Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Olgin JE, Pletcher MJ, Vittinghoff E, et al. Wearable cardioverter–defibrillator after myocardial infarction. N Engl J Med 2018;379:1205-15. DOI: 10.1056/NEJMoa1800781

SUPPLEMENTARY APPENDIX

TABLE OF CONTENTS

INVESTIGATORS AND ENROLLING SITES (numbers recruited)

USA: McLeod Cardiology Associates (103), Rajesh Malik; **Ochsner Medical System** (95), Daniel Morin; **Hartford Hospital** (74), Steven Zweibel; **Wellmont Holston Valley** (68), James Merrill; **Brown/Providence Hospital** (65), Peem Lorvidhaya; **University of KY Gill Heart Institute** (60), Samy Claude Elayi; **Geisinger Heart Institute** (59), Pughazhendi Vijayaraman; **Montefiore Medical Center** (53), Jay Gross; **University of North Carolina Chapel Hill** (52), J. Paul Mounsey; **Lenox Hill Hospital** (50), Nicholas Skipitaris; **Albany Associates in Cardiology** (47), Robert Phang; **University of MA Memorial Hospital** (46), Lawrence Rosenthal; **Stony Brook University** (41), Eric Rashba; **Oklahoma Heart Institute** (38), David Sandler; **Carilion Clinic** (37), Soufian AlMahameed; Presbyterian Heart Group Albuquerque (33), Lawrence Nair; **Chambersburg Hospital** (32), Aylmer Tang; **Wake Heart Research** (32), Robert Lee Jobe; **Long Island Jewish Hospital** (31), David Slotwiner; **Watson Clinic** (31), Neal Kavesh; **University Hospital-Case Medical Center** (28), Mauricio Arruda; **Columbia Providence Cardiology** (28), Venkateshwar Gottipaty; **North Ohio Heart Center** (27), Kara Quan; **St. Luke's-Roosevelt Hospital** (25), Emad Aziz; **Baylor University Medical Center** (25), Jay Franklin; **Massachusetts General Hospital** (19), Theofanie Mela; **Christiana Care Health Services** (19), Michael Stillabower; **Multicare Institute for Research** (18), Tariq Salam; **McFarland Clinic** (16), M. Imran Dotani; **Duke University** (16), Donald Hegland; **University of FL** (15), William Miles; **Mt Sinai New York** (14), Nicholas Skipitaris; **The Guthrie Clinic** (13), Edo Kaluski; **Dean Foundation** (13), Peter Lee; **University of TX Southwestern** (13), Richard Wu; **Cardiovasculary Consultants Heart Center** (13), Michael Gen; **Advocate Christ Hospital** (12), Manoj Duggal; **University of Colorado Denver** (12), Duy Nguyen; **UCSF** (12), Gregory Marcus; **St. Vincent Medical Group** (9), Sandeep Joshi; **University Cardiovascular Associates** (8), Sarah Taylor; **SJH Cardiology Associates** (7), Ali Al-Mudamgha; **Ohio State University** (7), Emile Daoud; **Huntington Hospital** (6), Paul Maccaro; **Melbourne Cardiac Institute** (6), Rajiv Chandra; **Wake Forest University Health Sciences** (6), Tony Simmons; **Alaska Heart & Vascular Institute** (6), Steven Compton; **Endovascular Research** (6), Romakota Reddy; **United Health Services** (5), Nicholas Stamato; **Heart Group/Deaconess Hospital** (5), Chandrashekar Kumber; **Marshfield Clinic** (5), John Hayes; **UCSD** (5), Ulrika Birgersdotter-Green; **St Francis Hospital Indianapolis** (4), Robert Kinn; **Indiana University School of Medicine** (4), Gopi Dandamudi; **Cleveland Clinic** (4), Mina Chung; **Louisville Cardiology** (4), Rudolph Licandro; **Methodist Hospital Houston** (4), Miguel Valderrabano; **Tufts Medical Center** (3), Jonathan Weinstock; **ProHealth Care Waukesha** (3), Waseemuddin Kazi; **Heart and Vascular Institute Safety Harbor** (3), Jonathan Hobson; **Vanderbilt Health** (3), Walter Clair; **Cardiovascular Associates of Mesa** (3), Andrew Kaplan; **Salinas Valley Memorial** (3), Harlan Grogin; **Brigham and Women's Hospital** (2), Bruce Koplan; **University of Pittsburgh** (2), David Schwartzman; **Emory University** (2), Angel Leon; **Western KY Heart and Lung** (2), Frank Schwender; **Turkey Creek Medical Center** (2), Malcolm Foster, III; **University of TX Health Science Center** (2), Anne Dougherty; **San Diego Cardiac Center** (2), Charles Athill; **Valley Hospital Ridgewood, NJ** (1), Gerald Sotsky; **Parkview Research Center Ft Wayne** (1), Mirro, Michael; **Liberty Cardiovascular Specialists** (1), Venkat Pasnoori; **FL Heart Group/FL Hospital** (1), George Monir; **Little Rock Cardiology Clinic** (1), Wilson Wong; **Cardiology Associates of Corpus Christi** (1), Wassim Choucair.

POLAND: Medical University of Lodz (108), Jerzy Krzysztof Wranicz; **Samodziedlny Publiczny Zaklad** (86), Piotr Wanczura; **American Heart of Poland-Chrzanow** (57), Aleksander Zurakowski; **Wojewodzki Szpital Zespolony Torun** (49), Grzegorz Skonieczny; **Institute of Cardiology Warsaw** (43), Milosz Marona; **II Oddzial Kardiologiczny Bielsko-Biała** (41), Leszek Kinasz; **Swissmed Vascular Gdansk** (36), Nader Elmasri; **Medical University of Warsaw** (34), Marcin Grabowski; **Medical University of Silesia Warsaw** (25), Maciej Sterlinski; **American Heart of Poland-Dabrowa Gornicza** (25), Marcin Debinski; **American Heart of Poland-Tychy** (22), Maciej Pruski; **Gdanski Uniwersytet Medyczny** (21), Grzegorz Raczak; **Indywidualna Specjalistyczna Praktyka Lekarskais Lodz** (14), Andrzej Lubinski; **EMED Centrum Uslug Medycznych** (10), Andrzej Przybylski; **Wojskowy Instytut Medyczny Warsaw** (9), Zbigniew Orski; **American Heart of Poland Kedzierzyn-Kozle** (9), Janusz Prokopczuk; **Centrum Medyczne LukaMed Chojnice** (8), Monika Lica-Gorzynska; **Specjalistyczna Poradnia Kardiologiczna Kielce** (8), Beata Wozakowska-Kapłon; **Jagiellonian Univesity Hospital Krakow** (2), Danuta Czarnecka; **American Heart of Poland-Polanica-Zdroj** (7), Hubert Krupa; **NZOZ Vitamed Bydogoszcz** (6), Robert Romanekl; **American Heart of Poland Ustron** (3), Bartosz Skwarna; **American Heart of Poland-Myszkow** (3), Artur Mendyk; **American Heart of Poland Nysa** (6), Karol Stania;

GERMANY: **Klinikum Links der Weser Bremen** (58), Rainer Hambrecht; **Universitätsmedizin Mannheim** (28), Martin Borggrefe; **Universitätsmedizin Göttingen** (22), Markus Zabel; **Klinikum der Stadt Ludwigshafen** (16), Thomas Kleeman; **Uniklinik Heidelberg** (11), **Dierk Thomas; Universität Mainz** (7), Thomas Munzel.

HUNGARY: Semmelweis University Budapest (6), Bela Merkely; **University of Debrecen** (3), Zoltan Csanádi.

STUDY GOVERNANCE AND OVERSIGHT

An overview of the governance and oversight of VEST is shown in Figure S1. The clinical sites were managed by the Clinical Coordinating Center at UCSF (Olgin, PI). Data collection systems were managed separately by the Data Coordinating Center at UCSF (Pletcher, PI). All study sites were directly contracted with and managed by the Clinical Coordinating Center as the study sponsor, and data was directly sent from the sites to the Data Coordinating Center. All members of the Clinical Coordinating Center were blinded to the data until the database was locked. The study was overseen from the beginning by the independent Data and Safety Monitoring Board (DSMB) (Table S1), originally appointed by the NIH, that operated throughout the study. The DSMB met at least twice per year to review the status of the study, review un-blinded data reports, approve any protocol or analysis plan changes and approve continuation of the study. The VEST Steering Committee (Table S2) was responsible for scientific and technical oversight of the study, protocol revisions and publications. The Executive Committee (Table S3) was responsible for general oversight, quality control and overseeing regular operations.

CLINICAL SITE MANAGEMENT AND MONITORING

The study began with 60 sites in the United States, which expanded due to lower than expected enrollment and site terminations (for lack of enrollment at those sites). In 2013, study sites in Germany, Poland and Hungary were added. At the end of the study, there were a total of 108 sites that enrolled at least 1 participant—76 in USA, 6 in Germany, 24 in Poland and 2 in Hungary. By the end of the study, of the 2302 participants randomized and followed, 1520 were from USA, 632 from Poland, 141 from Germany and 9 from Hungary (Table S6). The CONSORT diagram shows the flow of participants through the phases of the study in Figure S3. One site in the US (not included in the 76) was dismissed on June 24, 2014, and their participants (n=46) were excluded from analyses, at the request of the site IRB and approved by the study DSMB, due to irregularities found by the site IRB.

