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EFFECTIVENESS OF WEARABLE DEFIBRILLATORS: SYSTEMATIC REVIEW AND QUALITY OF EVIDENCE

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Objectives: The objectives of this systematic literature review were to identify all published literature on wearable defibrillators, assess the wearable defibrillator's efficacy and effectiveness in general and among specific patient groups, including post-myocardial infarction, post coronary artery bypass grafting or percutaneous coronary intervention, non-ischemic cardiomyopathy, and ischemic cardiomyopathy, and to evaluate the quality of evidence.
Methods: The search and synthesis was informed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement, and the quality of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation and the Newcastle Ottawa Scale.
Results: A total of thirty-six articles and conference abstracts from thirty-three studies were included in the review. It appears that wearable defibrillator use compared with no defibrillator use reduces the chance of ventricular tachycardia and ventricular fibrillation (VT/VF) associated deaths by an absolute risk reduction of approximately 1 percent, achieved by averting approximately 4/5th of all VT/VF associated deaths. The quality of evidence was low to very low quality, such that our confidence in the reported estimates is weak.
Conclusions: To validate beneficial results, further investigation using robust study designs conducted by independent researchers is warranted.

Keywords: Defibrillators, Medical device, Ventricular fibrillation, Ventricular tachycardia

Sudden cardiac arrest is defined as the abrupt loss of heart function and if untreated can result in sudden cardiac death (1). The cause of cardiac arrest is usually an abnormal or irregular heart rhythm (arrhythmia), and common arrhythmias that can lead to cardiac arrest include ventricular fibrillation (VF) and ventricular tachycardia (VT) (2;3). Early defibrillation is key to survival of a VT/VF related cardiac arrest and the probability of successful defibrillation decreases rapidly with time delays (4). In one large observational study, researchers found that people who were defibrillated within 2 minutes of a VT related cardiac arrest were admitted to the hospital alive in 80 percent of cases and alive after 1 month in 50 percent of cases, while people who were defibrillated after a 15-minute time delay, the proportion who arrived to the hospital alive and at 1 month was 15 percent and 5 percent, respectively (5).

A possible treatment option is the wearable cardioverter defibrillator (WD), a device that is worn like a vest, monitors the heart continuously, and if a VT/VF arrhythmia is detected will automatically deliver a shock to return the heart to a normal rhythm. It is often used as a bridge to the implantable cardioverter defibrillator (ICD, a device surgically placed to monitor the heart rhythm and when necessary automatically deliver therapy), or when ICD is inappropriate, interrupted or refused by the patient (6;7). It is also a clinical alternative to the automatic external defibrillator, a portable device that can be found in hospitals, ambulances, and the community setting, and has the benefit of not requiring a trained bystander to administer a shock.

While the WD is for adult patients who are at high risk of sudden cardiac arrest, indications for use are not as clearly outlined as they are for ICDs (8). For example, current ACC/AHA/ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death (9), only restates the use of the WD as approved by the FDA, which is: "for cardiac patients with transient high risk VF such those awaiting cardiac transplantation, those at very high risk after a recent myocardial infarction (MI), or an invasive cardiac procedure, or those requiring temporary removal of an infected implanted defibrillator for antibiotic therapy." The International Society for Heart and Lung Transplantation Guidelines for Care of Cardiac Transplant Candidates (10), gives a Class I recommendation (evidence and/or agreement that the treatment is beneficial, useful, and effective) to use a WD for "status 1B patients who are discharged from home given that the wait for transplantation remains significant" and gave a "C" level of evidence rating (evidence is based only on consensus opinion of experts, case studies, or is the standard of care) for that recommendation. While others have suggested the potential usefulness of the wearable defibrillator to include the following patient groups (6;11): newly diagnosed NYHA functional class III or IV heart failure and LVEF <35 percent,

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≤ 40 days post-MI and a measured LVEF ≤ 0.35, ≤ 90 post coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI or percutaneous transluminal coronary angioplasty [PTCA]) and LVEF ≤ 0.35, bridge to interrupted ICD therapy or heart transplantation, syncope of uncertain etiology but high risk for VT/VF, familial or inherited condition that increases risk of life-threatening VT such as QT syndrome or Brugada syndrome, and non-ischemic cardiomyopathy (NICM) and LVEF ≤ 0.35.

