Rapid Literature Review on Public Access to Defibrillation

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NSW GOVERNMENT

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Executive summary

- The incidence of out of hospital cardiac arrest (OHCA) is estimated to be 49.8 OHCA events per 100,000 person years in Sydney, NSW in 2010; no updated data is available. This is because apart from the Victorian Ambulance Cardiac Arrest Registry, NSW and Australia lacks a registry on OHCA.

- Globally, survival to hospital discharge after OHCA is poor, reported to be ~ 7% and 8%. Only up to 50% of OHCA events manifest heart rhythms that may respond to defibrillation. Survival after OHCA is critically dependent on time to defibrillation with each 1 minute delay in defibrillation reducing the probability of survival to discharge by 10-12%.

- Public Access defibrillation (PAD), involves a bystander, trained first responder (e.g. firefighters, police officers) or recruited trained volunteer initiating cardiopulmonary resuscitation (CPR) and external defibrillation via an automated external defibrillator (AED) before arrival of emergency medical services (EMS). PAD has been implemented in a number of countries. There is sufficient evidence, based on population-based cohort studies that PAD result in 2 to 3-fold increased survival compared to lack of PAD; and in some series survival of up to 50-70% can be achieved.

Where should they be placed – where is placement most effective?

- The optimal location where fixed AEDs should be placed is debated. There is sufficient evidence for placement in high public traffic areas such as airports, railway stations, or sites where short defibrillation times can be guaranteed (e.g. casinos) or where access to EMS is restricted (e.g. aircraft). Evidence for placement at other public places such as exercise facilities, athletic fields, community centres, shopping centres is limited, but is heavily influenced by public opinion and media attention. A paradox in the literature is that PAD has only been tested in public spaces where only ~40% of OHCA occur; the majority occur in private places and no evaluation of PAD has been performed in this setting. Furthermore, rural and remote regions have a higher contribution to OHCA (~60- 70% of cases), longer delays to EMS access, and poorer outcomes after OHCA, but PAD has not been adequately tested in these regions. Lastly, the uptake of PAD has been historically poor (~1% access AED during OHCA, despite availability) suggesting unrecognised potential for lives saved.

Where is this considered cost-effective?

- Cost benefit analyses on optimal location for AED placement have been very limited, heterogeneous in methodology and results, mostly outdated (~7 years old), and have lacked sophistication in analyses, having failed to take into account downstream costs of OHCA survival with or without residual neurologic impairment. Analyses do support placement of AEDs in high traffic public areas, casinos and aircraft. It has been consistently argued that broad dissemination of AEDs for the sake of raw coverage is not cost effective. Instead that targeted AED placement matching country and region-specific OHCA event rates in addition to efforts of improving universal *spatial and temporal accessibility to existing, functional* AED units is likely to be more cost effective.

When linked to emergency services, when first responders are guided to AED are outcomes improved? Do such programs promote AED use in community? Cost effectiveness?

- There is sufficient evidence, based on population-based cohort studies, that dual dispatch systems (simultaneous activation of trained professional first responders such as police or fire departments alongside with EMS) shorten time to defibrillation, increase rates of successful defibrillation, survival to hospitalisation and neurologically intact survival. Further, uptake of CPR and AED by first responders, in such countries continues to increase over time. Cost effectiveness analyses of such programs is limited.

- There is very limited data on expansion of such systems to include recruitment of volunteer bystander rescuers who are guided to location of OHCA in addition to advice about co-ordinates of a nearby AED by means of novel smartphone technologies. A number of logistic concerns have been raised by such studies that employ smartphone applications. Complex mathematical algorithms to optimise AED location, use of crowdsourcing mobile applications to assist creation of AED registries and drone- delivery of AED to OHCA locations have been suggested in theoretical or pre-clinical studies. Such applications appear promising, but are unlikely to contribute to enhancement of a PAD program in the immediate future.

- In some countries where rate of bystander CPR and AED were historically low (~1%), rates have dramatically increased (~15-20%) with implementation of successful PAD programs.

What are the enablers and barriers to the use of publicly accessible defibrillators in the community?

- Components of successful PAD include aggressive public awareness campaigns, dissemination of AEDs at public places notable for high incidence of OHCA, a dual dispatch system of EMS and trained professional first responder activation (with or without engagement of trained volunteer laypersons from a registry who are activated to reach a site of OHCA), a dynamically updated registry of AEDs location and functionality, regular maintenance of AEDs, structured training, retraining and certification of responders and a development of OHCA registry with regular reporting of outcomes. In Australia, only Victoria have most components of the PAD program and have reported dramatic improvements in bystander CPR and AED use and in survival to hospital discharge after OHCA

- A number of key barriers to bystander AED use have been identified including lack of universal availability in public spaces, lack of accessibility at all hours (especially at night, when most OHCA occur), lack of public awareness of the benefit of defibrillation, lack of training on how to perform BLS or to use AED, indifferent attitude by public to perform CPR and/or AED, lack of structured EMS support to guide laypersons on how to perform CPR or AED use during an OHCA, lack of functionality of implanted AEDs at public spaces, absence of a co-ordinated system of identifying AED locations, and failure by the public to recognise signage for an AEDs. The literature suggest that these factors appear to critical priorities that need optimisation, rather than widespread dissemination of using public funding for the sake of coverage alone.

Search Methodology

A Pubmed search was performed on July 14, 2017 with the following search terms, on a unrestricted time limit:

(a) "defibrillators"[MeSH Terms] OR "defibrillators"[All Fields] OR ("automated"[All Fields] AND "external"[All Fields] AND "defibrillators"[All Fields]) OR "automated external defibrillators"[All Fields];

(b) public[All Fields] AND access[All Fields] AND ("electric countershock"[MeSH Terms] OR ("electric"[All Fields] AND "countershock"[All Fields]) OR "electric countershock"[All Fields] OR "defibrillation"[All Fields]); and

(c) dual[All Fields] AND dispatch[All Fields].

The search revealed 17,843 citations, whose abstracts were reviewed manually on line; 352 citations were selected for full length manuscript review. A further 114 citations were added from review of reference lists of these manuscripts, and 9 websites and "grey literature" documents were added giving a total of 475 citations reviewed. After review of these 475 citations, 228 manuscripts were excluded due to duplications (3), for lack of relevance to the research questions in the review (156), and reviews, editorials or letters to the editor or limited relevance to the research questions (69). The final 247 citations reviewed are provided in the attached Endnote file. A reference list cited is provided at the end of this document. A summary of major studies cited in this review in available in Table 1. A summary of health economic evaluations evaluating the cost-effectiveness of public access defibrillators is provided in Table 2. Although the review requested manuscripts published till approximately 2005, some seminal studies were published prior to this date, so no time limit for publication inclusion was applied.

Preamble

Out of hospital cardiac arrest (OHCA) is defined as sudden and unexpected pulseless condition attributable to cessation or perturbation of cardiac mechanical activity, outside of a hospital facility.[1] For the scope of this review, traumatic OHCA (e.g. motor vehicle or industrial accidents) are excluded.

Incidence of OHCA

- The global incidence of OHCA when including adults and children is 35 per 100,000 person years; the incidence is 62 per 100,000 person years when restricted to adults alone.[2] In Sydney, Australia, the crude incidence of OHCA in 2009-2010 is 49.8 OHCA events per 100,000 person years (similar age-adjusted incidence).[3] In Victoria, the unadjusted state-wide incidence of OHCA in 2015-2016 was 99.2 events per 100,000 population, being higher in the rural (128.6) compared with metropolitan centres (89.7 events per 100,000 population).[4]

- OHCA affects more than 350,000 individuals in North America and 300,000 individuals in Europe.[5, 6]
- There is absence of systematic literature on incidence of OHCA across all populations in Australia; notably there is absence of a nationwide registry on OHCA in Australia, apart from data collected in the Victorian Ambulance Cardiac Arrest Registry.[4]
- Amongst young adults (aged 1-35 years) in Australia, the incidence of sudden cardiac arrest is 1.3 cases per 100,000 person years, when evaluated from autopsy studies.[7] Similar rates are reported from England and Wales (1.8 per 100,000 person years based on death certificates),[8] but higher from Denmark (2.8 per 100, 0000 person; 1.9/100,000 person years when considering autopsy cases only).[9]

Aetiology of OHCA

- The aetiology of OHCA is either: (a) malignant ventricular arrhythmia (ventricular tachycardia [VT] or fibrillation [VF]) leading to hemodynamic collapse or (b) pulseless electrical activity (electromechanical dissociation) where there is hemodynamic collapse despite near normal electrical activity or (c) asystole (absence of electrical or mechanical activity).[10]
- Cardiac defibrillation (external shock) will only revert VT or VF, not pulseless electrical activity or asystole. A shockable rhythm (VT or VF) is detected in ~25-50% of persons with OHCA; a percentage which has declined over the last 20 years.[11-17] This may be in part, due to success of internal cardiac defibrillators in preventing OHCA in at risk individuals.[16]
- The literature recognises that a greater proportion of OHCA cases may have VT or VF at the time of collapse, but by the time the rhythm is detected via an electrocardiogram, the rhythm may have deteriorated to asystole.[18, 19] When recorded soon after collapse, the proportion of OHCA with a shockable rhythm may be as high as 76%.[20, 21] It is thus plausible that the estimated proportion of OHCA with a shockable rhythm is underestimated in the literature.
- Despite advances in treatment and improved organisation of services targeting OHCA, it appears international survival rates to discharge from hospital after OHCA have remained relatively consistent at between 7% and 8% for the last 30 years.[22] In Australia, data from the Victorian Ambulance Cardiac Arrest Registry showed that survival to hospital discharge was 13%.[23] There has been minimal change over time (when comparing 2015- 2016 to 2006-2007).[4] Survival to hospital discharge was higher in metropolitan areas (11%) than rural areas (9%) of Victoria, Australia.[4] However, when resuscitation attempts are successful and patients survive to hospital discharge and beyond 12 months post OHCA, their quality of life is comparable to population norms, suggesting that an aggressive approach is worthwhile.[23]