Clinical site monitoring in the US, Germany, Hungary, and Poland was conducted throughout the entire VEST trial to ensure the integrity of the study. The UCSF VEST Clinical Coordinating Center (CCC) was responsible for coordination of the overall monitoring process, data collection associated with the study, and for overall study management. ZOLL, under the supervision of the UCSF Clinical Coordinating Center, provided field-based clinical monitoring duties. The UCSF Clinical Coordinating Center was responsible for oversight and training of all VEST study staff, including those employed/contracted directly with ZOLL for monitoring purposes. ZOLL contracted with the Contract Research Organization (CRO), Premier Research, to provide Clinical Research Associates (CRA) for monitoring in Germany. In Poland and Hungary, CRAs were directly contracted with ZOLL.

All VEST monitors and CRAs received training (i.e., ICH/GCP guidelines) and VEST study specific training by the UCSF Clinical Coordinating Center, as per the VEST Monitoring Plan prior to start of any work on the trial. The CCC reviewed qualifications and training of all monitors/CRAs to confirm that they were qualified to perform clinical monitoring activities as per US regulations and standards governing the VEST study.

Monitoring was performed using periodic in-person site visits, as well as remote electronic data monitoring on a daily basis. In-person monitoring visits were conducted throughout the duration of the clinical trial as a means of assessing regulatory and protocol compliance. Site monitoring visits were conducted up to 2 times per year at each actively enrolling site. After enrollment was completed, visits

were conducted at sites to continue monitoring of regulatory documentation and adherence to follow-up study procedures. The VEST Monitor, who conducted an in-person monitoring visit was required to document the monitoring visit using the VEST Monitoring Visit Report. The UCSF Clinical Coordinating Center reviewed and approved all completed Monitoring Visit Reports prior to sending the monitoring follow up letter to the Investigator. The Monitor and CCC then performed follow-up with the site to ensure implementation of any corrective actions with the Investigator and/or study staff.

ROLE OF SPONSORS

The Clinical and Data Coordinating Centers were initially funded by the NIH until 2010 and then by ZOLL thereafter. ZOLL funded the Coordinating Centers, US site and participant costs, through a grant to UCSF (Olgin, PI). Contracts with study sites in the US were between UCSF and the site while site contracts were between ZOLL and the site in the European sites. The NIH approved the protocol and governance and appointed the DSMB. ZOLL played no role in trial design, trial center selection, trial oversight, center supervision, data analysis, data interpretation, manuscript preparation, or the decision to submit for publication. There was one employee of ZOLL (Steve Szymkiewicz, MD) who served as a non-voting member of the Steering Committee. All data were processed and stored at the UCSF Data Coordinating Center with the exception of data transmissions from the WCD which went automatically to ZOLL and then to the UCSF Data Coordinating Center. ZOLL did participate in site monitoring as detailed above.

HISTORY OF THE STUDY

The study began in 2008 (first participant enrolled in 2009) as a "dual" study called VEST PREDICTS— Vest Prevention of Early Sudden Death Trial and PREDiction of ICd Treatment Study (NCT00628966).[1] This publication reports results from the VEST portion of the project. PREDICTS was an observational study into which participants of VEST entered after final follow-up (90 days after discharge from hospitalization for an index MI). PREDICTS participants received an implantable device, either an ICD (if clinically indicated) or an implantable loop recorder (ILR), to identify predictors of ventricular tachycardia and sudden death.[1] An ILR was implanted instead of an ICD in participants whose EF recovered to >35%. The purpose of PREDICTS was to develop a risk stratification algorithm that predicted future ICD shock or sudden death over 5 years in patients who were admitted for an acute MI with an EF ≤35% (the VEST population).

The Clinical and Data Coordinating Centers for VEST PREDICTS were funded by the NIH/NHLBI (U01HL089458 and U01HL089145, respectively) from September 1, 2007 to May 31, 2011, while ZOLL and Medtronic funded the site and participant costs of VEST and PREDICTS, respectively. GE Healthcare provided ECG equipment to the study, through a research contract to UCSF, but no direct funding for the study. Since VEST PREDICTS had been planned as an 8-year study, ZOLL and Medtronic were to fund the continuation of the Coordinating Centers at UCSF at the end of the planned NIH funding 5-year period to complete the study. However, due to slower than expected enrollment and financial considerations at the NIH and Medtronic, both the NIH and Medtronic decided to end funding in 2011, 1 year prior to the planned end of 5-years of NIH funding and 3 years prior to the planned end of Medtronic funding. Nevertheless, ZOLL continued funding of VEST and added funding for a VEST Registry. VEST continued enrollment as VEST and VEST Registry (NCT01446965). The original

protocol, latest protocol and summary of changes, including the analysis plans are included as a supplement. Outcomes reported in this manuscript are detailed in Table S5.

DESCRIPTION OF THE WEARABLE CARDIOVERTER DEFIBRILLATOR

The wearable cardioverter defibrillator (LifeVest® 4000, ZOLL, Pittsburgh, USA) consists of a monitor, worn at waist level, and sensing and therapy electrodes, assembled into a washable garment, that is worn on the patient's chest, as shown in Figure S2. The monitor contains the capacitors, the computing circuitry, and a rechargeable battery pack. It is capable of delivering a minimum of five 150-joule shocks at the end of battery life (battery packs are exchanged daily). The four dry ECG sensing electrodes are arranged as front-back and left-right lead pairs. There are three defibrillation electrodes, one over the apex of the heart and two located posteriorly for an apex-posterior defibrillation path. The self-gelling electrodes release a highly visible blue gel upon detection of a sustained ventricular arrhythmia just prior to defibrillation therapy. Each patient receives two battery packs, a battery charger, and two garments. An additional function of the battery charger is to receive data (ECG recordings and daily use time) from the monitor and transmit it to a central server.

The device algorithm assesses ECG quality while monitoring the cardiac signal for the presence of a treatable arrhythmia (i.e., VT or VF) and for asystolic episodes. The ECG quality is assessed through detection of loss of skin contact with individual electrodes, detection of high frequency interference, detection of signal clipping and the presence of artifacts. Both leads are used for arrhythmia monitoring but if one lead is compromised then the device uses the other in a single lead detection mode.

VT and VF have separate rate thresholds and the VT range additionally uses morphology matching for determining the presence of a treatable arrhythmia. A template of the morphology is obtained during device setup. The default thresholds were used in this study (150 BPM for VT and 200 BPM for VF). While the maximum output is 150 joules (default), each of the five shocks in a treatment sequence can be programmed from 75 to 150 joules. The default output was used in this study.

When the algorithm determines a treatable arrhythmia is present, it first goes through a 10 second silent phase to confirm the persistence of the arrhythmia. It then goes through a series of alarms, during which patients are trained to use the response buttons to inform the algorithm that they are conscious. As long as the response buttons are held, the device will not deliver a shock (aborted shock). When the patient loses consciousness and releases the response buttons, the series of alarms begin again. During the alarm sequence the cardiac signal continues to be evaluated by the algorithm and if the absence of an arrhythmia is determined, the alarm sequence is aborted. The series of alarms consists of 5 seconds of vibration followed by a two-tone siren for an additional 5 seconds. After 10 seconds the siren becomes louder, and after 15 seconds bystander warnings of a potential shock are given. The therapy electrodes release gel about 20 seconds into the alarm sequence. The shock delivery occurs after 25 seconds. Shocks are delivered synchronized but an unsynchronized shock will be delivered if the rhythm is unstable. In the VT threshold, the louder siren alarm lasts 35 seconds before proceeding to bystander warnings.

Asystolic episodes are triggered for rates less than 10 beats per minute. Cardiac complexes must be at least 0.1 millivolts from isoelectric to be sensed. Asystole alarms are designed to alert bystanders and instructs them to call for help.

The device records daily use and also stores ECG recordings. For arrhythmia detections, the device stores 30 seconds prior to and 15 seconds after the alarm from a pre-recording buffer. For asystole

detections, 5 minutes of ECG prior to the detection is stored in the ECG recording but no post-buffer is stored. Patients can also save a 45 second section of ECG by holding the response button for longer than 3 seconds (30 seconds prior to activation and 15 seconds afterwards). Event data are transmitted over wireless networks to a central monitoring service.

SAMPLE SIZE CALCULATION

Original sample size estimate of 4506. The original VEST sample size was estimated using data-based estimates of the following factors:

- Total mortality in the first 2 months following an MI in patients with EF≤35% is 5.1%. The VALIANT Study,[2] the EPHESUS Study,[3] and the DINAMIT Study[4] were studies reporting on all-cause and sudden death rates in the early period following an MI in populations similar to our study population. A meta-analysis of these study populations gives a summary estimate for overall mortality of 5.1%.
- Mortality due to sudden death in the first 2 months following an MI in patients with EF≤35% is 2.4%. A meta-analysis of sudden death rates in VALIANT, EPHESUS, and DINAMIT provides a summary estimate for the sudden death rate of 2.4%.
- Mortality due to ventricular arrhythmias in the first 2 months following an MI in patients with EF≤35% is 2.2%. The wearable defibrillator vest should be effective at reducing only sudden death due to a ventricular arrhythmia. The preliminary data from the wearable defibrillation vest shows that 91% of all sudden cardiac arrests are due to ventricular arrhythmias. This is consistent with estimates in the literature. Therefore, 91% of 2.4% would give us an expected mortality of 2.2% due to ventricular arrhythmia.
- The effectiveness of the wearable defibrillator to reduce sudden death due to ventricular arrhythmias will be 79.7%. Previous analyses show that the WCD conversion success rate is 98% for syncopal VT/VF. However, we estimated that approximately 90% of patients tolerate the WCD whereas 10% of patients stop wearing it within 1-2 days. The patients that do tolerate the device will wear it on average 21.7 hours per day or about 90.4% of each day. The overall effectiveness of the WCD used was 79.7% (98% x 90% x 90.4%).
- Given the above assumptions, we estimated an event rate of 5.1% in the control group and 3.3% in the wearable defibrillator group (35% reduction in mortality). The absolute reduction in mortality is the mortality from ventricular arrhythmia (2.2%) times the effectiveness of the WCD (79.7%) = 1.8%, so that the total mortality rate in the defibrillator WCD group is expected to be the mortality in the control group minus the absolute reduction or 5.1%-1.8% = 3.3%.
- Given the short follow-up period (2 months) and strong efforts to collect complete data, we anticipate minimal loss to follow-up and minimal crossover. Crossover in the treatment group (WCD group) was accounted for by the adherence rate estimate. Given that the WCD is only available by prescription, we expected that crossover from the control group to the treatment group would be exceedingly rare.

