KCE REPORT 294

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

STATIC AUTOMATED EXTERNAL DEFIBRILLATORS FOR OPPORTUNISTIC USE BY BYSTANDERS

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HEALTH TECHNOLOGY ASSESSMENT

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STATIC AUTOMATED EXTERNAL DEFIBRILLATORS FOR OPPORTUNISTIC USE BY BYSTANDERS

HANS VAN BRABANDT, SOPHIE GERKENS, NICOLAS FAIRON, CECILE DUBOIS, MARCEL VAN DER AUWERA, CHRISTOPHE VANSIMPSEN, DOMINIQUE ROBERFROID

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COLOPHON

Title:	Static automated external defibrillators for opportunistic use by bystanders
Authors:	Hans Van Brabandt (KCE), Sophie Gerkens (KCE), Nicolas Fairon (KCE), Cécile Dubois (KCE), Marcel Van Der Auwera (PFS Public Health), Christophe Vansimpsen (PFS Public Health), Dominique Roberfroid (KCE)
Project coordinator:	Dominique Paulus (KCE)
Senior supervisor:	Dominique Roberfroid (KCE)
Reviewers:	Audrey Cordon (KCE), Christian Léonard (KCE), Sabine Stordeur (KCE)
External experts:	Rufij Baeke (Heartsaver®), Ivan Blankoff (BEHRA [Belgian Heart Rhythm Association]; CHU Charleroi), Paul Calle (BeSEDiM [Belgian Society of Emergency and Disaster Medicine]; UGent), Marc Clevers (bvba CLINITEC, bvba RECOMEX), André De Landtsheer (VVIB-AMTI [Vereniging Voor Interne Bedrijfsartsen – Association des Médecins du Travail des services internes]), Thierry Hosay (Belgian Red Cross & ERC [European Resuscitation Council]), Tony Hosmans (Ecole Provinciale d'Aide Médicale Urgente, Liège), Mouloud Kalaai (IDEWE [Externe Dienst voor Preventie en Bescherming op het Werk]), Luc Ketele (Heartsaver®), Jorien Laermans (Rode Kruis-Vlaanderen), Frédérique Meulders (FAGG-AFMPS [Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten – Agence Fédérale des Médicaments et des Produits de Santé]), Pierre Mols (CHU Saint-Pierre, Bruxelles), Koen Monsieurs (UZA [Universitair Ziekenhuis Antwerpen]), Walter Renier (KULeuven), Christophe Scavée (Cliniques universitaires Saint-Luc), Peter Thiebaut (AED Partners), David Vancraeynest (Cliniques universitaires Saint-Luc), Marcel Van der Auwera (FOD Volksgezondheid), Steven Vercammen (EVapp [Emergency Volunteer Application]), Hans Verstraeten (Rode Kruis-Vlaanderen)
External validators:	Alexandre Ghuysen (ULG), Ruud W. Koster (Academisch Medisch Centrum, Universiteit van Amsterdam), Rik Willems (KULeuven)
Acknowledgements:	Tom Kooi (Heart Save Living), Nicolas Mpotos (AZ Sint Lucas & Volkskliniek, Gent), Frank Schrooyen (Heart Save Living, Defib Belgium NV), Patrick Van de Voorde (UZ Gent)
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Holder of intellectual property (patent, product developer, copyrights, trademarks, etc.): Tony Hosmans (Manual of first aid 3rd Ed 2016. Ed de la Province de Liège)

Participation in scientific or experimental research as an initiator, principal investigator or researcher: Paul Calle (co-author of a number of scientific publications related to defibrillators, without financial relation with the industry or an institution), Pierre Mols (Eureca One, Eureca Two, CAAM study, RCT in general on cardiac arrests)

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Consultancy or employment for a company, an association or an organisation that may gain or lose financially due to the results of this report: Peter Thiebaut (AED Partners), Marc Clevers (Clinitec, Recomex)

Presidency or accountable function within an institution, association, department or other entity on which the results of this report could have an impact: Walter Renier (Board member BRC), Steven Vercammen (EVapp)

Other possible interests that could lead to a potential or actual conflict of interest: Paul Calle (Advisor for the city of Gent on the use of defibrillators by bystanders), Jorien Laermans (Employee of Belgian Red Cross-Flanders, providing courses on first aid, including resuscitation and AED use, for the general public and commercial settings, and promoting AED use in Flanders), Hans Verstraeten (Participation in the project 'Hartveilig' by the Belgian Red Cross-Flanders that promotes the use of AED and organizes cursus related to reanimation and defibrillation)

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- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
- **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.**
- **Finally, this report has been approved by common assent by the Executive Board.**
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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AED	Automated External Defibrillator
AHA	American Heart Association
CPR	Cardiopulmonary Resuscitation
EMS	Emergency Medical Services
ERC	European Resuscitation Council
FPS	Federal Public Service
HTA	Health Technology Assessment
ICER	Incremental Cost-Effectiveness Ratio
OHCA	Out of Hospital Cardiac Arrest
PAD	Public Access Defibrillation
QALY	Quality-Adjusted Life-Year
RCT	Randomized Controlled Trial
SD	Standard Deviation
SR	Systematic Review of the literature
VF	Ventricular Fibrillation

SCIENTIFIC REPORT

1 BACKGROUND

1.1 Out of Hospital Cardiac Arrest

A cardiac arrest is defined by the absence of signs of circulation[1]. A victim who is unresponsive and not breathing normally is suspected to be in cardiac arrest[2]. An out of hospital cardiac arrest (OHCA) is a cardiac arrest that occurs outside a hospital setting.

OHCA is predominantly of cardiac origin ("primary cardiac arrest") and caused by ventricular fibrillation (VF)[3]. VF can be abolished by electrical defibrillation whereby the application of an electrical shock to the chest depolarises the heart and enables normal heart rhythm to resume.

A cardiac arrest of non-cardiac origin may be due to other medical causes (e.g. anaphylaxis, asthma, exsanguination), trauma, drug overdose, drowning, electrocution, asphyxia (airway obstruction, hanging, or strangulation)[1, 2].

Immediate cardiopulmonary resuscitation (CPR) of an OHCA victim provides a small but critical blood flow to the heart and brain, limiting brain damage and slowing down deterioration of the VF to asystole[1, 4]. Chest compressions are especially important if a defibrillation shock cannot be delivered within the first few minutes after collapse.

"First monitored rhythm" is defined as the first heart rhythm present when a monitor or a defibrillator is attached to the patient after a cardiac arrest[1]. Although most patients suffering OHCA have VF at the moment of collapse[3, 5], this rhythm gradually deteriorates to asystole, and only 25 to 50% of them still have VF by the time the first electrocardiogram is monitored[2].

"Shockable rhythm" refers to VF (or pulseless ventricular tachycardia) as the first monitored rhythm. In contrast to asystole, these rhythms are treatable by electric defibrillation.

The time dependency of shockability has been demonstrated in a recent UK study: the longer the EMS arrival time, the lower the proportion of shockable patients[6]. Patients who had their arrest witnessed by a bystander were more likely to be found in a shockable rhythm on EMS arrival. This effect was more pronounced in patients that received bystander CPR, and even more in whom an automated external defibrillator was used[6].

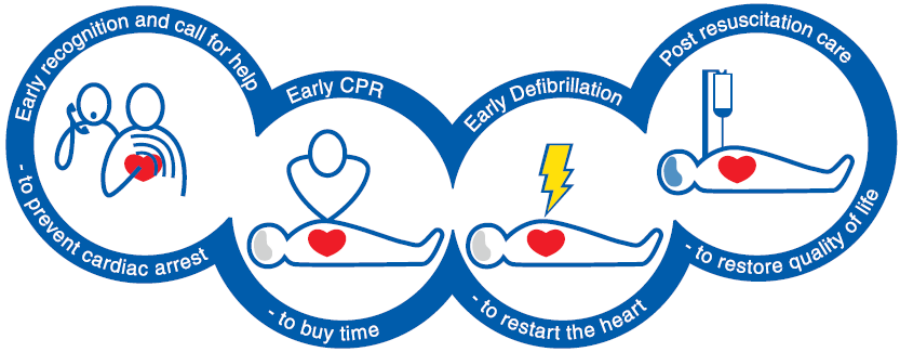
Factors impacting the time between collapse and (public access) defibrillation are described in section 6.1.

OHCA of cardiac origin which are witnessed and present a VF as first-monitored rhythm are called hereafter the Utstein comparator group.

1.2 Cardiopulmonary resuscitation and Automated External Defibrillators

The "chain of survival" of OHCA summarises the vital links for successful ressuscitation[2]. OHCA is diagnosed by the observation of an unconscious individual not breathing normally. Early recognition is critical to enable rapid activation of the EMS and promptly starting CPR.

Figure 1 – The chain of survival



Source: Perkins et al.[1]

While awaiting the arrival of the EMS, cardiopulmonary resuscitation (CPR) should be started and continued until a defibrillator is connected to the victim[2]. Originally defibrillators were operated by professional health care providers. Automated External Defibrillators (AEDs) have at first been developed to be used out of hospital by EMS personnel. They are connected to the chest of the victim, give spoken instructions and analyse the heart rhythm. If a shockable rhythm is detected, the AED automatically delivers an electric shock to the patient. In the semi-automatic mode, a button has to be pressed by the rescuer in order for the device to shock. Presently, most publicly available AEDs operate in a fully automatic mode.

AEDs can be static or mobile. Static AEDs remain at a given location (often fixed on a wall) and are intended for opportunistic use by bystanders. Mobile AEDs are often used by first responders, i.e. individuals responding to a medical emergency in an official capacity as part of an organised medical response team but who are not the designated transporter of the patient to the hospital[7]. First responders can be police officers, fire fighters, or life-saving crew members trained to perform basic life support until the EMS team arrives and who are called to the scene by emergency dispatch centres. However, a first responder can also be a lay rescuer that received a special training and can be alarmed via e.g. a text message. In that case, he can make use of a mobile AED or he may be informed where to find a static AED in the vicinity of the OHCA victim[8]. AEDs can be incorporated into a comprehensive public access defibrillation (PAD) programme involving training programmes, community groups of lay-volunteers, geolocation of AEDs, delivery of AEDs with drones, dispatched or non-dispatched first responders.

Public access defibrillation (PAD) programmes have been developed to promote the use of AEDs, with the aim of increasing survival from OHCA by reducing the time to defibrillation. The European Resuscitation Council (ERC)[9] and the American Heart Association (AHA)[10] have produced guidelines on PAD, both based on the International Liaison Committee on Resuscitation (ILCOR) systematic review[11, 12]. They recommend implementing PAD programmes in public places with a high density and movement of citizens, such as airports, railway stations, bus terminals, sport facilities, shopping malls, offices and casinos where cardiac arrests are usually witnessed and trained CPR providers can quickly be on scene. The ERC recommends AED placement in areas with at least 1 cardiac arrest every five years[9].

2 AIMS AND SCOPE

The first research question submitted to KCE concerned the clinical- and cost-effectiveness of the provision of publicly accessible automated external defibrillators (AED) intended for opportunistic use by bystanders who witness a cardiac arrest. The report focuses on the use of AEDs as a stand-alone intervention, i.e. not incorporated into a coordinated public access defibrillation (PAD) programme (see section 1.2), because this is currently the dominant practice in Belgium (see section 5.3). The question was not to advise the government about the most effective strategies for PAD, as the governmental involvement in PAD is very limited, but if it should support (also financially) the current practice or not (as currently most AEDs are privately owned).

A secondary question concerned the utility of the mandatory central registration of AEDs by the SPF Public Health.

3 METHODS

3.1 Systematic literature review

We performed a systematic literature review (SR) on the clinical effectiveness and cost-effectiveness of the provision of publicly accessible AEDs intended for opportunistic use by bystanders who witness a cardiac arrest. The literature search was organised in two steps, following KCE procedures for rapid HTA: identify a recent high-quality Health Technology Assessment (HTA) or systematic review (SR) to serve as the core evidence source; assess if an update of the core source is relevant based on the publication of more recent primary studies.

First we searched for HTA and SR without any date restrictions. The search was run on February 2, 2017 and updated on June 1, 2017. Having found the ILCOR systematic review[2, 12] and an HTA published by the Ireland's Health Information and Quality Authority (HIQA)[13], we designed our strategy to retrieve primary comparative studies published after January 1, 2013. The search was conducted the 8th February 2017 for Wiley databases and the 27th of February for Medline and Embase with a later update the June 1, 2017 and a final update the 10th of July for Embase. A separate search for cost-effectiveness studies was executed on June 1, with the addition of Econlit database.

The systematic searches of literature were conducted in the following databases:

- Medline (http://ovidsp.ovid.com/)
- Embase (http://www.embase.com/)
- The Cochrane library (http://onlinelibrary.wiley.com/cochranelibrary/search)
    - The Cochrane Database of systematic reviews, for part 1 of the search
    - DARE, for part 1
    - HTA database, for part 1

  - NHS Economic Evaluations Database, for part 1
  - The Cochrane Central Register of Clinical Trials (CENTRAL) for part 2
- Econlit database (via Ovidsp.com)

The search strategy excluded studies regarding children or animals. For Embase, the strategy excluded conference papers and duplicates from Medline.

No language limits were set in the strategies. Search strategies were based on the PICO presented in Table 1. Full details of the search strategy with date of the search and number of articles found and the resulting PRISMA flow diagrams are presented in Appendix.

All the results found during these searches were imported into an Endnote® database, with automatic duplicates removal turned on. We used both Endnote and an Excel template for screening references based on title and abstract.

Inclusion and exclusion criteria are presented in Table 1. The main factor of exclusion was the use of mobile AEDs, of highly sophisticated add-ons (texting, apps, geolocation of AEDs …), etc. as our focus is the use of static AEDs by bystanders. Observational studies with a non-comparative design (e.g. registries) were excluded because results might be confounded by many factors, i.e. the individuals to whom AED is applied are not necessarily similar to those with no AED, and these individual differences are generally not (fully) captured in routine registries, hampering in-depth adjustment of results for the effect of confounding factors. Moreover, other interventional or contextual factors might have changed between the start and the evaluation of the PAD programme and do not necessarily allow to assess the impact of PAD versus no PAD. However, relevant data from observational studies were extracted for the discussion whenever appropriate.

For the cost-effectiveness chapter, only full economic evaluations were selected, i.e. studies comparing at least two alternative treatments in terms of costs and outcomes and allowing to calculate an incremental cost-effectiveness ratio. Cost studies were for example not included.

Table 1 – PICO question used for literature search, and study selection criteria

	Inclusion criteria	Exclusion criteria
Population	Patients with out-of-hospital cardiac arrest	Individuals <18 yrs., in-hospital cardiac arrest.
Intervention	Provision of publicly accessible automated external defibrillator (PAD)	Use of mobile AEDs, studies on specific aspect of defibrillators (algorithms, brands, pads placement …).
Comparison	Traditional EMS response without PAD	
Outcome	Survival, safety, cost-effectiveness	
Study settings	HTA, SR, Randomized Controlled Trial (RCT), comparative observational studies with control group	Case reports. Meeting abstracts. Case series of OHCA. Non-comparative studies.

3.2 External experts and stakeholders

External experts were invited at two separate expert meetings (March 16, and June 19, 2017) in order to obtain a critical appraisal of the proposed methodology and the relevance and quality of the report. They also provided input on organisational issues, especially with respect to the Belgian EMS and PAD practice. On July 31st, a draft was sent for final on-line discussion.

Selection of experts was executed through contact with relevant professional associations and previously known experts and contacts: Belgian Resuscitation Council (BRC), Belgian College of Emergency Physicians (BeCEP), Belgian Society of Emergency and Disaster Medicine (BeSEDiM), Belgian Heart Rhythm Association (BeHRA), Belgian Red Cross-Flanders, and occupational physicians. We also invited industry representatives through their professional association beMedTech and via personal contact, but they showed no interest for participation. Commercial data on AEDs in Belgium were obtained from AED distributors. We also invited Heart Saver vzw to participate because of their field knowledge of AED use in Belgium.

External experts and stakeholders are mentioned in the colophon to this report.

3.3 Search for Belgian data on AED

Data on the number of AEDs in Belgium were extracted from the Federal Public Service (FPS) database (see section 5.2). For statistics on OHCAs and potential use of AED, we analysed data from the MUGREG/SMUREG registry. The MUG/SMUR is a second tier unit, staffed with emergency physicians and nurses. It is deployed when the presence of a physician at an emergency scene is considered crucial. By law, its interventions have to be registered. Finally, the Belgian data of the European EuReCa ONE study[14] were made accessible to us and re-analysed.

Additional data on Belgian AED practice were obtained from external clinical experts, Belgian distributors of AEDs, and through on-line searches. The following website were searched:

- GIN (http://www.g-i-n.net/)
- Greylit (http://greylit.org/)
- OpenGrey (http://www.opengrey.eu/)
- OpenAire (https://www.openaire.eu/)
- Bictel (http://www.bictel.be/)
- Scriptiebank (http://www.scriptiebank.be)
- NGC (https://www.guideline.gov/)
- Unicat(http://www.unicat.bet)

4 RESULTS

4.1 Effectiveness of PAD

Our search for SRs resulted in one recent HTA, and one consensus document that we in fact considered a genuine SR.

The HTA was published by Ireland's Health Information and Quality Authority (HIQA) on December 1, 2014[13]. Its search date was October 24, 2013. The consensus document on "Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" was produced by the International Liaison Committee on Resuscitation (ILCOR). Its search date was January 13, 2014. The resulting conclusions were co-published in 2015 in two journals: "Circulation" and "Resuscitation" under the name of "International Consensus on CPR and ECC Science with Treatment Recommendations" (CoSTR)[2, 12]. The search strategy and results for this SR are not available in print (in contrast to previous versions of the document) and could not be retrieved on-line. Therefore, and since the ILCOR review does not consider cost-effectiveness issues, we decided to select the HIQA HTA as the primary source document for the present report. We searched for additional primary studies (matching our PICO question) published after January 1, 2013. No comparative studies (either RCT or observational) were identified. Therefore, we base our analysis on the HIQA HTA[13].

