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Impact of Wearable Cardioverter-Defibrillator Compliance on Outcomes in the VEST Trial: As-Treated and Per-Protocol Analyses

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Abstract

BACKGROUND.—VEST did not demonstrate a significant reduction in arrhythmic death with the wearable cardioverter-defibrillator (WCD), but compliance with the device may have substantially affected the results. The influence of WCD compliance on outcomes has not yet been fully evaluated.

METHODS.—Using linear and pooled logistic models, we performed as-treated analyses omitting person-time in the hospital and adjusted for correlates of WCD compliance. To assess the impact of early stopping of WCD, we performed a per-protocol Kaplan-Meier analysis, censoring after the last day the WCD was worn. Interactions of potential effect modifiers with treatment assignment and WCD compliance on outcomes were investigated. Lastly, we used linear models to identify predictors of WCD compliance.

RESULTS.—A per-protocol analysis demonstrated a significant reduction in total (p<0.001) and arrhythmic (p=0.001) mortality. Better WCD compliance was independently predicted by cardiac arrest during index MI, higher maximum Cr, diabetes, prior heart failure, EF 25%, Polish enrolling center and number of WCD alarms, while worse compliance was predicted by

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being divorced, Asian race, higher BMI, prior PCI, or any WCD shock. Neither excluding time in hospital from the as-treated analysis nor adjustment for factors affecting WCD compliance materially changed the results. No variable demonstrated a significant interaction in either the intention-to-treat or as-treated analysis.

CONCLUSION.—Robust sensitivity analyses of as-treated and per-protocol analyses suggest that the WCD is protective in compliant patients with EF 35% during the first 3 months post-MI.

Keywords

Sudden death; Ventricular tachyardia; Myocardial infarction; Heart failure; Defibrillator; Wearable cardioverter-defibrillator

INTRODUCTION

The Vest Prevention of Early Sudden Death Trial (VEST)(1) demonstrated a high mortality rate in the control group in the 3 months post-MI in patients with reduced left ventricular ejection fraction (EF). This finding, consistent with older studies(2,3), was observed despite the fact that a high proportion of VEST participants 1) received modern therapy including PCI for acute management of their MI and guideline-directed medical therapy, and 2) had improvement in their EF by 3 months post-MI.(4) While VEST did not demonstrate a statistically significant reduction in arrhythmic death (the primary outcome) in the WCD arm with intention-to-treat analysis,(1) the as-treated analysis showed significantly lower arrhythmic death and total mortality rates when the WCD was worn.(1)

As-treated analyses, however, have the potential to be confounded by participant propensity to adhere and, in the case of VEST, by an "effect-cause" bias since patients may be more likely to remove the WCD during hospitalizations, during which mortality may be higher. It remains unclear whether optimal use of a WCD would improve outcomes.

VEST included extensive baseline measurements, follow-up and adjudication of clinical outcomes, and daily information on WCD use captured by the WCD device. We used these data to explore the impact of WCD compliance and hospitalizations on outcomes, including additional on-treatment analyses and effect modification analyses to determine factors that identify those most likely to benefit from the WCD. In addition, we sought to identify factors that predict WCD compliance.

METHODS

The details of the Vest Prevention of Early Sudden Death Trial (VEST) have been previously published.(1) The study was approved by the UCSF Institutional Review Board and all enrolling centers. In brief, VEST was an international, multi-site, unblinded, randomized trial in which patients admitted to the hospital for a myocardial infarction and who had an EF of 35% after the MI were enrolled and randomized in a 2:1 fashion to receive a ZOLL LifeVest wearable cardioverter defibrillator (WCD) plus guideline-directed medical therapy, or guideline-directed medical therapy alone. At 3 months, the primary outcome of arrhythmic death was assessed, as were pre-specified secondary outcomes of death from

any cause and non-arrhythmic death. The cause of death was adjudicated by an independent panel of experts who were blinded to the randomization group assignments and therefore did not have any rhythm or shock data from the WCD. All VEST participants are included in this analyses; those without any compliance data in the WCD arm (n=10) were excluded from those specific analyses involving wear-time.