To better understand the efficacy and effectiveness of the wearable defibrillator in general and among specific patient groups, we conducted a systematic literature review to identify all published scientific evidence. To our knowledge, no published systematic literature reviews on this topic currently exist. Specifically, we sought to answer the following research questions:

Research Question 1. How efficacious and/or effective are wearable defibrillators (WD) *compared to no WD use* among adult patients (≥ 18 years old) at high risk of sudden cardiac death?

Research Question 2. How efficacious and/or effective are wearable defibrillators *compared to other resuscitation methods* (i.e., ICD and external defibrillators) among adult patients (≥ 18 years old) at high risk of sudden cardiac death?

Research Question 3. Are WDs efficacious and/or effective for the following patient sub-groups?

1a. ≤ *40 days* post-MI and a measured LVEF ≤ 0.35
1b. >*40 days* post-MI and a measured LVEF ≤ 0.35
2a. ≤ *90 days* post CABG or PCI (PTCA) and LVEF ≤ 0.35
2b. > *90 days* post CABG or PCI (PTCA) and LVEF ≤ 0.35
3a. ≤ *3 months* non-ischemic cardiomyopathy (NICM) and LVEF ≤ 0.35
3b. > *3 months* non-ischemic cardiomyopathy (NICM) and LVEF ≤ 0.35
4. Ischemic cardiomyopathy

Research Question 4. What risks/harms do WDs pose to the patient?

Measures of efficacy and effectiveness were defined as: all-cause mortality, sudden cardiac death, VT/VF related death, VT/VF specific death, survival, accurate detection of VT/VF by the WD, sensitivity/specificity of the WD (e.g., appropriate/inappropriate shocks), and successful termination of arrhythmic events.

METHODS

A review protocol was developed and is available in the online supplementary section, which can be viewed online at http://dx.doi.org/10.1017/S026646231400004X. The search and synthesis was informed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (12;13). The databases PubMed, Embase, and Scopus were searched in November 2012 using the following search strategy (note that terms were entered exactly as they appear here): (wearable AND defibrillator*), (Lifecor OR Lifevest OR WEARIT OR BIROAD), and (Asahi Kasei and defib*). Searches were limited to English-language articles, and no date or country restrictions were set. The type of eligible studies included randomized control trials, quasi-experimental studies, and observational studies that tested the wearable defibrillator among non-pregnant adults (≥ 18 years old). Excluded were case reports and qualitative studies, as well as gray literature, commissioned reports, and journals and conference abstracts that were not peer-reviewed. Bibliographies of eligible studies and the "ACC/AHA/ESC guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death" (14) were screened to find articles and abstracts not identified in the search.

Titles and abstracts were first screened to identify eligible articles, and the full text of eligible articles was then screened for inclusion. A paper-based data extraction form was developed, piloted, and used to extract information from included studies. Table 1 lists all data that were extracted. We collected measures of absolute risk and when available relative effects, such as hazard ratios, relative risk, and odds ratios. Given the sparseness of

Table 1. Information Extracted from Each Study

Efficacy and effectiveness measures
1. All-cause mortality
2. Sudden cardiac death (VT/VF specific)
3. Survival
4. Sensitivity/specificity of WD (e.g., appropriate/inappropriate shocks)
5. Successful termination of arrhythmic events
Compliance and harms
1. Mean duration of use (# of days)
2. Mean patient compliance (# of hours used/day)
3. Reported harms and risks
Study characteristics
1. Manuscript type (peer-reviewed journal, juried conference abstract, non-juried conference abstract)
2. Funding, device manufacturer, and author affiliation
3. Study design and data sources (years of data analyzed)
4. Sampling method, power calculation, sample size, and loss to follow up
5. Location: US (regional), international, and urban/rural
6. Inclusion/exclusion criteria
7. Use of a comparison group
8. Analytic model and adjustments
9. Limitations
Patient characteristics
1. Demographics: age, sex, race, income
2. Baseline medical characteristics and indications of use
• Entire study and by sub-groups of interest