Role of Resuscitation in OHCA

A detailed review of principles of resuscitation in OHCA is available elsewhere.[18, 24]

- For the purpose of this review, principles of OHCA are underpinned by the concept of a "chain of survival" which comprises: (a) early access to emergency medical services (EMS); (b) prompt bystander cardiopulmonary resuscitation (CPR) providing basic life support (BLS); (c) prompt defibrillation using automated external defibrillator (AED); and (d) advanced life support.[18, 24]
- CPR and defibrillation can be provided by layperson bystanders, dispatched professional first person responders (e.g. police force, firefighters) or EMS personnel from the ambulance service.
- Bystander CPR improves survival to hospital discharge in persons with OHCA 3-4 fold, from 3.9% to 16.1%, based on a large systematic review from 79 studies involving 142,740 patients.[22]
- Prompt defibrillation within 3-5 minutes of collapse can lead to rates of survival to hospital discharge after OHCA as high as 50-70%.[15, 21, 25, 26]

- Each 1-minute delay in defibrillation reduces the probably of survival to discharge by 10- 12%. When bystander CPR is provided, the decline in survival is more gradual and averages 3–4% per minute delay to defibrillation, indicating the critical link between CPR and defibrillation in the "chain of survival".[19, 27-29]

- Median time from emergency call to EMS arrival is reported to be 5–8 min,[20, 30, 31] or 8– 11 min to a first shock.[15, 32] In Australia, the Australian Resuscitation Council reports that the median emergency-response time by ambulance services throughout Australia was between 7.5 minutes and 10 minutes.[33] In Victoria, Australia, the median state-wide response time to EMS treated events in 2015-2016 was 7.8 minutes (90th percentile time, 15.4 minutes), being longer in rural areas compared with the metropolitan region (median 9.9 minutes; 90th percentile time 21.4 minutes vs. median 7.4 minutes, 90th percentile 12.5 minutes).[4]

- About half of the variability in both, overall survival and survival with meaningful functional recovery after OHCA is attributed to variations in the rates of bystander CPR and AED use.[34] Hence, response of a layperson bystander with CPR and AED has a critical influence on survival.

Research Question 1: Evidence for Public Access Defibrillation.

Where they should be placed, where are they placed most effectively and where is this considered cost effective?

Summary and Recommendations

- *Guidelines in Europe and the U.S. support implementation of PAD programs and we found sufficient strength of evidence that PAD programs markedly improve survival to hospital discharge of OHCA (e.g. with government implemented program in U.S and Japan).*

- *PAD programs function best when incorporating dual dispatch EMS, strategic placement of AEDs, and a system of education and training of first responders (lay or professional first responders).*

- *The evidence supports AED placement in areas where response time of a bystander could potentially be guaranteed such as a casino, or at sites where EMS are not easily available or impractical such as airports and airplanes. We also found sufficient evidence to recommend that AEDs should be placed in high traffic public areas such as train stations, pedestrianised areas, shopping malls, sports stadiums. There was insufficient evidence to support AED placement at other public sites such as community centres, fitness facilities, stadiums, athletic fields, parks. Widespread dissemination of AEDs beyond the above sites hence cannot be recommended on current evidence.*

- *Cost effectiveness analyses also support AED placement in the sites listed above. There is no cost-effectiveness evidence to support widespread dissemination of AEDs and it is likely that wider dissemination is less cost-effective. Matching location of AED to sites of OHCA specific to a city/state will likely yield optimal placement.*

Since the mid 1990's, Public Access Defibrillation (PAD) programs have emerged.

- PAD is the process of where a bystander and/or trained professional (e.g. firefighters, police officers) or non-professional first responder initiates CPR and AED before EMS arrival in a person experiencing OHCA.[35] The program may have various elements, determined by the extent of Government initiatives, funding and policies but may include: structured training of laypersons, volunteers and professional first responders, a registry of AEDs and/or volunteer laypersons, dissemination of AEDs at places notable for high incidence of OHCA, a dual dispatch system of EMS and trained professional first responder activation with or without engagement of volunteer laypersons activated to site of OHCA with or without central instructions on where to locate an AED and how to perform CPR, maintenance of AEDs, structured retraining and certification and development and maintenance of a OHCA registry with regular reporting of outcomes.

- PAD programs are recommended by the 2015 guidelines from the American Heart Association and the European Resuscitation Council.[18, 36] Several countries have an established PAD including Japan, Austria, Denmark, Sweden, England and Wales, and in some counties or states in the United States of America.[37-42] On review of the published literature, most of these countries describe a form of dual dispatch program where trained professional first responders are activated simultaneously with ambulance which are AED equipped (Table 1). Formal government funded training of layperson bystander CPR and AEDs are offered in many of these countries and AED placement is encouraged in high public traffic areas, but are not mandated.

- In Victoria, Australia, a co-ordinated PAD is described.43 In response to OHCA, EMS equipped with AED and advanced life support paramedics is dispatched; in addition, some areas have a system of dual dispatch of firefighters and/or community emergency response teams trained in BLS and equipped with AEDs at the same time as EMS dispatch. Since 2002, AEDs have been placed at sites identified to have high incidence of OHCA, based on review of historical data including railway stations, the international airport, the casino and major tourist venues. OHCA rates and locations continue to be tracked and reported as part of the "Heart Maps" program,[44] and the Ambulance Victoria Ambulance Cardiac Arrest Registry.[4] The PAD programme supplies and installs AEDs (including maintenance), provided training of selected staff (such as security personnel), annual skills maintenance, clinical debriefing after an event and bimonthly peer support visits from an Ambulance Victoria paramedic. At airports and large shopping complexes in the capital city, AEDs are available for use by the public. At some public sites, volunteer first-aid agencies have AEDSs available for public use at selected workplaces, smaller shopping centres and sporting grounds around Victoria. An active effort has been made to create and maintain an AED registry via an "opt in" approach.[45] The locations of registered AEDs is identified in the computer aided dispatch system such that if a OHCA call is received from a site with a registered AED, the call-taker notifies the caller of the location of the AED and provides telephone instructions on its use.[43]

- There is strong evidence of markedly improved survival from PAD (Table 1). PAD has been reported to yield survival to hospital discharge rates of 50-70%, which are much higher than first-responder defibrillation and dispatched EMS defibrillation.[15, 17, 21, 26, 46, 47] On site AED, compared to dispatched AED confers a 2.5-fold increase in survival.[48, 49]

- There are numerous reports indicating improvement in survival after co-ordinated efforts at enhancing PAD in the USA; in one report, survival to hospital discharge increased from 8.2% to 10.4% from 2006-2010,[50] which was confirmed by reports from other groups in the USA.[15, 51-53] Similarly in Japan, neurologically intact survival at 1 month doubled with PAD (38.5%) compared to pre-PAD programme implementation (18.2%).[41] In Denmark, 30 day survival increased from 3.5% to 10.8% with PAD programs.[32] In the United Kingdom (UK), survival from OHCA improved from 12% to 32%.[30]

- Use of bystander CPR and PAD is associated with a 2-3 fold increase in survival after OHCA. [15, 20, 21 54, 55.40, 41]In a recently published meta-analysis of PAD, the overall survival to hospital discharge after OHCA treated with PAD was 40.0% (range 9.1- 83.3%). Defibrillation by non-dispatched lay first responders was associated with the highest survival with a median of 53.0% (range 26.0-72.0) while defibrillation by EMS- dispatched professional first responders (firefighters/police) was lower, with a median survival of 28.6% (range 9.0-76.0).[25]

- A program of nationwide dissemination of PAD, most successfully implemented in countries like Japan have reported earlier time to shock, overall survival and neurologically intact survival. [15, 21, 40, 41] In a large nationwide population based registry study in Japan of out of hospital cardiac arrests (n=43,762 patients), significant benefit was noted from PAD, compared to lack of PAD. Over a 9-year period (2005-2013), survival at 1 month with a favourable neurologic outcome using propensity-score matching was 2-fold higher with PAD than without PAD. Furthermore, there was a 33- fold increase in the number of survivors with a favourable neurologic outcome (from 6 in 2005 to 201 in 2013). However, the proportion receiving PAD was small (10.3% of all cardiac arrest), but did increase 16-fold during the study period (from 1.1% to 16.5%).[41] Bystander defibrillation, compared to EMS-only defibrillation translated to approximately 2-fold increase in neurologically intact survival.[56]

- There is sufficient evidence to indicate that bystander CPR and defibrillation uptake in the community is increasing in countries such as Japan (from 1.1% to 16.5% from 2005- 2013[41]) and the USA (from 14.1% to 23.1% from 2010-2013 in the CARES registry[53]). In Victoria, Australia, there was a 11-fold increase in public AED use from 2002/2003 to 2012/2013 from 1.7% to 18.5%.[43] With a dual dispatch system of firefighters and EMS capable of defibrillation in Sweden, the proportion of OHCA persons defibrillated before EMS arrival increased from 5% in 2008 to 20% in 2015.[49]