WCD Wear-Time and Compliance

All participants randomized to the WCD arm were monitored for wear-time and compliance through direct measurement by the device, as previously described.(1) For the purposes of these analyses, hourly wear-times per day throughout the study were evaluated. The date of early termination of WCD use was defined as the day on which there were 0 hours of wear-time on all subsequent days prior to the scheduled end of follow-up.

As-Treated and Per-Protocol Analyses

In our previous publication, we reported an as-treated analysis that compared event rates per person-month during periods when participants were and were not wearing the WCD. While this analysis was robust, the as-treated analyses were subject to bias from two sources which we further evaluate here:1) effect-cause bias—meaning that hospitalized patients may be more likely not to wear the WCD because of being hospitalized, and are at higher mortality risk due to the cause of their hospitalization; and 2) confounding by propensity to adhere— that is, patients who are more likely to wear the WCD may also be more likely to adhere to medications and other medical care or prescribed behavior. To test sensitivity to effect-cause bias, we omitted all person-time and events that occurred in the hospital, except those in-hospital deaths resulting from out-of-hospital cardiac arrests. To assess confounding by propensity to adhere, we adjusted for correlates of wear-time and early termination identified in the WCD compliance analyses described below using linear and pooled logistic models, and using backward stepwise deletion of potential predictors with P<0.05 to select a parsimonious model given the small numbers of events. Finally, to evaluate the impact of early stopping of WCD use, we performed a per-protocol analysis using Kaplan-Meier plots for time from randomization to death or censoring for ICD implant, by treatment assignment, with follow-up and events censored in the WCD group at the last day the WCD was worn (defined as all subsequent days with 0 hours wear-time). Between-group differences were assessed using unadjusted Cox models.

Effect Modification of Outcomes

Baseline predictors of highly adherent WCD use might be expected to behave as effect modifiers and increase estimates of WCD effectiveness. In order to determine whether these or other factors predict more or less benefit from the WCD, we chose plausible effect modifiers collected prior to randomization (i.e., demographics, prior diagnoses, and characteristics of the index MI hospitalization; Supplemental Table 1) and assessed their interactions with treatment assignment and wearing the WCD in both the intention-to-treat and as-treated analyses, respectively.

Predictors of WCD Wear-time

Extensive baseline data were collected at the time of enrollment and prior to hospital discharge. These included demographics, cardiovascular diagnoses prior to the index hospital admission, prior medications, smoking history, and information about the index MI hospitalization and discharge medications. Over the 3 months of follow-up, information about hospitalizations and emergency room visits as well as medications was also collected. In addition, through the automatic transmission of data from the WCD, we also collected data on WCD alarms as well as appropriate, inappropriate, and aborted shocks.

Statistical Analyses

Baseline characteristics of the sample are described using means, standard deviations, and proportions, then compared using t, F, chi-square, and Fisher's exact tests, as appropriate. The associations of those baseline characteristics with daily WCD wear-time hours were compared using linear models with robust standard errors to account for within-participant correlation of the repeated outcomes, and controlling for days since randomization, modeled as a restricted cubic spline. Time to final cessation of WCD use was modeled using pooled logistic models,(5) again with robust standard errors, and the baseline risk of stopping WCD use was captured by a restricted cubic spline in days since randomization. Finally, as-treated analyses were conducted using Poisson models for the number of deaths of each type among participants assigned to the WCD, accounting for time at risk. In this analysis, overall follow-up for each participant was divided into WCD wearing time and time when the WCD was not worn, with deaths assigned to one or the other period as appropriate. In this analysis, the as-treated effect of the WCD was captured by an indicator for WCD use. We also extended these Poisson models to assess the interaction of each of a pre-specified set of characteristics with the indicator of WCD use.