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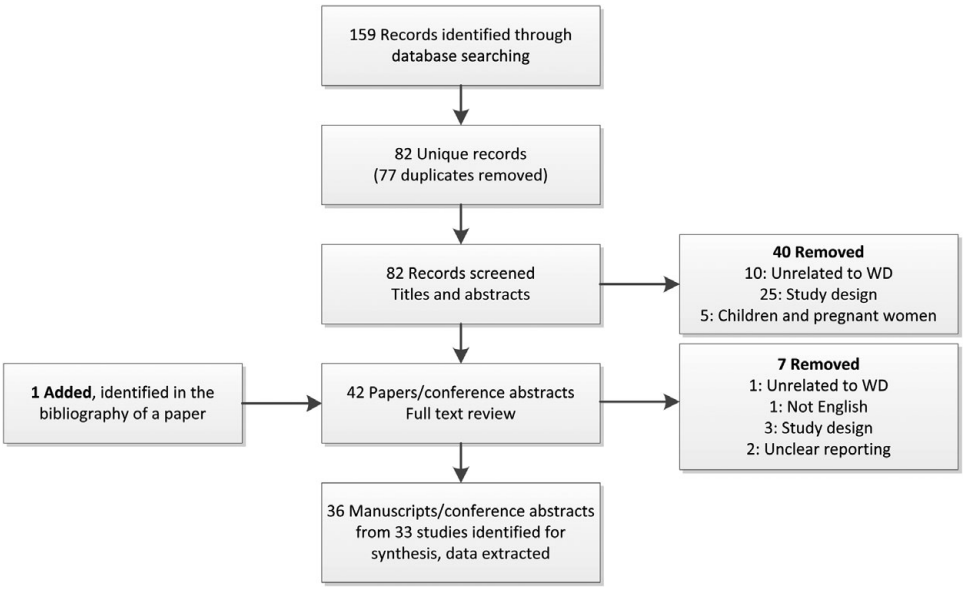

Figure 1. Phases of the systematic review: identification, screening, eligibility, and included.

data, meta-analysis was not possible. J.U. screened titles and abstracts, screened full papers, extracted data, and assessed quality of evidence. Uncertainties that arose about including/excluding studies and downgrading quality of studies were discussed with RSB until authors came to a consensus.

The Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach and software program was used to evaluate the overall body of evidence (15). The GRADE approach, when applied to a systematic review, classifies a body of work on a continuum—high, moderate, low, and very low—where "high" indicates a strong degree of confidence that the estimated effect reflects the true effect and "very low" indicates very little confidence. Individual studies were evaluated and marked down based on five domains: risk of bias, imprecision, inconsistency, indirectness of study results, and publication bias. Individual studies that showed no indication of risk of bias were then evaluated on three other domains to assess the possibility of raising scores: large effect, possible influence of confounding, and dose response gradient. Given that all included studies were observational, risk of bias was assessed for each individual study using the Newcastle-Ottawa Scale (16).

RESULTS

A total of thirty-six articles and conference abstracts from thirty-three studies were included in this review. As shown in Figure 1, the search yielded eighty-two unique records. Based on a review of titles, abstracts, and full texts a total of forty-seven records were excluded because of unsuitable study design (twenty-eight records), or were unrelated to wearable defibrillators (11), focused on children or pregnant women only (5), did not clearly report study results (2), or not published in English (1). One article identified in a bibliography was added. Data were extracted from each study and results from multiple papers from the same study were combined to avoid double counting.

Table 2 provides a description of the studies included in this review. Of the thirty-six articles and abstracts, twenty-eight (78 percent) were conference abstracts and eight (22 percent) were articles published in journals. The majority (thirty-two, 89 percent) were published in the past 5 years. Of the thirty-three studies, twenty-eight were retrospective cohort (85 percent), 2 were prospective cohort (6 percent), two tested the device on human subjects in a laboratory setting (6 percent), and 1 was a case-control (3 percent). Twenty-nine of the studies (88 percent) relied on secondary data, twenty-four of which used a database provided by the device manufacture, two relied on hospital chart reviews, and three did not report the source of data. On average, studies using secondary data included approximately 4 years of data (range: 0.5–8 years; median = 4.5). Sixteen of the studies were conducted in the United States, two in Germany, and geographic location was not reported for fifteen studies.