Using these estimated all-cause mortality rates of 5.1% (Control) and 3.3% (WCD arm), we used standard methods for tests of differences in proportions to estimate that a sample of 4506 participants, randomized 2:1 to the WCD and control, would provide 80% power in 2-sided tests with a type-I error rate of 5% to detect the hypothesized 1.8 percentage point reduction in total mortality.

Change of primary outcome and follow-up period, allowing for a reduction in sample size to 1890. In response to difficulties in recruitment, in December 2009, the VEST DSMB, Steering Committee and IRBs approved changing the primary outcome from all-cause mortality to sudden cardiac death, and also changing the follow-up period from 60 to 90 days. The updated sample size calculation was based on an increase of 25% in the expected control event rate, from the original meta-analytic estimate of 2.4% to 3.0%, due to the extension of follow-up from 60 to 90 days and an event rate of 1.0% in the WCD group, after accounting for expected adherence to the WCD of 70% and WCD efficacy of 98% during hours of use for the assumed 91% of sudden deaths that can be averted by an appropriate shock. In estimating the expected reduction in sudden death, we accounted for week-by-week declines in VEST compliance, based on the observed data, as well as in sudden death rates, following the pattern observed in VALIANT.[2]

Provision for sample size re-estimation. We recognized in computing the sample size that it was sensitive to our assumptions. Among those assumptions, the proportion of sudden deaths due to ventricular arrhythmia and the efficacy of the WCD in preventing those deaths were considered relatively solid, but the sudden death and WCD adherence rates were less certain. To address these uncertainties, in December 2009 the DSMB and Steering Committee approved updating the sample size at regular intervals during the conduct of the trial, using methods that do not inflate the type-I error rate. Specifically, we proposed using blinded VEST data to estimate the marginal sudden death rate, as well as unblinded data to estimate adherence in the WCD arm. In combination with our prior estimates of the proportion of sudden deaths due to ventricular arrhythmia and the efficacy of the WCD in preventing those deaths, this would allow us to re-estimate sudden death rates by group, and on that basis to re-calculate sample size. Because this procedure would be blinded to treatment assignment, no meaningful inflation of the type-I error rate was expected.[5]

Clarification of primary outcome definition. In September 2011, as recommended by the DSMB, the primary outcome definition was clarified and the final text in the protocol was changed from sudden death to combined “sudden death and death due to ventricular arrhythmia”.

Final sample size update to 2300. At several meetings during the course of the study, the DSMB considered but did not elect to change the sample size of 1890 agreed on in December 2009 However, in September 2015, in accord with the plan for sample size re-estimation approved in December 2009, the DSMB approved an increase in the sample size to 2300, which was estimated to provide 70% power. Following the December 2009 plan approved by the DSMB, these calculations did not use unblinded information on event rates by group; instead, they used then-current sample information on the marginal sudden death rate (1.66%) as well as average adherence to the WCD (58.6% or 14.1 hours per day). The implicit group-specific event rates consistent with prior assumptions about WCD efficacy and average adherence information were 1.15% in the WCD arm and 2.68% and in the Control arm.

ADJUDICATION AND DEFINITIONS OF OUTCOMES

Outcomes were adjudicated by an independent, blinded panel of adjudicators, who were all board-certified cardiologists. Hospitalization records, autopsy reports, death certificates and narratives of accounts from witnesses of the events (or circumstances of last being seen) were available to the adjudicators. Data from the WCD were not used in the adjudication of outcomes and records were redacted to remove any mention of WCD use; sham redaction was used in controls to maintain the

blinding. All outcomes were adjudicated by 2 independent adjudicators; a third adjudicator, blinded to the other two adjudications, was used to resolve discordant adjudications. Outcomes initially found to be indeterminate (could not clearly be classified as Sudden or Non-Sudden Death) were re-reviewed by a separate panel of blinded cardiologists.

The following definitions were used for adjudication of deaths:

1. *Sudden death*[6,7]—For *witnessed deaths*, sudden death was defined as an unexpected non-traumatic, non-self-inflicted fatality in otherwise stable participants who died within one hour of the onset of the terminal symptoms. For persons dying more than one hour after a cardiac arrest from a ventricular arrhythmia (eg. after a hospitalization from the cardiac arrest), the non-sudden death due to ventricular arrhythmia category was used (see below). For *unwitnessed deaths*, participants met the definition of sudden death if they were found dead within 24 hours of being well, assuming there was no evidence of another cause of death during that period. Unwitnessed deaths when the participant was found dead more than 24 hours after last being seen with no arrhythmia data, autopsy results or other information regarding the cause of death were adjudicated as *indeterminate* cause of death.
2. *Non-sudden death due to ventricular arrhythmia* was used when the most likely initiating cause of death was ventricular arrhythmia, but the definition of sudden death is not met. For example, this occurred when a person suffered a cardiac arrest from an acute ventricular arrhythmia, was admitted to the ICU, but did not die until several days after the arrest. This event type was included in the primary outcome definition (sudden death or death due to ventricular arrhythmia).
3. *Non-sudden death* was used when criteria were not met for either sudden death or non-sudden death due to ventricular arrhythmia; these deaths were not included in the primary outcome definition.
4. *Indeterminate* was used when there was insufficient information available to determine whether the death was sudden or non-sudden.

Our primary outcome was the combined outcome of sudden death and non-sudden death due to ventricular arrhythmia, which we refer to in the manuscript as “arrhythmic death”.

The following criteria were used for adjudication of myocardial infarction:

1. Diagnostic rise and/or fall of biomarkers and evidence of ischemia (symptoms of ischemia, new ischemic ST-T changes, new LBBB, new pathological Q waves, or new loss of viable myocardium or new regional wall motion abnormality); OR
2. Sudden death with cardiac arrest, and other evidence of MI; OR
3. PCI with normal baseline biomarkers and subsequent biomarker risk to >3 x ULN; OR
4. CABG with event biomarkers >5x ULN and evidence of infarction/vessel occlusion as documented by new LBBB or new pathological Q waves or new angiographically documented graft/vessel occlusion or pathological findings of acute MI; OR
5. Pathological findings of acute MI

The following criteria were used for adjudication of stroke:

1. Rapid onset of a neurologic deficit consistent with arterial obstruction or rupture lasting >24 hours and without evidence of another cause; OR

2. Imaging evidence of a new stroke in conjunction with clinical findings of a possible cerebrovascular event

The following criteria were used for adjudication of congestive heart failure:

1. New or worsening symptoms, including at least one of the following: dyspnea on exertion or dyspnea at rest, orthopnea, ankle swelling, or paroxysmal nocturnal dyspnea; AND
2. Objective evidence of heart failure, as indicated by at least one of the following: Rales, increased JVP, S3 gallup, cardiomegaly and/or pulmonary edema on CXR or CT, systolic and/or diastolic dysfunction on echocardiogram; AND
3. New or intensified intravenous/invasive therapy, as indicated by at least one of the following: intravenous diuretic, vasodilator, or inotropic medication, other invasive therapy intended to treat heart failure exacerbation (e.g., dialysis, ultrafiltration).

The following criteria were used for adjudication of a clinically significant arrhythmia (either ventricular tachycardia or ventricular fibrillation; or an other clinically significant arrhythmia):

1. New or worsening signs and symptoms (not met by incidental identification of an asymptomatic arrhythmia); AND
2. Evidence that an arrhythmia occurred by one or more of the following: direct review of the ECG tracing, documented cardioversion attempt (either electrical or pharmacologic), or initiation or elevation of the dose of a medication or the implantation of a device for the purpose of controlling the arrhythmia or complications of the arrhythmia (e.g., anticoagulation for atrial fibrillation); AND
3. Arrhythmia event must have been a cause of the hospitalization, or have led to the prolongation of it

SENSITIVITY ANALYSES OF OUTCOMES

At the time the Statistical Analysis Plan was finalized, the number of participants with unknown vital status or indeterminate cause of death was substantially larger than the expected number of primary events, and we expected this to hold at the end of the trial. On this basis, we decided that inverse probability weighting of the complete cases, based on multiple logistic models for unknown vital status and indeterminate cause of death, would be a better strategy for handling missing data than multiple imputation of the missing outcomes among patients with unknown vital status or indeterminate cause of death, using iterative chained equations. The rationale was that more outcomes would allow us to fit more elaborate models, thus making the assumption that the data were covariate-dependent missing-at-random more plausible. However, aggressive efforts to obtain missing vital status and cause of death continued until the data were locked, reducing the number of participants with unknown vital status and indeterminate cause of death to 22 and 4, respectively, forcing us to simplify our plan for the weighted analysis. After multiply imputing missing covariates, we explored logistic models in rough accord with the rule of thumb of 10 outcome events per predictor. The model most predictive of unknown vital status included only treatment assignment and country, which were complete. Inverse probability weights for the analysis of total mortality were then obtained using fitted probabilities from the selected logistic model for unknown vital status, fit to the final analysis dataset with 2302 observations. For the weighted analyses of the primary outcome and non-arrhythmic death, from which deaths with indeterminate cause

of death were omitted, the weights for the remaining deaths were modified so that the overall weighted number of deaths equaled the number of all-cause deaths with known vital status.