RESULTS

We observed a "U" shaped distribution of WCD wear-time, with 34% wearing the WCD for a median of 0 hours per day, and 53% wearing the WCD for a median of 22 hours (Figure 1). Figure 1C shows the timing of early discontinuation of wearing the WCD (i.e., all subsequent days had 0 hours). Thirty percent of participants stopped wearing the WCD within 1 month of randomization, 43% within 2 months, and 80% before the end of the planned 90 day follow-up period. The steepest part of this curve was in the first few days after randomization and, as expected, in the final days of the randomization period. It should be noted, as described in the Methods, participants who received an ICD were censored from this analysis at the time of ICD implantation.

Figure 2 shows the timing of death events in those participants randomized to the WCD group, in relation to wearing or not wearing the WCD and in relation to hospitalizations. Of the 48 deaths in the WCD group, only 12 (25%) occurred while the participant was wearing the WCD; this included 9 of the 25 arrhythmic deaths and 2 of the 21 non-sudden deaths.(1) Twenty-two of the 83 total deaths (6 arrhythmic deaths and 16 non-sudden deaths) in both groups occurred during a hospital admission. Of the 61 deaths (20 in the WCD group) due to

out of hospital events, only 11 (all in the WCD group) were wearing the WCD at the time of the event.

Predictors of WCD Compliance

The characteristics of the study participants are shown in Table 1, based on a mean wear-time of 90% (21.6 hours) vs <90% per day throughout the study, which was the pre-specified wear-time used for sample size calculation, and those who stopped wearing the WCD early during month 1, 2 or 3 of the study. Those who wore the WCD a mean of 90% tended to be from Polish enrolling sites, older, female, white and married, and had a lower BMI. There was a lower percentage of participants with a prior history of diabetes or prior PCI who wore the WCD a mean 90%. A greater percentage of patients who had a cardiac arrest during the index MI wore the WCD a mean of 90%.

The US sites had a higher percentage of participants who stopped wearing the WCD early. There was a higher percentage of males and widowed or divorced participants who stopped wearing the WCD early. The median BMI was higher in those who stopped wearing the WCD early. There was a higher percentage of participants with prior PCI or CABG or a prior diagnosis of hypertension who stopped wearing the WCD in the first 2 months. A higher percentage of participants who received thrombolytics during their index MI stopped wearing the WCD in the first and second month.

Using the WCD wear-time as a continuous variable, in multivariate analyses (Table 2) of differences in wear-time, Polish enrolling center, being divorced, BMI, prior PCI, cardiac arrest during index hospitalization, maximum creatinine during the index hospitalization, being in the hospital during follow-up, mean number of alarms in the prior 7 days, any appropriate or inappropriate shocks in the prior 7 or 90 days, and days from randomization were significant independent predictors of WCD wear-time (univariate analyses presented in Supplemental Table 2).

In multivariable analysis of predictors of stopping WCD wear early (Table 3), being from a Polish enrolling center, being Asian, divorced, having a prior diagnosis of diabetes or heart failure, EF 25% during the index MI, and any shock (appropriate or inappropriate) in the 7 days prior were significant independent predictors of discontinuation of wearing WCD early (univariate analyses presented in Supplemental Table 3).

As-Treated and Per-Protocol Analyses of Outcomes

Hospitalized patients may be less likely to wear the WCD in the hospital and at greater risk of death due to the illness that prompted hospitalization (effect-cause bias). We performed a sensitivity analysis to test for effect-cause bias, censoring events and time while patients were in the hospital (Table 4). Removing outcome events that occurred in the hospital did not materially change the significant protective effect of the WCD with respect to total mortality, arrhythmic death, and non-sudden death in as-treated analyses (Table 4).

In order to assess potential confounding by propensity to adhere, the as-treated analysis was performed adjusting for variables that predicted WCD wear-time in a multivariate analysis from Tables 2 and 3. After stepwise deletion (Table 4), only diabetes and prior PCI remained

significant covariates in the model. Adjustment for these variables did not materially change the rate ratios or p values for any of the outcomes in the as-treated analysis.