The HIQA HTA[13] included a systematic review of the literature published up to 24/10/2013 and indexed in Medline, Embase, Scopus, clinical trial registries (Cochrane Registry of Controlled Trials, ClinicalTrials.gov and the ISRCTN register) and the Cochrane Library (Database of Abstracts of Reviews of Effects [DARE], Cochrane Database of Systematic Reviews [CDSR] and the Health Technology assessment [HTA] database. The inclusion criteria are summarised in Appendix. Study quality was assessed using the Quality Assessment Tool for Quantitative Studies (http://www.ephpp.ca/tools.html). The quality of the SR was high as assessed with the AMSTAR grid (see appendix).

This HTA identified only one comparative study on the provision of static AEDs in public locations: the Public Access Defibrillation Trial, published in 2004[15]. HIQA graded the study high-quality. Fourteen studies on the use of mobile AEDs, carried and deployed by police first responders or fire fighter first responders or a combination of laypeople and first responders were also included. However, the latter approaches were out of scope in the present KCE report.

The PAD-trial studied the use of AEDs by trained volunteers in selected public areas at high risk of OHCA across the US. High risk locations were physical facilities with a history of at least one witnessed OHCA every two years on average, or where one could expect at least one OHCA during the study period, i.e. if the equivalent of at least 250 adults more than 50 years of age were present for 16 hours a day. Almost 1000 public areas (e.g. recreational facilities, shopping malls, residential complexes) were randomly assigned to Cardiopulmonary Resuscitation (CPR) or CPR+AED. A summary of findings is displayed in Table 2.

Table 2 – Main characteristics and summary of findings of the PAD trial

PICO	Description
Population	Individuals aged ≥8 years with an out-of-hospital cardiac arrest of cardiac cause were included. Patients with arrest and unconsciousness due to trauma and obvious drug overdose were excluded.
Intervention	11 015 trained (retraining after 3-6 months and at one or more additional times) volunteers in CPR+AED in 496 residential or public community groups[a] with the ability to deliver an AED within 3 minutes to a person having a cardiac arrest. Volunteers were alerted to events in various ways (e.g. overhead paging, security notification), depending on the facility's response plan Within each community, as many AEDs were installed as were needed to ensure that volunteers could deliver the device to a cardiac arrest victim within three minutes. 1 587 AEDs were placed, 85% of which in public locations (facilities where at least one out-of-hospital cardiac arrest could be expected every two years (equivalent of at least 250 adults more than 50 years of age present for 16 hours a day or if the facilities had a history of at least one witnessed out-of-hospital cardiac arrest every two years, on average)). Density of AEDs was unknown because the catchment population was unknown.
Comparator	8 361 volunteers across 497 community units (without a pre-existing PAD) trained in CPR
Outcomes	235 definite OHCA occurred over a period of 21.5±5.5 months. EMS-treated OHCA cases were 67% male and had a mean age of 70 years, 72% of arrests were witnessed. The prespecified primary outcome chosen was the number of survivors of definite OHCAs. Survivors to hospital discharge after a definite OHCA were 30 in the CPR+AED group vs. 15 in the CPR only group, yielding a twofold difference in survival (RR=2.0; 95%CI: 1.07 to 3.77; p=0.03).
Study type	RCT[b]

Source: PAD trial[15]

[a] The catchment population of the community unit is not reported. The community units were excluded if they were within a three minute EMS response catchment, had on-site medical personnel able to respond within three minutes, or had an existing defibrillation programme in place.

[b] The randomized groups were stratified according to center and stratified within each center according to location (residential vs. public)

There have been some methodological discussions over the way of computing results in the PAD trial. The authors of the PAD trial reported the results of the trial as the absolute number of outcome events in both groups (30 versus 15 survivors), rather than as a rate based on the total number of cardiac arrests, and applied a t-test with which the mean number of survivors per unit within strata were compared, yielding a statistically significant result, although statistical significance was borderline (p=0.03). The rationale given for this approach was that ascertainment and detection bias associated with the intervention would likely affect the calculation of rates. That is, more definite cardiac arrests were likely to be recorded in the intervention group, since volunteers with AED training were considered more likely to intervene, and AED electrocardiograms would facilitate better diagnosis of cardiac arrests. However, the authors of the HIQA HTA redid the computation based on risk ratio of survival in patients with a definite OHCA (30/128 (23%) in intervention vs. 15/107 (14%) in control, and reached a RR=1.67 (95%CI: 0.95-2.94; p=0.074) which was no more statistically significant, with a risk difference of 9% (95%CI: 0%-19%).

It is also worth noting that the study was designed to have an 80% power to detect a 2.1-fold difference in the number of survivors between groups. This can explains the imprecision around the point estimate, and the fact that the result was marginally non-significant. In the trial, OHCA incidence was lower than expected in public locations and survival from CPR was higher than expected, two factors which could also have reduced the study power.

On top of these statistical uncertainties, it should be noted that the PAD trial included an “optimally” trained lay-person-enacted response plan (11 000 volunteers and the deployment of 1 600 AEDs in selected high-risk places), i.e. the results cannot be extrapolated to implementation without such a response plan.

4.2 Safety

The Irish HIQA HTA briefly describes safety issues related to PAD and distinguishes 4 domains in this respect: device malfunction, injury to patients or users of the AED, failure to access or dispatch the AEDs, and adverse psychological effects on users[13]. In our view, the accessibility of AEDs is a rather organisational issue. Below we summarise the HIQA findings and supplement them with data provided by the external experts that were involved in the present report.

4.2.1 Injury to patients or providers

A systematic review published in 2009 found no accounts on immediate life-threatening conditions in rescuers inflicted by (any mode) defibrillation of a patient[2, 16]. Discharging a defibrillator directly to a healthy person’s chest can be lethal[16]. Two studies, both from Belgian researchers, established the safety of fully automatic defibrillation. One manikin study showed that untrained nursing students committed fewer safety errors using a fully automatic AED compared with a semi-automatic AED[2, 17]. A simulated cardiac arrest scenario on a manikin showed that safety was not compromised when untrained lay rescuers used a fully automatic AED rather than a semi-automatic device[2, 16]. There are no human data to determine whether these findings can be applied to clinical use[2].

4.2.2 AED malfunction

In 2 studies published in 1998 and involving 285 OHCA with shockable rhythm, a total of nine cases of device failure were reported[13, 18, 19]. In the PAD trial, no device failed to shock when indicated[13, 15].

An FDA report analysed all adverse event reports on AEDs where a patient died between the years 1993 and 2008[13, 20]. A total of 1 150 failed defibrillation attempts were identified. The most common device failures occurred during the attempt to charge and deliver the intended shock (45%) or when the device powered on, but failed to complete rhythm analysis (22%). A cause of device failure could be identified in approximately 80% of cases, with pads/connectors (24%) and battery/power (23%) being the most frequently cited components. The usefulness of these data however is

limited since the total number of AEDs/defibrillators is not known and it is also not clear if a (failed) device caused a fatality[21].

Belgian data from the Ghent area have been published on all AED applications from February 2012 until March 2014, used by EMS personnel[22]. The investigators analysed 837 ECG tracings, extracted from an AED (ZOLL AED PRO®), and applied on 135 consecutive patients. These AEDs were programmed in the semi-automatic mode, leaving the caregivers the opportunity to make a final decision whether or not to provide a shock. Of 837 tracings, 148 (18%) involving 35 patients, were classified by the investigators as shockable. Among these, 23 (16%), involving 13 patients, were not recognised by the AED (false-negatives). In six of these cases the omitted or delayed shock(s) were judged to be of clinical relevance. Of 689 tracings that were considered non-shockable, 25 (4%) were false-positively considered shockable by the device algorithm. On 10 occasions, the caregivers assumed the wrongful AED decision and did not deliver the shock. Fifteen inappropriate shocks were delivered but the non-shockable rhythm did never deteriorate to VF. A recent study reported that errors associated with AED use were rare[23].

According the HIQA HTA, the AED devices are generally regarded as reliable and safe when used properly. This claim has been confirmed by the external clinical experts who participated in the present report.

The information on AED malfunction we received from AED distributors was contradictory. On one hand, most of them declared that device-related malfunction is extremely rare. Distributors are able to recognise some malfunctions through the interrogation of devices after they have been used. The owner of an AED is able to interrogate himself the device after its use in order to obtain the electrocardiogram that has been stored before and after the shock. Most customers however do not perform this analysis but ask the AED distributor to do it for them. Most AED owners also dispose of a maintenance contract. This also allows distributors to detect some device malfunctions such as a depleted battery or withered defibrillation pads.

On the other hand, some distributors express their concern on the protection of AEDs against extreme temperatures or humidity conditions. User manuals stipulate that AEDs must be stored in conditions where temperature and humidity are kept between 0 and 50°C and 5%-95% humidity respectively. A “substantial number” of outdoor placed AEDs do not comply with this rule, according to an expert. However no exact data are available.

4.3 Epidemiology of OHCA

To describe the epidemiology of OHCA in Europe, we referred mainly to two sources. The first one was a literature review which included 30 studies performed in Europe[24]. In that study, incidence estimates of individual studies were weighted and averaged according to the size of the study population or to the person-years. Survival to hospital discharge was reported. The second one, the EuReCa ONE study, was a prospective, multi-centre (27 countries) study carried out during one month (October 2014) and including all OHCAs attended and/or treated by an Emergency Medical Service (EMS)[14]. Incidence rates for one month were extrapolated to incidence rates per 100 000 person-years. Survival rate was available only for patients in whom a CPR (by bystander or EMS) was attempted, and was derived from status at 30 days, or replaced by hospital discharge status in case of missing 30 days status.

4.3.1 Incidence of OHCA

The average yearly incidence of EMS-attended OCHA in Europe was estimated at around 85 per 100 000 person-years, and this figure was quite consistent in a review of studies[24] and in the more recent prospective EuReCa ONE study[14].The reported incidence of OHCA varies greatly across studies and populations, from 55 to 113 per 100 000 person-years in Europe[2]. Variations in data collection and definitions of OHCA play a role in that variation[24], e.g. in some registries children are excluded, others consider only cardiac arrests of cardiac origin. Even the definition of OHCA of cardiac cause may vary as according to the Utstein template definition, a cardiac cause is presumed in the absence of evidence for non-cardiac causes, i.e. depends upon the efforts to identify other causes[24]. A second contributing factor to geographical variations in OCHA incidence may be a varying distribution of risk factors of OHCAs. These are the conventional cardiac risk factors, including diabetes, smoking, high cholesterol, and high blood pressure.

When considering EMS-treated OHCA, the average incidence was estimated at 45.0 per 100 000 person-years in Europe, and 35.0 per 100 000 person-years for OHCA of cardiac origin[24]. The rate difference between EMS-attended and EMS-treated OHCAs can be explained by the high proportion of victims found dead at EMS arrival on the scene.

The average proportion of VF among EMS-treated OHCA of cardiac origin is low and was estimated between 22%[14] and 32%[24]. As a result, the average incidence of EMS-treated OHCA of cardiac origin with a VF, i.e. cases amenable to public access defibrillation, was estimated at 12.8 per 100 000 person-years in Europe[24]. The results from North-America and Australia were quite similar with 14.0 per 100 000 person-years and 14.9 per 100 000 person-years, respectively[24]. A more recent average estimate from the USA was also close to the European estimates at 11.9 per 100 000 (21% of non-traumatic OHCA)[25]. However, as explained above, shockability is highly time-dependent, and a reflection of how well the chain of survival (see point 1.2) functions. The proportion of all OHCA patients that belong to the Utstein comparator group varies between 3% and 27% in Europe[14, 24]. For example, in Amsterdam where the time from call to defibrillator connection was quite short (8 minutes), the % of shockable first rhythm was higher than in other studies at 45%[26]. It was 50% in Stockholm among the OCHA of cardiac origin bystander-witnessed[3].

In Europe in 2014, patients with an OHCA had a mean age of 66.5 (SD 18.6) years, and a median age of 70.0 years, (range 0–104).The majority of patients were male (66.3%)[14]. The majority of OHCAs occurred at home (overall average: 69.4%; range of country values: 46.4-79.9%)[14], as also reported in many other studies[6, 13, 15, 27-29]. This is an important element of information as PAD programs target victims of OHCA occurring in public locations.

4.3.2 Survival

Survival rate to hospital discharge of EMS-treated OHCA is globally low in Europe with a reported average between 9.4% [24] and 10.3% (in patients in whom CPR was started)[14]. It is similar to the 9.6% observed in the USA[27]. A recent estimate from 28 729 EMS-treated OCHA in England in 2014 reported a survival to hospital discharge of 7.9%[30]. Expectedly, survival rates following OHCAs are also extremely variable across countries. A 24-fold variance in survival (from 1.1% to 26.1%) has been reported[14, 31].

One contributing factor to such variation might be the utilization of varying definitions of OHCAs and varying quality of data collection. Obviously, survival rates are very sensitive to the denominator used as illustrated by Eisenberg et al.[32c]. However, disparities in survival rates are also observed between countries when an homogeneous category of patients is used (e.g. the Ustein Comparator Group in the EuReCa ONE study[14]), or across regions in a same country[33])

Such variation is indeed also a reflection of how effectively the chain of survival is implemented, as one of the main factors that influence survival rate is the rapidity of intervention after collapse[27]. Defibrillation of a VF within 3 to 5 min of collapse can produce survival rates as high as 50 to 70%[2, 34]. Each minute of delay to defibrillation reduces the probability of survival by 10 to 12%[2]. Patients presenting with asystole as their first monitored rhythm have a poor prognosis.

[c] The authors calculated survival rates of OHCA victims using eight different definitions of denominators. Survival rates ranged from 16% to 49%. The denominator for the lowest survival rate included all cases of OHCA for whom emergency medical services personnel started CPR. The denominator for the highest survival rate included all cases of witnessed collapse of presumed cardiac origin in whom the first recorded rhythm was ventricular fibrillation and in whom cardiopulmonary resuscitation was started by bystanders within 4 minutes and definitive care provided within 6 minutes.

4.3.3 Adverse psychological effects on providers

Only few adverse psychological effects associated with AED use[2, 35, 36].

4.4 Cost-effectiveness

4.4.1 Introduction

Economic evaluations are meaningful for interventions that has been proven to be effective, or to a latter extend for interventions that are expected to reduce costs. In the absence of this evidence and with the lack of robust Belgian data on current AED use, it is not possible to properly evaluate the cost-effectiveness impact of AED provision in Belgium. The aim of this section is therefore to only have a rapid look at the existing cost-effectiveness literature on AED and to identify main elements impacting the cost-effectiveness of this intervention.

As explained in the method section (see section 3.1), no additional relevant publications were identified after the HIQA HTA study. The HIQA HTA includes both a systematic review of economic evaluations and an economic evaluation of AED provision in Ireland[13]. The systematic review identified 4 studies assessing the cost-effectiveness of static AED provision across a range of public locations. We considered out of scope for the present report a fifth study that focused on OHCA occurring in casinos[37] because it concerned a closed private environment with the full-time presence of security guards with cardiopulmonary certification and well-trained in the used of AEDs. Such a study would therefore not allow us to make any conclusion about the opportunistic use of AEDs by bystanders in public locations. Finally, 5 economic evaluations were therefore selected (the 4 studies reviewed in the HTA and the HTA itself)[13, 38-41].

The quality of these five economic evaluations was assessed by a single economist using a standard quality assessment checklist for economic evaluations (see the appendix to this chapter). These studies are summarized and critically assessed in the next sections.

4.4.2 Main elements and critical appraisal of economic evaluations

4.4.2.1 Economic evaluations identified from the HIQA HTA

The design characteristics of the four economic evaluations identified by the HIQA HTA study are summarized in Table 3. It is important to highlight that AED deployment strategies analysed in those studies are targeted, i.e. they concerned area with a “high” OHCA incidence (1 cardiac arrest every 2 years or 1 cardiac arrest every 5 years), except in the Danish study where unguided AED placement strategies were also analysed[39]. As described in Table 4, positive assumptions in favour of AED interventions evaluations were also done in each study, i.e. an intervention expected within 3 minutes or an AED use in 100% of cases. It should nevertheless be noted that the Danish study also analysed the impact of reducing the AED use to 80% and 60% of cases[39].

From those studies[38-41], it appears that there is a clear association between the Incremental Cost-Effectiveness Ratio (ICER) and the annual probability of OHCA in the area of AED installation (see Table 5). For example, the Danish model assuming AED deployment only in public locations with a 50% annual probability of an OHCA calculated an ICER of $33 100/QALY, versus $40 900/QALY if the annual probability of OHCA was 20%. Moreover, unguided placement in the whole city resulted in an ICER of $108 700/QALY. The same study also showed that with a less positive assumption on the probability of AED use in case of OHCA (60% instead of 100%), results are worsened, with ICERs of $55 200/QALY with an annual probability of OHCA of 50%, $68 200/QALY with an annual probability of OHCA of 20%, and $181 700/QALY with an unguided placement[39].

Sensitivity analyses performed in those studies[38-41] showed that results were mostly sensitive to the OHCA incidence in the area of AED placement, the probability of AED use in case of OHCA, and the survival with or without AED. The study of Nichol et al.[40] also mentioned that if they were no ascertainment bias in the PAD trial, results would unlikely be cost-effective. The location of the OHCA (in a residence or in the public) also influenced results.

