencies or receiving
41 hospitals may enroll patients to provide an analysis of their program as well as to
42 benchmark the process and outcome of care compared to other participant's experience.
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56 **Data Acquisition**

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EMS providers and personnel responsible for maintenance of AEDs are encouraged to scan the individual identifier after each AED use. Upon scanning of the 2D matrix code, the date, time and location of use are automatically identified, recorded and transmitted to the dynamic registry. As well, users are asked to respond to a finite set of queries confirming the location of the AED as well as describing the reason for its scan. In the event of a clinical use, EMS providers who scan the individual identifier are queried about the patient's intended hospital destination to facilitate subsequent tracking of patient vital status at hospital discharge. After the event, EMS providers are queried about a finite set of patient and EMS factors to facilitate adjustment of outcomes for case-mix as well as assessment of rates of potential adverse events in a manner consistent with the Utstein template for reporting of outcomes after OHCA.⁽¹⁾ As well, investigators ascertain the subject's vital status at discharge from the receiving hospital. Anonymized quarterly reports are provided to participating EMS systems, which describe the process and outcome of care for patients with OHCA as an incentive to facilitate continued surveillance of AEDs, their use, and factors that contribute to positive clinical outcomes. The quality of the data included in the registry is monitored and improved by using regular checks and audits.

Data Elements

Baseline characteristics, covariates and outcomes included in the registry were developed and implemented by consensus of the executive committee. In doing so, emphasis was placed on developing a finite set of key variables so as to ensure that the registry was simple, sustainable and scalable. These can be revised periodically as required.

Data Quality Control

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3 The Dynamic AED Registry uses multiple mechanisms to ensure data
4 completeness and accuracy (Table 1). Monitoring and auditing use standardized data
5 quality checks. Events are adjudicated as required for pre-specified outcomes.
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9 10 ***Use of Data to Improve Care***

11 The Dynamic AED Registry provides feedback to participating sites including
12 periodic quality benchmarking. Participants have access to a repository of their own data
13 and tools to evaluate their local practice and conduct user-specified local data queries.
14 This is especially valuable for communities that alert lay responders to the need for
15 bystander CPR and AED need through dispatch-identified OHCA. Data are also provided
16 to FDA to address specific surveillance questions.
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24 ***Use of Data to Facilitate Research***

25 The data will be used to facilitate monitoring of enrollment in prospective
26 embedded evaluations of interventions in patients with cardiac arrest. For example, the
27 majority of vanguard sites are planning to participate in a large randomized prehospital
28 trial of active drug vs. placebo as soon as feasible in patients treated for OHCA. As sites
29 implement this trial, trial investigators can monitor whether all eligible patients were
30 enrolled by comparing the volume of patients enrolled in the AED registry to that
31 enrolled in the trial. As well, the characteristics of the patients who accrue to the trial can
32 be compared to data obtained from the AED registry. In order to adhere to patient
33 privacy requirements, data from the registry will not be linked to individual patients who
34 might also be enrolled in the clinical trial. Instead, aggregate statistics for the population
35 of all patients with OHCA treated within the study communities will be compared to
36 aggregate statistics for the patients enrolled in this trial. From such a comparison, the
37 generalizability of the trial results can be investigated.
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54 ***Innovative Methods***

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3 The Dynamic AED Registry uses multiple innovative methods to enhance
4 surveillance of AEDs.
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8 **a) Crowdsourcing**
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10 We have adapted crowdsourcing methods to find AEDs installed in public
11 locations for use by laypersons in major metropolitan areas that are participating in the
12 Dynamic AED Registry. Merchant pioneered use of crowdsourcing to identify AEDs
13 installed in community settings.⁽⁹⁾ According to these methods, help is solicited for tasks
14 usually performed by particular individuals from an undefined large group (i.e. a crowd).
15 Since the task is offered to a large group with diverse backgrounds, it has the potential to
16 attract individuals who are interested in the problem, likely to finish the task, and likely
17 to contribute innovative ideas. Based on methods developed by the Defense Advanced
18 Research Projects Agency (DARPA),⁽¹⁰⁾ adults were invited to identify AEDs installed in
19 community settings in Philadelphia County, PA. According to state law, AEDs installed
20 in community settings in Philadelphia County, PA should be registered with the local
21 EMS authority. Before the contest began, 57 devices were registered with Philadelphia
22 EMS. Monetary prizes were awarded to those individuals or teams who reported the
23 most AEDs as well as to those who were first to report any of 200 preselected AEDs.
24 During the contest, 313 individuals and teams identified 852 unique AEDs in 528
25 locations. These locations were in 94% of eligible census tracts and included a mix of
26 public (59%) and private (41%) locations. 50% of AEDs were identified as either non-
27 functional or having unknown functional status. The investigators concluded that
28 crowdsourcing is a feasible approach for identifying AEDs installed in community
29 settings in a large urban city.
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52 **b) Able to Track Individual Medical Devices**
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55 We have pioneered the use of an individual identifier to track AEDs or other MDs
56 through time and space in community settings. According to this method, each AED is
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3 tagged with a label which consists of a unique two-dimensional (2D) matrix code (QR
4 code, Denso Wave Inc., Chita-gun, Japan); then the QR code or 2D matrix code is
5 recorded as well as the location and status of the AED by using open-source software
6 native to any contemporary smartphone (e.g. Google Goggles, Google Inc., Mountain
7 View, CA); and finally these elements are automatically passed via the internet to a
8 secure and confidential database in real time (Provisional Patent # 61/498,424, Figure 1).
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10 The user is prompted to rescan the label after any use (Figure 2). Note that by design
11 each label has a unique alphanumeric code that provides built in redundancy with the 2D
12 matrix code. The user is queried to answer a finite set of questions when the smartphone
13 is connected to the database (Table 2). If the device has a clinical use, these queries
14 include verification of the intended receiving hospital for transported cases to facilitate
15 longitudinal follow-up of patient outcome to hospital discharge (Table 3). Using the
16 limited data collected in the field with the 2D matrix code, additional variables are
17 abstracted later from the subject's record to further characterize the process and
18 outcome of care.
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35 The method for scanning the 2D matrix code is deliberately platform
36 independent (i.e., agnostic). We opted to design and implement a website that can be
37 accessed by any web-capable smartphone rather than take on the burden of designing,
38 disseminated and maintaining multiple different smartphone applications. Most EMS
39 providers carry their own smartphone. Since no specific smartphone application is
40 required to access the website, our web developer is able to update this centrally as
41 needed.
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50 This device identifier complement's the FDA's Global Use Device Identification
51 Database (GUDID) initiative.⁽¹¹⁾ This establishes that: a unique device identifier number
52 is assigned by the device manufacturer to each version or model of a device. This
53 identifier is both in human-readable format and in machine-readable format. It is
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intended to contain information about the type of device as well as information about its manufacture. The primary difference is that GUDID does not require or enable tracking of the location of a device through time and space.