Among all studies, the mean age of patients was 59.3 years (SD = 3.71), and 72 percent (SD = 9) of participants were male. Race/ethnicity was reported in one study (17), and in that study 58 percent of participants were African American, Hispanic, or Asian. Information about patient income was not reported in any of the studies. The most common indications for WD use in the general WD patient population were non-ischemic cardiomyopathy, myocardial infarction, ICD explanation, ICD pocket infection, and VT/VF before ICD implantation.

Supplementary Table 1, which can be viewed online at http://dx.doi.org/10.1017/S026646231400004X, lists results for select outcomes, including predetermined measures of

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Table 2. Description of the Studies, Articles, and Abstracts Included in the Review

36 articles and abstracts	
Manuscript type	28 (78%): Juried conference abstracts
	0 (0%): Non-juried conference abstracts
	8 (22%): Article published in peer-reviewed journal
Publication year	32 (89%): Within the past 5 years
	4 (11%): > 5 years
33 studies	
Study design	28 (86%): Retrospective cohort
	2 (6%): Prospective cohort
	2 (6%): WCD tested in a lab
	1 (3%): Case-control
Data sources	29 (88%): Relied on secondary data
	24: Included use of a Zoll database
	3: Not reported (likely Zoll database given authors affiliation)
	2: Hospital chart reviews
	4 (12%): Collected primary data
Mean age[a]	59.3 years (SD = 3.71)
Sex (male)[a]	72% (SD = 9%)
Race/ethnicity	Reported in 1 study: 58% of participants were African American, Hispanic, or Asian

[a]Weighted based on study sample size.

efficacy and effectiveness, by study. Sixteen studies reported on all-cause mortality. Among patients prescribed a WD, on average 2.6 percent died (range, 0–60 percent) over the course of 75.2 mean days of WD use (range, 35–289 days). The causes of death was reported in four studies and included, heart failure, MI, peritonitis, complications of chemotherapy, and post shock asystole. Eleven studies reported on VT/VF related mortality (defined as # of patients who died of VT/VF related causes/sample population), and an average of 0.33 percent (range, 0–60 percent) of the study population died of VT/VF related causes over the course of 90.1 mean days of WD use (range, 41–93 days). Among those who experienced a VT or VF event, on average 22.1 percent died (range, 0–60 percent) due to VT or VF (based on six studies), over the course of 58.3 mean days of WD use (note only one of the studies reported on mean days of use).

Based on 10 studies that reported on VT/VF incidence, on average 1.4 percent (range, 0–5.7 percent) of WD users experienced a VT and/or VF event over the course of 62.7 mean days of WD use (range, 41.4–527 days), and based on fourteen studies the WD successfully terminated arrhythmic events in 96 percent of patients (defined as the # of patients with terminated VT/VF event(s)/# of patients who experienced a VT/VF event) over the course of 76.2 mean days of WD use (range, 41–93 days).

Research Question 1

Only one retrospective cohort study assessed the effectiveness of wearable defibrillators (WD) compared with no WD use (18). Zishiri et al. examined whether survival differed between patients discharged with a WD after CABG or PCI with a left ventricular ejection fraction (LVEF) of < or = to 35 percent compared with a similar patient group discharged without a WD (non-WD users). For the entire cohort of revascularized patients ($N = 4958$), survival for WD users was better compared with non-WD users over the course of 3 years (hazard ratio [HR], 0.54; 95 percent confidence interval [CI], 0.43–0.68; $p < .0001$). Data for WD-users came from a national database (database source unreported), while data for non-WD users came from the Cleveland Clinics' patient registry. The study did not report whether non-WD users were exposed to other resuscitation methods (e.g., ICD or AED). No studies reported all-cause mortality or VT/VF specific mortality.