Table 3 – Characteristics of economic evaluations identified by the HIQA HTA

	Nichol 2005[42] and 2009[40]	Folke 2009[39]	Walker 2003[41]	Cram 2003[38]
Population	Individuals with OHCA. Excluded: people with obvious traumatic injury or aged < 8 years.	Individuals with OHCA who were judged eligible for resuscitation attempt by the physician on location.	Individuals with OHCA.	Individuals with OHCA.
Country	United States and Canada	Copenhagen, Denmark	Scotland	United States
Intervention	• CPR; compared to • CPR + AED performed by trained lay responders **within 3 minutes** of event identification. Sites selection: areas with at least **1 cardiac arrest every 2 years**. The number of AED placed in these sites allowed an intervention within 3 minutes.	Various interventions: • EMS system alone; • **2005** AED **unguided placements**: 104 AEDs (driven by municipal or local initiative). • ERC guidelines: 125 AEDs placed in areas with at least **1 cardiac arrest every 2 years** within a 100-m radius. • AHA guidelines: 1104 AEDs placed in areas with at least **1 cardiac arrest every 5 years** within a 100-m radius. • **Unguided AED** coverage for the entire city: 10 394 AEDs.	• No AED provision; compared to • AED provision (n=31) in: • 4 major airports (4 AEDs per site => 16 AEDs), • 9 major railway stations (=> 11 AEDs), and • 4 major bus stations (1 AED per site => 4 AEDs) in Scotland.	• EMS equipped with AED; compared to • AED deployed as part of a public access defibrillation program • Site selection: public locations with at least a **1 cardiac arrest every 5 years**).
Design	Cost-utility analysis – Lifelong Markov Model	Cost-utility analysis; Method not clear.	Cost-effectiveness and cost-utility analyses.	Cost-utility analysis – Lifelong Markov Model
Perspective	Societal	Not specified (seems the health care payer)	Not specified (seems the health care payer)	Societal (but only direct costs are considered)

AED = Automated external defibrillator; CPR = Cardiopulmonary resuscitation; EMS = Emergency medical services; OHCA = Out of Hospital Cardiac Arrest; PAD = Public access defibrillation

Table 4 – Costs and effectiveness data used in economic evaluations identified by the HIQA HTA

	Nichol 2005[42] and 2009[40]	Folke 2009[39]	Walker 2003[41]	Cram 2003[38]
Clinical outcomes	'*Conditions*': AED places allowed an intervention within 3 minutes. Survivors to hospitals discharge: relative risk: 2.0 (95%CI 1.07-3.77) (Source: PAD study)[15] QoL: HUI-III	Assumption: Systematic use of AED (100%); Other rates are also tested (80% and 60%). 30-day survival rate: 25% with an AED program vs 13.9% without an AED program. QoL: HUI-III	Assumption: Same observed survival than for patients attended by an ambulance staff within 3 minutes. Based on the Scottish Ambulance Service database. Survival rate at discharge: AED: 16.7%; Without AED: 14.7%. QoL: HUI-III.	Assumption: Systematic use of the AED (100%). Probability of surviving to hospital discharge: EMS: 10%; AED: 25%. QoL: HUI-III and EQ-5D.
Costs*	Direct (medical and material costs) and indirect costs (productivity losses). 2004 US dollars	Only direct costs (medical and material costs) seem taken into account. 2008 US dollars	Direct costs (medical and material costs). 2001 pounds	Direct costs (medical and material costs). 2002 US dollars
Discounting	3% for both costs and outcomes	Not mentioned (0%?)	6% for costs and 1.5% for outcomes	3% for both costs and outcomes

**Costs data are not analysed in details in this report because they are not transferable to our setting. AED= Automated external defibrillator; EQ-5D = EuroQol instrument – 5 dimensions; EMS = Emergency medical service; HUI-III = Health Utilities Index Mark 3; US = United States.*

Table 5 – Results of economic evaluations identified by the HIQA HTA

Nichol 2005[42] and 2009[40]	Folke 2009[39]	Walker 2003[41]	Cram 2003[38]
$46 700/QALY ($23 100 – $68 600)	Compared to EMS alone: • 2005 AED unguided placements: between **$63 500/QALY and $105 900/QALY** according to the AED use assumption (100% vs 60%) • ERC guidelines: between **$33 100/QALY and $55 200/QALY** according to the AED use assumption (100% vs 60%) • AHA guidelines: between **$40 900/QALY and $68 200/QALY** according to the AED use assumption (100% vs 60%) • Unguided AED coverage for the entire city: between **$108 700/QALY and $181 700/QALY** according to the AED use assumption (100% vs 60%)	**£41 146/QALY**. Range in the univariate sensitivity analysis: **£23 403-£58 302**. The ranges and parameters tested where nevertheless not justified. With a decrease in survival gains (i.e. a survival rate at discharge of 16.2% instead of 16.7%), the ICER was **£53 549**.	Base case assumption on AED use and cardiac arrest incidence: **$30 000/QALY (**with a probability of 87% to be < $50 000/QALY). With different assumptions: ranged from **13 000/QALY in airports to $12 000 000/QALY** in retail stores.

AED= Automated external defibrillator; EMS = Emergency medical service; ICER = Incremental cost-effectiveness; QALY = Quality-adjusted Life-Year.

4.4.2.2 The economic evaluation performed in the HIQA HTA

The aim of this economic evaluation[13] is to assess the cost-effectiveness impact of the Irish Public Health (Availability of Defibrillators) Bill 2013 (hereafter called "Legislation"), proposing a substantial increase in the availability of static AEDs in a range of designated places for use by trained staff or members of the public in the event of a cardiac arrest in the vicinity.

The base case comparator was the situation at the time of the assessment, i.e. with medical emergency services, first responders groups, and out of 8 to 10 000 AEDs voluntarily placed (for which only 4670 were located in places proposed by the Legislation). This base case situation was compared to differed level of implementation of the legislation.

These different deployment programmes of static AEDs in public locations proposed by the legislation were all combined with the training of staff employed in these locations. The different level of implementation as well as other study characteristics are described in Table 6. As described in this table, the AED use rate was determined according to the number of OHCA that arrived within 200m of an AED placement and the probability of use in such situation observed in the Irish OHCA register database[13].

Table 6 – Description of the economic evaluation performed in the HIQA HTA

Elements	Description of the IRISH economic evaluation
Population	Individuals with OHCA attended by EMS and for which resuscitation is attempted.
Country	Ireland
Intervention	• Current process of care: EMS + ad hoc distribution of public AEDs + a limited number of police, fire-service or community first responder groups in various locations. • Deployment programmes of static AEDs in public locations combined with the training of staff employed in these locations: • 100% legislation: (38 400 additional AEDs) • PAD 15%: in site with an annual probability of at least one OHCA per 20 AEDs (1900 additional AEDs) • PAD 20%: in every building of type hospital and residential, transport and public administration (3100 additional AEDs) • PAD 25%: in every building of type hospital and residential, transport, public administration and retail (6800 additional AEDs) • PAD 45%: in every building of type hospital and residential, transport, public administration, retail, and arts & entertainment (15 300 additional AEDs) • PAD 55%: in site with an annual probability of at least one OHCA per 100 AEDs (19 600 additional AEDs)
Design	Cost-effectiveness and cost-utility analyses; Lifelong Markov Model
Perspective	Societal
Clinical outcomes	Assumption: The proportion of patients predicted to receive bystander defibrillation was based on the number of OHCA that occurred within 200 m of existing AED location. For the base case strategy, proportions observed in the Irish OHCA register database were used. Survival at discharge: EMS: 5.1%; CPR only: 5.5%; CPR + AED: 12.4% (Based on the Irish OHCA register database).
Costs	Direct (medical and material costs) and indirect costs (time and productivity losses) for patients, health service providers and the designated places; including an annual cost of AED database (€69 259). (€2013).
Discounting	5% for both costs and outcomes

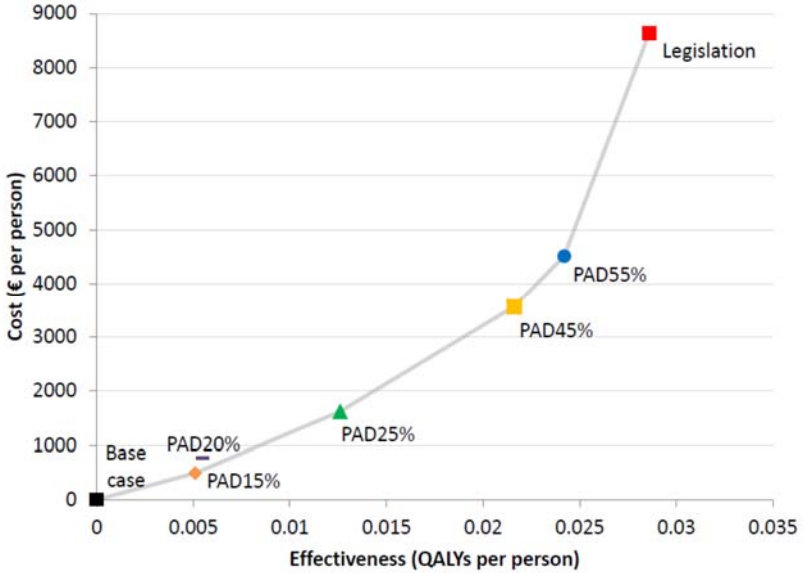
AED = Automated external defibrillator; CPR = Cardiopulmonary resuscitation; EMS = Emergency medical services; OHCA = Out of Hospital Cardiac Arrest; PAD = Public access defibrillation

Results of the study showed that, depending on the programme, the predicted average increase in the number of OHCA patients surviving to hospital discharge annually ranged from 1.7% (2 additional people per year) for PAD15% to 9.3% (10 additional people per year) for the full legislation[13].

Concerning the cost-effectiveness analysis, an extended dominance was observed for the strategy PAD20%, meaning that some combinations of strategies PAD15% and PAD25% leaded to a better impact on the quality adjusted life years gained at reduced costs (see Figure 2). This strategy was therefore excluded. For other strategies, PAD programmes that involved AED deployment in buildings with the highest OHCA incidence (i.e. PAD15%) was the most cost-effective approach compared to the current situation (see Table 7). Nevertheless, the ICER of this strategy was €95 640 per QALY, with a probability of 5% to be the most cost-effective approach at a threshold of €45 000/QALY (i.e. the threshold used in Ireland to determine the cost-effectiveness of an intervention). PAD programs were therefore not considered as cost-effective[13].

The budget impact analysis over a five-year time horizon showed that the implementation of a PAD programme would be associated with total incremental costs over five years ranging from €2 million to €20 million for the public sector (including the health sector), and €3.3 million to €85 million for the private sector, depending on which PAD programme is implemented. The majority of these additional costs were related to the procurement of AEDs[13].

Figure 2 – Cost-effectiveness plane (QALY)



Source: HIQA HTA[13]

Table 7 – Results of the economic evaluation performed in the HIQA HTA

Scenario	Costs	Incremental costs	QALYs	Incremental Qalys	ICER
Base case	€ 16 954	-	0.3004	-	-
PAD15%	€ 17 446	€ 492	0.3055	0.0051	€ 95 640/QALY
PAD25%	€ 18 577	€ 1 131	0.313	0.0075	€ 151 243/QALY
PAD45%	€ 20 518	€ 1 941	0.322	0.009	€ 214 108/QALY
PAD55%	€ 21 467	€ 949	0.3246	0.00254	€ 373 545/QALY
Legislation	€ 25 589	€ 4 122	0.329	0.0044	€ 928 450/QALY

PAD = Public access defibrillation; ICER = Incremental cost-effectiveness; QALY = Quality-adjusted Life-Year.

The univariate sensitivity analysis showed that results were mostly influenced by the relative risk of survival with and without AED use (at hospital discharge and/or hospital admission) and the number of (public or residential) OHCA within 200m of an AED (influencing the probability of AED use). Nevertheless, in each univariate sensitivity analysis performed, the ICER was superior to €45 000/QALY[13].

Different scenario analyses were also performed. The scenario analysis on the cost of AEDs for example indicated that even with a 60% reduction in the average cost of an AED, conclusions remained similar (ICER > $45 000). They also showed that if the use of AEDs by bystanders increased significantly (approximately 40%), the PAD15% strategy could become cost-effective. This scenario is based on the assumption that a PAD programme would increase AED use in case of a cardiac arrest event due to the (i) improved public awareness about OHCA, (ii) the increasing number of people trained in basic life support, and (iii) the use of an EMS-linked AED register. However, there is no evidence to indicate what magnitude of increase could reasonably be expected[13].

The authors also argued that a more cost-effective distribution of AEDs could be achieved using a deployment rule based on location-specific incidence rather than building type. Sufficient data to support such an analysis were nevertheless not available at the time of the HIQA HTA[13].

5 BELGIAN CONTEXT

5.1 Belgian AED legislation

The use of AEDs is regulated in Belgium by the Royal Decree of 21 April 2007 and the Ministerial Circular of 29 July 2011[d]. The Royal Decree authorises the use of an AED by professionals and lay rescuers alike in patients with an OHCA.

Formal registration of an AED at the Federal Public Service (FPS) Public Health by the owner, including its exact geographic location, is mandatory before its installation.

The Royal Decree also stipulates the terms and conditions for making an AED publicly[e] and permanently[f] available[g]. The AED has to be placed in a "sealed" (meaning that it cannot be opened unnoticed) case in the conditions required by the manufacturer. The case needs to specify the name of the owner, including his address, phone number, email. The Ministerial Circular of 29 July 2011 provides detailed instructions on a label with the FPS registration number that should be attached to the AED and the case.

At least every month, as well as after each use of the AED, the owner has to assess the function of the device (AED, battery, pads) in agreement with the instructions by the manufacturer, and has to check whether alarms have been produced by the device. When the AED has been used, the doctor of the patient who was shocked can request from the owner data stored by the AED. Yearly the owner has to report to the FPS all data recorded within the AED.

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d https://www.health.belgium.be/nl/e-services/automatische-externe-defibrillatoren-aed

e « publieke plaats » : elke plaats, inclusief winkels, scholen, bedrijfsgebouwen en –terreinen, stations, luchthavens, filmzalen en sportterreinen, waar mensen verzamelen en evenementen kunnen worden georganiseerd; « lieu public » : tout lieu, y compris les magasins, écoles, bâtiments et sites d'entreprise, gares, aéroports, salles de cinéma et terrains de sport, où des personnes se rassemblent et où des événements sont susceptibles d'être organisés;

f « permanent » : op langdurige en duurzame wijze; « en permanence » : de manière prolongée et durable;

g « ter beschikking stellen » : het gratis aanbieden van een automatische externe defibrillator voor gebruik in geval van een hartstilstand; « mettre à disposition » : proposer gratuitement un défibrillateur externe automatique destiné à être utilisé en cas d'arrêt cardiaque;

The Ministerial Circular formulates recommendations where an AED could most effectively be installed in a public place: public buildings, fitness and sport centres, industry zones, railway stations, airports, pharmacies… For identifying other places at high risk of OHCA, it refers to the Provincial Committees of Emergency Health Service [Commissie voor Dringende Geneeskundige Hulpverlening (CoDGH) - Commission de l'aide médicale urgente (COAMU)] "that know which places are at highest risk" (sic). Through an e-mail contact with all (10) provincial health inspectors in June 2017, it appears that no specific mapping of high risk locations is done.

AED malfunctions must be reported to the Federal Agency for Medicines and Health Products.

5.2 The AED registration anno 2017

Employees of the Federal Public Health Service that participated as co-authors for the present report assessed the current implementation of the AED registration procedure as anticipated by the federal law.

5.2.1 Data quality

The registration form (https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/defibrilateur_fr.pdf) as provided in the Appendix to the Royal Decree is often incorrectly filled out and in many instances; additional information has to be requested from the applicant through correspondence. Often, this additional information is not delivered. Hence, the database contains registered AEDs that have never been fully approved because of incompleteness. The most common missing items are the lambert coordinates and the topographic maps. In the first quarter of 2017, 472 new files were submitted, of which 90 (19%) were incomplete. Currently (June 2017), 8204 registrations are included in the database, of which 631 are incomplete.

In Art.7 the Royal Decree refers to the obligation to report operational changes related to the AED within one month. However, the Royal Decree does not describe how this should happen. On one hand, the Federal Public Health Service often receives queries related on this topic, on the other hand very few specific requests for changing existing registrations are submitted.

A monthly up-to-date extract from the database is made available since the beginning of 2014 through the website of the Federal Public Health Service. It is stipulated that it cannot be guaranteed the data are correct and complete. There are frequent parliamentary questions about the evolution of the number of registered AEDs in the database.

Presently, the database is not applicable to unequivocally locate the AEDs on a map. Overall the database is not suitable for statistical purposes.

5.2.2 Surveillance

AEDs need to be properly maintained. The Royal Decree provides for a control in its Art. 13: The health inspectors referred to in Article 10a of the Law of 8 July 1964 on urgent medical care, and the health inspectors of the FPS Public Health referred to in Article 5 of the Law of 12 June 2006, are authorised to monitor the implementation of the provisions of this Decree.

However, so far no AED on the Belgian territory has been controlled by a health inspector. Moreover, the yearly report of activity of the AED is not transmitted to the FPS Public Health.

5.2.3 Processing of an application for registration

Article 5, 7 ° of the KB of 21 April 2007 stipulates: The Directorate-General for Health and Crisis Management shall issue a registration number within one month after the form referred to in paragraph 1 has been received.

The processing of the application for AED registration includes the following steps:

- Receipt of registration applications (± 150 registrations per month)
- Input of applications in an Access database
- Verification of data. If all information is correct and complete, a registration number will be sent. In the other case, a letter is sent requesting for additional and/or corrected data.
- Modification of the database in response to acceptance of additional data, followed by sending a registration number
- Save a hard copy of all documents for each registration file

- Follow-up of the mailbox AED-DEA@health.fgov.be and answer telephone questions

In most cases, the goal of finishing an application within one month is not achieved because the current methodology is very labour intensive. The data provided by the applicant is also often incomplete and/or unreliable. It may take several months for the registration of an AED to be complete. In a worst case scenario, no registration number is assigned because missing / incorrect data is never completed.