The results of this weighted sensitivity analysis were qualitatively identical to the primary analysis. For the primary outcome of sudden death or death due to ventricular arrhythmia, the weighted model included 2276 participants (omitting those with unknown vital status and indeterminate cause of death) and yielded a relative risk of 0.67 (95% CI of 0.37, 1.2) with p=0.17. For non-arrhythmic death outcomes, the weighted model, estimated using the same 2276 participants, yielded a relative risk of 0.63 (95% CI of 0.33, 1.18) with p=0.14. For total mortality, the weighted model included 2280 participants (omitting those with unknown vital status) and yielded a relative risk of 0.64 (95% CI of 0.42, 0.97) with p=0.03.

EFFECT OF PROTOCOL CHANGES ON ANALYSES

As described above, the endpoint was changed early in the trial from total mortality within 60 days to the combined outcome of sudden death or death due to ventricular arrhythmias within 90 days. Table S7 compares the 244 participants enrolled under the 60-day protocol compared with the 2058 enrolled under the 90-day protocol. There are some statistically significant differences between these two groups, but we would not expect this to bias our results since randomization was balanced in both groups—66% of each group was randomized to WCD and 33% to Control.

The 244 participants enrolled before the protocol change were not followed through 90 days. Although the primary analysis does not account for this factor, adding an indicator for the longer follow-up to otherwise unadjusted log-binomial models for the effect of the WCD on study outcomes has no material effect (Table S10). In addition, log-rank tests in the survival analyses do account for length of follow-up and are consistent with the primary analysis results.

CORRECTION FOR MULTIPLICITY

The p values reported in the manuscript are not corrected for multiple hypothesis testing because it was not part of our pre-specified analysis plan. This becomes relevant to the finding of the associated decrease in total mortality, with an uncorrected p value of 0.04 (Table S9). With Bonferroni correction for two comparisons (viewing total mortality, the previous primary outcome, as uniquely important among the 11 secondary outcomes), the corrected p value becomes 0.08; and 0.45 if corrected for all 12 reported outcomes. However, Bonferroni correction assumes that one is testing completely independent hypotheses; but, in this case the mortality outcomes are not completely independent hypotheses since arrhythmic death and non-arrhythmic death are subsets of total mortality. Therefore, Bonferroni correction is overly conservative.[8] Using an alternative approach[8-10] that takes into account correlations between endpoints, the corrected p value for total mortality is 0.046 with adjustment for two comparisons (viewing total mortality, the previous primary outcome, as uniquely important among the secondary outcomes) and 0.22 with adjustment for all 12 outcomes. Therefore, the range of corrected p values from least conservative to most conservative range from 0.046 to 0.45.

WCD COMPLIANCE

Sites were instructed to emphasize the need to properly explain both arms of the trial during the consent process of participants, in particular obtaining their consent and willingness to comply with the results of the randomization. When randomized to the WCD, sites were instructed to specifically emphasize the need to wear the WCD as much as possible for the 3 months of the study. This included

discussions with the participant and their family and involved the study coordinator, site PI and treating physician.

The WCD monitors, records and transmits the amount of time the device is worn through impedance measurements from the electrodes. When WCD compliance was less than 15 hours in a 24-hour period for a participant, the site was alerted and asked to contact the participant to troubleshoot any problems with fitting, discomfort or alarms and reiterate the importance of wearing the WCD. When fitting or confusion about the operation of the device was the reason for not wearing the WCD, the participant underwent in-person refitting, troubleshooting re-education. This is similar to standard alerts for patients prescribed the WCD outside of the study.

The WCD wear-time is shown in Figure S4. Forty-three (2.8%) of participants randomized to the WCD arm never wore the WCD. Over the course of the 90 days, the proportion of participants who wore the WCD on a given day fell from 80.8% (CI: 78.8-82.8) just after randomization to 41.3% (CI 37.5, 44.9) at 90 days. Similarly, the average number of hours worn per day overall (including those who wore for 0 hours on a given day) also decreased over time from an average of 16.3±9.8 and median of 23.4 [IQR 7.4-23.9] hours per day after randomization to an average of 8.3±10.6 and median of 0 [IQR 0-22.2] hours per day at 90 days (Figure S4C). However, when worn, the number of hours worn per day remained high and fairly consistent over time—mean of 22.3±4.3 and median of 23.9 [IQR 23.3-24.0] hours per day after randomization and mean of 20.3±5.7 with a median of 23.2 [IQR 19.7-24.0] hours per day at 90 days. The distribution of wear-time was bimodal–the majority of those with low wear-time per day wore it for 0 hours, while those wearing it at all during the day typically wore it for more than 20 hours (Figure S4D).

The majority of deaths in the WCD group occurred in participants not wearing the WCD. Of the 48 deaths in the WCD arm, 36 occurred in participants who were not wearing the WCD at the time death. Of the 25 adjudicated sudden deaths in the WCD arm, 16 were not wearing the WCD at the time of death. One of these participants, for whom we have a detailed narrative about the circumstances of death, had removed the WCD to shower and died suddenly.

Our observed median wear-time of 23 hours per day in participants who wore the WCD is very similar to other previously published registry studies—median of 22.5 hours per day[11] and 21.7 hours per day.[12] However, overall compliance (taking into account 0 hour wear days) in our study (median of 18 hours per day) is lower than in these registries and lower than might be expected in clinical practice. There are some important distinctions when comparing compliance data in our open-label randomized trial compared to these registry studies. In our study, the denominator of the percentage wear-time is all participants who were randomized to that group, whereas in the registry, these were patients that were prescribed the WCD as part of clinical practice. There is both expressed and implied equipoise when presenting a randomized trial option to a patient that may not exist to the same extent in registries of patients receiving the WCD as part of clinical care; after all, part of the consent for our RCT is an understanding by the participant that there is a chance they may or may not receive the WCD. Despite best efforts in the study, this may create an implied “permission” to not wear the WCD and create a different participant decision-threshold to not wear the WCD compared to clinical practice (and registry) in which a patient is told the necessity of the treatment and likely with less equipoise presented. In an open-label such as this one, the participant is aware of the treatment so the “equipoise” in discontinuing an unknown therapy (for example, the participant does not know whether they are discontinuing a placebo or an actual treatment) in a double-blind trial does not exist, thus changing the calculus for

discontinuation in the presence of side-effects or discomfort. In addition, compliance in our RCT is based on wearing the WCD for the full 90 days of study; whereas the "end-point" for registry data is based on when the WCD was removed (last day worn). Thus, in our RCT, when the WCD was removed before 90 days or not worn for any day after randomization, those days counted as 0 wear days. In the registry studies, compliance timing started the first day the WCD was worn and ended the last day it was worn. These are both important distinctions that make comparing our overall compliance data (overall percent worn and overall total hours worn) to previously published registry results difficult; therefore, it may also be inappropriate to correlate the wear time seen in our study to patient compliance in clinical practice. The number hours of WCD when worn is more comparable to the data presented in registries (and likely closer to clinical practice) and are numerically similar to previous studies.[11-13] While it is generally true that adherence to therapies is often better in clinical trials due to greater supervision of care, this may not have been sufficient to overcome the issues related to equipoise in an open-label study. Importantly, the only additional scheduled appointment in the trial above standard of care is a 1-month phone follow up. The methods of ensuring WCD adherence using device measures and alert system to the study sites is identical to what is done in clinical practice.

AS TREATED ANALYSIS

Twelve participants (23% of all deaths) in the WCD group and none in the control group who died were wearing the WCD at the time of death (Table S12). One person removed the WCD for a shower in the WCD group just before he died. Among the 25 participants with adjudicated arrhythmic death, only 9 were wearing the WCD at the time of death, 4 of whom received appropriate shocks for VT/VF with conversion to sinus rhythm but subsequent recurrent VT/VF or agonal rhythm and 5 of whom had no ventricular tachyarrhythmias on the WCD at the time of death (Tale S12). Deaths and follow-up time after ICD implantation were omitted.

In order to assess impact of wearing the WCD on sudden death, non-arrhythmic death, and total mortality, we calculated event rates per 100 person-months of wearing the WCD compared to not-wearing the WCD and compared the two rates using Poisson regression. For arrhythmic death, there were 9 arrhythmic death events in 2,420 person-months of wearing time (rate 0.37 per 100 person-months) compared to 32 arrhythmic death events in 3,724 person-months of non-wearing time (rate 0.86), with a rate ratio of 0.43 (95% Poisson CI 0.21, 0.91; uncorrected p=0.03; Bonferroni corrected p=0.32). For non-arrhythmic death, there were 2 and 36 deaths, respectively (rates of 0.08 and 0.97; rate ratio 0.09; 95% CI 0.02, 0.35; uncorrected p<0.001; Bonferroni corrected p=0.009). For total mortality, there were 12 and 71 deaths, respectively (rates 0.50 and 1.91; rate ratio 0.26; 95% CI 0.14, 0.48; uncorrected and Bonferroni corrected p<0.001). Adjustment for age, education, EF, and revascularization had essentially no effect on these estimates. Analysis using Cox models gave qualitatively similar results. If wearing and non-wearing time were otherwise comparable, this analysis might estimate the efficacy of the WCD. However, these results should be interpreted with caution since greater wearing time is almost surely confounded by propensity to adhere; for example, those that wear the WCD may be more compliant with other aspects of their care. In addition, patients may be required to remove the WCD in hospitalizations preceding non-arrhythmic death, resulting in an effect-cause artifact. Further analyses will be required in future publications to better understand the impact of these potential biases.

SUPPLEMENTAL FIGURES

Figure S1: Overview of study governance and oversight.