Research Question 2

Only one retrospective cohort study compared the effectiveness of WDs with other resuscitation methods (19). Chung et al. assessed 3-month and 3-year survival among WD patients from a national database maintained by the device manufacture compared with patients undergoing first ICDs placement at one center (data from the Cleveland Clinic Electrophysiology Laboratory). Authors report no significant survival differences between groups at 3-months of use (HR, 0.83; 95 percent CI, 0.60–1.14; $p = .26$) and 3-years (HR, 0.92; 95 percent CI, 0.79–1.07; $p = .29$), even after adjusting for age and sex in Cox proportional hazards analysis ($p = .71$). Mortality rates between WD patients versus ICD patients were not significantly different at 3 months (3.6 percent versus 4.4 percent, $p = .256$), 6 months (6.3 versus 7.6; $p = .13$), 1 year (10.1 versus 11.0; $p = .38$), 2 years (15.6 versus 16.7; $p = .34$), 3 years (20.5 versus 22.1; $p = .29$), and 4 years (22.2 versus 27.9; $p = .279$).

Research Question 3

1a. ≤ 40 days *post-MI and a measured LVEF ≤ 0.35*
1b. >40 days *post-MI and a measured LVEF ≤ 0.35*

Four studies (three retrospective and one prospective cohort) assessed the effectiveness of WD use among post-MI patients (19–22). None of the studies specifically reported whether WD use started ≤ or> 40 days post-MI. Three of the studies described patients as having a "recent MI" or starting WD use "following discharge." The fourth study did not describe a timeframe. Only one study reported outcomes disaggregated by LVEF level. All-cause mortality was reported in one study and in that study no deaths (0/43) occurred within 90-days following discharge. Two studies reported on VT/VF related mortality (defined as the # of patients who died of VT/VF related causes/study population),

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and on average 0.52 percent (2/384) of the study population died of these causes over 58.3 mean days of WD use (only one study reported on mean days of use). Of those who experienced a VT/VF event, on average 18 percent (2/11) died due to VT or VF (based two studies) over 58.3 mean days of WD use (only one study reported on mean days of use). Thirty- and 90-day survival was reported in one study, and in that study, among those resuscitated by a WD, 87 percent survived 30-days after resuscitation and 82 percent survived 90-days after resuscitation. Based on two studies that reported on VT/VF incidence, on average 2.8 percent (11/384) of WD users experienced a VT and/or VF event over the course 58.3 (range, 3–146) mean days of WD use. Among those who experienced a VT/VF event, on average 82 percent (9/11) experienced successful termination of one or more arrhythmic events (based on the same two studies). No studies reported on inappropriate shocks.

2a. *2a.* $\leq$ 90 days *post CABG or PCI (PTCA) and LVEF* $\leq$ *0.35*
2b. *2b.* $>$ 90 days *post CABG or PCI (PTCA) and LVEF* $\leq$ *0.35*

Three retrospective cohort studies assessed the effectiveness of WD use among post-CABG and/or PCI patients (18;19;22). Two of the studies reported outcomes specifically for patients who began WD use $\leq$ 90 days post-revascularization (2a), while one study did not specify a timeframe. All studies included patients with a LVEF $\leq$ 0.35. One study reported on VT/VF related mortality and in that study 0.41 percent (1/243) of the study population died of VT or VF related causes (defined as # of people who died of VT/VF causes/study sample) over the course of 59.8 $\pm$ 32 days (mean or median days not specified). Of those who experienced a VT/VF event in the aftermath of a CABG or PCI, one study reported that 7 percent (raw numbers not reported) of revascularized patients died over "approximately 2 months of WD use" while in another study 50 percent (1/2) died over the course of 59.8 $\pm$ 32 days (mean or median days not specified). One study compared survival differences between WD users (patients in a national database) and non-WD users (patients discharged without a WD at the Cleveland Clinic) among a cohort of patients who underwent revascularization (CABG or PCI). For the entire cohort of patients, 3-year survival for WD users was better compared with non-WD users over the course of 3 years (HR, 0.54; 95 percent CI, 0.43–0.68; $p < .0001$). The study did not report whether non-WD users were exposed to other resuscitation methods (e.g., ICD or AED). Among propensity score matched CABG patients in that same study, survival was better among WD users than non-WD users (HR, 0.42; 95 percent CI, 0.23–0.74; $p = .002$) over the course of 3-years, and similar trends were reported for PCI patients (HR, 0.33; 95 percent CI, 0.21–0.52; $p < .0001$). Ninety-day mortality was 3 percent (after CABG) and 2 percent (after PCI) among patients discharged with WDs compared with 7 percent (CABG) and 10 percent (PCI) among patients discharged without a WD (p-values for difference and raw numbers were not reported). One study reported on VT/VF incidence and in that study 0.82 percent (2/243) of WD users experienced a VT and/or VF event over the course of 46.5 median days of WD use. Among those who experienced a VT/VF event, 50 percent (1/2) experienced successful termination of one or more arrhythmic events over the course of 59.8 $\pm$ 32 days (mean or median days not specified) as reported in one study. No studies reported on all-cause mortality and inappropriate shocks for this patient group.