5.2.4 *Third party initiatives*

The Belgian Red Cross-Flanders, the Belgian Cardiologic League, the EMURgency project (http://emurgency.eu/) and others are active in the field of registration and visualisation of AEDs on geographic maps. We compared the number of AED locations in the two largest municipalities of Flanders on the website www.hartveilig.rodekruis.be with that of the Federal Public Health Service. This showed that the number of locations in the Belgian Red Cross-Flanders database (n = 60) was higher for the municipality of Antwerp than in the FPS (n = 41), while for Ghent the opposite was found: n = 36 in the Belgian Red Cross-Flanders database and n = 118 in that of the FPS.

5.3 Current use of AED in Belgium

Data on the use of AEDs in Belgium were obtained from several sources. All of them however suffered from severe limitations with regard to data quality and completeness. Thus critical information is lacking on the number of AEDs available to the public, their accessibility on a 24/7 basis, and their operational reliability. Furthermore, we retrieved few data on the CPR training level of the general population and on its awareness of AEDs or acceptance for using them.

Although several Belgian experts are involved in CPR research and guideline production on a European level, only few Belgian data on AED use have been published in peer reviewed journals. Furthermore, although both the registration of publicly available AEDs, and interventions by EMS physicians (MUG/SMUR) are mandatory by law, the resulting databases are reportedly far from complete.

5.3.1 *Unpublished data provided by external experts*

The following data are obtained from external experts involved in this report. They have repeatedly stressed that reliable data on CPR and AED use in Belgium are lacking. The deployment of AEDs in Belgium is predominantly done by private actors (e.g. managers of sports clubs, building owners). It is estimated that ±70% of the devices is privately owned. They are mostly installed indoor, e.g. at an industrial or commercial site (reception, medical service …). The remaining 30% is installed outdoor with 25% of them being static (e.g. street, market place) and 5% mobile (e.g. police). The placement of AEDs is not coordinated. Some high risk public places, as defined by the legislation, are not covered (e.g. metro in Brussels). Elsewhere, several AEDs can be very close to each other.

Since 2003 an estimated 14 000 AEDs have been sold in Belgium. The operational lifetime of an AED is 7 to 8 years. It is estimated that presently 10 000 devices are still operational, i.e. 0.9 per 1000 inhabitants. As a comparison, in the Netherlands 0.6 devices are installed per 1000 inhabitants[43], versus 3.4 per 1000 in Japan[44], and 1.7 to 2.0 in Ireland[13]. The price of an AED ranges from 1 100 to 1 995 €, depending on the presence of specific features such as battery capacity, full or semi-automatic mode, synchronous/asynchronous defibrillation mode, etc.

It is assumed that the owner of an AED always contacts the distributor of the device after it has been used, in order to renew the pads and to interrogate the device to recover electrocardiograms stored before and after a shock. This practice should enable distributors to assess how often a particular AED is used, but reportedly these data are not stored. One distributor estimates that of 8 000 AEDs, one is used every day (this would mean a use of once per 22 years).

In January 2017, the Belgian Heart Rhythm Association conducted an on-line survey on the understanding of sudden death and CPR in the general population[h]. It involved 3761 individuals. Ninety-seven percent was not able to correctly define a cardiac arrest. Two thirds never followed a CPR course, and 39% of respondents never saw an AED. Sixty percent claimed that they would use an AED in case it was needed. When told that an AED provides spoken instruction to the user (only 35% of respondents were aware of this), 82% would use it.

Up to now, Belgium has no compulsory training of CPR/AED during the secondary school cursus to the contrary of several other European countries. According to experts, 2 initiatives were recently developed in the French speaking part of Belgium (http://www.minipop.be/fr/accueil.html; http://lfbs.org/fr/formation-58c17c95a1e48.html). The number of students trained is of course very small (a few hundred per year) because these are initiatives by non-profit organizations with limited means. During their studies to become gym teachers, some of them are also trained to later be able to teach BLS to students. In Flanders it is part of the curriculum (Vak Overschrijdende Eind Termen) since 2010, which means every school has to do "something" about CPR. The Flemish ministry of Education launched a website "EHBO op school" in order to give some expert guidance on content and facilitate the instruction of first aid and CPR-AED (https://onderwijs.vlaanderen.be/nl/wat-moeten-je-leerlingen-minimaal-kunnen). However, there is still no obligation to do so.

5.3.2 Peer reviewed publications

Among the list of publications that we obtained from our original literature search, we identified 3 that reported on AED use in Belgium ("Belgium" in title or abstract). We also asked our expert group to point to us relevant publications they were aware of.

In 2011, a retrospective telephone survey was performed in 51 fitness centres in the French speaking part of Belgium[45]. The aim was to assess the number of centres that had an AED available. The authors also studied the number of OHCAs and the use of an AED in these cases. In 5 (6.8%) centres there was an AED available. The main reasons for not acquiring an AED were the costs involved in 13 centres, whereas in 14 it was the perceived futility of the device in view of the close proximity of a hospital or fire station. Overall 5 cases of cardiac arrest occurred, of which 2 occurred in a centre disposing of an AED. Two cardiac arrests were unwitnessed. Two victims died despite the use of an AED, and one was successfully resuscitated in a centre without an AED. In all cases the fitness centre was located within 10 km from the nearest hospital or fire station.

In another survey, 85 volunteers were randomly selected among visitors in a hospital's main entrance[46]. Participants were given a 19-item questionnaire to assess demographic data, evaluate general knowledge of CPR and AEDs, and estimate willingness to use such a device. Less than half the volunteers had been trained in CPR or felt they could intervene in a cardiac arrest. Fifty-one (60%) participants attested that they did not feel capable of using an AED in a real life situation. The major reasons given were: 'I don't know how the device works' (45%), 'I am too stressed' (4%), and 'I am afraid to harm the victim' (2%). However, when put in situation in a simulation room with a CPR manikin and an AED placed visibly in the corner of the room, 74% (63/85) of the volunteers performed CPR and 62% (53/85) delivered an electrical shock. Among the latter, 47% (25/53) had stated they did not feel able to use an AED in the pre-test questionnaire. This study tends to show that a majority of volunteers do not feel self-

h http://www.knokke-heist.be/nieuws/initiatiesessies-voor-reanimatie-en-gebruik-van-defribillator ; additional data provided by L. Discart, VADEMECOM.

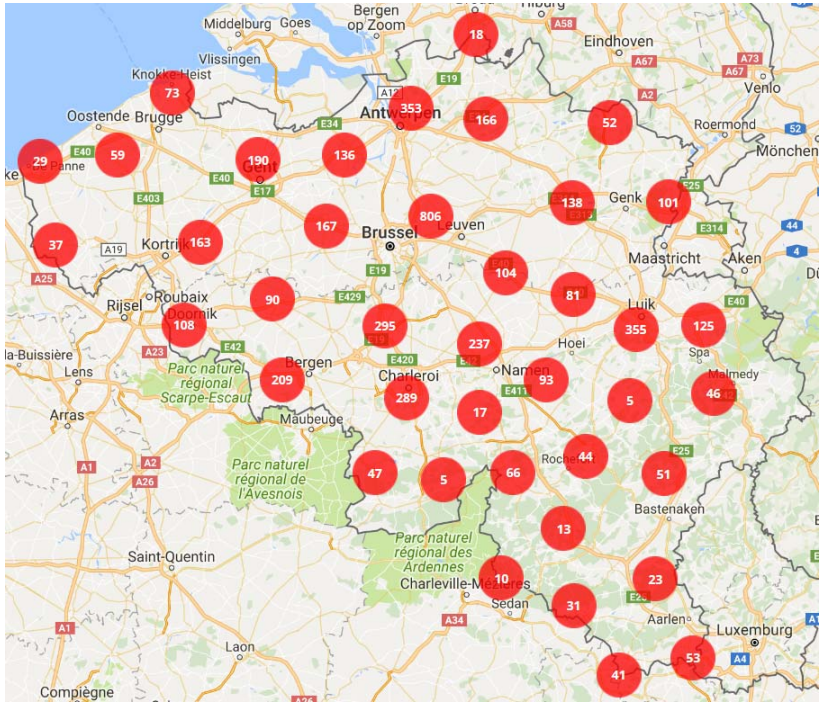
confident in performing resuscitation, but may apply it when confronted with the situation. Whether such findings are valid in a real-life situation is questionable: the sample size was moderate, participants might not be representative of the general population (visitors of a general hospital volunteering to participate), and the simulation room within the hospital and with a visible AED might induce specific behaviours.

The EuReCa ONE study included data about Belgium[14]. In order to isolate the Belgian results, the corresponding dataset was provided to us by Prof. Mols (Hospital St-Pierre, Brussels) and were analyzed in Stata 12.0. In October 2014, data on 105 OHCAs were registered by 14 MUG/SMUR services located either in Brussels, Flanders or Wallonia, covering 15% of the general population. The mean age was 69.6 (±54.1) (median 70 years) and 65.7% were males. 74.3% of OHCA occurred at private home, and only 17.1% (18/105) in public location (7.6% occurred in rest house and 1% in workplace). The vast majority of OHCAs were of medical/cardiac origin (85.7%; 90/105). Overall, 63.8% of OCHAs were witnessed. This proportion amounted to 88.9% in public locations, and 44.4% (8/18) were witnessed by a passer-by or a family member. An AED was reportedly available in 69.5% of the OCHAs (73/105; missing data in 12/105), and used in 46.7% of overall OHCAs (49/105) and in 47.8% (43/90) of OHCAs of cardiac origin. The vast majority of users was the EMS (85.7%; 42/49). Most of the 7 remaining users had some training in resuscitation (1 MD; 3 rescuers; 1 policeman; 2 others). Eventually, a shock was given in 15 cases, i.e. in 14.3% (15/105) of all OCHAs. In the OCHAs of cardiac origin, this proportion amounted to 15.6% (14/90). The overall survival was 9.5% (95%CI: 4.7%; 16.8%; 10/105), 10% (95%CI: 4.7%; 18.1%; 9/90) in OCHAs of cardiac origin, and 33% (95%CI: 10%; 65%; 4/12) in the Utstein comparator group. In conclusion, a minority of OHCAs occurred in public location, and although 44% of those cases were witnessed by a bystander, an AED was used by a bystander in none of these cases.

5.3.3 *On-line AED databases*

In section 5.2 we discussed the Federal Public Health Service's AED database. It was concluded that it was incomplete and did not provide reliable data on the number, the location, or the reliability of publicly available AEDs in Belgium. The Belgian Heart Rhythm Association, in cooperation with the FPS, produced a map of Belgium indicating the geographic locations of the AEDs that are registered in the Federal Public Service's database (Figure 3). Obviously, the limitations mentioned with respect to the database also apply to this map, especially since geolocations of AEDs in the database are reported to be incomplete.

Figure 3 – Location of AEDs according the Belgian Heart Rhythm Association

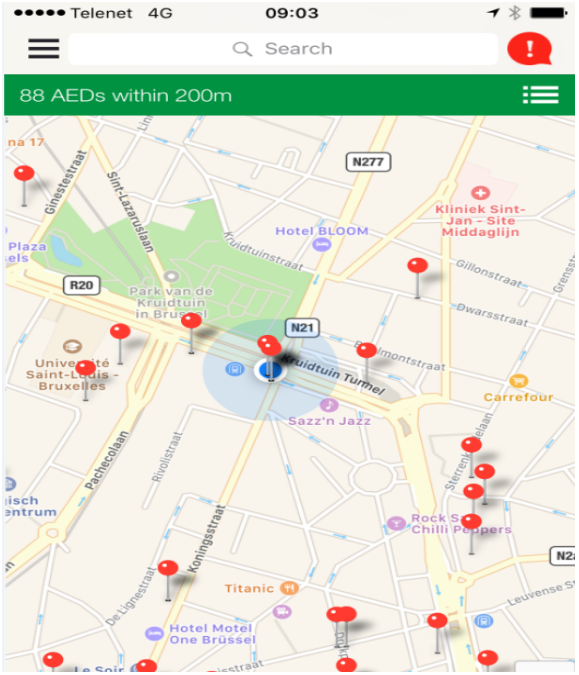


Source: http://www.mijnhartritme.be/index.php?lang=1

Red Cross Flanders reports on its website their presumed location of AEDs in Flanders (www.rodekruis.be/hartveilig). As mentioned before these data do not match with those of the FPS.

StayingAlive is a smartphone application enabling to localise nearby AEDs that are registered in the database, everywhere in the world. A test of the application on June 1, 2017 revealed 88 AEDs available within 200m of the KCE entrance.

Figure 4 – Cell phone screenshot of AED locations in the vicinity of the KCE



Source: Staying Alive: http://www.stayingalive.org/en.php

5.3.4 *The MUGREG – SMUREG registry*

The "Mobiele Urgentie Groep (MUG)" or "Service Mobile d'Urgence (SMUR)" is deployed when the presence of a physician at an emergency scene is considered crucial. The SMUReg-MUGReg is a compulsory registration of SMUR – MUG interventions data for all authorised SMUR – MUG functions in Belgium. This data collection was introduced as a paper-based registration. From April 2008 onwards the registration is submitted via an electronic portal (i.e. via SMUReg-MUGReg web application) which is regulated by the Royal Decree of 27 April 200[i].

The time between the SMUR – MUG intervention and the recording of the data is maximum seven days. The file contains SMUR – MUG data about emergency call and intervention of SMUR – MUG [47];

- patient data and clinical status;
- data on clinical interventions.

Box 1 – Limitations of the SMUReg – MUGReg

- Missing fields and possible mistake in some fields despite internal checks included at the level of the SMUR – MUG form;
- The flag for cardiac arrest is not an automatic field and is ticked by the physician on the SMUR – MUG form;
- No information on the quality of appropriateness of the care is available in the registry.

The external experts involved in this report - some of them participating in this registry – contend that the data included in the registry are incomplete and not fully reliable.

[i] https://www.health.belgium.be/nl/e-services/automatische-externe-defibrillatoren-aed

Each year the FPS publishes a summary report of the MUGREG – SMUREG registry on-line. Below, we summarise relevant data from the most recent report (2015, published June 24, 2016). Additional data related to the use of AEDs have been provided by the FPS upon our request.

5.3.4.1 The 2015 MUGREG/SMUREG registry report

In 2015, 116 377 interventions of the MUG/SMUR were registered (EMS interventions). The following data are related to 10 855 of "primary" interventions that were categorised as "cardiac arrest". The mean age of these patients was 65.32 years (median 68.00; IQR 55.00-79.00). The mean time interval between the 112 emergency call and the arrival of the MUG – SMUR was 16.70 min (median: 12.00; IQR: 8.60-16.60). 8 327 (76.7% died on the scene). Only 20.2% were still alive at hospital entrance.

In the database, cardiac rhythm at arrival and departure of the MUG/SMUR is registered. It includes the following entries: sinus rhythm, atrial fibrillation, supraventricular rhythm, asystole, ventricular fibrillation (VF), ventricular tachycardia (VT), pulseless electrical activity (PEA, previously known as electromechanical dissociation), AV block, and pacemaker rhythm (Table 8).

Table 8 – First monitored cardiac rhythm in resuscitated cardiac arrest victims

			Survival to hospital admission	
	n	% of Total	n	%
AV BLOCK	16	0,4	13	81,3
ASYSTOLE	2907	69,1	756	26,0
PULSELESS ELEC ACTIVITY	456	10,8	218	47,8
SINUS RHYTHM	135	3,2	77	57,0
SUPRAVENTRICULAR	10	0,2	7	70,0
VF	596	14,2	372	62,4
VT	52	1,2	43	82,7
ATRIAL FIBRILLATION	34	0,8	21	61,8
TOTAL	4206	100,0	1507	35,8

Source: Rapport Annuel Smur 2015/Jaarrapport MUG 2015. Total number of resuscitated patients differs across the report (4092 or 4206).

Of 4 206 resuscitated patients (CPR), only 648 (15%) have a shockable rhythm (VF or VT) registered. This is a lower proportion than reported in international literature (between 22%[14] and 32%[24]). Asystole represents the most often entered cardiac rhythm in the database (2907/4206=69.1%).

5.3.4.2 Data on AED use in Belgium according the MUGREG/SMUREG registry

Since year 2012, there were approximately 11 000 EMS interventions for cardiac arrest registered yearly (Figure 5). Around 80% of the cardiac arrest were deemed of cardiac origin, i.e. not caused by an external agent (fall, accident, burns…). Further analysis concern only cardiac arrest of cardiac origin. The median age of patients was around 70 years (IQR: 57y-80y) and in 6 cases out of 10 were males. In 2015, there were 9 353 OHCA of cardiac origin. Therefore, the incidence of EMS-attended OHCA of cardiac origin would be 82.8 per 100 000 person-years in Belgium. This figure is similar to the one reported for Belgium in the EuReCa One study[14] (82 per 100 000 person-years EMS-attended and/or treated OHCAs with CPR attempted

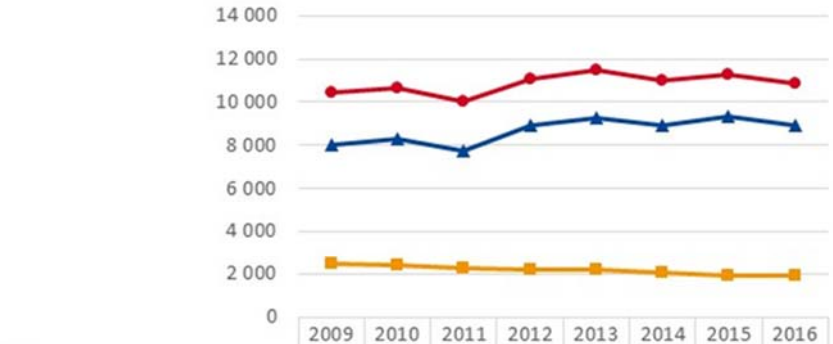
(either by EMS or bystander)j and close to European estimates (86.4 EMS-attended OHCA per 100 000 person-years)[24]. The Figure 6 displays the incidence per district. It can be seen that there were more interventions per 100 000 inhabitants in Veurne (Furnes) and in some of the districts along the French border than in the North of Belgium (due to the protection of privacy, the data by municipalities were not available at the time of this report).