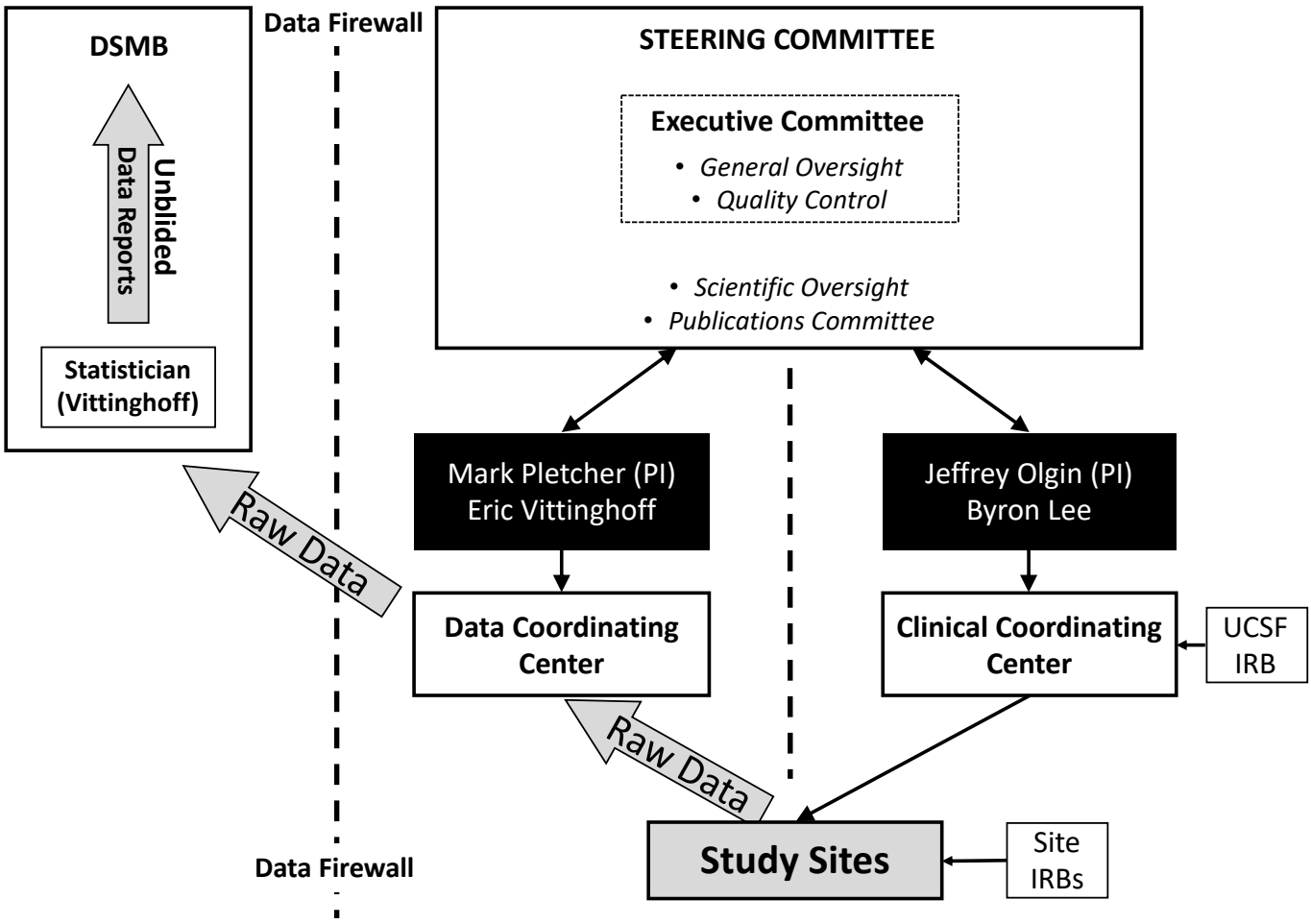


Figure S2: The ZOLL® LifeVest® wearable cardioverter-defibrillator.

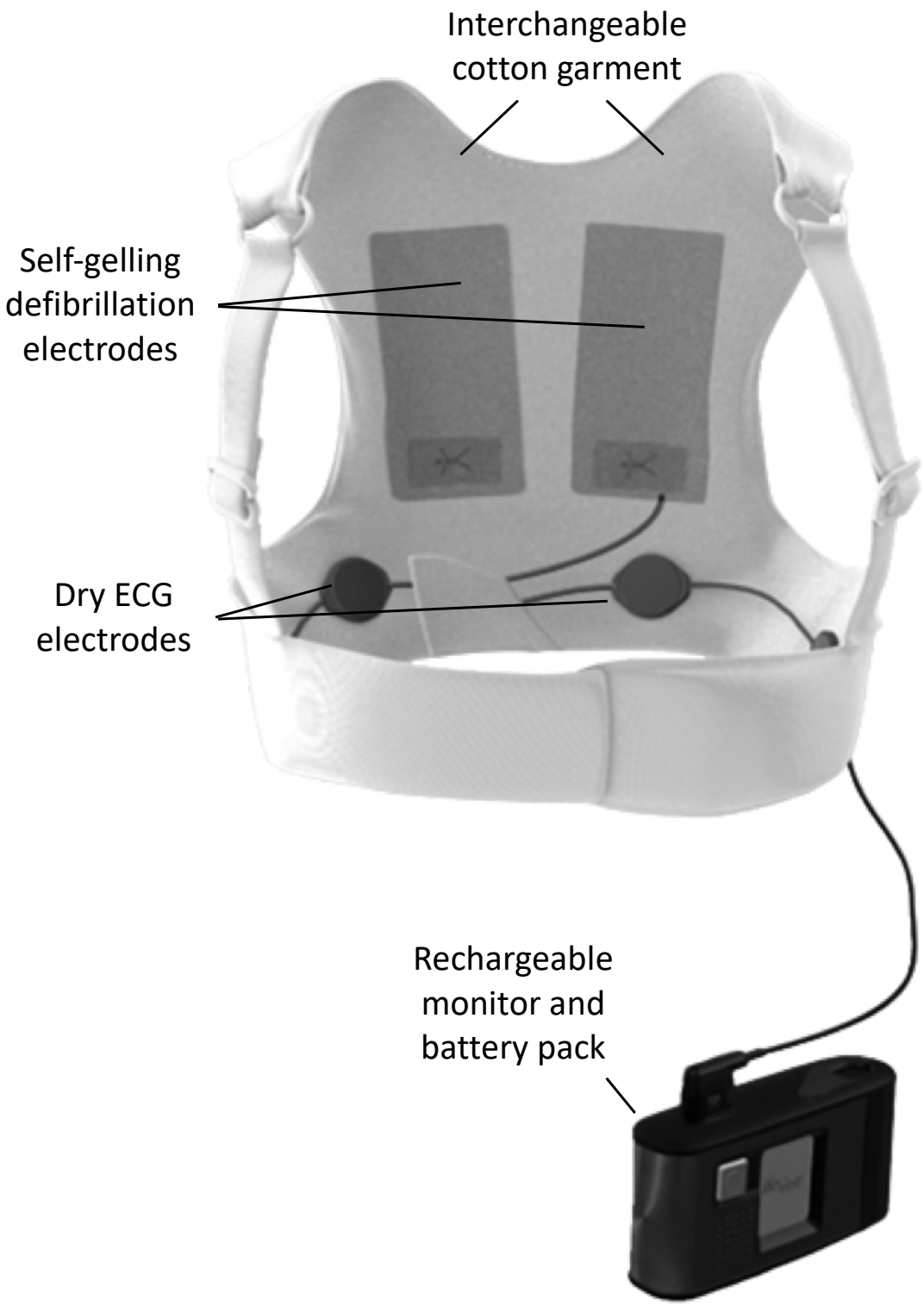
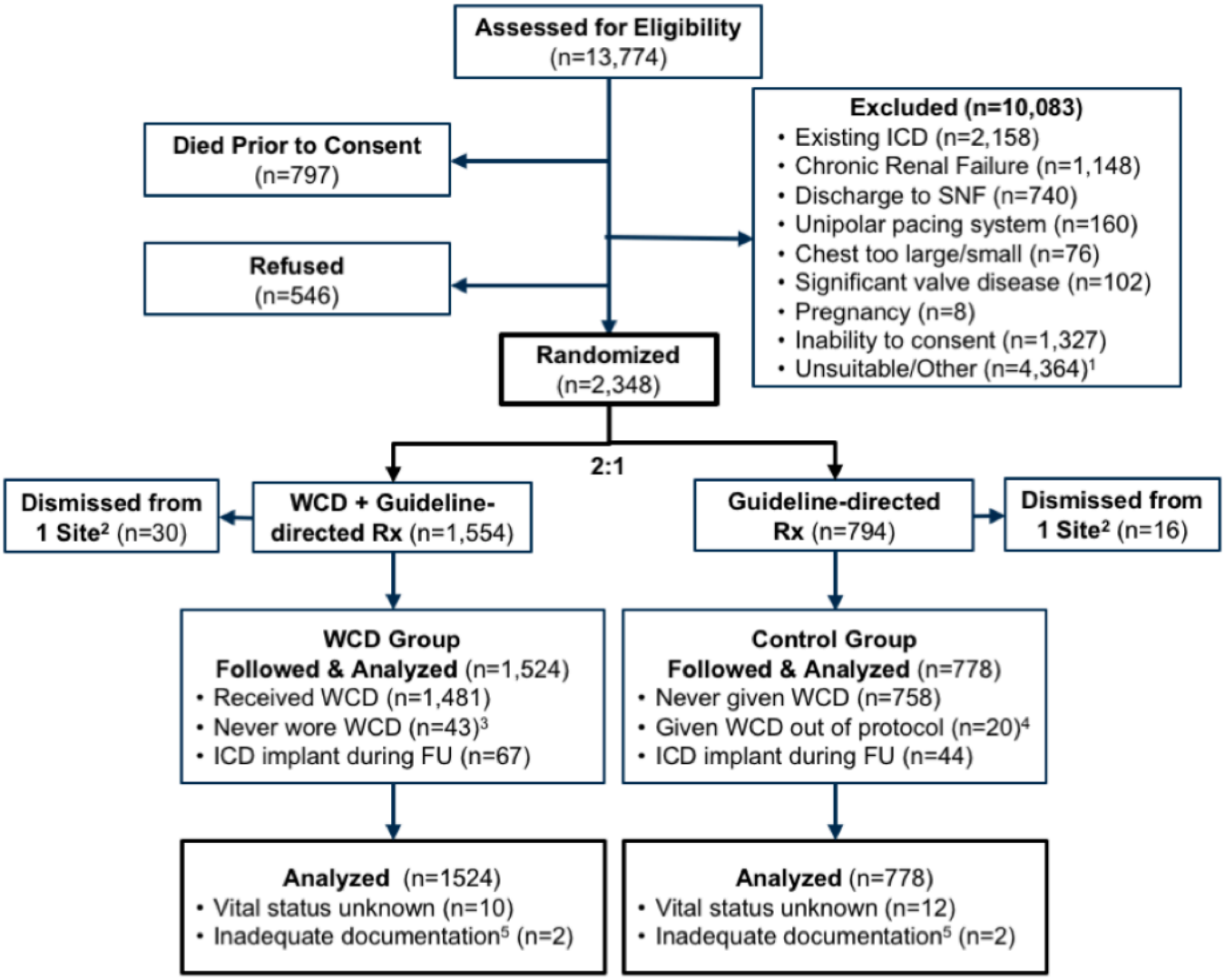