3a. *3a.* $\leq$ 3 months *non-ischemic cardiomyopathy (NICM) and LVEF* $\leq$ *0.35*
3b. *3b.* $>$ 3 months *non-ischemic cardiomyopathy (NICM) and LVEF* $\leq$ *0.35*

Four retrospective cohort studies assessed the effectiveness of WD use among NICM patients (17;19;23;24). None of the studies specifically reported whether WD use started $\leq$ or $>$ 3 months after NICM diagnosis. Three of the studies described patients as "newly diagnosed," with "recent NIMC," or prescribed a WD "during medical optimization in the ICD qualification period." The fourth study did not describe a timeframe. All studies included patients with a LVEF $\leq$ 0.35. Two studies reported all-cause mortality, and on average 3.7 percent (12/325) of patients died over 54.9 mean days of WD use. Two studies reported on VT/VF related mortality, and on average 0.14 percent (1/712) of the study population died of these causes over the course of 52.6 mean days of WD use. Of those who experienced a VT/VF event, one study reported that 25 percent (1/4) died over the course of 59.8 $\pm$ 32 days (mean or median not specified). Based on three studies that reported on VT/VF incidence, on average 0.57 percent (5/871) of WD users experienced a VT and/or VF event over the course of 52.6 $\pm$ 69.9 mean days (mean duration of use reported only in one of the studies). Among those who experienced a VT/VF event, on average 80 percent (4/5) experienced successful termination of one or more arrhythmic events over 52.6 $\pm$ mean days of WD use (two studies). Inappropriate shocks occurred in 0.61 percent (2/325) of WD users on average over 52.6 mean days of use (two studies). No studies reported on survival.

4. Ischemic cardiomyopathy

Three retrospective cohort studies assessed the effectiveness of WD use among ICM patients (24–26). All-cause mortality was reported in one study and in that study no deaths (0/53) occurred over 135 $\pm$ 127 days of WD use (mean or median days not specified). The same study also reported VT/VF incidence was 0 percent over the course of 135 $\pm$ 127 days of WD use. In a study in which VT/VF was induced during an electrophysiological study, the WD successfully terminated 100 percent (12/12) of events. No studies reported on VT/VF related mortality, VT/VF specific mortality, survival, or inappropriate shocks.

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Research Question 4

Inappropriate shocks occurred among 1.6 percent (range, 0.63–3 percent days) of WD users as reported in fifteen studies (fourteen retrospective and one prospective) over the course of 60.4 mean days of WD use (range, 41–527 days). Patients used the WD daily for an average of 19 hours per day (based on thirteen studies—twelve retrospective and one prospective) for 74 days (range, 41–527 days, based on eleven studies). Other reported harms included a burn from an inappropriate shock, discomfort and lifestyle issues to the point of discontinued use, and unspecified adverse reactions.