- Professional first responder defibrillation (e.g. by police force) is associated with superior outcomes compared to EMS-guided defibrillation. In Switzerland, professional first responder defibrillation led to improvement in median of 5 minutes for initiation of CPR, a median 3-minute improvement in time to first defibrillation, a 1.8-fold improvement in proportion of patients with return of spontaneous circulation, a 1.7-fold increase in successful field resuscitation and subsequent admission to hospital, and a 2.1-fold increase in survival to hospital discharge.[57]
- Overall, strong evidence emerges in the literature that survival and neurological survival are markedly better with bystander CPR and defibrillation, followed by first-responder CPR and defibrillation, and lowest for when dispatched EMS-delivered defibrillation.[53] These outcomes are critically linked to time to successful defibrillation with delays correlating with lower likelihood of survival. Indeed, data from Ambulance Victoria in 2015-2016 supports this, showing survival to hospital discharge after OHCA when the person was defibrillated by the public was 55%, 38% when defibrillated by professional first responders and 28% when defibrillated by EMS.[4]
- The benefit of PAD in adult populations is transferrable to the paediatric population (aged less than 17 years).[58] PAD resulted in a 3-fold increase in neurologically intact survival, however neurologically favourable survival could not be seen in patients with an unwitnessed cardiac arrest or arrest due to a non-cardiac cause.[58]

Public Access Defibrillation: Evidence behind where they should be placed

There is much debate in the literature about where AEDs should be placed namely whether there should be widespread dissemination of AEDs versus restricted placement at sites considered to be high risk venues for OHCA. A number of recent studies have focused on development of novel smart-phone applications to recruit layperson responders for CPR and defibrillation.[59] There is recent interest in modelling drone technologies to facilitate rapid delivery of AED at sites of OHCA.[60] A number of studies have used complex mathematical modelling techniques taking into account historical data of OHCA coupled with location and availability of registered AEDs.[61-63]

- The American Heart Association (AHA) recommends that AEDs be placed in areas of high population density, such as airplanes, airports, sports arenas, gated communities, office complexes, physician offices, and shopping malls.[64, 65] Calculations based on historical data of the location of OHCA have been used to give recommendations for sites of AED installation. The AHA recommends installation at sites that experience OHCA once every 5 years and the European Resuscitation Council at sites of OHCA once every 2 years.[66, 67]
- There is evidence to support that AED placement should occur in places where response time of a bystander could potentially be guaranteed such as a casino, or at sites where EMS are not easily available or impractical such as airports and airplanes, respectively.[26, 68, 69] The evidence for AED placement at other public sites such as community centres, fitness facilities, stadiums, athletic fields, parks is limited. In the PAD trial, rates of OHCA that were treatable with defibrillation were highest in fitness centres (5.1 per 1,000 person years of exposure) and golf courses (4.8) and lowest in office complexes (0.7) and hotels (0.7). Survival from treatable CA was highest in recreational complexes (0.5), public transportation sites (0.4), and fitness centres (0.4) and lowest in office complexes (0.1) and residential facilities (0.0).[70] The frequency of OHCA in public places was estimated in a study from Copenhagen, Denmark with the highest in major train stations (1.8 arrests every 5 years per area), large public square and pedestrianized areas (0.6 arrests every 5 years per area), whereas high schools (0.18) and primary schools were the lowest (0.09).[71] Data from the New South Wales Ambulance Service in 2012 shows that the majority of calls that were classified as 'cardiac or respiratory arrest or death' came from residential areas (69%), and only 6% came from a public or community area.[72] Similarly, data from Ambulance Victoria showed that most EMS attended OHCA events in 2015-2016 were at private residences (76%) with 14% of events occurring in a public place.[45] There has been a notable lack of concerted efforts to address

OHCA in fitness centres in Australia.[73]

- In casinos, where there is widespread camera surveillance and every person is monitored by a security guard, use of AEDs led to 53% survival to hospital discharge, and as high as 74% if the time from collapse to shock was <3 minutes. [26]
- In aircraft, survival rates to hospital discharge in OHCA persons who had a witnessed arrest with a shockable rhythm were 26-40%%.[68, 69] The argument for AED placement in aircraft is strengthened by the fact that the length of time it takes to divert a plane and obtain ground access to defibrillation is likely to yield very poor survival.
- In airports, where there is thoroughfare of a large number of public, a high rate of neurologically intact survival to hospital discharge with defibrillation is reported (61%); this increased to 75% if the time elapsed from collapse to defibrillation is <5 minutes.[74] When AEDs are available for public access in airports, their use was associated with significantly shorter time to defibrillation, longer duration of resuscitation and survival to hospital admission compared with group-dispatched AEDs where defibrillation was performed only by paramedics.[48]
- Application of PAD program in a busy metropolitan subway system in Brazil transporting ~4.5 million people per day was reported in a recent study. The program involved training their security officer employees (laypersons) in CPR and use of AED; additionally, AEDs were installed at each subway station. Survival to discharge amongst OHCA with a shockable rhythm was significantly higher (43%) once the program was fully functional compared to initial phase of program introduction (0%).[75]
- OHCA in schools is estimated to occur in 1 of 111 schools annually, with a higher incidence in colleges (1 per 8 colleges) than high schools (1 per 125) and primary schools (1 per 200). The estimated annual incidence of cardiac arrest was 0.18 per 100,000 person-years among students and 4.51 per 100,000 person-years for school faculty and staff.[76]
- A small number of observational, non-controlled studies with a small number of cases of sudden cardiac arrest, show that AED installation in schools and colleges was associated with increased hospital survival.[77-80] Survival rate in schools with an AED program varies from 64-72% if a shockable rhythm is noted.[76, 77, 79, 81] Despite this data, only 17 of 50 states (34%) in the USA have legislation for installation of AED in schools; the remaining states have no legislation. It was noted that requirements are far from comprehensive in these 17 states, and it was estimated that 35 million public elementary and secondary students attend school in states where there is no legislative requirement for a school AED.[82]
- There is limited data on the outcomes of OHCA occurring during exercise in the era of PAD[83-85] In one study from the USA, the incidence of OHCA at health clubs and traditional fitness centres was 0.024 arrests/site each year or 1 arrest every 42 years. The rate was higher rate at indoor tennis facilities, ice arenas, bowling alleys and community centres than at traditional exercise facilities, with one arrest every 11, 13, 27 and 51 years/site, respectively.[85] In Japan, 0.3-0.7% of all OHCAs occurred during exercise.[83, 84] The reported survival rates are high (56-77%),[83-85] and are higher with than without PAD (77% versus 35% in one study).[84]
- There is evidence for efficacy of PAD at public places, when stratified by location. In a large Japanese cohort study, the proportion of neurologically favourable outcome was 28.0% at railway stations, 51.6% at sports facilities, 23.3% in public buildings, and 41.9% in schools. However, early defibrillation, irrespective of bystander or EMS was associated with neurologically favourable outcome, such that each 1-minute increment was associate with a 11% lower chance of a neurologically favourable outcome. [86]

Cost effectiveness analyses for Public Access Defibrillation

- OHCA draws significant media and fund-raising attention. In 2010 alone an estimated 200,000 AEDs were sold and the market was expected to double every 2 years.[87] The cost of each unit is estimated to be $USD2,000[65] which equates to $200 million expenditure in USA alone in 1 year. This would account for only 13.5% of the costs of running a PAD program, and does not taken into repair, maintenance and replacement costs of the AED as well as expenses related to training and re-training of laypersons and first-responders.[88]
- There are a number of significant limitations in cost-effectiveness analyses (see Table 2):

(a) the number of published studies are very few (7 manuscripts, representing 2.9% of references cited in this review) and with the exception of one manuscript (published in 2015), most were published in or before 2010;

(b) there was significant heterogeneity in the analysis methods with a high degree of variability in the results;

(c) a common finding was the lack of sophistication in the cost-effective analyses. The analyses did not account for all downstream costs associated with OHCA including equipment and hospitalisation costs following defibrillation, the residual quality of life of the survivor in addition to their residual social and economic productivity, neurologic damage of survivors, and further reliance on health care resources.[89]

(d) whilst there has been cost-effective analysis of AED placement at various locations, apart from two studies, there has been a lack of systematic evaluation of the cost-effectiveness of a PAD programmes.[90, 91]

- A clear message in the literature is that broad dissemination of AEDs for the sake of raw coverage is not cost effective. Instead, targeted AED placement matching country and region-specific OHCA event rates in addition to efforts of improving accessibility of existing AED units is likely to be more cost effective. [20, 35, 62, 92, 93] Furthermore, different approaches are needed for public versus private coverage and metropolitan versus rural area coverage. Cost effectiveness data supports placement of AEDs in public places, especially if the location can be optimised.[89, 94]
- There are increasing reports in the literature that complex modelling frameworks may be necessary to help identify priority places for deploying AEDs based on transportation time to the nearest hospital and population size of the communities.[95] Complex mathematical optimization techniques can augment planning of public AED deployment programs.[61, 62] One such example is modelling using spatiotemporal localisation, where factors such as location and actual availability during the day are taken into account to improve the coverage of AEDs, rather than increased the number of publicly accessible AEDs per se.[63]
- Although PAD programs have demonstrated a significant survival benefit, the benefit is limited to those who have an OHCA in a public setting. There are a number important considerations when considering whether AED should be in public places:

  (a) only 16-40% of all OHCA occur in public places, the rest occur in private homes; 96

  (b) there are fundamental differences in patients who experience OHCA at public versus public places. Persons experiencing OHCA at home are older, more likely to encounter a bystander not trained in CPR, and less likely to perform it even when trained, were more likely to arrest at night.[92, 97] The odds of a shockable rhythm were 2-fold higher and the odds of survival 2.5-fold higher in a public setting than at home.[96] These characteristics suggest that fundamentally different strategies are needed in addressing OHCA in public versus private places.[97] Only one prior study has examined private home AED use, showing no benefit from AED use, but the population recruited (survivors of anterior myocardial infarction who were not eligible for a defibrillator) were very high risk.[98] No prior study has examined a PAD programme unique to OHCA occurring in private homes.