Sample Size and Analysis

Enrollment of AEDs and patients with OHCA in this cohort study is ongoing. As such, there is no maximum expected enrollment necessary to detect a significant difference between groups, as there would be in a clinical trial. The primary analysis will be descriptive. If 95% of AEDs are ready for use, enrollment of 10,000 AEDs annually will yield precision (measured as half of the 95% confidence interval) of 0.4% in the estimate of readiness for use. If 10% of patients treated for OHCA survive to discharge, enrollment of 2500 patients annually will yield precision of 1.9% in the estimate of survival to discharge.

Ethics and Dissemination

The Dynamic AED Registry is the first registry to be conducted under a grant of authority for public health surveillance from FDA. As such, these activities have been determined by multiple institutional review boards (IRBs) to not be subject to human subjects' regulations and to exercise the public health exception within the Health Insurance Portability and Accountability Act (HIPAA, 45 CFR 164.512(b)). These methods are adaptable to public health surveillance of other MDs.

Discussion

Lay use of AEDs before the arrival of EMS providers on scene increases survival after OHCA.⁽⁴⁾ Large numbers of AEDs have been placed in public locations to improve the community response to cardiac arrest.⁽⁵⁾ It is sometimes difficult to determine whether these devices are maintained in a state of readiness for use or whether they functioned as intended when applied to someone in presumed cardiac arrest. Importantly, there is no widely-deployed method of tracking their location and use in

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3 community settings. We describe the implementation and maintenance of a dynamic
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5 registry for surveillance of AEDs through time and space.
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8 This registry serves multiple purposes, including public health surveillance of
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10 AEDs, quality improvement of AED use as well as overall EMS care, and serving as a
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12 framework for embedded research studies. We note that local and multicenter registries
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14 of patients with OHCA are often used for multiple purposes. For example, the ROC
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16 cardiac arrest registry⁽¹²⁾ measured the public health impact of cardiac arrest in
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18 participating communities,⁽¹³⁾ provided a mechanism for local quality improvement⁽¹⁴⁾ as
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20 well as a mechanism for embedded randomized trials.⁽¹⁵⁻¹⁷⁾ Unfortunately funding for
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22 ROC has ceased, and the ROC registry collated too many variables to be sustainable over
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24 the long term without dedicated funding.
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27 The Dynamic AED Registry has several strengths. By design, it is simple,
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29 sustainable and scalable. Since the registry functions under a grant of authority for
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31 public health surveillance, the base surveillance and quality improvement functionality is
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33 not subject to human subjects' research regulations and is exempted from HIPAA. Data
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35 collected for public health surveillance can, subject to appropriate permissions, can be
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37 used to improve the process and outcome of care for patients with OHCA in participating
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39 communities. Like other registries, it can also be used as a framework for embedded
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41 prospective research evaluations of existing or next-generation defibrillators, as well as
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43 other interventions intended to improve outcomes after OHCA.
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46 What does the Dynamic AED Registry offer over other registries? It tracks the
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48 location and use of individual AEDs in diverse communities. This identifies the specific
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50 AED used, allowing verification of the diagnostic algorithm in no-shock advised cases. It
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52 supports passive reporting of potential AED failure that is supposed to occur. AED
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54 manufacturers have recognized the value of and subsequently invested in the Dynamic
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56 AED Registry to provide ongoing safety and effectiveness data, which can be useful as
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3 real-world evidence to support regulatory decisions for AEDs. Recognizing that data
4 collated in different resuscitation registries may not be comparable, the academic
5 leadership of the Dynamic AED Registry is working with leaders of other resuscitation-
6 related registries to encourage harmonization of data elements, quality control
7 techniques, outcomes and adverse event classification.
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11 This registry has some limitations. The robustness of the data collated by it
12 depend in part upon the completeness of case finding by EMS providers and
13 participating sites may have variable success in enrolling consecutive AEDs or patients..
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15 Based on a comparison of patients not enrolled vs. enrolled in a registry intended to
16 enroll consecutive patients with acute coronary syndrome, patients who are not included
17 in a registry may have higher risk, receive poorer quality of care and have a higher
18 mortality than those who are included.⁽¹⁸⁾ Such selection bias limits the ability of
19 registries to reliably assess the effectiveness of study interventions.⁽¹⁹⁾
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23 At present, the Dynamic AED registry has a small footprint but this is expected to
24 grow over time. Although crowdsourcing methods are used to identify AEDs that were
25 placed in public locations, it is not feasible to apply crowdsourcing in every urban and
26 rural community. Instead, the registry is evolving to include prospective tagging of AEDs
27 through manufacturers as they are placed in public locations. The distribution of AEDs
28 by geography may be non-random (i.e., one manufacturer may have more devices placed
29 in a given community than another). Since geographic region is a strong predictor of
30 outcome after OHCA,⁽²⁰⁾ comparison of outcomes by different manufacturers needs to
31 account for differences in geography.
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35 The Center for Devices and Radiological Health (CDRH) of the US Food and
36 Drug Administration (FDA) of the US is responsible for regulating firms who
37 manufacture, distribute, or import MDs sold in the US. MDs are instruments or related
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3 articles which are intended for use in the diagnosis or treatment of disease, are applied
4 externally or internally to patients to affect the structure or function of their body, and
5 do not achieve their purpose through chemical action or metabolism.⁽²¹⁾ FDA relies on
6 registries for post-market surveillance of MDs to ensure their safety and efficacy. The US
7 congress has directed the agency to implement an active system capable of identifying
8 safety issues and communicating them in a timely manner to patients, providers and the
9 public.⁽²²⁾ Policy makers have suggested that increased surveillance of MDs is necessary
10 to enhance and maintain patient safety.⁽²³⁾ The Institute of Medicine (IOM) made
11 recommendations about how to improve the approval process and post-market
12 surveillance of MDs.⁽²⁴⁾ As well, the IOM made recommendations about how to improve
13 outcomes after OHCA that included the establishment and maintenance of a sustainable
14 method of national surveillance of the process and outcome of care of all patients with
15 OHCA.⁽²⁵⁾ Experts have recommended post-market surveillance of any AED introduced
16 for in-hospital, emergency medical services, or public access defibrillation.⁽²⁶⁾