As regards the number of shocks by an AED before the arrival of the SMUR-MUG, the field on the SMUR-MUG form was unfortunately left empty in the vast majority (around 85%) of cases. If we consider that missing information can be assimilated to no shocks, in the majority of the cases (93%) there were no shocks in the period before the arrival of the SMUR-MUG service. In 2016, AED shocks were given before the arrival of the SMUR-MUG service in 6% of the cases and mainly by the ambulance staff (only 24 occurrences reported for bystanders).

AED shocks given by the SMUR-MUG team were reported in around 15% of the cases. However, the same problem of missing information was encountered (75%).

The overall percentage of survival at hospital arrival was 20%. That percentage was around 53% in patients with an AED shock given either before the arrival of the SMUR-MUG or by the SMUR-MUG.

Figure 5 – Evolution number of primary interventions for cardiac arrest (2009 – 2016)

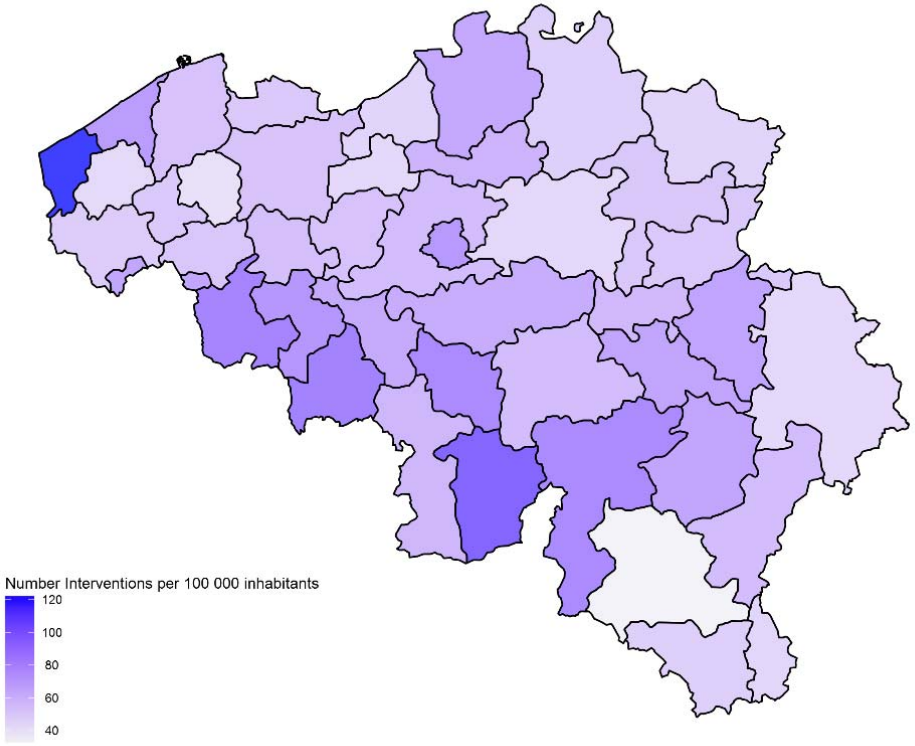


	2009	2010	2011	2012	2013	2014	2015	2016
All interventions for cardiac arrest	10 470	10 676	10 011	11 063	11 451	11 008	11 292	10 880
Not caused by external agent	8 001	8 267	7 749	8 905	9 287	8 939	9 353	8 939
Caused by external agent	2 469	2 409	2 262	2 158	2 164	2 069	1 939	1 941

Source: Federal Public Service (FPS) Health, Food Chain Safety and Environment: Mobile Intensive Care Units (MICU) data 2009-2016

j The study by Grasner et al was based on OHCA occurred in 27 European countries in October 2014. Figures from Belgium are based on cases in whom a CPR was attempted in a population covered by 14 EMS in Flanders, Brussels and Wallonia (14% of the total population)

Figure 6 – Mean number of primary interventions for cardiac arrest – cardiac origin per 100 000 inhabitants (2012-2016)



5.4 What results could be expected from PAD in Belgium?

We set up a number of scenarios to figure out the benefit of PAD at the population level. The baseline of EMS-attended OCHAs of cardiac origin in Belgium in 2015 was 82.8 per 100 000 person-years. In all scenarios, the % of OHCA of cardiac origin occurring in public locations (30%) and witnessed by a bystander (50%) were maintained constant as these parameters are not amenable to changes (except if the public area is fully covered by video surveillance, which is unlikely). The survival rate of EMS-treated OCHA of cardiac origin was set at 10%, consistently with the results of many studies (see section 4.3.2). In all scenarios, we also considered that all currently EMS-treated OCHAs were shockable, a realistic hypothesis if the time of intervention decreases dramatically. The factors that were variables across scenarios are the % of bystander applying CPR and/or AED, as a reflection of public awareness and training, and the survival rate following the utilization of public AED, as a reflection of rapidity of intervention and high accessibility of AED. Given what we know of the current practice of CPR/AED in Belgium and that in many countries, the use of AED by bystander remains low (for example, in Japan, a shock by public AED was delivered in only 10% of the Utstein comparator group with a survival rate of 38%[48]), scenarios 2 and 3 are probably the closest to the Belgian reality. The scenario 7 which implies that 50% of the bystander-witnessed OCHA of cardiac origin occurring in a public location would be shocked within 2 minutes after collapse would allow a gain of 3.7 survivors per 100 000 person-years, or 421 extra survivors. However, this scenario is unlikely within the current Belgian practice, but could be reached with other strategies. For example, in the North Holland province of The Netherlands, where 2 ambulances together with a first responder are dispatched for every suspected OHCA, an AED was used in nearly 60% (but a minority by bystander) and the survival rate in patients with a shockable first rhythm (45% of the cases) was 36%[26]. A survival rate of 70% with public AEDs in the Utstein comparator group was reported in Stockolm[3].

Table 9 – Gain in survival according to different scenarios

	PAD by bystander among bystander-witnessed OHCA	Survival % in the Utstein comparator group when a shock is delivered by a bystander	Overall survival rate per 100 000 person-years	Absolute numbers of survivors per year	Increased in survival rate per 100 000 person-years	Increased survivors numbers per year
1	0%	0%	8.3*	936		
2	2%	30%	8.3	941	0.05	6
3	10%	30%	8.5	964	0.2	28
4	30%	30%	9.0	1 020	0.7	84
5	50%	30%	9.5	1 076	1.2	140
6	50%	50%	10.8	1 216	2.5	281
7	50%	70%	12.0	1 357	3.7	421

** The survival rate was set at 10% for EMS-attended OHCA as described in the international literature and in Belgium*

6 DISCUSSION

6.1 Clinical effectiveness of PAD

We retrieved only one comparative study (a randomised controlled trial)[15] assessing the clinical effectiveness of AEDs in public locations. Survivors to hospital discharge after a definite OHCA were 30 in the CPR+AED group vs. 15 in the CPR only group, yielding a twofold difference in survival (RR=2.0; 95%CI: 1.07 to 3.77; p=0.03). As explained in section 4.1, there have been some methodological discussions over the way of computing results in the PAD trial. Based on risk ratio of survival in patients with a definite OHCA (30/128 (23%) in intervention vs. 15/107 (14%) in control groups, the RR was 1.67 (95%CI: 0.95 to 2.94; p=0.074). There are thus quite statistical uncertainties regarding the effect of the PAD program.

It should be noted that 11 000 optimally trained volunteers in selected public areas at high risk of OHCA were mobilized to deliver a shock within 3 minutes after collapse. The expected effect of PAD by lay bystanders is likely to be even lower, all other conditions being kept equal. In the North Holland Province of the Netherlands, it was estimated that 0.36 lives per 100 000 person-years were saved because of the use of onsite AEDs[43], whereas in Japan it was 0.16 per 100 000 person-years[44], and these figures are close to the simulation made for Belgium (see section 5.4).

How to explain the limited impact of PAD on a society level? There are two main reasons:

1. The Utstein comparator group, the target group of PAD, is relatively small.
    a. A minority of OCHA occur in public locations (around 30%) [6, 13-15, 27-29], and only around 50% of OHCA (33%-54%) is witnessed by a bystander[3, 7, 13, 29, 30, 44]. These two conditions reduce considerably the proportion of OHCA which management could be improved with PAD. These two conditions are interrelated (i.e. they do not simply sum up) but studies report rarely the category “OHCA witnessed by bystander in a public location”. An exception is the study by Ringh where 54% of OHCA of cardiac origin were witnessed and 45% of those were in public location, so in total there were only 20% of OHCA of cardiac origin witnessed by a bystander in public location[3].
    b. Not all OCHA are of cardiac origin (usually around 80%)
    c. Not all OCHA of cardiac origin will present a shockable initial rhythm, 20% of VF is often reported in the literature. However, this percentage very much depends of the time elapsed between collapse and first rhythm assessment (see point 2). Even in advanced PAD programs, the % of initial shockable rhythm did not go higher than 50%[3, 26].

Based on these figures, it can be inferred that only around 8% of all OCHAS are bystander-witnessed shockable OHCA of cardiac origin[k]. For example, in Japan, they represented only 7.5% of all OHCAs in whom resuscitation was attempted, between 2005 and 2013[44]. Therefore, although PAD makes a difference in survival of patients in the Utstein comparator group, this difference is diluted in the overall picture.

1. The occurrence of AED use by bystander remains low.
    a. In England in 2014, PAD use was reported in only 2.4% of the 16 811 non-EMS witnessed cases[30]. In Denmark in 2010, an AED was used by a bystander in 2.2% of OHCA although the proportion of OCHA witnessed by a bystander was 53.9% and a CPR was initiated by a bystander in 44.9%[49]. In Copenhagen in 2015, an AED was applied prior to ambulance arrival in 3.8% (20/521) of OHCAs in whom resuscitation was attempted[50]. In the USA, 2.1% (289/13769) had an AED applied before EMS arrival[29]. Even settings where efforts had been put to improve the accessibility and use of AED, the % remained low. In the PAD trial cited above, a shock was delivered with a public AED in 34.4% (44/128) of definite OCHA in the intervention group, whereas an AED could be reached by a trained volunteer within 3 minutes[15]. In Japan, where the density of AED was greatly increased (from 10 961 in 2005 to 428,821 in 2013 for 127 million inhabitants, only 10% (4499/43776)

[k] 20% witnessed in public locations*80% of cardiac origin*50%VF

of the OHCA of cardiac origin with VF and witnessed by a bystander received public-access defibrillation (Utstein comparator group)[48]. In Stockholm, 15.6% of bystander witnessed OHCA of cardiac origin in public location were shocked[3]. Accessibility to the device is part of the problem. In a Danish study, it was found that only 9.1% of all AEDs were accessible 24 hours a day, seven days a week and that AED coverage decreased by 53% during the evening, night-time and weekends, which is when 62% of all cardiac arrests in public locations occurred[51]. Another study in Copenhagen reported that among AED located within 100 m of the OHCA, only 15% were accessible[50].

b. When an AED is used, it might be with too much delay. Blom et al. have reported survival rates stratified by time elapsed between collapse and shock: 71.1% for 0-2 min; 63.4% for 2-4 min; 52.4% for 4-6 min; 42.3% for 6-8 min[26]. This might explain that the survival rate with PAD was below 40% in a number of observational studies (36.0% (1018/2,858) in the Netherlands[26]; 32.7% (8,573/26,165) in the USA[25]; and 38.4% (1731/4,499) in Japan in the Utstein comparator group[44]). A similar average survival rate of 29.7% was reported for the Utstein comparator group in the study by Grasner, without consideration regarding who administered the shock[14].

6.2 Cost-effectiveness

Given the lack of robust evidence on the effectiveness of AED use by lay bystanders in public locations as well as the lack of robust Belgian data on current AED use, it was not possible to properly evaluate the cost-effectiveness impact of AED provision in Belgium. Nevertheless, our review of the literature allowed us to identify the main elements impacting the cost-effectiveness of this intervention. The analysis has shown that results were mostly influenced by the incidence of OHCA in the area of AED locations, the probability of AED use in case of OHCA and the relative risk of survival after (bystander) defibrillation compared to other interventions. The four economic evaluations identified by the HIQA HTA were rather optimistic concerning these parameters[38-41].

In ideal conditions, i.e. with the intervention of well-trained people to both CPR and AED use expected within three minutes or with a 100% probability of AED use in case of cardiac arrest, three out of these four studies showed that a targeted use of AED in high incidence area could be considered as cost-effective compared to no AED[38-40]. Nevertheless, as described in section 6.1, it is possible that in practice and in non-specific area, an AED would only be used in around 2% of cases. Moreover, a significant impact of AED use on the survival at discharge was assumed (e.g. a RR of 2.0; 95%CI 1.07-3.77 was used in the model performed by Nichol et al. based on the study of Hallstrom et al[15]). If the risk ratio recalculated by the authors of the HIQA HTA had been used, i.e. 1.67 (95%CI: 0.95-2.94), results would be worst (non-significant impact). It should also be mentioned that the study of Nichol et al.[38] added that if they were no ascertainment bias in the PAD trial, results would unlikely be cost-effective.

The fourth study (Walker et al.)[41] concluded that other alternatives would provide better value for money. It should nevertheless be noted that this study assumed few difference in patients survival with or without AED (i.e. the survival rate at discharge was 16.7% with AED and 14.7% without AED) compared to other studies based on the assumption that survival after AED use was similar than for patients attended by an ambulance staff within 3 minutes.

The economic evaluation performed in the HIQA HTA was more realistic and used estimates observed in their national OHCA register databases.

This study concluded that compared to the current situation, PAD programs were not cost-effective. Nevertheless, they added that some elements could improve the cost-effectiveness of a PAD program, such as focusing on high incidence area (rather than focusing on specific building types), improving public awareness of OHCA, increasing the number of people trained in basic life support, and implementing an EMS-linked AED register. They nevertheless added that there is currently not enough evidence to analyse the magnitude of such an impact.

Results were also highly influenced by the base case comparator used in the analysis. In the Irish study, the base case scenario was based on the current situation, in which around 9000 AEDs were already deployed on a voluntary basis. Results were therefore dependent of the effectiveness of this base case situation. It should also be noted that the strategy of no AED provision was not investigated but removing all AEDs already bought has no sense. The cost-effectiveness of a public PAD program will therefore depend of the "current situation" in terms of AED unguided provision in each country.

It should also be noted that all studies identified focused on AED provision and not on all possible interventions to improve survival. Alternative strategies such as the training of first responders groups or other strategies to reduce the response times should also be considered. Moreover, in those studies, same hospitalization costs for survivors were assumed (with or without the use of an AED) while the study of Berdowski et al.[52] showed that for survivors, in-hospital health care costs were lower for patients treated with AED onsite than for patients treated with dispatched AED or without AED. This could be taken into account in further economic evaluations.

According to this analysis, the statement that AED used by lay bystander in public location would provide value for money is therefore quite doubtful.

6.3 The way forward?

No firm recommendation can be generated concerning the provision of static AEDs to be used by bystanders in Belgium, given the lack of high-quality evidence on the effectiveness and cost-effectiveness of such program. This is not to say that static AEDs by lay bystanders have no potential to save lives, but, as explained in section 6.1, their impact on overall OHCA mortality will remain limited, particularly if other difficulties identified in the chain of survival in the Belgian setting are not addressed. The results of the 2015 MUGREG/SMUREG registry (median time for arrival=12 min; VF/VT rate as initial rhythm in 15%) underscores the need for improvements. As stated by the Global Resuscitation Alliance the main principle is to shorten as much as possible the time period between collapse and defibrillation[l]. The European Resuscitation Council (ERC)[9] and the American Heart Association (AHA)[10] provided guidelines to shorten this delay, based on the ILCOR recommendations[11]. These recommendations, which have been translated in French (https://resuscitation.be/fr/directives/basic-life-support-new/) and in Dutch (https://resuscitation.be/nl/richtlijnen/basic-life-support-new/) by the Belgian Resuscitation Council, focused on early recognition of OHCA and call for help, high-performance CPR, and early access to an AED.

6.3.1 Early recognition and call for help

ERC guidelines emphasise that bystanders should suspect cardiac arrest and start CPR if the victim is (1) unresponsive and (2) not breathing normally[2]. As explained in section 5.3.1, the level of awareness of the Belgian population might be low. Survival rate could increase if early recognition allows reducing the time to shock[26]. For example, the Netherland Heart Foundation launched in 2007 the "6minute zone" campaign aiming to raise awareness in the community to increase the number of resuscitation attempts in which a defibrillation shock was delivered within 6 minutes after the first call. This campaign reduced effectively the time of intervention[26]. Similar campaign could be also implemented in Belgium.

l https://foundation915.files.wordpress.com/2016/07/a-call-to-establish-a-global-resuscitation-alliance-2016.pdf

6.3.2 Provision of high-performance CPR

6.3.2.1 CPR training for the general public

Bystander CPR slows down VF deterioration[4]. Increasing occurrence of bystander CPR presumably also increases the number of cases where EMS personnel will undertake resuscitation efforts. The proportion of CPR in OHCA varies widely in Europe. In the EuReCa One study, 33% of the confirmed cases of OHCA had no CPR attempted, and in cases where a CPR was attempted, 47% on average was attempted by a bystander, with a range between 6.3% and 78.0% among countries[14]. As explained in sections 5.3.1 and 5.3.2, the level of training of the Belgian population might be low to moderate. Two recent studies showed that national initiatives to increase bystander CPR have improved substantially survival rates in Denmark and Sweden (although the co-occurrence of other related initiatives hinders making a strong causal relationship)[49, 53]. Quality of the CPR is also important for a better survival[54, 55]. There is a need to **raise public awareness on the importance of early CPR resuscitation**. Understanding the facilitators to use CPR by bystanders is important to increase the effectiveness of training[56]. Mandatory training in CPR could be considered to be part of the school curriculum as this is already the case in Norway, Denmark, and 27 states in the USA[57], as well as in high schools and companies. For both training and awareness raising, wide dissemination and promotion of educational videos could be made through mass media.