  (c) most of the data examining location of OHCA focus on urban areas, however urban areas contributed only up to 31% of the total number of OHCA cases, with the remainder occur in less populated areas.[99] In Australia there were significant regional and inter-hospital disparities in OHCA survival rates.[100] Survival of OHCA is lower in rural than metropolitan communities.[45] Such findings were also reported in the United States with substantial proportion of the variation in outcomes from different counties that was explained by variability in bystander use of CPR and AEDs.[34]

(d) there is a notably poor correlation reported between location of OHCA and location of AEDs.[101, 102] In one study, one in 5 OHCAs occurred near an inaccessible AED at the time of the OHCA.[63] In only a minority (6.6%) of

OHCA cases, was an AED location within 100 m.[103] A study from the Swedish Register for Cardiopulmonary Resuscitation showed that whilst the incidence of OHCA was similar in residential (47%) and non-residential settings (43%), much fewer AEDs were present in residential settings (28% vs. 69%), and the median distance between OHCA location and the AED was larger in residential settings (288 m vs. 188 m).[104] Recent attempts have focused on identifying optimal AED locations based on the incidence of OHCA using geographical information systems.[104]

(e) the uptake of lay-person bystander defibrillation is low (<1% to 2.3%) and is significantly varied according to country.[10, 105] The Pan Asian Resuscitation Outcomes Study (PAROS), a registry of 7 Asian countries reviewed 66,780 OHCA cases and found that <1.0% of these arrests received bystander defibrillation.[105] However it is reported that the percentage of patients receiving PAD in some countries is increasing.[32, 41, 43, 49, 52, 53] In Australia, data from the Victorian Ambulance Cardiac Arrest Registry showed significant improvement in rates of bystander CPR and defibrillation (almost 3-fold increase), event survival (1.5 fold increase), and survival to hospital discharge (2.8-fold increase) between 2011 to 2012 compared with 2001-2010.[100] Use of public AEDs increased almost 11-fold between 2002/2003 and 2012/2013, from 1.7% to 18.5%, respectively.[43] In Japan, use of PAD increased from 1.1% in 2005 to 16.5% in 2013.[41], from 5% in 2008 to 20% in 2015 in Sweden [49], from 1.1% in 2001 to 2.2% in 2010 in Denmark[32], and from Proportion of PAD increased from 0.82% in 1999 to 2.05% in 2002 in the United States.[51]

- When AEDs are placed at high density sites such as airports, large aircrafts and casinos, the cost effective analysis equates to an average cost of USD$30,000-$50,000 per year of life saved.35, [106, 107] This falls in the cost-effective range of other medical interventions that are considered useful.[89]
- In aircraft, AEDs equate to USD$35,000 per life year when >200 passengers are carried and increases to USD$94,700 when all aircrafts are covered.[35, 107]
- When targeting large public spaces such as shopping centres and ports venues, the cost per life saved is much higher: USD$500,000 to USD$2 million; at large industrial sites, golf courses, health clubs, and community centres the cost is from $USD1 million up to USD$10 million.[35] However placement at the latter sites draws the most media and fund raising attention and it is noted, that it may raise awareness of AEDs in the community.[35, 106]
- In a cost-effectiveness analysis from Ireland, authors found widespread dissemination of static AEDs is unlikely to be cost effective, but needed to be at targeted locations with the highest incidence of OHCA, be supported by efforts to increase AED utilisation in addition to linkage with an EMS-linked AED register.[108] The incremental cost effectiveness ratio for the most comprehensive PAD scheme (universal coverage) was Euro 928,450 per quality-adjusted life year, whereas it was 10 fold lower at Euro 95,640 per quality-adjusted life year if a targeted programme involving AED placement in transport stations, medical practices, entertainment venues, schools and fitness facilities was employed.[108]
- In a cost-effective analysis from Copenhagen Denmark, targeted deployment of AEDs according to the location of a cardiac arrest resulted in USD $33,100 to $41,000 per additional quality-adjusted life year, whereas unguided AED placement in every 100 by 100 metre area in the entire city (which would cover all OHCA), had an estimated cost of USD $108,700 per quality-adjusted life year.[71]
- In a cost-effectiveness study from Brecia county, Italy, the authors calculated that a program of training volunteer and layperson use of AEDs compared to a historical cohort of predominantly EMS-delivered defibrillation became more cost-effective over time parallel with the success of the program. The quality-adjusted life year saved amounted to Euro 39 388 during the start-up phase of such a program and to Euro 23 661 at steady state.[90]
- In a Canadian study, indiscriminate dissemination of static AEDs was found not to be a cost-effective means of outcomes following OHCA. In Canadian dollars, the cost per quality-adjusted life year was $12,768 when AEDs were deployed in hospitals, $511,766 when deployed in office buildings, $87,569 when deployed in homes of high-risk patients but increased sharply to $2,360,023 when deployed in an unrestricted

manner to apartment buildings.[109]

- When taken together the fact that a minority of arrests occur in public places, that bystander AED rates are low in some countries, that only 40% of OHCA are reversible due to a shockable rhythm and that overall survival rates are low, one group of Scottish researchers estimated that even if AEDs were installation in sites as ubiquitous as fire extinguishers, overall survival would increase only from 5% to 6.5%[110]
- Despite the success of PADs and widespread dissemination of AEDs, there is limited appreciation of the fact that it is difficult to determine whether these devices are maintained in a state of readiness for use or whether they functioned as intended when applied to someone in presumed cardiac arrest. Some recent efforts are focused on tracking their location and readiness for use in community settings, using a tracking system. Each AED is assigned a 2D matrix code which is then recorded and the location and status of the AED tracked using a smartphone; these elements are automatically passed via the internet to a secure and confidential database in real time, which could be linked a centralised dispatch service for OHCA. The project is only in the planning phase with no outcome data reported.[111]

Research Question 2: Outcomes and cost-effectiveness OHCA programs that involve AED registries and recruitment of first responders (professional and/or bystander).

i. When linked to a call to emergency services and responders are alerted and guided to an AED to assist, are survival outcomes improved?

ii. Do such programs promote or reduce AED use in the community?

iii. What is the cost-effectiveness or cost-utility of such programs?

iv. What is the health service context for such programs eg are emergency medical services equipped with AEDs?

Summary and Recommendations

- *The evidence supports that when PAD programs are implemented they include a dual dispatch system of EMS (equipped with AEDs) and professional trained first responders (e.g. police officers and fire fighters) as this leads to improved survival to hospital discharge in persons with OHCA.*
- *There is a paucity of information on AED registries, but such a registry, especially when integrated into a registry of lay person trained first responders and a communication system to alert bystanders of the location of a OHCA and the location of an AED could have a significant impact on OHCA survival rates.*
- *There is no cost effectiveness data on AED or first responder registries.*
- There is paucity of AED registries globally and in Australia. Reporting of AEDs is not mandatory in all countries, but is encouraged. Novel technology aimed at tracking AED location through time and space is proposed, but only a protocol has been reported with no outcome data reported thus far.[111] A crowdsourcing exercise to enable creation of a registry of AED location has shown promising initial results.[112]
- There is significant amount of literature on the use of dual dispatch systems (where trained professional first responders such as police and fire personnel and EMS are activated simultaneously) and more recently, some studies have used crowdsourcing to increase the number of community layperson responders to OHCA.[13, 14, 49, 59, 91, 113-119] Reports show increase in survival with a dual dispatch system, and an increase in the uptake of bystander and/or first responder CPR and defibrillation with such systems being implemented.[49, 115-117]
- It is unclear if such dual dispatch or crowdsourcing activities increase the awareness of AEDs in the community as there was no specific study answering this question. One study reported a pilot program “MyHeartMap Challenge”, to organize public reporting of AED location throughout Philadelphia, a major US metropolitan city. Public were encouraged to use mobile phones to identify and report AED locations. A total of 1429 AEDs were identified by members of the public in almost all postcodes. The authors propose that such a program would be useful for creating an initial baseline database of AEDs at a particular time point, which could serve as a foundation for a data repository, which

could then be routinely validated and maintained over time, and perhaps linked to an EMS or dual dispatch or voluntary layperson register.[112]