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33 Our registry can be placed in the context of FDA's evolving medical device
34 regulatory process (Table 4) as well as in the context of other resuscitation-related
35 registries. It is a next-generation registry implemented with the multiple purposes of
36 surveillance of MDs as well as measurement and improvement of the process and
37 outcome of care for patients in real-world settings, as well as serving as a framework for
38 embedded studies of the effectiveness of defibrillator as well as other interventions in
39 patients with OHCA. The Dynamic AED Registry is designed to evolve into a
40 comprehensive but scalable and sustainable national registry in the US. Multiple other
41 resuscitation-related registries exist in the US and the rest of the world that seek to
42 characterize the process and outcome of care related to OHCA.⁽²⁷⁾ However, to the best of
43 our knowledge, none are capable of tracking clinical and non-clinical use of individual
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3 AEDs including vital status at hospital discharge. As well, some have experienced
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5 challenges related to sustainability.
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8 Multiple other registries exist that describe the process and outcome of care for
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10 patients with OHCA. In the US, the Resuscitation Outcomes Consortium (ROC) Cardiac
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12 Arrest Registry enrolled such patients in geographic sites that were selected by a
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14 competitive process to participate in a clinical research network.⁽¹²⁾ This registry
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16 included all patients with non-traumatic OHCA assessed or treated by participating EMS
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18 providers. Data reported by participating EMS agencies was routinely screened for
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20 missing cases by comparing the observed number of cases in any month to the expected
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22 number for that agency as estimated by averaging the observed cases over a 12-month
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24 period. As a consequence of this, the incidence of EMS-treated OHCA enrolled in this
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26 registry increased by 25% over time.^(13, 28) The registry used multiple methods to monitor
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28 and improve data quality and completeness. It was intended to facilitate case
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30 identification and data collection for ROC intervention trials so it used more than 200
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32 variables to characterize each enrolled episode. The registry informed the design and
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34 implementation of multiple pragmatic trials in patients with OHCA,^(15, 17, 29-31) and
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36 secondary analyses about the association between patient and treatment
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38 characteristics.^(13, 32-40) Although funding to support data collection in US ROC sites has
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40 ceased, most sites are continuing to enroll cases in this registry during ROC's current no-
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42 cost extension phase. We adapted and extended the ROC registry as a simple, sustainable,
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44 registry focused on tracking the process and outcome of care associated with use of AEDs.
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49 The Cardiac Arrest Registry to Enhance Survival (CARES) Registry initially
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51 focused on enrollment of cardiac arrest of presumed cardiac etiology, but has broadened
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53 its inclusion criteria to include cardiac arrest of any etiology.⁽⁴¹⁾ Since there is at least a
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55 two-fold variation in the reported proportion of cardiac arrests that are of non-cardiac
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57 etiology,^(42, 43) assessments of the effectiveness of interventions for OHCA that include
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3 only cases with presumed cardiac etiology may be susceptible to selection bias. Reports
4 from CARES emphasize survival among patients with witnessed VF rather than among
5 all treated patients. Importantly, the likelihood that an initial rhythm will be VF depends
6 in part on the time of rhythm assessment.⁽²⁾ A consequence of emphasizing survival in
7 this subpopulation rather than all patients treated for OHCA is that assessments of the
8 effect of interventions intended to improve survival (e.g. AEDs) may be susceptible to
9 bias or confounding. CARES reports that 32 states contribute data to it, but the
10 catchment population within each ranges from 50 to 100 percent.⁽⁴⁴⁾ As well, multiple
11 EMS agencies that participate in CARES report that 100% of their cases received
12 bystander CPR and 100% survived to discharge, which suggests that they may be missing
13 cases that did not receive bystander CPR (and did not have a good outcome).^{p 16, 17 in (44)}
14 Collectively, these observations suggest that the external validity of CARES data may
15 require further assessment. CARES was initially funded by the Centers for Disease
16 Control. It is currently funded by the American Heart Association and Medtronic
17 Foundation, as well as a subscription-based funding model.

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The National Emergency Medical Services Information System (NEMSIS) is an
electronic documentation system that is intended for use in every local EMS system.⁽⁴⁵⁾
Local data are collated by each state or territory, and then contributed to a national data
warehouse. Over 90% of states and territories have a NEMSIS-compliant system.⁽⁴⁶⁾
Challenges to use of NEMSIS for public health surveillance of AEDs include that many
states are working to revise data elements, improve data capture and ensure compliance
with the latest NEMSIS data standard. Another challenge is that historically NEMSIS has
had limited hospital outcome data. NEMSIS is supported by state public health
departments.

The PulsePoint program incorporates information about AED locations (as
opposed to individual AEDs) into dispatch software used by Public Safety Answering

Points to improve the community response to OHCA. The Dynamic AED Registry provides location information to PulsePoint to supplement and periodically update their location information. When a dispatcher identifies that someone has had OHCA in a community that is participating in the PulsePoint program, citizens who have previously downloaded a location-aware application to their smartphone are alerted to the event if they are close to the patient. They can then respond to provide CPR and use a nearby AED before the arrival of EMS providers on scene. PulsePoint does not routinely collate outcome on patients with OHCA for whom citizens are activated. As of May 25, 2016, the PulsePoint program has been adopted by more than 1,600 EMS agencies that are primarily based in the US.⁽⁴⁷⁾ PulsePoint is supported by a subscription-based funding model.

Lay use of AEDs before the arrival of EMS providers on scene increases survival after OHCA. Large numbers of AEDs have been placed in public locations to improve the community response to cardiac arrest. These devices may be moved or may not be ready for use when needed. Our dynamic AED registry surveys the location of AEDs dynamically through time and space so as to improve the community response to and outcome of OHCA.

Contributorship Statement

GN and RM contributed to the study conception and design. MD, SY, DS, TV and RM contributed to acquisition of data. GN, JBE, MD, SY, DS, TV and RM participated in drafting the article, revising it for critically important intellectual content and gave final approval of the submitted version.

Funding Statement

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3 This work is supported by 1U01FD004587-04 from the Food and Drug
4 Administration, Silver Spring, MD and ZOLL Medical Corporation, Chelmsford, MA.
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10 **Competing Interests**

11 The Dynamic AED Registry is funded by the Food and Drug Administration, Silver
12 Spring, MD and ZOLL Medical Corporation, Chelmsford, MA. No other competing
13 interests are declared.
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Figure 1: Use of Unique Device Identifier for AED Surveillance



Peer review only

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Figure 2: Two Dimensional Matrix Code for AED Tagging



**Help Save
Lives!**
Scan QR code
AFTER use
or service.

aed.uwctc.org/m/8fbg5cb

sw only

Table 1: Techniques for Optimizing Data Quality Control

	Applied to all Dynamic AED Registry Data	Applied to Post- Approval Studies
Site training and support from Registry staff for queries	Yes	Yes
Data cleaning: data integrity checks utilizing range validation and other measures	Yes	Yes
Audit portion of data	Yes	Yes
Collection of source documents and verification of pre-specified key events	No	Yes
Adjudication of selected outcomes	Yes	Yes
Potential adverse events	No shock advised by AED but first EMS rhythm shockable	Yes

review only

Table 2: Questions for EMS Upon Scanning After Clinical Use

Question	Definition
Device Not Used	Medic, bystander or other person tried to apply AED to patient but was unable to use device; Reason device not used.
Date of Cardiac Arrest	Date cardiac arrest occurred.
Time of Cardiac Arrest	Time cardiac arrest occurred.
Age	Patient's age in years.
Gender	Patient's gender.
Destination Hospital	Hospital to which patient was transported.
First Responder Agency	Name and state-assigned code number from First Responder vehicle.