Quality of Evidence and Risk of Bias

Table 3 provides a synthesis of the results and quality of evidence for questions 1 and 2, and Supplementary Table 2, which can be viewed online at http://dx.doi.org/10.1017/S026646231400004X, contains a synthesis of the results and quality of evidence for question 3. Overall, we found that the body of evidence related to the effectiveness of wearable defibrillators has several notable limitations and received an average of 4.2 stars of a possible 9 on the Newcastle-Ottawa Scale. This mid- to lower-end score indicates that considerable threats to internal validity were present in the majority of studies. Using the GRADE approach, we found that evidence for the majority of outcomes (89 percent, seventeen of nineteen) received a rating of "very low quality" and only evidence pertaining to the patient group "ischemic cardiomyopathy" received a "low quality" rating (11 percent, two of nineteen outcomes). Overall, limitations included: no randomized control trials identified, only one study compared WD use with no use, only one study compared the WD with an another resuscitation method, relative effect estimates (relative risk or odds ratios) were not reported in any of the studies, the majority of studies do not discuss how missing data was addressed, patient loss to follow up went unreported, the device manufacturer was the sole source of data for most studies, and for the majority of studies at least one author was affiliated with the device manufacturer. The majority of evidence comes from retrospective cohort studies (twenty-eight studies) of which only nine used a comparison group. Retrospective designs are inherently prone to selection bias—participants who are retrospectively chosen for a WD study from the manufacturer's database may be inherently different from those who never received a WD (e.g., eligibility, sex, health care usage)—in addition, differential loss to follow up between WD users and non-users may bias results (27).

DISCUSSION

Summary of Evidence

This review included thirty-six articles and conference abstracts from thirty-three studies. Although based on low quality evidence, with the majority of study authors affiliated with the device manufacturer, it seems likely that the use of WDs compared with no defibrillator use reduces the chance of VT/VF associated deaths by an absolute risk of approximately 1.4 percent to an absolute risk of approximately 0.33 percent (an absolute risk reduction of approximately 1 percent, achieved by averting approximately 4/5ths of all VT/VF-associated deaths). Magnitude of effect from WDs is qualitatively consistent across high risk patient groups (e.g., post-MI with EF $<$ 35 percent, post-CABG or PCI (PTCA) with EF $<$ 35 percent). Therefore, it seems likely that WDs prevent approximately 1 percent of deaths in high risk groups for which implantable defibrillators are not viable clinical options, a difference that many practitioners would consider clinically significant. Due to the sparseness of data, it is difficult to make inferences about the heterogeneity of WD-associated benefit across different high risk groups. However, it is possible that magnitude of benefit attributable to WD may be modestly greater for post-MI patients than for post-CABG patients.

This review found that the overall body of evidence on the efficacy and effectiveness of WD use was of low to very low quality, such that our confidence in the reported estimates is weak. Notable limitations that hindered quality scores include: all studies were observational, the few studies that included a control group drew controls from a source different from the exposure group, strong indication of publication bias in that the majority of papers were authored by investigators affiliated with the device manufacturer, no discussion on how missing data and patients lost to follow up were handled in the analysis, and majority of evidence was published in conference abstracts without proceeding journal publications. Two randomized trials are currently under way (ClinicalTrials.gov ID Nos. NCT00628966 and NCT01446965), which will play an important role in producing estimates that can validate or refute the current body of observational studies.

Limitations of Review

This review has several limitations, the most notable are discussed here. First, it is possible that not all studies related to WD efficacy and effectiveness were identified in our search, which may have contributed to publication bias. However, we pilot tested our search strategy with several search engines, tested varying combination of words, and opted for a strategy that erred on the side of greater sensitivity and modest specificity (i.e., casting the widest possible net that would ensure inclusion of the most relevant studies with the tradeoff that many "false positives" would also be captured). We also culled bibliographies of published and gray literature to ensure we identified citations that may have been missed in the formal search. Second, we did not contact study authors to clarify methodological ambiguity (primarily treatment of missing data and loss to follow up) and instead relied on what was reported, which could have implications on the quality of evidence scores. However, we do not believe overall GRADE scores would have improved given that all individual studies had multiple indications of risk

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Table 3. Synthesis and Quality of Evidence for Questions 1 and 2

Research question 1: How efficacious and/or effective are wearable defibrillators (WD) *compared to no WD use* among adult patients (≥ 18 years old) at high risk of sudden cardiac death?