Figure S3: CONSORT Diagram.



[1]Inability to follow-up such as homelessness, language barriers, left against medical advice, poor study candidate due to drug or alcohol abuse, or enrolled in another research study

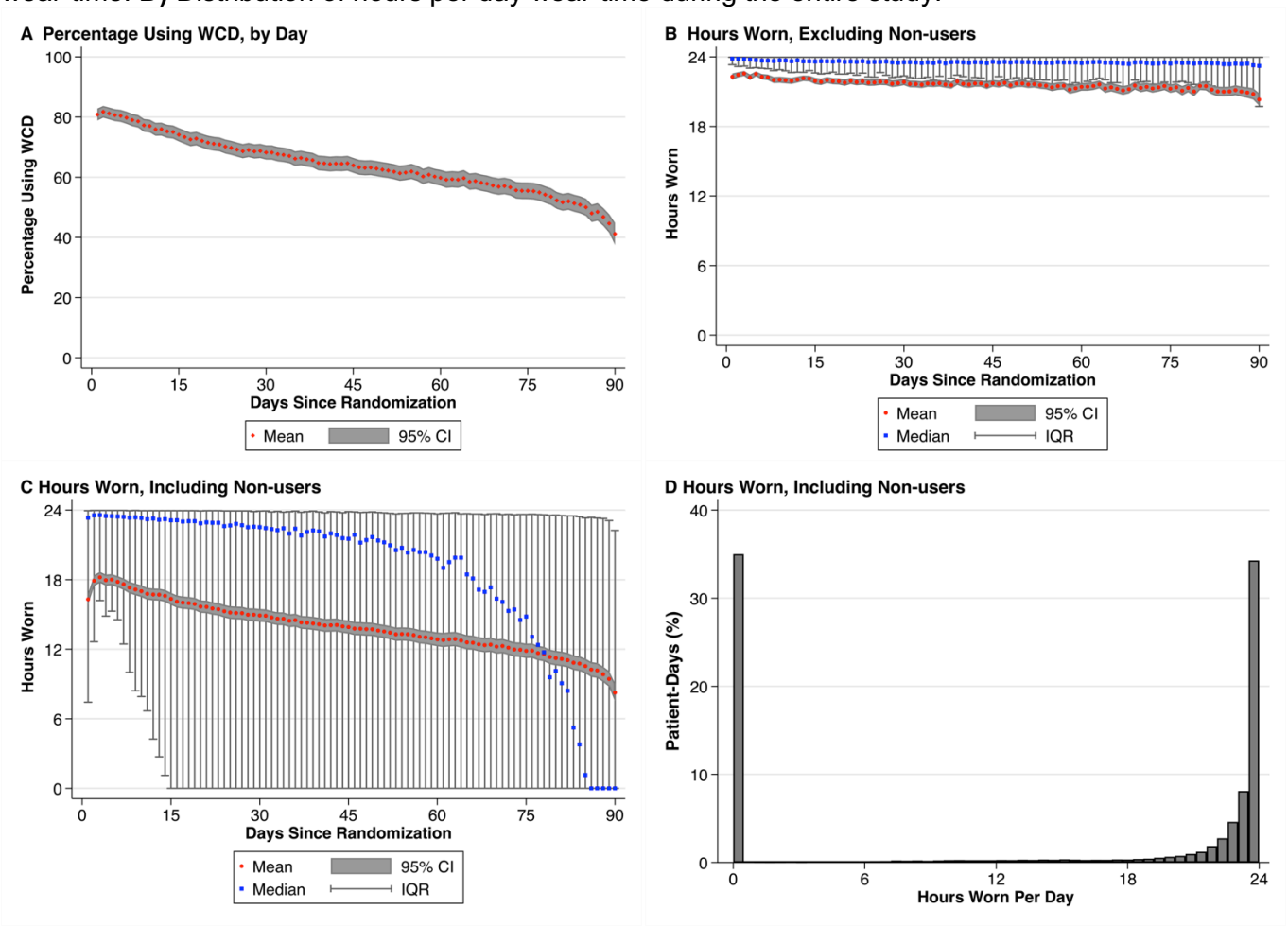
[2]One site was dismissed due to an irregularity at the site found by the IRB. All participants from this site were removed from the study on 6/24/14 and excluded from analyses and enrollment totals.

[3]Withdrew consent prior to receiving WCD or refused WCD fitting.

[4]Received WCD by prescription outside of protocol by treating MD

[5]Clinical documentation inadequate for determination of sudden vs. non-sudden death; these deaths were considered "Indeterminate" and were not counted as meeting the primary outcome definition in our primary analysis.

Figure S4: Wearable cardioverter-defibrillator wear-time in the WCD group over the duration of the study. Day 0 is considered the time of randomization. **A)** Percentage of participants who wore the WCD at all on any given day. The red points show observed percentages, and the black line shows the fitted values from a GEE logistic regression using a 3-knot restricted cubic spline to model the effect of time. **B)** The hours per day that the WCD was worn when the WCD was worn at all (i.e. excluding non-users in the WCD group with wear-time of 0 hours per day) over the duration of the study. **C)** The hours per day that the WCD was worn over duration of the study, including non-users in the WCD group with 0 hours wear-time. **D)** Distribution of hours per day wear-time during the entire study.



SUPPLEMENTAL TABLES

Table S1. Data Safety Monitoring Board members.

Name	Institution	Expertise
Robert Myerburg, MD (chair)	University of Miami	Cardiology
Felicia Cohn, PhD	UC Irvine & Kaiser Permanente	Medical Ethics
Jeffrey Goldberger, MD	University of Miami	Cardiology
George Howard, DrPH	University of Alabama, Birmingham	Biostatistics
Jay Mason, MD	Covance Cardiac Safety Services	Cardiology
Bruce Patsy, MD, PhD	University of Washington	Clinical Trials

Table S2. Steering Committee members.

Name	Institution
Jeff Olgin, MD	University of California San Francisco
Byron Lee, MD	University of California San Francisco
Mark Pletcher, MD	University of California San Francisco
Eric Vittinghoff, PhD	University of California San Francisco
Alfred E. Buxton, MD	Beth Israel Deaconess Medical Center
Eugene H. Chung, MD	University of Michigan
Stephen Hulley, MD	University of California San Francisco
Daniel P. Morin, MD	Ochsner Health System
Eric Rashba, MD	Stony Brook University
Steven Zweibel, MD	Hartford Hospital
Martin Borggrefe, MD, PhD	University Medical Center Mannheim
Krystof Wranicz, MD, PhD	Medical University of Lodz
*Steven J. Szymkiewicz, MD**	ZOLL, Inc.

*Non-voting member

Table S3. Executive Committee members.

Name	Institution
Jeff Olgin, MD	University of California San Francisco
Byron Lee, MD	University of California San Francisco
Mark Pletcher, MD	University of California San Francisco
Eric Vittinghoff, PhD	University of California San Francisco

Table S4. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1. Patients identified in the hospital or within ***7 days*** after discharge with a diagnosis of an acute MI (STEMI or Non-STEMI) 2. LV ejection fraction ≤35%, determined at the following time point: a) if no PCI, **≥8° after MI** b) if acute PCI occurs,**≥8° after PCI** c) if CABG is planned (before or within 7 days of discharge), **most recent assessment at least 48° post CABG**. 3. Age ≥18 years	1. Existing ICD or indication for an ICD 2. Existing unipolar pacemakers/leads 3. Chronic renal failure requiring hemodialysis after hospital discharge *4.* Chest circumference too small/large for WCD 5. Participants discharged to a skilled nursing facility with anticipated stay >7 days 6. Pregnancy 7. Inability to consent 8. Any condition/circumstance that makes the participant unsuitable for the study

Table S5. Outcomes in VEST and those reported in this manuscript.