Table 3: Patient Outcome Variables

Variable	Definition
Emergency Department Disposition	Final disposition of patient from Emergency Department: patient documented to be discharged from ED alive, patient documented to die in ED, transferred to a different hospital, admitted to same hospital.
Vital Status at Discharge	Patient's vital status at discharge from hospital: died in hospital, discharged alive, not yet determined.
Neurologic Status at Discharge	Patient's neurologic status based on Cerebral Performance Category (CPC) at discharge from hospital: good cerebral performance, moderate cerebral disability, severe cerebral disability, coma/vegetative state.

Table 4: Dynamic AED Registry in Context of FDA Approval Process for Medical Devices

	Premarket		Hybrid	Post-market		
			Dynamic AED Registry			
	Phase I	Phase 2	Phase 3	Post-Approval	Post-market	Clinical Registry
Aim	Safety	Efficacy	Safety, Efficacy and Effectiveness		Effectiveness	
Inclusion criteria	Restrictive		Either	Broad		
Intervention	Tight protocol		Either	Implemented in usual clinical practice		
Cointervention	Based on protocols for many aspects of care		Either	Based on local practice; monitored but minimal control		
Adherence to protocol	Required		Either	Expected and considered in sample size and analysis plan		
Events	Related to biologic effect (e.g. conversion out of shockable rhythm)		Either		Related to patient outcome (e.g. survival)	
Analysis	Treatment received		Both	Intention to treat		
Sample size	Usually < 1,000		Either		Usually > 1,000	
Data Burden	Large		Core supplemented by study-specific	Minimal and simple core		
Study Management	Significant interventions and support from research staff		Minimal support and interventions from research team			

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Figure 1: Use of Unique Device Identifier for AED Surveillance

254x69mm (300 x 300 DPI)

peer review only

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Figure 2: Two Dimensional Matrix Code for AED Tagging

240x139mm (300 x 300 DPI)

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BMJ Open

Public Health Surveillance of Automated External Defibrillators in the United States: Protocol for the Dynamic Automated External Defibrillator Registry Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2016-014902.R2
Article Type:	Protocol
Date Submitted by the Author:	10-Feb-2017
Complete List of Authors:	Elrod, JoAnn; University of Washington Merchant, Raina; Penn Medicine Social Media and Health Innovation Lab Daya, Mo; Oregon Health and Science University, Emergency Medicine Youngquist, Scott; University of Utah School of Medicine, Emergency Medicine; Salt Lake City Fire Department Salcido, David; University of Pittsburgh, Emergency Medicine Valenzuela, Terence; University of Arizona College of Medicine, Emergency Medicine; Tucson Fire Department Nichol, Graham; University of Washington, ; University of Washington
Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Epidemiology, Emergency medicine, Cardiovascular medicine
Keywords:	STATISTICS & RESEARCH METHODS, PUBLIC HEALTH, Cardiac Epidemiology < CARDIOLOGY

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**Public Health Surveillance of Automated External Defibrillators in the
United States: Protocol for the Dynamic Automated External Defibrillator
Registry Study**

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22 Supported by 1U01FD004587-04 from the Food and Drug Administration, Silver Spring,
23 MD and ZOLL Medical Corporation, Chelmsford, MA.
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30 Word Count:
31 Abstract 380
32 Body, not including figure, table or references 4,586
33
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3 **Introduction** Lay use of automated external defibrillators (AEDs) before the arrival of
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5 Emergency Medical Services (EMS) providers on scene increases survival after out-of-
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7 hospital cardiac arrest (OHCA). AEDs have been placed in public locations may be not
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9 ready for use when needed. We describe a protocol for AED surveillance that tracks these
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11 devices through time and space to improve public health, and survival as well as
12
13 facilitate research.

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15 **Methods and Analysis** Included AEDs are installed in public locations for use by
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17 laypersons to treat patients with OHCA before the arrival of EMS providers on scene.
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19 Included cases of OHCA are patients evaluated by organized EMS personnel and treated
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21 for OHCA.
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25 Enrollment of 10,000 AEDs annually will yield precision of 0.4% in the estimate of
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27 readiness for use. Enrollment of 2,500 patients annually will yield precision of 1.9% in
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29 the estimate of survival to hospital discharge.
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32 Recruitment began on Mar 21, 2014 and is ongoing. AEDs are found by using multiple
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34 methods. Each AED is then tagged with a label which is a unique two-dimensional (2D)
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36 matrix code; the 2D matrix code is recorded and the location and status of the AED
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38 tracked using a smartphone; these elements are automatically passed via the internet to
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40 a secure and confidential database in real time. Whenever the 2D matrix code is
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42 rescanned for any non-clinical or clinical use of an AED, the user is queried to answer a
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44 finite set of questions about the device status. The primary outcome of any clinical use of
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46 an AED is survival to hospital discharge. Results are summarized descriptively.
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49 **Ethics and Dissemination** These activities are conducted under a grant of authority
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51 for public health surveillance from the Food and Drug Administration. Results are
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53 provided periodically to participating sites and sponsors to improve public health and
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55 quality of care.
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Strengths and Limitations of This Study

- Study tracks individual automated external defibrillators over time
- Outcome is ascertained by public health surveillance
- Study has potential for selection bias due to incomplete case finding

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Introduction

Out-of-hospital cardiac arrest (OHCA) is defined as a sudden and unexpected pulseless condition attributable to cessation of cardiac mechanical activity.⁽¹⁾ Cardiac arrest has multiple etiologies, and the etiology of arrest influences treatment decisions. Underlying mechanisms for non-traumatic cardiac arrest are crudely categorized as a) conductive abnormalities of the myocardium leading to arrhythmias, b) chronically weakened myocardium leading to end-stage pump failure, and c) acute occlusion of a coronary artery leading to myocardial infarction. Of these mechanisms of OHCA, resuscitation is generally most successful for isolated conductive abnormalities or for acute coronary thrombosis that is treated rapidly. Acute occlusion is common among patients with a first recorded rhythm of ventricular fibrillation (VF), which hereafter includes pulseless ventricular tachycardia as well as rhythms interpreted as shockable by an automated external defibrillator (AED). Recognition⁽²⁾ and successful treatment of VF is highly time-dependent.⁽³⁾ AEDs are medical devices (MDs) intended to simplify and improve treatment of OHCA. The timely use of AEDs by laypersons in conjunction with cardiopulmonary resuscitation (CPR including manual chest compressions with or without ventilation) is the only field intervention that has been shown to significantly increase the number of individuals who survive to discharge after OHCA.⁽⁴⁾

Since the effectiveness of use of AEDs by laypersons was demonstrated more than a decade ago, more than 2.4 million AEDs have been sold for use by laypersons in the United States (US).⁽⁵⁾ As more of these AEDs are placed in the community, the Food and Drug Administration (FDA) has received reports of potential adverse events associated with them. Since the overall number of AEDs installed is not public information and it is difficult to track individual AEDs through time and space, agency staff have experienced challenges in trying to interpret these reports.⁽⁶⁾ As well, each major manufacturer of AEDs in the US has recalled their devices to address one or more