- When dual dispatch systems are reported in a study, all such systems have EMS that are equipped with AEDs (Table 1).
- A crowdsourcing mobile device application, "Pulse Point" notifies laypersons within 400 metres of a suspected cardiac arrest to facilitate resuscitation. One study reported major logistical challenges with the application.[120] Only 32% of users received the notification, only 23% responded; of those who responded 28% did not arrive at the scene. Of those who did arrive, only 32% found a person who was unconscious and not breathing normally. However, of those who did arrive and found the person suffering an OHCA, 79% performed CPR.[120] Limitations of this report were that AED use was not incorporated, however most recent review of the Pulse Point website does incorporate guidance to the responder of the location of the nearest AED.[114] Issues identified with this application were technical aspects of the notifications (audio volume, precision of location information), excessive activation radii, insufficient user density in the community, and suboptimal cardiac arrest notification specificity.[120] Outcome data from this application has not been reported.
- In Stockholm, Sweden, investigators recently reported the utility of a mobile-phone system that was activated to locate trained volunteers who were within 500 metres of patients with OHCA at the same time as activation of ambulance, fire, and police services. If needed, telephone instructions were given on how to perform CPR. Responders were then dispatched to the patients (the intervention group) or not dispatched to them (the control group). The study showed increased in CPR rates to 62% with responder dispatch compared to 48% without responder dispatch.[113] The extent of benefit was low, and the study did not target AED application, where the major survival benefit is expected to occur.
- There are a number of positive reports of increased survival after implementation of a dual dispatch system in Sweden.[49, 115-117] In the most recent of these reports, a system of dual dispatch of professional first responders alongside EMS (police, firefighters) was implemented from 2008. The system resulted in significant increase in proportion of patients defibrillated before EMS arrival (5% in 2008 to 20% in 2015). When comparing OHCA defibrillated before EMS, versus those defibrillated with EMS, there was a 3-minute improvement in time to defibrillation and an improvement in 30- day survival in patients with VF from 22% to 28%. On site defibrillation was associated with a 2.5-fold increase in 30-day survival compared to dispatched defibrillation.[49] Similarly in the USA, a dual dispatched system of police force with AEDs along with EMS, compared to EMS alone resulted in shortening of call to arrival times by 1.5 minutes, and improved survival to 17% from 9%.[121]
- There may be difference in efficacy of dual dispatch systems according to the population density of the region where the system is applied. Whilst city areas (population density ≥6000 people/Km2), suburban areas (3000-5999 people/km2) and urban areas (250-2999 people/Km2) experience a survival benefit with a dual dispatch system of EMS plus professional first responders, such a system did not provide a benefit in rural areas (<250 persons/Km2).[117]
- In the Netherlands, dispatching local lay rescuers living <1000m radius of the patient suffering OHCA received a text message to go to the patient directly, or were directed to retrieve an AED first. This system resulted in OHCA persons being defibrillated at a mean of 2 minutes and 39 seconds earlier compared to EMS.[59] However, there are limitation of this system; one study reported that only 18% of alerts initiated an action from the registered layperson. Reasons for no action were that laypersons were not in the patient's vicinity (41%) or noticed alerts late (35%). When alerts initiated a layperson action, 51% logged difficulties in retrieving AEDs (51%), finding addresses (29%), or were prohibited by traffic (5%) in reaching the location and/or accessing the AED.[59]
- A report from a mixed urban and rural area in North-western Switzerland showed that dual dispatch, compared to EMS alone showed a significant 6-minute reduction in reaching the site of OHCA with first responder reaching before EMS in 87% of instances. A comparative evaluation of survival was not performed.[118]
- In Zurich, Switzerland, a dual dispatch system of police force trained in BLS and AED activated

simultaneously with EMS was reported. Compared to EMS only approach prior to system implantation, CPR was started 3 minutes earlier and defibrillation delivered 6 minutes earlier. Outcomes were significantly better with a dual dispatch system including ~2-fold increase in incidence of return of spontaneous circulation, hospital admission and survival to hospital discharge.[57]

- In Rochester, Minnesota, United states, a system which dispatches AED-equipped police, fire-rescue and ambulance personnel simultaneously reported rate of survival to hospital discharge after OHCA of 46% survival in persons where the initial rhythm was VF.[14]
- Only one study has examined the cost effectiveness of a dual dispatch system.[91] The estimated number of additional saved lives was 16 per year, yielding a benefit-cost ratio of 36. The cost per quality-adjusted life years Euro 13,000, and the cost per saved life was Euro 60,000, concluding that the cost-effectiveness per quality of life year was modest.[91]
- In the only randomised trial of dual dispatch responses (police or fire brigade trained in CPR and AED use) versus EMS only attendance, time to first defibrillation was a median of 101 seconds earlier with dual dispatch response vs. EMS only response.[31] However, there was limited improvement in return of spontaneous circulation (57% vs. 48%) and no difference in discharge from hospital (18% vs. 15%).[31]
- Following state-wide initiatives to improve bystander and first-responder efforts in North Carolina from 2010-2013, the rates of bystander CPR and first-responder defibrillation increased from 14.1% to 23.1% over the study period, as did survival with favourable neurological outcome from 7.1% to 9.7%.[53]

Research Question 3: What are the enablers and barriers to the use of publicly accessible defibrillators in the community?

Summary and Recommendations

- *Enablers include implementation of a formal PAD program which includes training of professional first responders.*
- *Possible enablers are include raising public awareness, public education program, a focus on education of first responders including laypersons (bystanders) and improving access by improving awareness of the location of AEDs and ensuring the AED's functionality.*
- *A registry of AED locations and system for ensuring functional would be an initial logical step.*
- *Registries that enable audit of outcomes are likely to ensure safety and improved outcomes.*
- There are many potential barriers to bystander AED use, including availability, legal liability, awareness, training, technological limitations, and psychological factors. [71, 74, 122- 125]
- Although the success of PAD is noted in many studies, the rate of layperson use of AED remained low (0.6% in Netherlands,[21] 1.74% in Hamphsire, UK,[126], 2.1% with PAD trial in the USA,20 3.5% in Japan [127], 3.8% in Ireland[128], 2.2% in Denmark32), despite the fact that outcomes are much better when PAD is utilised.[127] In Australia, the Victorian Ambulance Cardiac Arrest Registry reported public use of AEDs at 6.7% of all OHCA cases.[43] Thus although favourable outcomes of PAD are demonstrated, utilisation of available equipment is vastly suboptimal. Further one study reported that only 15.1% of all OHCA occurred 100 metres of an accessible AED.[128] This suggests that education, awareness, and training are likely more important than widespread dissemination of public-access AEDs.[127]
- Although barriers to AED use are noted, reports suggest that training can be easily accomplished with good results. Training professional first responders such as police officers to operate AEDs can be achievable with minimal hours of training (3-4 hours), and additionally improves BLS skills.[129] Despite minimal hours of upfront training (4 hours in one study), these trained first responders can significantly shorten response time and time to defibrillation.[118] When layperson

first responders are trained in CPR and AED use, data from the PAD trial showed that the approach is safe with a very low rate of adverse patient events or volunteer events. Only 2 patients experienced adverse event of a rib fracture; 7 volunteers had adverse events (one had a muscle pull, four experienced significant emotional distress and two reported pressure by their employee to participate). Importantly, there were no inappropriate shocks and no failure to shock when shock was indicated by the AED.[130] Furthermore, trained laypersons tend to retain their skills for CPR (80% at 1 year) and AED use (90% at 1 year).[131] Minimal re-training (~10 minutes) may be necessary over time to allow laypersons to retain skills.[132]Successful training also seems to correspond to successful on-field performance by trained professional first responders.[133]

- Even when AEDs are installed, functionality is not universal when tested. In a study from the Netherlands, authors noted that 40% of the AEDs were not visible (range 21-64), 29% were not indicated with a sign (range 19-41), 7% had an empty battery (range 0-23), 16% of the defibrillator pads had expired (range 0-31). Overall 71% of the AEDs were available for use (range 61-93), 70% were in a good condition (range 46-82) and 70% were employable (range 58-93).[134] This suggest that significant investment is needed to maintain appropriate AED action.
- Effective signage has been recognised as barrier to more widespread use of AEDs in public spaces. Lack of recognition of the symbol of AED is a potential problem, even when universal sign endorsed by the International Liaison Committee on Resuscitation is used.[135] Public consultation in conjunction with expert designer has been identified as one possible solution to promote recognition of a public AED location.[136] Crowdsourcing could be used in an attempt promote awareness about AEDs and their locations.[137]
- A number of facilitating factors that led to bystander CPR and AEDs were identified by semi-structured qualitative interviews with CPR-trained lay bystanders in Denmark.1[38] These included: prior knowledge that intervention is crucial in improving survival, that it cannot cause substantial harm, and that the AED will provide guidance through CPR. Other factors were prior hands-on training in AED use; and during CPR performance, factors such as teamwork, using the AED voice prompt and a ventilation mask. Demonstration of leadership and feeling a moral obligation to act were also predictors of facilitating factors.[138] Amongst Flemish lifeguards trained for BLS/AED use, BLS/AED performances decayed significantly with increased age and longer time since certification, highlighting the need for ongoing refresher courses for first-responders to maintain skills.[139]
- Lack of public knowledge, confidence in using a defibrillator and the inability to locate a nearby device may be more important than a lack of defibrillators themselves.[140] In Hong Kong, only 33% of the surveyed public had knowledge of the location of an AED and 18% were willing to use it.[141] In a semi-structured open quantitative questionnaire delivered to over 1000 members of the public in a busy urban shopping centre in the UK, only 5.1% knew where or how to find their nearest public access defibrillator, only 3.3% of people would attempt to locate a defibrillator in a cardiac arrest situation, and even fewer (2.1%) would actually retrieve and use the device.[140] In the Netherlands, amongst 1018 surveyed participants, only 47% of respondents were willing to use an AED, and more than half (53%) were unable to recognize an AED.[142] These findings suggest that efforts focused at improving this link of underused PAD may be more important than increased investment to fund more AED installations.
- AED placement in schools and athletic facilities is argued for given the high survival rate (60%) and relative high incidence of use (0.7%), in one small study.[143] In a questionnaire developed to identify barriers to implementation and use AEDs in schools in Denmark, teachers reported perception that an AED was potentially dangerous, overtly technical, and difficult to use with ambiguity amongst the interviewed group as to whether students were the correct target group and the appropriate age at which they should receive training. Furthermore, teachers lacked knowledge about how they work and are operated, and were unaware about whether AEDs were already in place at their campus and how to access them.[144] In Japan, one study reported that 18% of defibrillators were located >5 minute from the farthest point in the school.[145]
- A noted problem is the survival rate of out of hospital cardiac arrest is also influenced by the AED density and rate of BLS education within a

region. In a French study, significant variation in AED density (5 to 3339 per 100,000 persons per 1000 km2) and BLS- educated people (955 to 36,636 per 100,000 persons) was noted amongst 19 surveyed districts. Notable, the mean survival rate was two-folds higher with AED density above the median of all surveyed districts and four-fold higher with BLS-education above the median of all surveyed districts. BLS-education, not AED density was independently associated with survival. These findings carry important implications that BLS-education and not just AED placement is a key factor in planning public health policies targeting out of hospital cardiac arrest.[146]