Quality assessment						Summary of findings					
						No of patients		Effect			
No of studies	Design	Quality, average NOS risk of bias rating	Consistency	Directness	Other modifying factors	Group A	Group B	Relative (95% CI)	Absolute risk	Quality	Importance
1	Retrospective cohort	Serious, NOS = 5	–	Not serious	Publication bias suspected	WD = 809	Non-WD = 4149	HR 0.54 (0.43–0.68)	Not reported	Very low quality [a]	Critical

Research question 2: How efficacious and/or effective are wearable defibrillators *compared to other resuscitation methods* (i.e., ICD and external defibrillators) among adult patients (≥ 18 years old) at high risk of sudden cardiac death?

Quality assessment						Summary of findings					
						No of patients		Effect			
No of studies	Design	Quality, average NOS risk of bias rating	Consistency	Directness	Other modifying factors	Group A	Group B	Relative (95% CI)	Absolute risk	Quality	Importance
All-cause mortality (# of deaths from all causes/study sample)											
1	Observational design	Serious, NOS = 6	–	Not serious	Publication bias suspected	WD = 2207	ICD = 1677	–	3-months, WD vs. ICD: 3.6% vs. 4.4% (CI not reported, p = 0.26) 3-year, WD vs. ICD: 20.5% vs. 22.1% (CI not reported, p = 0.29)	Very low quality[b]	Important
Survival											
1	Observational design	Serious, NOS = 6	–	Not serious	Publication bias suspected	WD = 2207	ICD = 1677	3-month: HR 0.83 (0.60–1.14) 3-year: HR 0.92 (0.79–1.07)	–	Very low quality[b]	Critical

a. Retrospective design, non-exposed cohort drawn from a different source than exposed cohort, no statement on how missing data was handled, and no statement on the proportion of patients lost to follow up. Authors report use of an adjusted model but variables not reported. Propensity score matching was used but not clear on which variables matching occurred and how similar groups were after matching. In all studies, at least 1 author was employed by the device manufacturer. Limited generalizability since cohort only includes revascularized patients.

b. Retrospective design, non-exposed cohort drawn from a different source than exposed cohort, no statement on how missing data was handled, and no statement on the proportion of patients lost to follow up. At least 1 author was employed by the device manufacturer and data for the exposed cohort came from a database maintained by the device manufacturer.

HR, hazard ratio; ICM, ischemic cardiomyopathy; NICM, non-ischemic cardiomyopathy; LVEF, left ventricular ejection fraction; NOS, Newcastle-Ottawa Scale (rating out of a possible 9 stars where 9, minimal threats to internal validity); VT/VF, ventricular tachycardia/ventricular fibrillation; WD, wearable cardioverter defibrillator.

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of bias, and scores could only be raised if there were no indications of risk of bias. Finally, only one reviewer extracted data from a large pool of studies and thus data may have been missed and mistakes made.

Conclusion and Policy Implication

This review did not find data that would suggest that the wearable defibrillator is superior to implantable defibrillators. Therefore, wearable defibrillators need only be considered in groups for whom implantable defibrillators are not a viable clinical option (for example, during a designated window of inoperability after MI). It would be reasonable to link use of WDs to gathering of additional evidence regarding whether shorter "bridge" periods to ICDs are safe (40 days post-MI and 90 days post-CABG or PCI). Should new evidence emerge that suggests a shorter time interval to ICD implantation is safe, then coverage would likely be affected.

WDs are associated with serious adverse events; in particular inappropriate shocks, which may be associated with burns, psychological trauma, and other adverse events. Because the chance of a WD patient receiving an inappropriate shock is slightly greater than the chance of a WD patient receiving an appropriate shock (1.6 percent versus 1.5 percent), it may be reasonable to require evidence of shared decision making and patient valuation of the possible harm from adverse events before WDs are used.

SUPPLEMENTARY MATERIAL

Supplementary Tables 1 and 2: http://dx.doi.org/10.1017/S026646231400004X

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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