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3 potential safety issues over the past five years. A need for a more comprehensive
4 surveillance system has been identified.⁽⁷⁾ Specifically, FDA's advisory panel
5 recommended "Registry information should be established to collect more data. An
6 active reporting registry would help with recalls and would help to maintain the quality
7 and confidence of the data collected. Sold devices could be tracked prospectively, and
8 long term device performance would be captured."
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11 In this paper we describe the rationale for and design of an ongoing dynamic
12 registry for surveillance of AED location and use. This registry has been created through
13 a partnership of academics, FDA, key stakeholders and manufacturers of AEDs. The
14 long-term goals of the registry are to provide reliable, valid and sustainable post-market
15 surveillance of AEDs; to provide important and timely information to patients, providers
16 and the public to improve MD device development including the quality of AEDs and the
17 quality of care for patients with OHCA; and to provide a framework for prospective
18 embedded studies of the effectiveness of next-generation AEDs. The Dynamic AED
19 Registry represents a novel approach to AED surveillance, leverages a clinical registry
20 infrastructure, and can be applied to other MDs that are mobile in time and space.
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37 **Methods and Analysis**

38 ***Study Populations***

39 Included AEDs are those:

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42 a) Pre-existing in community settings and
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44 i. Identified by crowdsourcing techniques, or
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46 ii. Identified by manufacturer or distributor.
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49 b) Newly installed in community setting:
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51 i. Identified by owner during at time of installation, or
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53 ii. Identified by manufacturer at time of sale.
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56 Included patients are those treated for OHCA:
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- a) Evaluated by organized EMS personnel and receive attempts at external defibrillation (by lay, police or EMS), or
- b) Receive chest compressions by organized EMS personnel.

Although a minority of patients with OHCA have an AED applied by a layperson before the arrival of EMS providers on scene,^{p 339 of (8)} we monitor all cases of EMS-treated cardiac arrest in participating communities to obtain complete case finding. Monitoring the outcome of every AED use is necessary to identify those uses that may have caused or contributed to survival or death (21CFR803), since the majority of patients treated for OHCA die.

To date, studies reported from smaller selective registries were difficult to interpret because of potential selection bias and lack of knowledge of the overall population. This potential selection bias should be mitigated as the Dynamic AED Registry evolves over time to include a high percentage of treated patients in the US.

Several strategies are used to achieve a high rate of enrollment in the Dynamic AED Registry. Initially AEDs were enrolled by their identification in community settings by using crowdsourcing techniques.⁽⁹⁾ According to these methods, individuals or teams of volunteers register to participate in a scavenger hunt contest. Those who identify the most AEDs during the contest period receive a prize. As well, the first individual or team to report one of a finite number of pre-selected AED receive a prize.

Now, enrollment has been extended to include prospective registry of AEDs sold by a manufacturer for use by lay persons in public locations. We also collate information about individual AEDs reported by laypersons who have registered online and then used their smartphone. (<https://heartmap.uwctc.org/> accessed on May 25, 2016)

Individual device identifiers are provided by the investigators to owners or responsible individuals of these AEDs, with information about the purpose and methods of AED surveillance, as well as instructions on where to apply the identifier to the AED and how

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3 to register the AED in the dynamic registry by scanning the identifier. A series of
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5 individual identifiers are provided to each sponsoring manufacturer for inclusion with
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7 the product registration materials provided with AEDs newly sold for use in community
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9 settings.
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11 Organizations that provide physician oversight and AED readiness services
12 encourage client participation by placing an individual identifier on each AED under
13 their supervision then scanning the identifier to record information about the location of
14 the device in our secure database. With permission of the client, this information is
15 shared with the relevant EMS dispatch center so as to improve the community response
16 to OHCA for the client's staff and customers. The lightweight and portability of AEDs
17 makes them easily movable. If the AED is moved later and then the identifier is
18 rescanned, we provide information about the updated location of the device to the
19 oversight organization so that the location of the AED is known at all times.
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22 Participating EMS agencies are recruited as interest and resources allow. Initially,
23 this included a mix of EMS agencies that participated in the Resuscitation Outcomes
24 Consortium (funded by the National Institutes of Health, American Heart Association
25 and other agencies), are participating in the Mission:Lifeline Cardiac Resuscitation
26 program (funded by American Heart Association) or associated with a dispatch center
27 using software to enable faster lifesaving AED response within the community
28 (PulsePoint Responder, PulsePoint Foundation, San Ramon, CA). These vanguard sites
29 included Philadelphia, PA, Pittsburgh, PA, Portland, OR, Salt Lake City, UT, Seattle, WA,
30 and Tucson, AZ. We expect that participation will expand over time to include as many
31 EMS agencies as possible throughout the US. Furthermore, EMS agencies or receiving
32 hospitals may enroll patients to provide an analysis of their program as well as to
33 benchmark the process and outcome of care compared to other participant's experience.
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36 **Data Acquisition**

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EMS providers and personnel responsible for maintenance of AEDs are encouraged to scan the individual identifier after each AED use. Upon scanning of the 2D matrix code, the date, time and location of use are automatically identified, recorded and transmitted to the dynamic registry. As well, users are asked to respond to a finite set of queries confirming the location of the AED as well as describing the reason for its scan. In the event of a clinical use, EMS providers who scan the individual identifier are queried about the patient's intended hospital destination to facilitate subsequent tracking of patient vital status at hospital discharge. After the event, EMS providers are queried about a finite set of patient and EMS factors to facilitate adjustment of outcomes for case-mix as well as assessment of rates of potential adverse events in a manner consistent with the Utstein template for reporting of outcomes after OHCA.⁽¹⁾ As well, investigators ascertain the subject's vital status at discharge from the receiving hospital. Anonymized quarterly reports are provided to participating EMS systems, which describe the process and outcome of care for patients with OHCA as an incentive to facilitate continued surveillance of AEDs, their use, and factors that contribute to positive clinical outcomes. The quality of the data included in the registry is monitored and improved by using regular checks and audits.

Data Elements

Baseline characteristics, covariates and outcomes included in the registry were developed and implemented by consensus of the executive committee. In doing so, emphasis was placed on developing a finite set of key variables so as to ensure that the registry was simple, sustainable and scalable. These can be revised periodically as required.