- In rural areas, long distances and low population densities make it difficult to reach OHCAs. Patients in rural areas of Australia are less likely to survive OHCA.[100] Such findings are also seen in Ireland.[147] In one study from a rural community in North Carolina, USA, placement of AED in private vehicle of first responders resulted in increased utilisation of AEDs.[148] Population density of >100 persons per square mile was the strongest predictor of survival to hospital discharge after OHCA in one study.[149]

- AED availability is also influenced by availability at different times of the day, with one study from Denmark reporting that only 9% of installed AEDs are available at all hours of the day. This limitation in AED accessibility at the time of cardiac arrest decreased AED coverage by 53.4% during the evening, night-time, and weekends, which is when 61.8% of all cardiac arrests in public locations occurred. Hence uninterrupted availability in addition to strategic placement warrants attention if public-access defibrillation is to improve survival after out-of-hospital cardiac arrest.[124]

- One novel solution to the long EMS response times in urban and rural settings is the use of a drone network than can theoretically deliver AEDs to a OHCA location. In a simulation modelling study utilising data from 53,702 OHCAs that occurred in the 8 regions of the Toronto Regional Rescue network, authors suggested that such a drone- delivered AED network could shorten significantly shorten time to AED accessibility. In urban regions, the 90th percentile of AED arrival time could be reduced by 6 minutes and 43 seconds relative to historical EMS response times in the region. In the most rural region, the 90th percentile could be reduced by 10 minutes and 34 seconds. Such technology could offer a promising solution if all legislative and logistic technologic hurdles were addressed.[60]

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Table 1: Summary of Selected Studies Referenced in this Review

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Berdowski et al, Circulation 2011[21]	North Holland, Netherlands	2833 OHCA; 2006-2009	Population-based cohort study	Effect of onsite defibrillation vs. dispatched professional first responder defibrillation vs. EMS- administered defibrillation on outcomes following OHCA	EMS carries AED, dual dispatch system (EMS and fire fighter/ police simultaneously), AEDs located in public places	• On site defibrillation compared with. EMS-AED reduced time to shock from 11 to 4.1 minutes, had greater neurological intact survival (49.6% vs. 14.3%) • Dispatched professional first responder defibrillation reduced the time from call to first shock to 8.5 minutes from 11 minutes • Every year, onsite AEDs saved 3.6 lives per 1 million inhabitants; dispatched professional frist responder AEDs saved 1.2 lives per 1 million inhabitants
Blom et al, Circulation 2014[15]	North Holland, Netherlands	6133 OHCA; 2006-2012	Population-based cohort study; ARREST registry of all OHCA	Whether neurologically favourable survival after OHCA arrest significantly increased over the study period	EMS carries AED, dual dispatch system (EMS and fire fighter/ police), AED in public places	• Neurologically favourable survival rates significantly increased over the study period from 16.2% to 19.7%, although only in patients with a shockable rhythm • Rates of AED use tripled (21.4% to 59.3%) • Time from EMS call to defibrillation device connection reduced by 1.9 minutes
Capucci et al, Circulation 2002[150]	Piacenza, Italy	354 OHCA; 1999-2001	Population-based cohort study	Whether participation of layperson closest to AED trained to use AED without any CPR requirement (called "Piacenza Progetto Vita [PPV] results in improved outcomes after OHCA	• Simultaneous activation of EMS with AED and first responder with AED • Layperson closest to AED trained to use AED without any CPR requirement • Laypersons were volunteers who were given official training and were part of an accessible register	PPV compared to EMS had: • Shorter EMS call to arrival time (4.8 vs. 6.2 minutes) • Greater overall survival (10.5% to 3.3%) • Greater survival from shockable arrhythmias (44% vs. 21%)

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Chan et al, Circulation 2014[51]	USA, >23 states	70, 027 OHCA throughout USA; 2005-2012	Population-based cohort study; CARES registry set up for all OHCA events in participating centres since 2005	To assess if there were any improvement in survival following OHCA in USA over time.	Data from geographically diverse EMS across multiple states.	• Increases survival from 5.7% in 2005 to 7.2% in 2008 to 8.3% in 2012 (both in shockable and non- shockable rhythms) • Rates of bystander CPR increased, as did rates for AED use (1.9% to 4.2%)
Culley et al, Circulation 2012[52]	King County, Washington, USA	50 OHCA; 1999-2002	Population-based cohort study	To evaluate the frequency and outcome of non-EMS AED use in a community experience.	• EMS activation, onsite AEDS. • Voluntary Community Responder AED Program and registry of PAD AEDs. • During the 4 years, 475 AEDs were placed in a variety of settings, and more than 4000 persons were trained in cardiopulmonary resuscitation and AED operation.	• 1.33% of OHCA were treated by PAD. • Proportion of PAD increased from 0.82% in 1999 to 2.05% in 2002. • 50% of PAD person survived till discharge.
Drezner et al, Circulation 2009[77]	USA	2006-2007	Population-based cohort study	To analyse effectiveness of emergency response planning for OHCA in a large cohort of US high schools that had onsite AED programs.	On site AEDs and EMS activated AED	• 94% of OHCA received bystander CPR, 83% received an AED shock. • 64% survived to hospital discharge

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Folke et al, Circulation 2010[92]	Copenhagen, Denmark	4828 OHCA; 1994-2005	Population-based cohort study	Whether areas suitable for placement of automated external defibrillators could be identified on the basis of demographic characteristics and characterized individuals with OHCA in residential locations.	• On site AEDs, EMS activated AEDs. • AEDs available for public- access defibrillation have been registered online in a Danish AED network (the Heart Start Network, www.hjertestarter.dk), dispatcher can identify local AED close to OHCA site or initiate its delivery from nearest site	• Home OHCA persons, compared with public OHCA were older, had longer EMS response times, with arrests occurred more often at night, VF was the presenting rhythm less often, and had worse 30- day survival (3.2% versus 13.9%)
Girotra et al, Circulation 2016[34]	USA, >23 states	96,662 OHCA; 2005-2014	Population-based cohort study; CARES registry set up for all OHCA events in participating centres since 2005	To understand reasons behind survival variation in OHCA in USA.	Data from geographically diverse EMS across multiple states	• There was marked variation in rates of survival to discharge (range, 3.4%-22.0%) and survival with functional recovery (range, 0.8%-21.0%) between counties. • Bystander CPR and AED use accounted for 41% of the survival variation, increasing to 50.4% after adjustment of county-level sociodemographic factors.
Myerberg et al, Circulation 2002[121]	Miami-Dade County, Florida, USA.	420 OHCA; 1999-2001	Population based cohort study	To examine if dual dispatched system improves OHCA survival compared to EMS only system	Dual dispatch of police force with AED simultaneous with EMS equipped with AED at time of OHCA call	• 1.5-minute improvement in call to arrival with defibrillation by the police force compared to EMS. • Police arrived to 56% of OHCA calls before EMS. • Improvement in OHCA survival rate from 9% with EMS to 17.2% with police force AED.
Weisfeldt et al, JACC 2010[20]	USA and Canada	13,769 OHCAs; 2005-2007	Population based cohort study	To examine the association between AED application and survival to hospital discharge	• ROC Epistry Cardiac Arrest • Registry • 215 geographically diverse sites in US and Canada	• With PAD program, 2.1% had an AED applied before EMS arrival. • Overall survival to hospital discharge was 7%. • Survival was 9% with bystander CPR but no AED, 24% with AED application, and 38% with AED shock delivered. • AED application was associated with 1.75-fold greater likelihood of survival.

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Malta-Hansen, JAMA 2015[53]	US	4961 OHCA; 2010-2013	Population based cohort study	To examine the association between resuscitation efforts for OHCA by various groups	EMS carries AED, layperson and professional first responder AED. Statewide initiatives to improve bystander and first-responder interventions (layperson training in COR and AED, professional first responder training in AED	• Bystander CPR and first-responder defibrillation increased from 14.1% to 23.1% over the study period • Neurologically favourable survival increased from 7.1% to 9.7% over the study period. • Survival was highest following bystander CPR and defibrillation 33.6%, followed by 25.2% in first- responder CPR and defibrillation, 24.2% following bystander CPR and first-responder defibrillation and lowest (15.2%) in EMS-alone given CPR and defibrillation
Nakahara, JAMA 2015[56]	Japan	16917 OHCA; 2005-2012	Population based cohort study	To examine the association between bystander intervention and survival	EMS with AED, PAD program of bystander CPR and defibrillation	• Bystander-only defibrillation increased from 0.1% to 2.3%, bystander defibrillation combined with EMS defibrillation increased from 0.1% to 1.4%. • Compared to EMS only delivered defibrillation, bystander-only defibrillation was associated with a 2-fold increase in neurologically intact survival as was combined bystander and EMS defibrillation (odds ratio 1.5), but no defibrillation was associated with significantly lower survival (odds ratio 0.43).