Outcomes		Data source	Adjudicated?	Included in manuscript?
Sudden death mortality + ventricular arrhythmia death	**Primary**	Records, interviews*	Yes	Yes
All-cause (total) mortality	Secondary	Records	Yes	Yes
Cause-specific mortality				
Non-sudden death	Secondary	Records	Yes	Yes
Non-Sudden Fatal MI	Secondary	Records	Yes	No
Fatal Congestive Heart Failure	Secondary	Records	Yes	No
Other Cardiac Death	Secondary	Records	Yes	No
Fatal Stroke	Secondary	Records	Yes	No
Other Non-cardiac Death	Secondary	Records	Yes	No
Indeterminate Cause of Death	Secondary	Records	Yes	Yes
Non-Fatal Events (Hospitalizations)				
All	Secondary	Records	No	Yes
Cardiovascular or study-related	Secondary	Records	Yes	Yes
MI	Secondary	Records	Yes	No
Atrial fibrillation	Secondary	Records	Yes	No
Congestive heart failure	Secondary	Records	Yes	No
Stroke	Secondary	Records	Yes	No
WCD Events				
Ventricular Tachyarrhythmia	Secondary	LifeVest	Yes	No
WCD Shocks delivered	Secondary	LifeVest	Yes	Yes
Sustained VT	Secondary	LifeVest	Yes	No
Inappropriate Shock	Secondary	LifeVest	Yes	Yes
Time to 1st episode of VT/VF	Secondary	LifeVest	Yes	No
Adverse Events				
Device-attributable Death or Hospitalization	Secondary	Records	Yes	Yes
Device-related Symptom or Sign	Secondary	Checklist	No	Yes
Other Adverse Event	Secondary	Data Form	No	Yes
Vest Compliance	Secondary	LifeVest	No	Yes
ICD Implantation	Secondary	Data Form	No	Yes
Quality of Life	Secondary	Instrument	No	No
Resource Utilization/Cost	Secondary	Data form	No	No

*Includes information from medical records, death certificates, interviews of next-of-kin or personal physicians, and National Death Index searches

Table S6: Enrollment and event rate by country.

	WCD Group	Control Group	Total
Total Enrolled	**1524**	**778**	**2302**
US, n (% of total)	1004 (66%)	516 (66%)	1520 (66%)
Poland, n (% of total)	419 (27%)	213 (27%)	632 (27%)
Germany, n (% of total)	95 (6%)	46 (6%)	141 (6%)
Hungary, n (% of total)	6 (0.4%)	3 (0.4%)	9 (0.4%)
Total Mortality	**48**	**38**	**86**
US, n (% of total)	34 (71%)	26 (68%)	60 (70%)
Poland, n (% of total)	9 (19%)	10 (26%)	19 (22%)
Germany, n (% of total)	5 (10%)	2 (5%)	7 (8%)
Hungary, n (% of total)	0 (0%)	0 (0%)	0 (0%)
Total Sudden Death Mortality	**25**	**19**	**44**
US, n (% of total)	19 (76%)	14 (74%)	33 (75%)
Poland, n (% of total)	4 (16%)	4 (21%)	8 (18%)
Germany, n (% of total)	2 (8%)	1 (5%)	3 (7%)
Hungary, n (% of total)	0 (0%)	0 (0%)	0 (0%)
Total non-sudden death Mortality	**23**	**19**	**42**
US, n (% of total)	15 (65%)	12 (63%)	27 (64%)
Poland, n (% of total)	5 (22%)	6 (32%)	11 (26%)
Germany, n (% of total)	3 (13%)	1 (5%)	4 (10%)
Hungary, n (% of total)	0 (0%)	0 (0%)	0 (0%)

Table S7. Comparison of characteristics of participants enrolled before and after protocol change to extend follow-up to 90 days.

Characteristics	60 days	90 days	P value
N	244	2058	
WCD, n(%)	160 (65.6%)	1364 (66.3%)	0.83
Age, mean ± SD	59.5 ± 12.5	61.3 ± 12.5	0.03
Men, n(%)	166 (68.0%)	1519 (74.1%)	0.04
BMI, Mean ± SD	29.0 ± 5.5	28.3 ± 5.5	0.07
Smoker, n(%)	80 (32.9%)	754 (36.8%)	0.23
Race, n(%)			0.02
White	188 (77.4%)	1727 (84.4%)	
Black	29 (11.9%)	189 (9.2%)	
Asian	8 (3.3%)	29 (1.4%)	
Native American/Alaskan	7 (2.9%)	30 (1.5%)	
Pacific Islander/Hawaiian	0 (0%)	1 (0.0%)	
Mixed	7 (2.9%)	27 (1.3%)	
Hispanic, n(%)	18 (7.4%)	101 (4.9%)	0.10
Baseline medical conditions			
DM, n(%)	83 (34.0%)	660 (32.1%)	0.66
HTN, n(%)	157 (64.3%)	1338 (65.2%)	0.41
Prior MI, n(%)	63 (25.8%)	510 (24.9%)	0.83
Prior CABG, n(%)	27 (11.1%)	176 (8.6%)	0.34
Prior PCI, n(%)	73 (29.9%)	503 (24.5%)	0.08
Prior CHF, n(%)	42 (17.2%)	351 (17.1%)	0.45
NYHA Classification, n(%)			0.008
I	115 (47.1%)	902 (44.0%)	
II	79 (32.4%)	736 (35.9%)	
III	45 (18.4%)	282 (13.7%)	
IV	5 (2.0%)	59 (2.9%)	
INDEX MI HOSPITALIZATION			
Left Ventricular Ejection Fraction (Qualifying), mean ± SD	27.9 ± 6.0	28.3 ± 6.0	0.39
Left Ventricular Ejection Fraction*			0.48
<25%	54 (22.1%)	395 (19.2%)	
25% - 35%	190 (77.9%)	1654 (80.6%)	
>35%	0 (0%)	3 (0.1%)	
PCI during index hospitalization	211 (86.5%)	1714 (83.9%)	0.30
Thrombolytics during index hospitalization	46 (18.9%)	143 (7.0%)	<0.001
CABG during index hospitalization	0 (0%)	26 (1.3%)	0.08
Cardiac Arrest or ventricular fibrillation	33 (13.5%)	206 (10.1%)	0.10
Pulmonary edema requiring intubation	38 (15.6%)	212 (10.4%)	0.01
Intra-aortic balloon pump	45 (18.4%)	221 (10.8%)	<0.001
Cardiogenic shock	28 (11.5%)	187 (9.2%)	0.24
Atrial fibrillation during hospitalization	28 (11.5%)	219 (10.7%)	0.72
Creatinine max (median, 25-75%)	1.1 (0.9 - 1.3)	1.1 (0.9 - 1.3)	0.63

*Ejection fraction ≤35% was an inclusion criterion for the study. Ejection fraction >35% represents a protocol violation.

Table S8. Reasons for early ICD implant

	WCD Group (n/N=67/1524*)	Control Group (n/N=44/778*)	P value
Reason for early ICD implant			0.35
Cardiac arrest or WCD shock	15	6	
Sustained ventricular tachyarrhythmia	4	1	
Bradycardia	0	1	
Heart failure treatment (required CRT)	5	1	
Syncope and inducible ventricular tachyarrhythmia	0	1	
Protocol violation	24	18	
Unknown reason	19	16	

IQR = Interquartile range

*n/N = n is the number of participants with an early ICD implant and N is the number of participants in the group

Table S9. P value corrections for multiplicity.

Event	RR	Uncorrected		Bonferroni-Correction*		Correction Accounting for Correlation**		Prioritized Correction Accounting for Correlation***	
		95% CI	P	95% CI	P	95% CI	P	95% CI	P
Arrhythmic Death	0.67	0.37-1.21	0.18						
Total Mortality	0.64	0.43-0.98	0.04	0.35-1.19	0.45	0.37-1.13	0.22	0.42-1.0	0.05
Non-arrhythmic Death	0.63	0.33-1.19	0.15	0.25-1.59	1.0	0.26-1.53	0.74		
Indeterminate Death	0.51	0.04-7.05	0.83	0.01-26.46	1.0	0.01-25.83	1.0		
Rehospitalization, any cause	0.96	0.85-1.09	0.51	0.8-1.15	1.0	0.81-1.14	0.99		
Rehospitalization, CV Cause	0.98	0.84-1.16	0.83	0.78-1.24	1.0	0.79-1.22	1.0		
Recurrent myocardial infarction	0.85	0.55-1.30	0.44	0.45-1.58	1.0	0.47-1.53	0.99		
Stroke	0.89	0.38-2.12	0.80	0.25-3.16	1.0	0.26-3.06	1.0		
Congestive heart failure	0.85	0.61-1.19	0.35	0.53-1.39	1.0	0.54-1.35	0.96		
Ventricular tachyarrhythmia	0.61	0.34-1.10	0.10	0.26-1.44	1.0	0.27-1.40	0.59		
Atrial fibrillation	0.82	0.27-2.49	0.72	0.16-4.16	1.0	0.17-4.04	1.0		
Other significant arrhythmia	1.36	0.33-8.0	0.92	0.19-20.39	1.0	0.19-19.74	1.0		

*Bonferroni-corrected p value is informally defined as the minimum of 1 and K times the uncorrected p value, where K is the number of tests. Usually the procedure is defined by comparing the uncorrected p value to the adjusted cutoff 1-alpha/K. We could ask to present the corrected 1-alpha/K CI instead.

**Bonferroni correction is overly conservative when outcomes are correlated. Hypotheses testing for secondary outcomes are not completely independent (eg. arrhythmic death is a subset of total mortality). Therefore, a less conservative approach to multiplicity for correlated outcomes was used. For each endpoint, the Dubey-Armitage-Parmar procedure uses the average of its correlations with the other 11 endpoints. As expected the average correlation of the Death, any cause outcome with all 11 others is much lower than with the other two mortality endpoints.

***Dubey-Armitage-Parmar procedure used to adjust for two comparisons, viewing with original primary outcome of total mortality being as uniquely important among the secondary outcomes.