Data Quality Control

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3 The Dynamic AED Registry uses multiple mechanisms to ensure data
4 completeness and accuracy (Table 1). Monitoring and auditing use standardized data
5 quality checks. Events are adjudicated as required for pre-specified outcomes.
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9 10 ***Use of Data to Improve Care***

11 The Dynamic AED Registry provides feedback to participating sites including
12 periodic quality benchmarking. Participants have access to a repository of their own data
13 and tools to evaluate their local practice and conduct user-specified local data queries.
14 This is especially valuable for communities that alert lay responders to the need for
15 bystander CPR and AED need through dispatch-identified OHCA. Data are also provided
16 to FDA to address specific surveillance questions.
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24 ***Use of Data to Facilitate Research***

25 The data will be used to facilitate monitoring of enrollment in prospective
26 embedded evaluations of interventions in patients with cardiac arrest. For example, the
27 majority of vanguard sites are planning to participate in a large randomized prehospital
28 trial of active drug vs. placebo as soon as feasible in patients treated for OHCA. As sites
29 implement this trial, trial investigators can monitor whether all eligible patients were
30 enrolled by comparing the volume of patients enrolled in the AED registry to that
31 enrolled in the trial. As well, the characteristics of the patients who accrue to the trial can
32 be compared to data obtained from the AED registry. In order to adhere to patient
33 privacy requirements, data from the registry will not be linked to individual patients who
34 might also be enrolled in the clinical trial. Instead, aggregate statistics for the population
35 of all patients with OHCA treated within the study communities will be compared to
36 aggregate statistics for the patients enrolled in this trial. From such a comparison, the
37 generalizability of the trial results can be investigated.
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54 ***Innovative Methods***

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3 The Dynamic AED Registry uses multiple innovative methods to enhance
4 surveillance of AEDs.
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7 **a) Crowdsourcing**
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10 We have adapted crowdsourcing methods to find AEDs installed in public
11 locations for use by laypersons in major metropolitan areas that are participating in the
12 Dynamic AED Registry. Merchant pioneered use of crowdsourcing to identify AEDs
13 installed in community settings.⁽⁹⁾ According to these methods, help is solicited for tasks
14 usually performed by particular individuals from an undefined large group (i.e. a crowd).
15 Since the task is offered to a large group with diverse backgrounds, it has the potential to
16 attract individuals who are interested in the problem, likely to finish the task, and likely
17 to contribute innovative ideas. Based on methods developed by the Defense Advanced
18 Research Projects Agency (DARPA),⁽¹⁰⁾ adults were invited to identify AEDs installed in
19 community settings in Philadelphia County, PA. According to state law, AEDs installed
20 in community settings in Philadelphia County, PA should be registered with the local
21 EMS authority. Before the contest began, 57 devices were registered with Philadelphia
22 EMS. Monetary prizes were awarded to those individuals or teams who reported the
23 most AEDs as well as to those who were first to report any of 200 preselected AEDs.
24 During the contest, 313 individuals and teams identified 852 unique AEDs in 528
25 locations. These locations were in 94% of eligible census tracts and included a mix of
26 public (59%) and private (41%) locations. 50% of AEDs were identified as either non-
27 functional or having unknown functional status. The investigators concluded that
28 crowdsourcing is a feasible approach for identifying AEDs installed in community
29 settings in a large urban city.
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52 **b) Able to Track Individual Medical Devices**
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55 We have pioneered the use of an individual identifier to track AEDs or other MDs
56 through time and space in community settings. According to this method, each AED is
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3 tagged with a label which consists of a unique two-dimensional (2D) matrix code (QR
4 code, Denso Wave Inc., Chita-gun, Japan); then the QR code or 2D matrix code is
5 recorded as well as the location and status of the AED by using open-source software
6 native to any contemporary smartphone (e.g. Google Goggles, Google Inc., Mountain
7 View, CA); and finally these elements are automatically passed via the internet to a
8 secure and confidential database in real time (Provisional Patent # 61/498,424, Figure 1).
9
10 The user is prompted to rescan the label after any use (Figure 2). Note that by design
11 each label has a unique alphanumeric code that provides built in redundancy with the 2D
12 matrix code. The user is queried to answer a finite set of questions when the smartphone
13 is connected to the database (Table 2). If the device has a clinical use, these queries
14 include verification of the intended receiving hospital for transported cases to facilitate
15 longitudinal follow-up of patient outcome to hospital discharge (Table 3). Using the
16 limited data collected in the field with the 2D matrix code, additional variables are
17 abstracted later from the subject's record to further characterize the process and
18 outcome of care.
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35 The method for scanning the 2D matrix code is deliberately platform
36 independent (i.e., agnostic). We opted to design and implement a website that can be
37 accessed by any web-capable smartphone rather than take on the burden of designing,
38 disseminated and maintaining multiple different smartphone applications. Most EMS
39 providers carry their own smartphone. Since no specific smartphone application is
40 required to access the website, our web developer is able to update this centrally as
41 needed.
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50 This device identifier complement's the FDA's Global Use Device Identification
51 Database (GUDID) initiative.⁽¹¹⁾ This establishes that: a unique device identifier number
52 is assigned by the device manufacturer to each version or model of a device. This
53 identifier is both in human-readable format and in machine-readable format. It is
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intended to contain information about the type of device as well as information about its manufacture. The primary difference is that GUDID does not require or enable tracking of the location of a device through time and space.

Sample Size and Analysis

Recruitment began on Mar 21, 2014. Enrollment of AEDs and patients with OHCA in this cohort study is ongoing. There is no planned end. As such, there is no maximum expected enrollment necessary to detect a significant difference between groups, as there would be in a clinical trial. The primary analysis will be descriptive. If 95% of AEDs are ready for use, enrollment of 10,000 AEDs annually will yield precision (measured as half of the 95% confidence interval) of 0.4% in the estimate of readiness for use. If 10% of patients treated for OHCA survive to discharge, enrollment of 2500 patients annually will yield precision of 1.9% in the estimate of survival to discharge.

Ethics and Dissemination

The Dynamic AED Registry is the first registry to be conducted under a grant of authority for public health surveillance from FDA. As such, these activities have been determined by multiple institutional review boards (IRBs) to not be subject to human subjects' regulations and to exercise the public health exception within the Health Insurance Portability and Accountability Act (HIPAA, 45 CFR 164.512(b)). These methods are adaptable to public health surveillance of other MDs.

Discussion

Lay use of AEDs before the arrival of EMS providers on scene increases survival after OHCA.⁽⁴⁾ Large numbers of AEDs have been placed in public locations to improve the community response to cardiac arrest.⁽⁵⁾ It is sometimes difficult to determine whether these devices are maintained in a state of readiness for use or whether they functioned as intended when applied to someone in presumed cardiac arrest. Importantly, there is no widely-deployed method of tracking their location and use in