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Wissenberg, JAMA 2013[32]	Denmark	29,111; 2001-2010	Population based cohort study	To examine temporal changes in bystander resuscitation attempts and survival during a 10-year period in which several national initiatives were taken to increase rates of bystander resuscitation and improve advanced care.	EMS with AED; fixed AEDs; PAD program for bystander CPR and defibrillation. Several national initiatives rolled out in since 2001: implementation of mandatory resuscitation training in elementary schools (since January 2005), also when acquiring a driver's license (since October 2006), combined with an increase in voluntary first aid training; (2) free distribution of ~150 000 CPR self- instruction training kits between 2005 and 2010; (3) nationwide improvement of telephone guidance from emergency dispatch centres to bystanders witnessing a cardiac arrest, including the addition of health care professionals at dispatch centres, starting from 2009; (4) large increase in the number of automated external defibrillators located outside hospitals (approximately 15 000 were in place by 2011) (5) efforts to improve advanced care with updates of clinical guidelines, including introduction of therapeutic hypothermia starting from 2004, and increasing focus on early revascularization; and (6) overall strengthening of the EMS system with training of the ambulance personnel, including implementation of paramedics, mobile emergency care units staffed with specialized anesthesiologists dispatched as rendezvous with basic life support ambulances, or both.	• Bystander CPR increased from 22.1% to 44.9%. • Bystander defibrillation rates remained low, but increased 1.1% to 2.2%. • Increased rates of survival to hospital from 7.9% to 21.8%. • Improvement in 30-day survival 3.5% to 10.8% and 1-year survival 2.9% to 10.2%.
Caffrey et al, NEJM, 2002[74]	O'Hare, Midway, and Meigs Field airports, Chicago, USA.	21 OHCA; 1999-2001	Observational study	Whether random bystanders witnessing OHCA would retrieve and successfully use automated external defibrillators.	AEDs placed at brisk 60-to-90- second walk apart throughout passenger terminals; back up EMS. AED use promoted by public-service videos in waiting areas, pamphlets, and reports in the media.	• 11/21(52%) of OHCA person successfully defibrillation. • 8/21 (38%) survived to hospital. • 10/18 (56%) of patients who had a shockable rhythm survived and were neurologically intact at 1 year. • 19/21 (90%) of operators were 'Good Samaritan' volunteers. • 4/21 (19%) had OHCA without a nearby AED and all of these persons died.

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Hallstrom et al NEJM 2004[55]	USA and Canada	993 OHCA; 2000-2003	Randomised controlled trial	To evaluate if trained volunteer laypersons performed CPR plus defibrillation leads to better outcomes compared to CPR alone in persons who have experienced OHCA.	Eligible community units (e.g., shopping malls and apartment complexes) randomised to a CPR- only response system or a CPR plus AED response system. Lay volunteers trained in either CPR alone or in CPR and the use of AEDs.	• CPR plus AED was associated with a 2-fold higher percentage of patients who survived to hospital discharge compared to CPR only.
Kitamura et al, NEJM 2010[151]	Japan	312,319 OHCA; 2055-2007	Population-based cohort study	To evaluate the effect of nation-wide dissemination of public- access AEDs on the rate of survival after an OHCA.	EMS equipped with AEDs, widespread dissemination of AEDs at public areas, including schools, medical and nursing-facilities, work places, sports and cultural facilities, and transportation facilities, depending on both public and private initiatives.	• Bystander shock was given in 3.7% of patients with OHCA with a shockable rhythm. • Bystander shock rates increased from 1.2% to 6.2%. • 14.4% of persons who had bystander witness OHCA who had VF survived had neurologically intact survival at 1 year. • 31.6% of OHCA persons who had bystander shock had neurologically intact survival ay there was a 9% reduction in neurologically intact survival with every 1-minute increase in tie to defibrillation regardless of type of provider. • Mean time to shock was reduced from 3.7 to 2.2 minutes. • With increase in public AEDs from fewer than 1 per square kilometre of inhabited area to 4 or more, the annual number of patients per 10 million population who survived with minimal neurologic impairment increased from 2.4 to 8.9.

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Kitamura, NEJM 2016[41]	Japan	43,762 persons with bystander-witnessed VF arrests of cardiac origin; 2005-2013	Population-based cohort study	To evaluate the effect of dissemination of public- access AEDs for VF cardiac arrest at the population level..	EMS equipped with AEDs, widespread dissemination of AEDs at public areas, including schools, medical and nursing facilities, work places, sports and cultural facilities, and transportation facilities, depending on both public and private initiatives	• 10.3% of persons with bystander-witnessed VF arrests of cardiac origin received bystander defibrillation with a significant increase over time (1.1% in 2005 to 16.5% in 2013). • Neurologically intact survival rates at 1 month doubled with PAD than without PAD (38.5% from 18.2%). • Estimated number of neurologically intact survivors attributed to use of PAD increased from 6 in 2005 to 201 in 2013.
Valenzuela et al, NEJM 2000[26]	USA (casinos in 5 states)	105 persons with OHCA in whom VF was in the initial rhythm; 1997-1999	Observational study	To evaluate outcomes when the easily available AEDs are used by nonmedical personnel for OHCA in casinos.	Casino security instructed in use of AEDs; AEDs located such that target interval ≤3 minutes from collapse to the first defibrillation. Defibrillation first (if feasible), followed by manual CPR	• 53% of OHCA with VF as the initial rhythm survived to hospital discharge. • Survival rate for defibrillation ≤3 minutes was 74%, for >3 minutes was 49%.
Colquhoun et al Resuscitation 2008[39]	England and Wales	1530 OHCA; 1999-2005	Population-based cohort study	To evaluate outcomes of a National c Defibrillator Program on survival of persons with OHCA.	National Defibrillator Program comprising of (1) EMS equipped with AEDs (2) AEDs placement in busy public places identified from routine ambulance data as sites where cardiac arrest was liable to occur such as airports and major railway stations; AEDs kept in unlocked protective cabinets within 200m walking distance from any part of the premises to which the public has access; staff working at these sites volunteered to be trained over 4 hours to provide BLS and to use Mobile AEDs placed amongst community first responders where EMS response times expected to be long such as rural areas; also included professional first responders	• Static AED use, compared to mobile AED (e.g. EMS-delivered or mobile first responder AED) resulted in: a. Higher incidence of return of spontaneous circulation (39% vs. 10%) b. Higher incidence of hospital discharge (26% vs. 2.9%)

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Lijovic et al, Resuscitation 2014[43]	Victoria, Australia	2270 OHCA; 2002-2013	Population-based cohort study	To assess the impact of bystander defibrillated OHCA persons vs. EMS- defibrillated persons on survival.	EMS equipped with AEDs; AEDs at fixed locations	• 93.4% of OHCA persons were first defibrillated by EMS compared to 6.7% by bystander using public AED. • There was 11-fold increase in public AED use between 2002/2003 and 2012/2013, from 1.7% to 18.5%. • First defibrillation occurred sooner in bystander defibrillation vs. EMS defibrillation (5.2 versus 10.0 min). • Survival to hospital discharge for bystander defibrillated patients was significantly higher than for those EMS defibrillated patients (45% versus 31%). • First defibrillation by a bystander using an AED was associated with a 62% increase in the odds of survival to hospital discharge compared to first defibrillation by EMS.
Claessen et al, Am J Emerg Med 2017[49]	Western Sweden	6675 OHCA; 2008-2015	Population-based cohort study	To assess the impact of dual dispatch first responders alongside emergency medical services for the treatment of OHCA	Dual dispatch of EMS equipped with AED and firefighters for OHCA; on site AEDs used when available.	• 15% of all VF cases were defibrillated before EMS arrival; 46% of such patients with public. • Proportion of patients defibrillated before EMS arrival increased 5% in 2008 to 20% in 2015. • 30-day survival increased in patients with VF from 22% to 28%. • On-site defibrillation conferred a 2.45-fold increase in 30-day survival compared to dispatched defibrillation.
Ringh et al, Resuscitation 2015[17]	Stockholm, Sweden	6532; 2066-2012	Population-based cohort study	To evaluate the effect of a PAD program on outcomes of patients with OHCA.	SALSA project comprised of (a) dual dispatch of fire-fighters and police in parallel with standard EMS and (b) a structured PAD program consisting of property owners, site managers and security companies of traditionally high incidence sites such as big shopping malls, transportation hubs and air- ports were approached with an offer to participate with a free instructional training in standard BLS and AED use; (c) onsite “unregulated” AEDs used by laypersons purchased over the counter by private owners.	• Sites within the PAD program increased from 60 to 135 while the number of unregulated AEDs outside the PAD program increased from 178 to 5016. • 69% of OHCA were defibrillated by the EMS, 11% by first responders and 16% by public AEDs. • 1-month survival was 31% EMS-defibrillation cases, 42% by first responders and 70% when defibrillated by a public AED.

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Saner et al, Resuscitation 2013[118]	Switzerland	1334 OHCAs; 2001-2008	Population-based cohort study	To evaluate the effect of a system based on minimally trained first responders dispatched simultaneously with EMS of the local hospital in a mixed urban and rural area in Northwestern Switzerland on survival of OHCA persons.	EMS with AEDs; minimally trained first responders (voluntary firefighters) with 4 hours of training in BLS and AED use.	• First responders reached patients 6 minutes earlier than EMS, reaching before EMS in 87% of cases. • 75% were defibrillated by first responders. • 14% of OHCA persons defibrillated by first responders were discharged form hospital in a neurologically good condition.
Stein et al, Resuscitation 2017[57]	Zurich, Switzerland	1393 OHCA; 2004-2015	Population-based cohort study	To evaluate if a system of dual dispatch of police officer trained in BLS and AED use in addition to EMS resulted in improved outcomes in treatment of OHCA persons.	Dual dispatch of EMS with AEDs and trained police officers with BLS skills and AED in period 2 (2010- 2015) was compared to EMS only system prior to the former program implementation in period 1 (2004-2009)	• In period 2, compared with period 1, police dispatch started CPR 3 minutes earlier, and performed defibrillation 6 minutes than EMS. • In period 2, compared to period 1, there was a significant increase in proportion of patients with: a) return of spontaneous circulation (35.8% vs. 24%); b) hospital admission 32.2% vs. 21.4% c) survival to hospital discharge (13.6% vs.6.9%). • The odds of return of spontaneous circulation were 2.6-fold higher and hospital admission were 2.8- fold if defibrillation was performed by trained first responders than EMS.