6.3.2.2 Telephone-CPR by EMS dispatchers

EMS dispatchers represent a critical link in the chain of survival. They must be able to diagnose cardiac arrest in order to provide Telephone CPR (T-CPR) guidance or identify close-by AEDs. They should be considered the team leader for a resuscitation effort until the EMS arrives at the scene. In order to diagnose cardiac arrest, the dispatcher needs as quickly as possible an answer to two questions: (1) is the patient conscious (awake)? and (2) is the patient breathing normally? If the answer is no to each question, the dispatcher should immediately provide telephone assistance on CPR to the bystander. Such a strategy was deemed effective in several case reports, with a steep increase in the rate of bystander-CPR[57, 58]. The quality of CPR could also be improved [59]. However, diagnosing cardiac arrest and providing T-CPR can be difficult and stressful, resulting in delays[60] or even failed dispatch[61m]. This emphasizes the need for standardized procedures and well-trained dispatchers. T-CPR has been implemented in all 112 dispatch centres in Belgium for 4-5 years. A study in Liège reported a significant increase in bystanders CPR[62]. However, some experts mentioned that that there is currently huge variability of T-CPR by 112 dispatchers both in terms of simply happening and also in terms of quality. Of note, T-CPR does not seem to decrease the psychological impact of resuscitation on the witness[63].

In the coming years, smart technologies may allow strengthening the agency between the EMS dispatcher and the bystander at the side of the victim of an OHCA. For example, video feeds could allow the dispatcher to see the CPR quality live and adapt his/her advices[64].

[m] This Swedish study published in 2009 reported that the most common reason for dispatch failures and delays were difficulties identifying true cases of OHCA at the time of the emergency call. AED-equipped first responders were dispatched to only 66% of treated cardiac arrests.

6.3.3 Maximise the use of existing AEDs

6.3.3.1 AED number and location

Although the AED density per 1000 inhabitants is lower in Belgium than in other countries (e.g. Ireland, Japan), there is no one-for-all recommendation in terms of dispatch and number of AEDs. We don't know if the current number and dispatch is appropriate or not. The current Belgian legislation, following European and US guidelines, already recommends **targeting the placement of AEDs in high risk public places**[n] (airports, railway stations, bus terminals, sport facilities, shopping malls, offices and casinos)[2, 12]. However, as demonstrated in the HIQA HTA[13], simply increasing the number of AEDs, even in high-incidence locations, will result in high costs and no cost-effectiveness.

6.3.3.2 Accessibility and traceability

A second important issue is the accessibility and traceability of AEDs. For now, most of AEDs in Belgium are placed indoor (offices, train station, shops…). Most of them are not available on a 24/7 base. That indoor public AEDs are not accessible on a permanent basis (e.g. during public holiday or in the evenings) is difficult to overcome. To increase accessibility to AED and reduce time to defibrillation, other strategies that the stand-alone static AEDs for opportunistic use by bystanders, can be considered. There are two main ones[34]:

- Professional first responders (police, fire fighters) with mobile AEDs and dispatched by the emergency medical dispatch centre (112).
- Lay first responders dispatched by the 112 service (activated by a text-message) using either a mobile AED or being guided to the closest static AED[8].

The first approach increases the incidence of PAD. In North-Holland, currently more than 50% of all defibrillations is done by AED (personal communication R.W. Koster). However, the survival in defibrillated patients is lower than in those defibrillated by a bystander[34]. While local fixed AEDs may reduce the time to defibrillation most and therefore may result in dramatically increased survival (to 50-70%) , the smaller benefit in response time and therefore less dramatic increase in survival of mobile AEDs may effectively save more lives because it can be applied in the whole population[43]. The second approach is promising but more evidence is needed[8].

F**acilitating the retrieval of neighbouring AEDs** by increased visibility is crucial. That can be done with clear and systematic advertisement outside the building and/or with mapping apps (e.g. staying alive). The listing of AEDs done by the FPS Public Health should be kept updated and easily accessible to any user. Automatic geolocation of the AED would help to keep the mapping up to date[39]. Such mapping could also be used to referring bystanders of OHCAs to existing AEDs by EMS dispatchers[50].

6.3.3.3 Appropriate use of AED

As for CPR, raising awareness and training is an important first step in the utilization of AED. Explaining that the device is fully automatic and will provide all necessary information may help to decrease fear of use. Insisting that the bystander will not be held legally responsible in case of resuscitation failure is also important. And as for CRP, EMS dispatchers can provide guidance on the use of AEDs. This role could also be played by volunteers, as it is done in other countries (the Netherlands, Ireland). When the AED is used appropriately, the error rate is reportedly low[23]. The ERC also recommends considering the development of a team with responsibility for monitoring, maintaining the devices, training and retraining individuals who are likely to use the AED, and identification of a group of volunteer individuals who are committed to using the AED[2, 12]. Ensuring that accessible AEDs are well functioning is also crucial, particularly as the

[n] The MUGREG – SMUREG registry could be useful to define such places, provided that the registry contains accurate locations and is comprehensive (see section 6.3.4).

majority of AEDs will serve very rarely. A maintenance contract with a specialized company should be compulsory, and maintenance should be done yearly.

6.3.4 Data collection and quality control

Good-quality data are important to improve the utilization and monitoring of AEDs. Our study has demonstrated that many data are already collected and available. However, their validity is questionable and it is quite impossible today to have a clear picture of PAD in Belgium (see section 5). Therefore, we suggest to make the utilization of existing registers more efficient.

1. The registration of AED by the PFS Public Health, which is compulsory, should be optimised, i.e. every AED placed should be registered. There is a need to simplify the registration by AED owners, e.g. by online registration. Also, providing the address where the AED stands should be sufficient, i.e. providing the lambert coordinates and the topographic maps should not be on the shoulders of the AED owner. Companies in charge of AED placement and maintenance could be charged of that responsibility (concentration on fewer actors). The register should be updated in real-time. It could serve as a crucial base for geographical mapping and facilitating of AED retrieval in case of OHCA.
2. The centralized registration of AED utilization which is mentioned in the Belgian law should be implemented (the current legislation stipulates that a report activity of each AED should be submitted yearly to the FPS Public Health). In principle, when an AED is used the company in charge of its maintenance will be called upon to check the device. This company could send the report to the FPS Public Health.
3. A centralized registration of EMS-attended OHCA is already in place (the MUGREG-SMUREG registry). However, strong quality procedure should be implemented to allow using the collected data for epidemiology and evidence-based policy.

6.4 Study limitations

Our study presents some limitations. First, the scope was narrow, following the research question submitted to KCE, and focuses on the provision of static AEDs to be used by bystanders. We have shown that there is no robust evidence regarding this approach, and that its effect as a stand-alone intervention will remain limited at the population level. Alternative, more integrative, approaches to increase PAD have been proposed. Although we discuss these alternatives in our report, we did not review systematically the evidence in that domain. Second, our choice of including only studies with a comparative design to avoid bias might seem too exclusive. However, a very recent systematic review confirmed that among the 44 observational studies retrieved, 77% had a critical risk of bias[65]. In the five observational studies included (rated “serious risk of bias”) where AED was applied to patients with all rhythms or only shockable rhythms, the OR were around 1.7 for survival at hospital discharge.

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APPENDICES

APPENDIX 1. SEARCH STRATEGIES

Appendix 1.1. Search for systematic reviews and guidelines

This is the initial search, the latest strategy is the one used during the search for economic studies (see below).

Appendix 1.1.1. Medline

Date	2017-02-02	
Database	Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions(R)	
Search strategy		
1	defibrillators/	1380
2	automat*.ab,ti,kw.	182565
3	1 and 2	581
4	extern*.ab,ti,kw.	280219
5	3 and 4	536
6	"automat* external defib*".ab,ti,kw.	1380
7	((AED or AEDs) and (defibrillation or fibrillation)).ab,ti,kw.	520
8	"public access defibrillation".ab,ti,kw.	230
9	"out-of-hospital defibrillation".ab,ti,kw.	25
10	5 or 6 or 7 or 8 or 9	1526
11	limit 10 to systematic reviews	88
12	Out-of-Hospital Cardiac Arrest/	2176
13	1 and 12	197
14	limit 13 to systematic reviews	8
15	exp *Cardiopulmonary Resuscitation/	10655
16	(cardiopulmonary and resuscitation).ti.	5203
17	15 or 16	12415

18	(neonatal or pediatric or child or children or infant? or 'delivery room' or newborn? or neonate?).ti.	895185
19	in-hospital.ti.	12466
20	((emergency or critical care or intensive care) adj1 (department? or unit? or environment or physician? or practitioner?)).ti.	47887
21	18 or 19 or 20	946331
22	17 not 21	10975
23	exp clinical pathway/	5542
24	exp clinical protocol/	146458
25	exp consensus/	7382
26	exp consensus development conference/	10498
27	exp consensus development conferences as topic/	2525
28	critical pathways/	5542
29	exp guideline/	28727
30	guidelines as topic/	34969
31	exp practice guideline/	22190
32	practice guidelines as topic/	96792
33	health planning guidelines/	3972
34	(guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.	37032
35	(position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw.	22487
36	(standards or guideline or guidelines).ti,kf,kw.	86801
37	((practice or treatment* or clinical) adj guideline*).ab.	29226
38	(CPG or CPGs).ti.	5015
39	consensus*.ti,kf,kw.	19128
40	consensus*.ab. /freq=2	18691
41	((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw.	15469
42	recommendat*.ti,kf,kw.	31885
43	(care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw.	41700
44	(algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw.	5551

45	(algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kf,kw.	7137
46	or/23-45	497033
47	22 and 46	1428
48	limit 47 to last 5 years	337
49	remove duplicates from 48	331
50	11 or 14	94
51	remove duplicates from 50	91
52	49 not 51	319
Notes	Line 51: SR, Line 52: Guidelines This search was improved and run again along with the search for economic studies, see below.	

Appendix 1.1.2. Embase

Date	2017-02-02	
Database	Embase	
Search strategy		
#1	'automated external defibrillator'/exp OR 'automated external defibrillator'	1760
#2	(automat* NEAR/3 extern* NEAR/3 defibrillat*):ab,ti	1876
#3	aed:ab,ti OR aeds:ab,ti AND (defibrillation:ab,ti OR fibrillation:ab,ti)	842
#4	'public access defibrillation':ab,ti	312
#5	'out-of-hospital defibrillation':ab,ti	27
#6	(workplace NEAR/3 defibrillat*):ab,ti	5
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	2756
#8	'out of hospital cardiac arrest'/exp	5330
#9	'defibrillator'/exp	54985
#10	#8 AND #9	781
#11	#7 OR #10	3110

#12	'meta-analysis'/exp OR 'meta-analysis' OR 'systematic review'/exp OR 'systematic review'	272412
#13	#11 AND #12	49
#14	#13 NOT [medline]/lim	13
#15	#14 NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim)	7
#16	'resuscitation'/exp/mj	50837
#17	cardiopulmonary:ti AND resuscitation:ti	6465
#18	#16 OR #17	51265
#19	neonatal:ti OR pediatric:ti OR child:ti OR children:ti OR infant:ti OR infants:ti OR 'delivery room':ti OR newborn*:ti OR neonate*:ti	1116521
#20	'in hospital':ti	17588
#21	((emergency OR 'critical care' OR 'intensive care') NEAR/1 (department* OR unit OR units OR environment OR physician* OR practitioner*)):ti	63724
#22	#19 OR #20 OR #21	1185833
#23	#18 NOT #22	45790
#24	'clinical pathway'/exp	7140
#25	'clinical protocol'/exp	78338
#26	'consensus'/exp	46112
#27	'consensus development'/exp	17402
#28	'practice guideline'/exp	388014
#29	'position statement':ab,ti OR 'position statements':ab,ti OR 'policy statement':ab,ti OR 'policy statements':ab,ti OR 'practice parameter':ab,ti OR 'practice parameters':ab,ti OR 'best practice':ab,ti OR 'best practices':ab,ti	29754
#30	standards:ti OR guideline:ti OR guidelines:ti	102131
#31	((practice OR treatment* OR clinical) NEAR/5 guideline*):ab	72890
#32	cpg:ti OR cpgs:ti	5824
#33	consensus*:ti	21541
#34	((critical OR clinical OR practice) NEAR/2 (path OR paths OR pathway OR pathways OR protocol*)):ab,ti	21573
#35	recommendat*:ti	37233
#36	(care NEAR/2 (standard OR path OR paths OR pathway OR pathways OR map OR maps OR plan OR plans)):ab,ti	63492

#37	(algorithm* NEAR/2 (screening OR examination OR test OR tested OR testing OR assessment* OR diagnosis OR diagnoses OR diagnosed OR diagnosing)):ab,ti	6955
#38	(algorithm* NEAR/2 (pharmacotherap* OR chemotherap* OR chemotreatment* OR therap* OR treatment* OR intervention*)):ab,ti	9869
#39	#24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38	649802
#40	#23 AND #39	3660
#41	#23 AND #39 AND [2013-2017]/py	1103
#42	#41 NOT [medline]/lim	716
#43	#42 NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim)	280
Notes	Line 15: Systematic reviews Line 43: Guidelines This search was improved and run again along with the search for economic studies, see below and got a last update to correct a mistake.	

Appendix 1.1.3. Cochrane

Cochrane was searched on 2nd of February 2017 then updated during the search for primary studies. See update below for search strategy.

Appendix 1.2. Search for primary studies

Appendix 1.2.1. Medline

Date	2017-03-06	
Database	Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions(R)	
Search strategy		
1	Electric Countershock/	13586
2	cardioversion?.ti.	2371
3	cardiac electroversion?.ti.	1
4	defibrillators/	1393
5	1 or 2 or 3 or 4	14900
6	Out-of-Hospital Cardiac Arrest/	2202
7	exp "non-medical public and private facilities"/	186954
8	6 or 7	189131
9	5 and 8	414
10	"automat* extern* defib*".ab,ti,kw.	1387
11	((AED or AEDs) and defibrillat*).ab,ti,kw.	802
12	(public adj3 defibrillat*).ab,ti,kw.	314
13	(out-of-hospital adj3 defibrillat*).ab,ti,kw.	123
14	(community adj3 defibr*).ab,ti,kw.	30
15	(workplace adj3 defib*).ab,ti,kw.	5
16	(bystander? adj3 defib*).ab,ti,kw.	48
17	10 or 11 or 12 or 13 or 14 or 15 or 16	1658
18	9 or 17	1847
19	"AED plus".ab,ti,kw.	8
20	cardiolife.ab,ti,kw.	1
21	lifepak.ab,ti,kw.	45
22	"zoll aed pro".ab,ti,kw.	0

23	"heart start".ab,ti,kw.	3
24	powerheart.ab,ti,kw.	2
25	defibtech.ab,ti,kw.	1
26	"aed 7000".ab,ti,kw.	0
27	heartstart.ab,ti,kw.	57
28	heartsine.ab,ti,kw.	3
29	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28	113
30	18 or 29	1922
31	limit 30 to yr="2012-2017"	668
32	limit 31 to animals	11
33	limit 31 to human	549
34	32 not 33	4
35	31 not 34	664
36	limit 35 to "all child (0 to 18 years)"	107
37	limit 35 to "all adult (19 plus years)"	252
38	35 not (36 not 37)	609
39	randomized controlled trial.pt.	448767
40	controlled clinical trial.pt.	91958
41	randomized.ti,ab.	418791
42	placebo.ti,ab.	188884
43	drug therapy.fs.	1938969
44	randomly.ti,ab.	272674
45	trial?.ti,ab.	819565
46	groups.ti,ab.	1701756
47	39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	4202862
48	exp animal/ not humans/	4325121
49	47 not 48	3640734

50	38 and 49	103
51	38 not 50	506
52	remove duplicates from 51	490
53	remove duplicates from 38	591
54	remove duplicates from 50	101
55	limit 54 to yr="2014 -Current"	64
56	limit 53 to yr="2014 -Current"	383
Notes		

Appendix 1.2.2. Embase

Date	2017-02-08	
Database	Embase	
Search strategy		
1	'cardioversion'/exp OR cardioversion*.ti OR electroversion*.ti OR countershock.ti	17759
2	'out of hospital cardiac arrest'/exp	5374
3	'airport'/exp	1555
4	'workplace'/exp	30512
5	'sporting event'/exp	998
6	'market'/exp	15881
7	'school'/exp	310031
8	#2 OR #3 OR #4 OR #5 OR #6 OR #7	361835
9	#1 AND #8	273
10	'automated external defibrillator'/exp	1364
11	'automat* extern* defib*':ab,ti	1858
12	aed:ab,ti OR aeds:ab,ti AND defibrillat*:ab,ti	1271
18	((bystander* OR workplace OR community OR public OR witness* OR 'out-of-hospital' OR layperson* OR 'lay rescuer*' OR 'lay people') NEAR/3 (aed OR aeds OR defib*)):ab,ti	892
19	#10 OR #11 OR #12 OR #18	2924