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3 community settings. We describe the implementation and maintenance of a dynamic
4 registry for surveillance of AEDs through time and space.
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7 This registry serves multiple purposes, including public health surveillance of
8 AEDs, quality improvement of AED use as well as overall EMS care, and serving as a
9 framework for embedded research studies. We note that local and multicenter registries
10 of patients with OHCA are often used for multiple purposes. For example, the ROC
11 cardiac arrest registry⁽¹²⁾ measured the public health impact of cardiac arrest in
12 participating communities,⁽¹³⁾ provided a mechanism for local quality improvement⁽¹⁴⁾ as
13 well as a mechanism for embedded randomized trials.⁽¹⁵⁻¹⁷⁾ Unfortunately funding for
14 ROC has ceased, and the ROC registry collated too many variables to be sustainable over
15 the long term without dedicated funding.
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18 The Dynamic AED Registry has several strengths. By design, it is simple,
19 sustainable and scalable. Since the registry functions under a grant of authority for
20 public health surveillance, the base surveillance and quality improvement functionality is
21 not subject to human subjects' research regulations and is exempted from HIPAA. Data
22 collected for public health surveillance can, subject to appropriate permissions, can be
23 used to improve the process and outcome of care for patients with OHCA in participating
24 communities. Like other registries, it can also be used as a framework for embedded
25 prospective research evaluations of existing or next-generation defibrillators, as well as
26 other interventions intended to improve outcomes after OHCA.
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29 What does the Dynamic AED Registry offer over other registries? It tracks the
30 location and use of individual AEDs in diverse communities. This identifies the specific
31 AED used, allowing verification of the diagnostic algorithm in no-shock advised cases. It
32 supports passive reporting of potential AED failure that is supposed to occur. AED
33 manufacturers have recognized the value of and subsequently invested in the Dynamic
34 AED Registry to provide ongoing safety and effectiveness data, which can be useful as
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3 real-world evidence to support regulatory decisions for AEDs. Recognizing that data
4 collated in different resuscitation registries may not be comparable, the academic
5 leadership of the Dynamic AED Registry is working with leaders of other resuscitation-
6 related registries to encourage harmonization of data elements, quality control
7 techniques, outcomes and adverse event classification.
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14 This registry has some limitations. The robustness of the data collated by it
15 depend in part upon the completeness of case finding by EMS providers and
16 participating sites may have variable success in enrolling consecutive AEDs or patients.
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18 Based on a comparison of patients not enrolled vs. enrolled in a registry intended to
19 enroll consecutive patients with acute coronary syndrome, patients who are not included
20 in a registry may have higher risk, receive poorer quality of care and have a higher
21 mortality than those who are included.⁽¹⁸⁾ Such selection bias limits the ability of
22 registries to reliably assess the effectiveness of study interventions.⁽¹⁹⁾
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33 At present, the Dynamic AED registry has a small footprint but this is expected to
34 grow over time. Although crowdsourcing methods are used to identify AEDs that were
35 placed in public locations, it is not feasible to apply crowdsourcing in every urban and
36 rural community. Instead, the registry is evolving to include prospective tagging of AEDs
37 through manufacturers as they are placed in public locations. The distribution of AEDs
38 by geography may be non-random (i.e., one manufacturer may have more devices placed
39 in a given community than another). Since geographic region is a strong predictor of
40 outcome after OHCA,⁽²⁰⁾ comparison of outcomes by different manufacturers needs to
41 account for differences in geography.
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52 The small footprint of the registry impacts on its representativeness, and may be
53 associated with selection bias. Communities choose to participate or not participate in
54 the registry. To the extent that participating communities have greater (or lesser)
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3 survival than other communities, the registry may over (under) estimate the
4 effectiveness of AEDs.
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8 It is plausible that incomplete identification and scanning of QR codes may
9 impact on the registry's representativeness and may be associated with selection bias. To
10 try to mitigate this, participating communities are encouraged to track and report all
11 patients with OHCA treated by EMS providers, regardless of whether they are initially
12 identified as having been treated with an AED by a layperson.
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18 The Center for Devices and Radiological Health (CDRH) of the US Food and
19 Drug Administration (FDA) of the US is responsible for regulating firms who
20 manufacture, distribute, or import MDs sold in the US. MDs are instruments or related
21 articles which are intended for use in the diagnosis or treatment of disease, are applied
22 externally or internally to patients to affect the structure or function of their body, and
23 do not achieve their purpose through chemical action or metabolism.⁽²¹⁾ FDA relies on
24 registries for post-market surveillance of MDs to ensure their safety and efficacy. The US
25 congress has directed the agency to implement an active system capable of identifying
26 safety issues and communicating them in a timely manner to patients, providers and the
27 public.⁽²²⁾ Policy makers have suggested that increased surveillance of MDs is necessary
28 to enhance and maintain patient safety.⁽²³⁾ The Institute of Medicine (IOM) made
29 recommendations about how to improve the approval process and post-market
30 surveillance of MDs.⁽²⁴⁾ As well, the IOM made recommendations about how to improve
31 outcomes after OHCA that included the establishment and maintenance of a sustainable
32 method of national surveillance of the process and outcome of care of all patients with
33 OHCA.⁽²⁵⁾ Experts have recommended post-market surveillance of any AED introduced
34 for in-hospital, emergency medical services, or public access defibrillation.⁽²⁶⁾
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54 Our registry can be placed in the context of FDA's evolving medical device
55 regulatory process (Table 4) as well as in the context of other resuscitation-related
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registries. It is a next-generation registry implemented with the multiple purposes of surveillance of MDs as well as measurement and improvement of the process and outcome of care for patients in real-world settings, as well as serving as a framework for embedded studies of the effectiveness of defibrillator as well as other interventions in patients with OHCA. The Dynamic AED Registry is designed to evolve into a comprehensive but scalable and sustainable national registry in the US. Multiple other resuscitation-related registries exist in the US and the rest of the world that seek to characterize the process and outcome of care related to OHCA.⁽²⁷⁾ However, to the best of our knowledge, none are capable of tracking clinical and non-clinical use of individual AEDs including vital status at hospital discharge. As well, some have experienced challenges related to sustainability.

Multiple other registries exist that describe the process and outcome of care for patients with OHCA. In the US, the Resuscitation Outcomes Consortium (ROC) Cardiac Arrest Registry enrolled such patients in geographic sites that were selected by a competitive process to participate in a clinical research network.⁽¹²⁾ This registry included all patients with non-traumatic OHCA assessed or treated by participating EMS providers. Data reported by participating EMS agencies was routinely screened for missing cases by comparing the observed number of cases in any month to the expected number for that agency as estimated by averaging the observed cases over a 12-month period. As a consequence of this, the incidence of EMS-treated OHCA enrolled in this registry increased by 25% over time.^(13, 28) The registry used multiple methods to monitor and improve data quality and completeness. It was intended to facilitate case identification and data collection for ROC intervention trials so it used more than 200 variables to characterize each enrolled episode. The registry informed the design and implementation of multiple pragmatic trials in patients with OHCA,^(15, 17, 29-31) and secondary analyses about the association between patient and treatment

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3 characteristics.^(13, 32-40) Although funding to support data collection in US ROC sites has
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characteristics.^(13, 32-40) Although funding to support data collection in US ROC sites has ceased, most sites are continuing to enroll cases in this registry during ROC's current no-cost extension phase. We adapted and extended the ROC registry as a simple, sustainable, registry focused on tracking the process and outcome of care associated with use of AEDs.