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Van Alem et al, BMJ 2003[31]	Amsterdam, The Netherlands	469 OHCA; 2000-2002	Randomised trial	To evaluate if a system of dual dispatch (EMS plus trained professional first responder of police or fire brigade) yields superior outcomes compared with EMS only activation in treatment of persons with OHCA	• EMS-dispatch (control) versus EMS plus police or fire brigade (experimental) who were CPR and AED capable as a controlled clinical trial. • Initial random allocation of AED to first responders in four of the eight participating regions; each region switched from control to experimental, and vice versa, every four months.	• Experimental arm had shorter median time interval between collapse and first shock (668 seconds vs. 769 seconds). • No significant difference in persons discharged form hospital between the experimental and control arms (18% vs. 15%). • Higher rate of return of spontaneous circulation in the experimental vs. control arm (57% vs. 48%).
Hansen et al, Circulation 2013[124]	Copenhagen, Denmark	1864 public OHCA, 1994-2011	Population-based cohort study	To assess how AED accessibility affects the coverage of OHCA	AEDs available for public-access defibrillation have been registered online in a Danish AED network (the Heart Start Network, www.hjertestarter.dk), dispatcher can identify local AED close to OHCA site or initiate its delivery from nearest site .	• Only 9.1% of all AEDs were accessible at all hours. • Limited AED accessibility decreased coverage of cardiac arrests by 4.1% during the daytime on weekdays and by 53.4% during the evening, night- time, and weekend, which is when 61.8% of all cardiac arrests in public locations occurred. • Uninterrupted availability, not only strategic placement of AEDs is needed.

Study Name, Journal, Year	Country of Origin	Number of Patients, study period	Study design	Primary Question	EMS and AED system Summary	Main Findings
Ringh et al, NEJM 2015[113]	Stockholm, Sweden	6532 OHCA; 2012-2013	Blinded, randomised controlled trial	To evaluate if rates of bystander-initiated CPR could be increased with the use of a mobile-phone positioning system that could instantly locate mobile-phone users and dispatch lay volunteers who were trained in CPR to a patient nearby with out-of-hospital cardiac arrest	• Lay volunteers trained in CPR recruited through advertising campaigns and at CPR training courses and called "short- message-service lifesavers." • OHCA activation involves dispatch of an ambulance and first responders (i.e., fire and police vehicles) and, if needed, the provision over the telephone of instructions on how to perform CPR. • Volunteers within a radius of 500 m from the patient received a computer-generated telephone call and a text message with information on the patient's location were randomised to be dispatched to the patients (the intervention group) or not dispatched to them (the control group). • Volunteer performed CPR.	• Rate of bystander-initiated CPR was significantly higher (62%) in the intervention group than the control group 48%.

Table 2: Summary of Health Economics Evaluations Referenced in this Review

Author	Country	Intervention	Cost- effective?*	Cost-effectiveness result	Health system 'enablers'	Costs included	Economic evaluation method	Determinants of cost- effectiveness	Quality assessment score** [152]
Moran et al. Resuscitation 2015[108]	Ireland	Different PAD placement in public places across Ireland	No	ICER for most comprehensive option = €928,450/ QALY, while for the most targeted program (transport stations, medical practices, entertainment venues, non-primary schools and fitness facilities) = €95,640/ QALY.	Study in response to proposed legislation mandating placement in particular public areas	Irish health service costs, device suppliers and training providers to train respondents	Cost-utility analysis (decision analytic model)	ICER results were most affected by the rate of survival to hospital admission and discharge for those receiving bystander defibrillation and the estimated number of OHCAs occurring in public areas within 200 m of an AED.	0.83

Author	Country	Intervention	Cost- effective?*	Cost-effectiveness result	Health system 'enablers'	Costs included	Economic evaluation method	Determinants of cost- effectiveness	Quality assessment score** [152]
Sund et al. Eur J Health Econ 2012[91]	Sweden	Dual dispatch of ambulance and fire services for OHCAs	Yes	Cost benefit ratio = 36	Fire trucks equipped with AED	Equipment, training costs, healthcare costs, callouts for fire services, overheads and increased dispatch centre costs.	Cost benefit analysis	Cost-benefit ratio was influenced most by assumptions around the value of a statistical life, effectiveness (number of lives saved) of early defibrillation. The result was not dramatically affected by varying costs.	0.7
Sharieff and Kaulback Int J Technol Assess Health Care 2007[109]	Canada	Positioning of AEDs in different locations: in far reaches of hospitals, apartment buildings, office buildings, homes of high risk patients, homes of people >55	Yes in hospitals and high risk patient homes, No everywhere else	Cost per QALY was $12,768 in hospital settings, $87,569 in homes of high-risk patients, $511,766 in office buildings, $2,360,023 in apartment buildings, and $1,529,371 in homes of people older than 55 years of age.	Firefighters and 30% of police responders have machines under current response system.	Price of machines and price of training. There were no healthcare costs.	Cost-utility analysis (decision analytic model)	The cost-effectiveness results were most influenced by the likelihood of a cardiac arrest in the area.	0.79
Cappato et al. Eur H J 2006[90]	Italy	Deployment of AEDs across the County of Brescia for use by trained volunteers and laypersons.	Yes	Additional cost per QALY gained €39,388 during the start up phase and €23,661 in 'steady state'	Recent law allowing the use of AEDs by non-medical personnel	Costs of AEDs and maintenance, training costs, medical costs including diagnostic, cardiac and surgical procedures, ICD implants, outpatient and hospital costs	Cost-utility analysis	Not stated. The majority of the costs were accounted for by the cost of the AED.	0.62

Author	Country	Intervention	Cost- effective?*	Cost-effectiveness result	Health system 'enablers'	Costs included	Economic evaluation method	Determinants of cost- effectiveness	Quality assessment score** [152]
Cram et al. J Gen Intern Med 2005[94]	US	In home AED targeting different groups of American adults (all American adults over 60, adults with multiple risk factors, adults with previous myocardial infarction and adults with ischemic cardiomyopathy unable to receive an implantable defibrillator) plus standard EMS response	Generally not	Cost per QALY differed by the cohorts: • All adults over 60 - $216,000 per QALY gained • Multiple risk factors - $132,000 • Previous MI – 104,000 • Ischemic cardiomyopathy – $88,000	EMS provide defibrillation in base case	Medical costs, machine costs, training costs - all estimated from the literature	Cost-utility analysis (decision analytic model)	Cost effectiveness were most influenced by the relative risk of cardiac arrest for the patient cohort and the time to defibrillation	0.84
Nichol et al. Circulation 2003[106]	US	Targeted (and trained) non-traditional responders to provide defibrillation with AED in a casino	Yes	Compared with standard EMS, defibrillation by targeted non- traditional responders had an incremental cost per QALY gained of $56,700	EMS provide defibrillation in base case	Hospital and device costs	Cost-utility analysis (decision analytic model)	Cost effectiveness was most sensitive to changes in time to defibrillation, rate of cardiac arrests and whether responders are paid during training.	0.89
Kuisma et al. Resuscitation 2003[88]	Finland	Public Access Defibrillation in sites with at least one cardiac arrest per year (7 sites) with trained responders	NA	Total cost = 110,270 euro for three year trial, time benefit to reaching patient 4.8 minutes per arrest	Responders trained to use PAD	Market prices, salaries, medical supervision	Cost consequence analysis (not stated)	Costs were predominantly made up of non-machine costs	0.5

Author	Country	Intervention	Cost- effective?*	Cost-effectiveness result	Health system 'enablers'	Costs included	Economic evaluation method	Determinants of cost- effectiveness	Quality assessment score** [152]
Groenevald et al. JAMA 2001[107]	US (aero-plane s)	AED deployment on aeroplanes - either across all aircraft or selectively on larger capacity planes (>100 or >200). Different strategies of either training all flight attendants or selectively choosing some were also modelled.	Yes	• AEDs on passenger aircraft with more than 200 passengers would cost $35,300 per QALY gained. • AEDs on aircraft with capacities between 100 and 200 persons would cost an additional $40,800 per added QALY compared with deployment on large-capacity aircraft only. • Full deployment on all passenger aircraft would cost an additional $94 700 per QALY gained compared with limited deployment on aircraft with capacity greater than 100	NA (training provided to flight attendants at private cost)	Airline costs, published wage data, published estimates of medical costs for cardiac arrest, AED-manufacturers provided costs for AEDs	Cost-utility analysis (decision analytic model)	Cost effectiveness results were proportional to number of passenger hours covered by the strategy, the effectiveness of AEDs in improving survival and the rate of cardiac arrests on board	0.87

Abbreviations: AED – Automatic External Defibrillators; EMS – Emergency Medical Services; ICER – Incremental Cost Effectiveness Ratio; MI – Myocardial infarction; NA – Not applicable; OHCA – Out of hospital cardiac arrest; PAD – Public access defibrillation; QALY- Quality adjusted life year; US – United States of America.

*As assessed by individual study authors.

**Quality score calculated based on the methodology proposed by La Torre et al. (2011) which is based on 35 items across three main sections: study design, data collection and analysis and interpretation of results[1].

1. La Torre, G., et al., Development of a weighted scale to assess the quality of cost-effectiveness studies and an application to the economic evaluations of tetravalent HPV vaccine. Journal of Public Health, 2011. 19(2): p. 103-111.

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