20	#9 OR #19	3182
21	'aed plus':ab,ti	18
22	cardiolife:ab,ti	3
23	lifepak:ab,ti	86
24	'zoll aed pro':ab,ti	7
25	'heart start':ab,ti	12
26	powerheart:ab,ti	5
27	defibtech:ab,ti	3
28	'aed 7000':ab,ti	0
29	heartstart:ab,ti	90
30	heartsine:ab,ti	12
31	#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30	217
32	#20 OR #31	3322
33	#32 AND (2014:py OR 2015:py OR 2016:py OR 2017:py)	869
34	#33 AND 'animal'/exp	828
35	#33 AND 'human'/exp	818
36	#33 NOT (#34 NOT #35)	859
37	#36 AND ([adolescent]/lim OR [child]/lim OR [embryo]/lim OR [fetus]/lim OR [infant]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim)	103
38	#36 AND ([adult]/lim OR [aged]/lim OR [middle aged]/lim OR [very elderly]/lim OR [young adult]/lim)	281
39	#36 NOT (#37 NOT #38)	789
40	#39 NOT ('conference abstract'/it OR 'conference paper'/it OR 'conference review'/it OR 'editorial'/it OR 'letter'/it)	408
41	#40 NOT [medline]/lim	190
44	#41 NOT ([editorial]/lim OR [letter]/lim OR 'case report'/de)	158
45	#44 AND (random*:ab,ti OR 'clinical trial'/de OR 'clinical trial' OR 'health care quality'/exp)	70
46	#44 NOT (random*:ab,ti OR 'clinical trial'/de OR 'clinical trial' OR 'health care quality'/exp)	88
Notes		

Appendix 1.2.3. Cochrane

Date	08/02/17 14:09:55.421	
Database	Cochrane Database of Systematic Reviews	
Search strategy		
#1	[mh ^"Electric Countershock"]	870
#2	[mh ^defibrillators]	87
#3	#1 or #2	918
#4	[mh "Out-of-Hospital Cardiac Arrest"]	154
#5	MeSH descriptor: [Public Facilities] explode all trees	154
#6	#4 or #5	308
#7	#3 and #6	28
#8	"automat* extern* defib*":ab,ti	135
#9	((AED or AEDs) and defibrillat*):ab,ti	97
#10	(public near/3 defibrillat*):ab,ti	35
#11	(out-of-hospital near/3 defibrillat*):ab,ti	22
#12	(community near/3 defibr*):ab,ti	2
#13	(workplace near/3 defib*):ab,ti	0
#14	#8 or #9 or #10 or #11 or #12 or #13	170
#15	#7 or #14	182
#16	"AED plus":ab,ti	1
#17	cardiolife:ab,ti	0
#18	lifepak:ab,ti	8
#19	"zoll aed pro":ab,ti	1
#20	"heart start":ab,ti	1
#21	powerheart:ab,ti	1
#22	defibtech:ab,ti	0
#23	"aed 7000":ab,ti	0

#24	heartstart:ab,ti	5
#25	heartsine:ab,ti	1
#26	#16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25	18
#27	#15 or #26	195
#28	#15 or #26 Publication Year from 2012 to 2017	63
Notes		

Appendix 1.3. Search for economic studies and update of previous searches

Appendix 1.3.1. Medline

Date	2017-06-06	
Database	Medline OvidSP	
Search strategy		
1	(AED or AEDs).mp.	7705
2	(SAED or saeds).mp.	744
3	1 or 2	8446
4	Heart Arrest/	26477
5	atrial fibrillation/	46115
6	Ventricular Fibrillation/	16715
7	cardiac arrest.ab,ti,kw.	27176
8	heart arrest.ab,ti,kw.	1568
9	cardiopulmonary arrest.ab,ti,kw.	2018
10	asystol*.ab,ti,kw.	3842
11	4 or 5 or 6 or 7 or 8 or 9 or 10	102197
12	Out-of-Hospital Cardiac Arrest/	2373
13	"Out-of-Hospital Cardiac Arrest".ab,ti,kw.	3850
14	ohca.ab,ti,kw.	1458

15	12 or 13 or 14	4814
16	Electric Countershock/	14027
17	defibrillators/	1435
18	cardioversion?.mp.	5716
19	electroversion?.mp.	33
20	countershock?.mp.	14214
21	defibrillat*.mp.	28083
22	16 or 17 or 18 or 19 or 20 or 21	37649
23	15 and 22	1208
24	11 or 15 or 22	124633
25	3 and 24	990
26	bystander*.ab,ti,kw.	8616
27	community.ab,ti,kw.	388784
28	public.ab,ti,kw.	341230
29	witness*.ab,ti,kw.	20839
30	layperson*.ab,ti,kw.	1223
31	'lay rescuer*'.ab,ti,kw.	120
32	'lay people'.ab,ti,kw.	971
33	out-of-hospital.ab,ti,kw.	7936
34	workplace?.ab,ti,kw.	32917
35	outdoor.ab,ti,kw.	15341
36	public access.ab,ti,kw.	1098
37	publicly accessible.ab,ti,kw.	897
38	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37	769507
39	22 and 38	2518
40	automated.mp.	116562
41	semi-automated.mp.	4091

42	semiautomated.mp.	2815
43	automatic.mp.	72612
44	semiautomatic.mp.	2174
45	semi-automatic.mp.	2668
46	40 or 41 or 42 or 43 or 44 or 45	183026
47	22 and 46	3507
48	external.mp.	292908
49	47 and 48	1548
50	"AED plus".ab,ti,kw.	8
51	cardiolife.ab,ti,kw.	1
52	lifepak.ab,ti,kw.	46
53	"zoll aed pro".ab,ti,kw.	0
54	"heart start".ab,ti,kw.	3
55	powerheart.ab,ti,kw.	2
56	defibtech.ab,ti,kw.	2
57	"aed 7000".ab,ti,kw.	0
58	heartstart.ab,ti,kw.	57
59	heartsine.ab,ti,kw.	3
60	50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59	115
61	"automat* extern* defib*".mp.	1446
62	(automat* adj2 external adj2 defibrillat*).mp.	1461
63	60 or 61 or 62	1542
64	23 or 25 or 39 or 49 or 63	3562
65	64 not (editorial or letter).pt.	3341
66	65 not case reports.pt.	3108
67	66 not (exp animals/ not human/)	3041
68	remove duplicates from 67	2950

69	limit 68 to systematic reviews	183
70	exp clinical pathway/	5812
71	exp clinical protocol/	153643
72	exp consensus/	7939
73	exp consensus development conference/	10910
74	exp consensus development conferences as topic/	2610
75	critical pathways/	5812
76	exp guideline/	30042
77	guidelines as topic/	36238
78	exp practice guideline/	23295
79	practice guidelines as topic/	101397
80	health planning guidelines/	4080
81	(guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.	38653
82	(position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw.	23897
83	(standards or guideline or guidelines).ti,kf,kw.	90315
84	((practice or treatment* or clinical) adj guideline*).ab.	30791
85	(CPG or CPGs).ti.	5172
86	consensus*.ti,kf,kw.	20122
87	consensus*.ab. /freq=2	19615
88	((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw.	16248
89	recommendat*.ti,kf,kw.	33462
90	(care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw.	43679
91	(algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw.	5973
92	(algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kf,kw.	7566
93	or/70-92	520009
94	68 and 93	367
95	94 not 69	274

96	randomized controlled trial.pt.	464985
97	controlled clinical trial.pt.	94185
98	randomized.ti,ab.	437449
99	placebo.ti,ab.	195057
100	drug therapy.fs.	2003038
101	randomly.ti,ab.	282969
102	trial?.ti,ab.	854923
103	groups.ti,ab.	1762709
104	96 or 97 or 98 or 99 or 100 or 101 or 102 or 103	4349079
105	exp animal/ not humans/	4412730
106	104 not 105	3770935
107	68 and 106	701
108	107 not (69 or 94)	591
109	limit 108 to yr="2013-2017"	138
110	Economics/	27115
111	exp "Costs and Cost Analysis"/	211967
112	Value of Life/ec	247
113	pharmacoeconomi*.ti,ab,kw.	3570
114	(economic adj1 evaluati*).ti,ab,kw.	9427
115	budget*.ti,ab,kw.	24688
116	cost-effectiveness.ti,ab,kw.	48948
117	cost-utility.ti,ab,kw.	3700
118	cost-mini*.ti,ab,kw.	1348
119	cost-benefit*.ti,ab,kw.	10189
120	letter.pt.	973639
121	editorial.pt.	441144
122	historical article.pt.	348027

123	animals/ not humans/	4379649
124	110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119	285909
125	or/120-123	6072803
126	124 not 125	259515
127	68 and 126	122
128	limit 127 to yr="2013-2017"	13
129	128 not (69 or 94 or 109)	8
130	68 not (69 or 94 or 109 or 129)	2347
131	limit 130 to yr="2013-2017"	513
Notes		

Appendix 1.3.2. Embase

See below for update

Appendix 1.3.3. Cochrane

Date	01/06/17 16:52:10.336	
Database	Cochrane Database of Systematic Reviews	
Search strategy		
#1	(AED or AEDs)	975
#2	(SAED or saeds)	11
#3	#1 or #2	985
#4	[mh "Heart Arrest"]	1502
#5	[mh "atrial fibrillation"]	3392
#6	[mh "Ventricular Fibrillation"]	504
#7	cardiac arrest:ab,ti,kw	2674
#8	'heart arrest':ab,ti,kw	2950
#9	cardiopulmonary arrest:ab,ti,kw	1397
#10	asystol*:ab,ti,kw	218

#11	#4 or #5 or #6 or #7 or #8 or #9 or #10	7816
#12	[mh "Out-of-Hospital Cardiac Arrest"]	167
#13	"Out-of-Hospital Cardiac Arrest":ab,ti,kw	626
#14	ohca:ab,ti,kw	197
#15	#12 or #13 or #14	631
#16	[mh "Electric Countershock"]	876
#17	[mh defibrillators]	1141
#18	cardioversion*	1063
#19	electroversion*	4
#20	countershock*	915
#21	defibrillat*	3418
#22	#16 or #17 or #18 or #19 or #20 or #21	4398
#23	#15 and #22	168
#24	#11 or #15 or #22	10643
#25	#3 and #24	127
#26	bystander*:ab,ti,kw	244
#27	community:ab,ti,kw	25023
#28	public:ab,ti,kw	12013
#29	witness*:ab,ti,kw	562
#30	layperson*:ab,ti,kw	147
#31	'lay rescuer*':ab,ti,kw	40
#32	'lay people':ab,ti,kw	386
#33	out-of-hospital:ab,ti,kw	990
#34	workplace*:ab,ti,kw	1849
#35	outdoor:ab,ti,kw	554
#36	public access:ab,ti,kw	1887
#37	publicly accessible:ab,ti,kw	38

#38	#26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37	39951
#39	#22 and #38	376
#40	automated	5222
#41	semi-automated	194
#42	semiautomated	98
#43	automatic	2997
#44	semiautomatic	80
#45	semi-automatic	95
#46	#40 or #41 or #42 or #43 or #44 or #45	8012
#47	#22 and #46	468
#48	external	21260
#49	#47 and #48	200
#50	"AED plus":ab,ti,kw	1
#51	cardiolife:ab,ti,kw	0
#52	lifepak:ab,ti,kw	9
#53	"zoll aed pro":ab,ti,kw	1
#54	"heart start":ab,ti,kw	1
#55	powerheart:ab,ti,kw	1
#56	defibtech:ab,ti,kw	0
#57	"aed 7000":ab,ti,kw	0
#58	heartstart:ab,ti,kw	6
#59	heartsine:ab,ti,kw	1
#60	#50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59	20
#61	"automat* extern* defib*"	160
#62	(automat* near/2 external near/2 defibrillat*)	161
#63	#60 or #61 or #62	175
#64	#23 or #25 or #39 or #49 or #63	487

#65	#23 or #25 or #39 or #49 or #63 Publication Year from 2014 to 2017	166
Notes	Records found in the Cochrane systematic review database: 43 Records found in CENTRAL: 168 Records found in DARE: 14 Records found in NHS EED: 25 Records found In HTA database: 7	

Appendix 1.3.4. Econlit

Date	2017-06-01	
Database	Econlit <1886 to April 2017>	
Search strategy		
1	(AED or AEDs).mp.	8
2	(SAED or saeds).mp.	0
3	1 or 2	8
4	fibrillation.ab,ti,kw.	12
5	cardiac arrest.ab,ti,kw.	7
6	heart arrest.ab,ti,kw.	1
7	cardiopulmonary arrest.ab,ti,kw.	1
8	asystol*.ab,ti,kw.	0
9	4 or 5 or 6 or 7 or 8	21
10	"Out-of-Hospital Cardiac Arrest".ab,ti,kw.	1
11	ohca.ab,ti,kw.	0
12	10 or 11	1
13	cardioversion?.mp.	0
14	electroversion?.mp.	0
15	countershock?.mp.	1
16	defibrillat*.mp.	11
17	13 or 14 or 15 or 16	12
18	12 and 17	1

19	9 or 12 or 17	29
20	3 and 19	0
21	bystander*.ab,ti,kw.	73
22	community.ab,ti,kw.	22590
23	public.ab,ti,kw.	97132
24	witness*.ab,ti,kw.	2563
25	layperson*.ab,ti,kw.	29
26	'lay rescuer*'.ab,ti,kw.	0
27	'lay people'.ab,ti,kw.	32
28	out-of-hospital.ab,ti,kw.	20
29	workplace?.ab,ti,kw.	4633
30	outdoor.ab,ti,kw.	359
31	public access.ab,ti,kw.	112
32	publicly accessible.ab,ti,kw.	31
33	21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32	122926
34	17 and 33	4
35	automated.mp.	967
36	semi-automated.mp.	8
37	semiautomated.mp.	2
38	automatic.mp.	2035
39	semiautomatic.mp.	4
40	semi-automatic.mp.	18
41	35 or 36 or 37 or 38 or 39 or 40	2978
42	17 and 41	0
43	external.mp.	23225
44	42 and 43	0
45	"AED plus".ab,ti,kw.	0

46	cardiolife.ab,ti,kw.	0
47	lifepak.ab,ti,kw.	0
48	"zoll aed pro".ab,ti,kw.	0
49	"heart start".ab,ti,kw.	0
50	powerheart.ab,ti,kw.	0
51	defibtech.ab,ti,kw.	0
52	"aed 7000".ab,ti,kw.	0
53	heartstart.ab,ti,kw.	0
54	heartsine.ab,ti,kw.	0
55	45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54	0
56	"automat* extern* defib*".mp.	0
57	(automat* adj2 external adj2 defibrillat*).mp.	0
58	55 or 56 or 57	0
59	18 or 20 or 34 or 44 or 58	4
Notes		

Appendix 1.4. Embase search final update

Search date: July-10 2017

Search performed using embase.com

This search is an update of the search done while searching for economic studies. It corrects a mistake in search years. SR, guidelines, economic studies, RCT and other primary studies were all exported again.

Exported lines:

76 for systematic reviews

95 for guidelines

98 for RCT

119 economic studies

122 all studies

Line	Search expression	Hits
#122	**#120** AND (**2013**:py OR **2014**:py OR **2015**:py OR **2016**:py OR **2017**:py)	**253**
#121	**#120** AND (**2013**:py AND **2014**:py OR **2015**:py OR **2016**:py OR **2017**:py)	**123**
#120	**#75** NOT (**#76** OR **#93** OR **#96** OR **#117**)	**410**
#119	**#117** NOT (**#76** OR **#93** OR **#96**)	**21**
#118	**#117** AND (**2013**:py OR **2014**:py OR **2015**:py OR **2016**:py OR **2017**:py)	**22**
#117	**#75** AND **#116**	**51**
#116	**#99** OR **#100** OR **#101** OR **#102** OR **#103** OR **#104** OR **#105** OR **#106** OR **#107** OR **#108** OR **#109** OR **#110** OR **#111** OR **#112** OR **#113** OR **#114** OR **#115**	**624184**
#115	**'cost benefit*'**:ti,ab	**12700**
#114	**'cost mini*'**:ti,ab	**2028**
#113	**'cost utility'**:ti,ab	**5357**
#112	**'cost effectiv*'**:ti,ab	**139156**
#111	**budget***:ti,ab	**30825**
#110	(**economic** NEAR/1 **evaluati***):ti,ab	**12419**
#109	**pharmacoeconomi***:ti,ab	**6987**
#108	**'health care cost'**/exp	**248355**
#107	**'pharmacoeconomics'**/exp	**184386**
#106	**'economic evaluation'**/exp	**258028**
#105	**'cost of illness'**/exp	**16679**
#104	**'cost control'**/exp	**59019**
#103	**'cost minimization analysis'**/exp	**2975**
#102	**'cost consequence analysis'**/exp	**13**
#101	**'cost utility analysis'**/exp	**7518**
#100	**'cost effectiveness analysis'**/exp	**124072**
#99	**'cost benefit analysis'**/exp	**74269**
#98	**#96** AND (**2013**:py OR **2014**:py OR **2015**:py OR **2016**:py OR **2017**:py)	**202**
#97	**#96** NOT (**#76** OR **#93**)	**204**