Table S10. Prespecified weighted sensitivity analysis accounting for indeterminate causes of death and missing vital status.

	N	RR (95% CI)	P
Arrhythmic death			
Unweighted model	2302	0.67 (0.37-1.21)	0.18
Weighted model	2276	0.67 (0.37-1.20)	0.17
Total mortality			
Unweighted model	2302	0.64 (0.43-0.98)	0.04
Weighted model	2280	0.64 (0.42-0.97)	0.03
Non-arrhythmic death			
Unweighted model	2298	0.63 (0.43-0.98)	0.04
Weighted model	2276	0.64 (0.42-0.97)	0.03

Table S11. Analyses with and without adjustment for length of follow up in the first 244 participants.

	RR (95% CI)	Uncorrected P Value
Sudden death + ventricular arrhythmia death (1° outcome)		
Unadjusted log binomial regression model	0.67 (0.37, 1.21)	0.18
Model adjusted for length of follow-up	0.67 (0.37, 1.21)	0.18
Non-sudden death		
Unadjusted log binomial regression model	0.63 (0.33, 1.19)	0.15
Model adjusted for length of follow-up	0.63 (0.33, 1.18)	0.15
Death, any cause		
Unadjusted log binomial regression model	0.64 (0.43, 0.98)	0.04
Model adjusted for length of follow-up	0.64 (0.42, 0.97)	0.04

Table S12. A. Participants who had an appropriate shock and died at any point in the study; and **B.** participants who were wearing the WCD at the time of death but did not receive a shock.

A. Participants wearing the WCD who had an appropriate shock and died.						
Event	**Clinical Scenario**	**Adjudicated cause of death**	**Timing of Death from WCD Event**	**WCD Initial Rhythm**	**WCD Shock**	**WCD Outcome**
1	One hour of chest pain led to 911 call. Collapsed while on the phone with emergency personnel.	Sudden death	Immediate*	VT	Appropriate	WCD therapy aborted then shock converted to ventricular escape rhythm. VF recurred & external shocks were unsuccessful.
2	WCD shock led to ICD implant. VT storm 2 weeks later led to hospitalization. Died in the hospital.	Non-sudden death due to ventricular arrhythmia	2 weeks later	VT	Appropriate	WCD therapy aborted then shock converted to SR. Patient survived to ICD implant and died 2 weeks later.
3	Collapsed at home. Found by a family member.	Sudden death	Immediate	VT	Appropriate	WCD therapy aborted then shock converted to SR. VT recurred & became asystole.
4	Collapsed at home. Found by spouse. EMT started resuscitation in the field and stopped in the ED.	Sudden death	Immediate	VF	Appropriate	WCD therapy aborted then shock converted to SR. VT and VF recurred & became asystole.
5	Found dead at home by spouse.	Indeterminate cause of death	Immediate	VT	Appropriate	WCD therapy aborted then shock converted to a ventricular escape rhythm.
6	Hospitalized for chest pain. Cardiac arrest in hospital wearing the WCD. Autopsy showed MI & septal rupture.	Sudden death	Immediate	VT	Appropriate	WCD shock converted to SR. VT recurred with ineffective shocks.
B. Participants wearing the WCD at the time of death who did not have an appropriate shock.						
1	Collapsed at a casino. EMT found asystole. Resuscitation was unsuccessful.	Sudden Death	NA	IVR	None	Accelerated idioventricular rhythm became asystole.
2	Chest pain prompted 911 call. Collapsed at home in front of EMT. Asystole found. Resuscitation in ED was stopped per the family's wishes.	Sudden death	NA	Sinus Bradycardia	None	Sinus bradycardia became asystole.
3	Found dead at home by niece.	Sudden death	NA	IVR	None	Ventricular escape rhythm became asystole.
4	Felt tired & went to see the doctor. In waiting room, became diaphoretic & 911 was called. Pronounced dead in the ED. (No hospital	Non-sudden death	NA	SR	None	SR became sinus bradycardia.

	records available)					
5	Re-hospitalized for STEMI; Revascularization was incomplete & continued angina. Hospital day 31, angina was treated with morphine & later found dead by nursing staff.	Sudden death	NA	SR	None	SR became asystole.
6	Found dead in bed.	Sudden death	Immediate	CHB	None	2:1 AV block leading to CHB with slow ventricular escape.
7	Recently hospitalized for sepsis. Collapsed at home. EMT found PEA. Resuscitated & hospitalized but support withdrawn 7 days later.	Non-sudden death	NA	SR	None	SR became artifact likely due to resuscitation.

WCD=wearable cardioverter defibrillator; EMT=emergency medicine technician; ED=emergency department; SR=sinus rhythm; VT=ventricular tachycardia; VF=ventricular fibrillation; IVR=idioventricular rhythm; STEMI=ST segment elevation myocardial infarction; AV=atrioventricular; CHB=complete heart block; PEA=pulseless electrical activity; NA=not applicable since there was no "event" detected on the WCD. *Immediate death defined as no period of survival after the WCD event. The primary outcome of arrhythmic death included sudden deaths and non-sudden deaths due to ventricular arrhythmias.

Table S13. Adverse events identified by sites

EVENT NUMBER	EVENT TYPE	CAUSE	Comment	WCD Related
1	Hospitalization	Aborted shock	Participant aborted shock after alarm. No ventricular arrhythmias found.	Definite
2	Death	No shock	Collapsed wearing the WCD but no shock. Bystander CPR and EMT found in PEA (participant #7, Table S12).	Possible
3	Hospitalization	Inappropriate Shock	Received inappropriate shock & went to ED with dyspnea.	Definite
4	Hospitalization	Aborted shock	Participant aborted shock during an alarm and developed chest pain and went to the ED	Definite

WCD=wearable cardioverter defibrillator; CPR=cardiopulmonary resuscitation; EMT=emergency medicine technician; ED=emergency department; PEA=pulseless electrical activity.

Table S14. Prespecified symptoms reported during follow-up*

Characteristics	WCD Group (N=1421)	Control Group (N=714)	P value
Fatigue, n (%)	510 (36.1%)	274 (38.7%)	0.24
Back pain, n (%)	283 (20.0%)	137 (19.4%)	0.71
Trouble sleeping, n (%)	551 (39.0%)	264 (37.3%)	0.44
Dizziness, n (%)	344 (24.4%)	166 (23.4%)	0.64
Fainting, n (%)	59 (4.2%)	36 (5.1%)	0.34
Nausea, n (%)	132 (9.3%)	85 (12.0%)	0.06
Headache, n (%)	259 (18.3%)	136 (19.2%)	0.62
Palpitations, n (%)	327 (23.1%)	182 (25.7%)	0.19
Chest pain, n (%)	265 (18.8%)	151 (21.3%)	0.16
Shortness of breath, n (%)	548 (38.8%)	321 (45.3%)	0.004
Rash in any location, n (%)	216 (15.3%)	50 (7.1%)	<0.001
Rash on torso, n (%)	184 (13.0%)	27 (3.8%)	<0.001
Itch in any location, n (%)	243 (17.2%)	45 (6.4%)	<0.001
Itch on torso, n (%)	205 (14.5%)	22 (3.1%)	<0.001

*VEST participants in both WCD and Control Groups were asked "Since your last visit, have you experienced new or worsening…" and given a checklist of symptoms corresponding to the entries in the table above. Note that Rash on torso and Itch on torso were only asked of those that indicated any rash.

REFERENCES

1. Brooks GC, Lee BK, Rao R, et al. Predicting Persistent Left Ventricular Dysfunction Following Myocardial Infarction: The PREDICTS Study. J Am Coll Cardiol 2016;67:1186-96.
2. Solomon SD, Zelenkofske S, McMurray JJ, et al. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. N Engl J Med 2005;352:2581-8.
3. Pitt B, White H, Nicolau J, et al. Eplerenone reduces mortality 30 days after randomization following acute myocardial infarction in patients with left ventricular systolic dysfunction and heart failure. J Am Coll Cardiol 2005;46:425-31.
4. Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. N Engl J Med 2004;351:2481-8.
5. Gould AL. Interim analyses for monitoring clinical trials that do not materially affect the type I error rate. Stat Med 1992;11:55-66.
6. Priori SG, Aliot E Fau - Blomstrom-Lundqvist C, Blomstrom-Lundqvist C Fau - Bossaert L, et al. Task Force on Sudden Cardiac Death of the European Society of Cardiology.
7. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation 2006;114:e385-484.
8. Sankoh AJ, Huque Mf Fau - Dubey SD, Dubey SD. Some comments on frequently used multiple endpoint adjustment methods in clinical trials. Stat Med 1997;16:2529-42.
9. Armitage P, Parmar M. Some approaches to the problem of multiplicity in clinical trials. Proceedings of the XIIth International Biometrics Conference; 1986; Seattle.

10. Dubey S. Adjustment of p-values for multiplicities of intercorrelating symptoms,. Proceedings of the VIth International Society for Clinical Biostatisticians; 1985; Germany.
11. Kutyifa V, Moss AJ, Klein H, et al. Use of the wearable cardioverter defibrillator in high-risk cardiac patients: data from the Prospective Registry of Patients Using the Wearable Cardioverter Defibrillator (WEARIT-II Registry). Circulation 2015;132:1613-9.
12. Chung MK, Szymkiewicz SJ, Shao M, et al. Aggregate national experience with the wearable cardioverter-defibrillator: event rates, compliance, and survival. J Am Coll Cardiol 2010;56:194-203.
13. Feldman AM, Klein H, Tchou P, et al. Use of a wearable defibrillator in terminating tachyarrhythmias in patients at high risk for sudden death: results of the WEARIT/BIROAD. Pacing Clin Electrophysiol 2004;27:4-9.