The Cardiac Arrest Registry to Enhance Survival (CARES) Registry initially focused on enrollment of cardiac arrest of presumed cardiac etiology, but has broadened its inclusion criteria to include cardiac arrest of any etiology.⁽⁴¹⁾ Since there is at least a two-fold variation in the reported proportion of cardiac arrests that are of non-cardiac etiology,^(42, 43) assessments of the effectiveness of interventions for OHCA that include only cases with presumed cardiac etiology may be susceptible to selection bias. Reports from CARES emphasize survival among patients with witnessed VF rather than among all treated patients. Importantly, the likelihood that an initial rhythm will be VF depends in part on the time of rhythm assessment.⁽²⁾ A consequence of emphasizing survival in this subpopulation rather than all patients treated for OHCA is that assessments of the effect of interventions intended to improve survival (e.g. AEDs) may be susceptible to bias or confounding. CARES reports that 32 states contribute data to it, but the catchment population within each ranges from 50 to 100 percent.⁽⁴⁴⁾ As well, multiple EMS agencies that participate in CARES report that 100% of their cases received bystander CPR and 100% survived to discharge, which suggests that they may be missing cases that did not receive bystander CPR (and did not have a good outcome).^{p 16, 17 in (44)} Collectively, these observations suggest that the external validity of CARES data may require further assessment. CARES was initially funded by the Centers for Disease Control. It is currently funded by the American Heart Association and Medtronic Foundation, as well as a subscription-based funding model.

The National Emergency Medical Services Information System (NEMSIS) is an electronic documentation system that is intended for use in every local EMS system.⁽⁴⁵⁾

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3 Local data are collated by each state or territory, and then contributed to a national data
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5 warehouse. Over 90% of states and territories have a NEMSIS-compliant system.⁽⁴⁶⁾
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7 Challenges to use of NEMSIS for public health surveillance of AEDs include that many
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9 states are working to revise data elements, improve data capture and ensure compliance
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11 with the latest NEMSIS data standard. Another challenge is that historically NEMSIS has
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13 had limited hospital outcome data. NEMSIS is supported by state public health
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15 departments.
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19 The PulsePoint program incorporates information about AED locations (as
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21 opposed to individual AEDs) into dispatch software used by Public Safety Answering
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23 Points to improve the community response to OHCA. The Dynamic AED Registry
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25 provides location information to PulsePoint to supplement and periodically update their
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27 location information. When a dispatcher identifies that someone has had OHCA in a
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29 community that is participating in the PulsePoint program, citizens who have previously
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31 downloaded a location-aware application to their smartphone are alerted to the event if
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33 they are close to the patient. They can then respond to provide CPR and use a nearby
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35 AED before the arrival of EMS providers on scene. PulsePoint does not routinely collate
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37 outcome on patients with OHCA for whom citizens are activated. As of May 25, 2016, the
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39 PulsePoint program has been adopted by more than 1,600 EMS agencies that are
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41 primarily based in the US.⁽⁴⁷⁾ PulsePoint is supported by a subscription-based funding
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43 model.
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47 Lay use of AEDs before the arrival of EMS providers on scene increases survival
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49 after OHCA. Large numbers of AEDs have been placed in public locations to improve the
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51 community response to cardiac arrest. These devices may be moved or may not be ready
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53 for use when needed. Our dynamic AED registry surveys the location of AEDs
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55 dynamically through time and space so as to improve the community response to and
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57 outcome of OHCA.
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Contributorship Statement

GN and RM contributed to the study conception and design. MD, SY, DS, TV and RM contributed to acquisition of data. GN, JBE, MD, SY, DS, TV and RM participated in drafting the article, revising it for critically important intellectual content and gave final approval of the submitted version.

Funding Statement

This work is supported by 1U01FD004587-04 from the Food and Drug Administration, Silver Spring, MD and ZOLL Medical Corporation, Chelmsford, MA.

Competing Interests

The Dynamic AED Registry is funded by the Food and Drug Administration, Silver Spring, MD and ZOLL Medical Corporation, Chelmsford, MA. No other competing interests are declared.

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Figure 1: Use of Unique Device Identifier for AED Surveillance

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5 **Figure 2: Two Dimensional Matrix Code for AED Tagging**
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Table 1: Techniques for Optimizing Data Quality Control

	Applied to all Dynamic AED Registry Data	Applied to Post- Approval Studies
Site training and support from Registry staff for queries	Yes	Yes
Data cleaning: data integrity checks utilizing range validation and other measures	Yes	Yes
Audit portion of data	Yes	Yes
Collection of source documents and verification of pre-specified key events	No	Yes
Adjudication of selected outcomes	Yes	Yes
Potential adverse events	No shock advised by AED but first EMS rhythm shockable	Yes

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Table 2: Questions for EMS Upon Scanning After Clinical Use

Question	Definition
Device Not Used	Medic, bystander or other person tried to apply AED to patient but was unable to use device; Reason device not used.
Date of Cardiac Arrest	Date cardiac arrest occurred.
Time of Cardiac Arrest	Time cardiac arrest occurred.
Age	Patient's age in years.
Gender	Patient's gender.
Destination Hospital	Hospital to which patient was transported.
First Responder Agency	Name and state-assigned code number from First Responder vehicle.

Table 3: Patient Outcome Variables

Variable	Definition
Emergency Department Disposition	Final disposition of patient from Emergency Department: patient documented to be discharged from ED alive, patient documented to die in ED, transferred to a different hospital, admitted to same hospital.
Vital Status at Discharge	Patient's vital status at discharge from hospital: died in hospital, discharged alive, not yet determined.
Neurologic Status at Discharge	Patient's neurologic status based on Cerebral Performance Category (CPC) at discharge from hospital: good cerebral performance, moderate cerebral disability, severe cerebral disability, coma/vegetative state.

Table 4: Dynamic AED Registry in Context of FDA Approval Process for Medical Devices

	Premarket		Hybrid	Post-market		
			Dynamic AED Registry			
	Phase I	Phase 2	Phase 3	Post-Approval	Post-market	Clinical Registry
Aim	Safety	Efficacy	Safety, Efficacy and Effectiveness		Effectiveness	
Inclusion criteria	Restrictive		Either	Broad		
Intervention	Tight protocol		Either	Implemented in usual clinical practice		
Cointervention	Based on protocols for many aspects of care		Either	Based on local practice; monitored but minimal control		
Adherence to protocol	Required		Either	Expected and considered in sample size and analysis plan		
Events	Related to biologic effect (e.g. conversion out of shockable rhythm)		Either		Related to patient outcome (e.g. survival)	
Analysis	Treatment received		Both	Intention to treat		
Sample size	Usually < 1,000		Either		Usually > 1,000	
Data Burden	Large		Core supplemented by study-specific	Minimal and simple core		
Study Management	Significant interventions and support from research staff		Minimal support and interventions from research team			

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Figure 1: Use of Unique Device Identifier for AED Surveillance

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Figure 2: Two Dimensional Matrix Code for AED Tagging
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