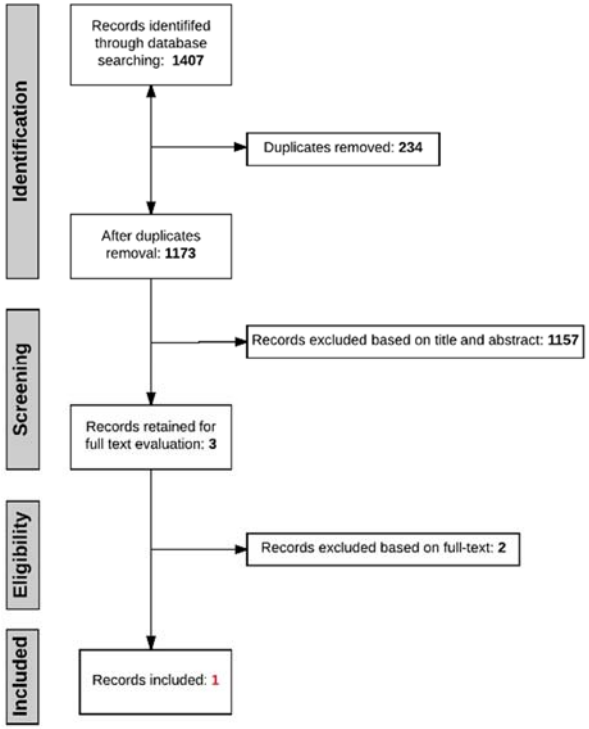
#96	**#75** AND (**random***:ab,ti OR **'clinical trial'**/de OR **'clinical trial'** OR **'health care quality'**/exp)	**372**
#95	**#93** NOT **#76**	**169**
#94	**#92** NOT **#76**	**682926**
#93	**#75** AND **#92**	**179**
#92	**#77** OR **#78** OR **#79** OR **#80** OR **#81** OR **#82** OR **#83** OR **#84** OR **#85** OR **#86** OR **#87** OR **#88** OR **#89** OR **#90** OR **#91**	**682936**
#91	(**algorithm*** NEAR/2 (**pharmacotherap*** OR **chemotherap*** OR **chemotreatment*** OR **therap*** OR **treatment*** OR **intervention***)):ab,ti	**10429**
#90	(**algorithm*** NEAR/2 (**screening** OR **examination** OR **test** OR **tested** OR **testing** OR **assessment*** OR **diagnosis** OR **diagnoses** OR **diagnosed** OR **diagnosing**)):ab,ti	**7372**
#89	(**care** NEAR/2 (**standard** OR **path** OR **paths** OR **pathway** OR **pathways** OR **map** OR **maps** OR **plan** OR **plans**)):ab,ti	**67963**
#88	**recommendat***:ti	**38790**
#87	((**critical** OR **clinical** OR **practice**) NEAR/2 (**path** OR **paths** OR **pathway** OR **pathways** OR **protocol***)):ab,ti	**22697**
#86	**consensus***:ti	**22487**
#85	**cpg**:ti OR **cpgs**:ti	**5975**
#84	((**practice** OR **treatment*** OR **clinical**) NEAR/5 **guideline***):ab	**77090**
#83	**standards**:ti OR **guideline**:ti OR **guidelines**:ti	**105628**
#82	**'position statement'**:ab,ti OR **'position statements'**:ab,ti OR **'policy statement'**:ab,ti OR **'policy statements'**:ab,ti OR **'practice parameter'**:ab,ti OR **'practice parameters'**:ab,ti OR **'best practice'**:ab,ti OR **'best practices'**:ab,ti	**31847**
#81	**'practice guideline'**/exp	**409174**
#80	**'consensus development'**/exp	**21245**
#79	**'consensus'**/exp	**47775**
#78	**'clinical protocol'**/exp	**80953**
#77	**'clinical pathway'**/exp	**7353**
#76	**#75** AND (**'meta-analysis'**/exp OR **'meta-analysis'** OR **'systematic review'**/exp OR **'systematic review'**)	**23**
#75	**#74** NOT **'case report'**/de	**827**
#74	**#73** NOT [medline]/lim	**926**
#73	**#72** NOT (**'conference abstract'**/it OR **'conference paper'**/it OR **'conference review'**/it OR **'editorial'**/it OR **'letter'**/it)	**4053**
#72	**#70** NOT **#71**	**10286**

#71	**'animal'**/exp NOT **'human'**/exp	**4876283**
#70	**#23** OR **#25** OR **#44** OR **#54** OR **#69**	**10488**
#69	**#65** OR **#66** OR **#67** OR **#68**	**2696**
#68	**'automated external defibrillator'**/exp	**1447**
#67	(**automat*** NEAR/2 **external** NEAR/2 **defibrillat***):ab,ti	**1926**
#66	**'automat* extern* defib*'**:ab,ti	**1917**
#65	**#55** OR **#56** OR **#57** OR **#58** OR **#59** OR **#60** OR **#61** OR **#62** OR **#63** OR **#64**	**222**
#64	**heartsine**:ab,ti	**12**
#63	**heartstart**:ab,ti	**92**
#62	**'aed 7000'**:ab,ti	**0**
#61	**defibtech**:ab,ti	**3**
#60	**powerheart**:ab,ti	**5**
#59	**'heart start'**:ab,ti	**13**
#58	**'zoll aed pro'**:ab,ti	**8**
#57	**lifepak**:ab,ti	**87**
#56	**cardiolife**:ab,ti	**3**
#55	**'aed plus'**:ab,ti	**18**
#54	**#52** AND **#53**	**2053**
#53	**external**:ab,ti	**305070**
#52	**#22** AND **#51**	**4917**
#51	**#45** OR **#46** OR **#47** OR **#48** OR **#49** OR **#50**	**197337**
#50	**'semi automatic'**:ab,ti	**3640**
#49	**semiautomatic**:ab,ti	**2635**
#48	**automatic**:ab,ti	**74165**
#47	**semiautomated**:ab,ti	**3215**
#46	**'semi automated'**:ab,ti	**6277**
#45	**automated**:ab,ti	**125814**

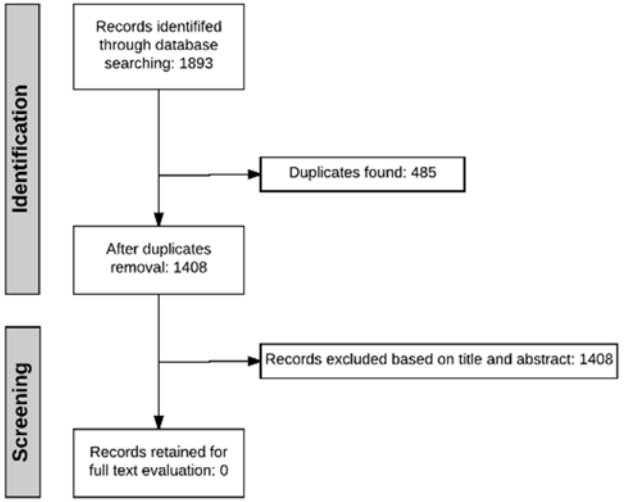
#44	**#22** AND **#43**	**8598**
#43	**#26** OR **#27** OR **#28** OR **#29** OR **#30** OR **#31** OR **#32** OR **#33** OR **#34** OR **#35** OR **#36** OR **#37** OR **#38** OR **#39** OR **#40** OR **#41** OR **#42**	**1221576**
#42	**'school'**/exp	**320734**
#41	**'market'**/exp	**16449**
#40	**'sporting event'**/exp	**1020**
#39	**'workplace'**/exp	**32109**
#38	**'airport'**/exp	**1615**
#37	**'publicly accessible'**:ab,ti	**1024**
#36	**'public access'**:ab,ti	**1389**
#35	**outdoor**:ab,ti	**18932**
#34	**workplace***:ab,ti	**39148**
#33	**'out-of-hospital'**:ab,ti	**11610**
#32	**'lay people'**:ab,ti	**1244**
#31	**'lay rescuer*'**:ab,ti	**211**
#30	**layperson***:ab,ti	**1448**
#29	**witness***:ab,ti	**26397**
#28	**public**:ab,ti	**400465**
#27	**community**:ab,ti	**460739**
#26	**bystander***:ab,ti	**11177**
#25	**#3** AND **#24**	**1699**
#24	**#11** OR **#15** OR **#22**	**267203**
#23	**#15** AND **#22**	**1942**
#22	**#16** OR **#17** OR **#18** OR **#19** OR **#20** OR **#21**	**80955**
#21	**defibrillat***:ab,ti	**31699**
#20	**countershock***:ab,ti	**594**
#19	**electroversion***:ab,ti	**40**
#18	**cardioversion***:ab,ti	**8308**

#17	**'defibrillator'**/exp	**56235**
#16	**'cardioversion'**/exp	**18092**
#15	**#12** OR **#13** OR **#14**	**7996**
#14	**ohca**:ab,ti	**3081**
#13	**'out-of-hospital cardiac arrest'**:ab,ti	**6257**
#12	**'out of hospital cardiac arrest'**/exp	**5819**
#11	**#4** OR **#5** OR **#6** OR **#7** OR **#8** OR **#9** OR **#10**	**215870**
#10	**asystol***:ab,ti	**5655**
#9	**'cardiopulmonary arrest'**:ab,ti	**2817**
#8	**'heart arrest'**:ab,ti	**571**
#7	**'cardiac arrest'**:ab,ti	**39957**
#6	**'heart ventricle fibrillation'**/exp	**29573**
#5	**'atrial fibrillation'**/exp	**116660**
#4	**'heart arrest'**/exp	**75091**
#3	**#1** OR **#2**	**14138**
#2	**saed**:ab,ti OR **saeds**:ab,ti	**667**
#1	**aed**:ab,ti OR **aeds**:ab,ti	**13475**

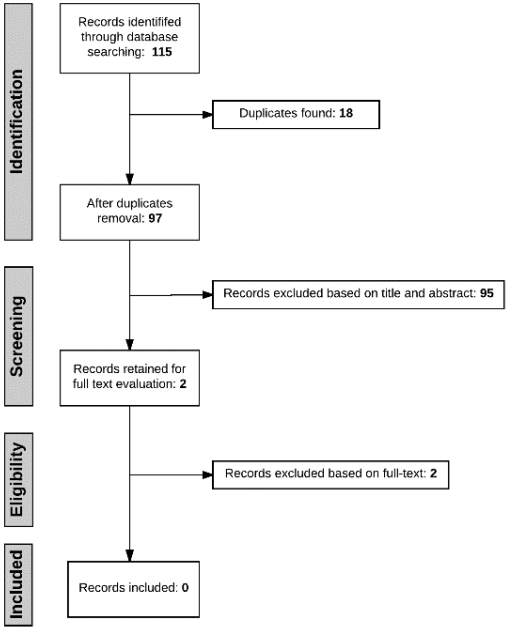
Appendix 1.5. PRISMA for systematic reviews and guidelines



Appendix 1.6. PRISMA for primary studies



Appendix 1.7. PRISMA for economic studies



APPENDIX 2. INCLUSION CRITERIA FOR THE SR OF THE HIQA HTA

PICO	Description
Population	All adults and children with sudden cardiac arrest in any location except for hospitals or other high dependency care facilities
Intervention	Public access defibrillation interventions that include the provision of static AEDs in publicly-accessible locations, and used opportunistically by trained or untrained volunteers or bystanders (studies involving community groups of trained lay-volunteers or lay responders such as police and firefighters were also eligible)
Comparator	Routine emergency medical services
Outcomes	Primary outcome was survival to hospital discharge
Study type	Any type of comparative studies. Descriptive studies (e.g. case reports, case series) were ineligible.

APPENDIX 3. QUALITY APPRAISAL OF THE HIQA HTA

AMSTAR EVALUATION OF THE HIQA HTA[13]

Article Name: Health Technology Assessment (HTA) of Public Access Defibrillation

1. Was an 'a priori' design provided?
The research question and inclusion criteria should be established before the conduct of the review.

Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."

- ☐ Yes
- ☐ No
- ☑ Can't answer
- ☐ Not applicable

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2. Was there duplicate study selection and data extraction?
There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.

Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.

- ☑ Yes
- ☐ No
- ☐ Can't answer
- ☐ Not applicable

Justification:

- Preliminary screening of all returned results was undertaken by a single person to eliminate duplicates and studies that were clearly not relevant. Assessment of the eligibility of studies and identification of multiple reports from single studies was performed independently by two people according to the inclusion criteria shown in Table 4.1. Disagreements were resolved by discussion, or if necessary, by a third person.

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3. Was a comprehensive literature search performed?
At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.

Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).

- ☑ Yes
- ☐ No
- ☐ Can't answer
- ☐ Not applicable

Justification:

A search was performed in Medline, Embase, Scopus, clinical trial registries (Cochrane Registry of Controlled Trials, ClinicalTrials.gov and the ISRCTN register) and the Cochrane Library (Database of Abstracts of Reviews of Effects [DARE], Cochrane Database of Systematic Reviews [CDSR] and the Health Technology assessment [HTA] database) for studies examining the effectiveness of public access defibrillation interventions.

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4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?
The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.

Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SINGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.

Justification:
This is not clearly stated, but reference lists of included studies were also searched.

- [x] Yes
- [ ] No
- [ ] Can't answer
- [ ] Not applicable

---

5. Was a list of studies (included and excluded) provided?
A list of included and excluded studies should be provided.

Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."

Justification:
Only a list of included studies was provided. But as regards provision of public AED, only one study was retrieved.

- [x] Yes
- [ ] No
- [ ] Can't answer
- [ ] Not applicable

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6. Were the characteristics of the included studies provided?
In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.

Note: Acceptable if not in table format as long as they are described as above.

Justification:

- [x] Yes
- [ ] No
- [ ] Can't answer
- [ ] Not applicable

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7. Was the scientific quality of the included studies assessed and documented?
'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.

Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).

- [x] Yes
- [ ] No
- [ ] Can't answer
- [ ] Not applicable

Justification:

Study quality was assessed using the Quality Assessment Tool for Quantitative Studies(103;104) developed by the Effective Public Health Practice Project, Canada.

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8. Was the scientific quality of the included studies used appropriately in formulating conclusions?
The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.

Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.

- [x] Yes
- [ ] No
- [ ] Can't answer
- [ ] Not applicable

Justification:
GRADE was not used given the retrieval of only one study. But there was a thorough discussion on the statistics and the uncertainties around the results.

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9. Were the methods used to combine the findings of studies appropriate?
For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?).

Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.

- [ ] Yes
- [ ] No
- [ ] Can't answer
- [x] Not applicable

Justification:

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10. Was the likelihood of publication bias assessed?
An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken).

Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

Justification:

- ☐ Yes
- ☐ No
- ☐ Can't answer
- ☑ Not applicable

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11. Was the conflict of interest included?
Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.

Justification:

- ☑ Yes
- ☐ No
- ☐ Can't answer
- ☐ Not applicable

Shea *et al. BMC Medical Research Methodology* 2007 7:10 doi:10.1186/1471-2288-7-10

APPENDIX 4. QUALITY ASSESSMENT CHECKLIST FOR ECONOMIC EVALUATIONS

Study design	Nichol 2005[42] and 2009[40]	Folke 2009[39]	Walker 2003[41]	Cram 2003[38]	HIQA HTA[13]
The research question is stated	Yes	Partially	Partially	Partially	Yes
The economic importance of the research question is stated	Yes	Yes	Yes	Yes	Yes
The viewpoints of the analysis are clearly stated and justified	Yes	No	No	Yes	Yes
The rationale for choosing the alternative programmes or interventions compared is stated	Yes	Yes	Partially	Yes	Yes
The alternatives being compared are clearly described	Yes	Yes	Yes	Yes	Yes
The form of economic evaluation used is stated	Yes	Partially	Yes	Partially	Yes
The choice of form of economic evaluation is justified in relation to the questions addressed	Yes	Yes	Yes	Yes	Yes

Data collection	Nichol 2005[42] and 2009[40]	Folke 2009[39]	Walker 2003[41]	Cram 2003[38]	HIQA HTA[13]
The sources of effectiveness estimates used are stated	Yes	Yes	Yes	Yes	Yes
Details of the design and results of effectiveness study are given (if based on a single study)	Yes	Partially	Partially	Partially	Yes
Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)	NA	No	NA	Partially	Partially
The primary outcome measure(s) for the economic evaluation are clearly stated	Yes	Partially	Yes	Partially	Yes
Methods to value health states and other benefits are stated	Yes	Partially	Yes	Yes	Yes
Details of the subjects from whom evaluations were obtained are given	Yes	Yes	No	No	Yes
Productivity changes (if included) are reported separately	No	NA	NA	NA	Yes
The relevance of productivity changes to the study question is discussed	Yes	NA	NA	NA	Yes
Quantities of resources are reported separately from their unit costs	No	No	No	No	Yes
Methods for the estimation of quantities and unit costs are described	Yes	Partially	Partially	Partially	Yes
Currency and price data are recorded	Yes	Yes	Yes	Yes	Yes
Details of currency or price adjustments for inflation or currency conversion are given	Yes	Yes	Yes	Yes	Yes

Details of any model used are given	Yes	No	No	Yes	Yes
The choice of model used and the key parameters on which it is based are justified	Partially	Partially	Partially	Partially	Yes

NA = Not appropriate

Analysis and interpretation of results	Nichol 2005[42] and 2009[40]	Folke 2009[39]	Walker 2003[41]	Cram 2003[38]	HIQA HTA[13]
Time horizon of costs and benefits is stated	Yes	No	No	Yes	Yes
The discount rate(s) is stated	Yes	No	Yes	Yes	Yes
The choice of rate(s) is justified	Yes	NA	Yes	Yes	Yes
An explanation is given if costs or benefits are not discounted	NA	No	NA	NA	NA
Details of statistical tests and confidence intervals are given for stochastic data	Yes	Partially	No	No	Yes
The approach to sensitivity analysis is given	Yes	No	Partially	Partially	Yes
The choice of variables for sensitivity analysis is justified	Partially	No	No	Partially	Yes
The ranges over which the variables are varied are stated	Yes	Yes	Yes	Yes	Yes
Relevant alternatives are compared	Yes	Yes	Yes	Yes	Yes
Incremental analysis is reported	Yes	No	No	No	Yes
Major outcomes are presented in a disaggregated as well as aggregated form	Yes	No	No	No	Yes
The answer to the study question is given	Yes	Partially	Yes	Partially	Yes
Conclusion follow from the data reported	Yes	Partially	Yes	Partially	Yes
Conclusions are accompanied by the appropriate caveats	Yes	Partially	Partially	Partially	Yes

NA = Not appropriate