To determine the impact of early stopping of WCD wear on outcomes, a per-protocol analysis was performed. Because of the time-dependent nature of early stopping of the WCD (Figure 1) and the falling risk of events over time,(1–3) a survival analysis was performed by randomization group but censoring participants at the time that they stopped wearing the WCD as part of a per-protocol analysis (Figure 3). In this analysis, the hazard ratio for total mortality was 0.25 (CI: 0.13, 0.48; p<0.001) in WCD users versus control, 0.38 (CI: 0.17, 0.86; p=0.02) for arrhythmic death, and 0.09 (CI: 0.02, 0.39; p=0.001) for non-sudden death. In addition, as seen in Figure 3, the mortality curves continue to separate during follow-up. This suggests that even with progressively lower rates of death over the 90 days, the benefit of wearing the WCD continued throughout the 90 day period.

Effect Modification of Outcomes

In order to determine whether there are particular demographic or clinical characteristics that identified people at higher or lower risk of events in VEST that might benefit most from the WCD, we evaluated whether the effects were modified by factors likely to impact efficacy of the WCD on the intention-to-treat and as-treated analyses (Supplemental Table 4). Because events were limited, we selected covariates that were plausible modifiers of outcomes (Supplemental Table 1) in this analysis using backward deletion with a retention criteria of p<0.01. No analyses demonstrated a significant interaction for any of the variables for either the intention-to-treat or as-treated analyses. However, there was a trend for participants with a cardiac arrest (interaction p=0.08), pulmonary edema (interaction p=0.07) and Cr<1.5 (interaction p=0.06) towards lower mortality in the WCD group in the intention-to-treat analysis (Supplemental Table 2).

DISCUSSION

In an intention-to-treat analysis of VEST, the WCD did not statistically significantly reduce arrhythmic death, the primary outcome, but did show a reduction in total mortality.(1,6) The impact of WCD wear-time and limitations of precisely adjudicating cause of death in the absence of rhythm at the time of death (as adjudication was blinded to WCD rhythm in both control and WCD group) on the power of the outcomes has been previously described.(1,6) In the WCD group, only 25% of the total deaths and 55% of the out of hospital deaths occurred while wearing the WCD; an as-treated analysis showed a significant reduction in total and arrhythmic mortality during times of wearing the WCD.(1) This analysis compared events during person-months while wearing the WCD to events during person-months while not wearing the WCD, thus each person in the WCD group (except for the 2.8% in the WCD group who never wore the WCD) contributed some to each period. As a result, confounding due to factors at the individual level (e.g., propensity to adhere) are minimized though not eliminated, since those wearing the WCD the least will contribute more to the non-wear time than those who are most compliant. In the analysis reported herein, we identified predictors of WCD wear-time; adjustment for these factors in the as-treated analyses did not materially change these results. In addition, there was little impact of censoring in-hospital time and

events, suggesting no material impact of an "effect-cause" bias (i.e., bias due to the fact that patients may be more likely to remove the WCD during hospitalization, at which time mortality may be high). This modified as-treated analysis further supports the conclusion that there may be benefit to wearing the WCD to prevent out of hospital events.

To specifically assess the impact of early discontinuation of the WCD on outcomes, we performed a per-protocol analysis in which participants in the WCD group were censored on the last day of any WCD wear-time (i.e., when all subsequent WCD wear-times were 0 hours per day). This analysis showed a significant reduction in both overall mortality and arrhythmic death in the WCD group. As with the above as-treated analysis, this analysis is still subject to confounding by propensity to adhere, but the data do suggest that those who wear the WCD longer during the post-MI benefit from the WCD with lower mortality and arrhythmic death over the entire 90-day period. As with the intention-to-treat analyses, both the as-treated and per-protocol analyses showed a reduction in arrhythmic and non-arrhythmic mortality. Although there is no clear mechanism to explain a benefit of the wearable cardioverter–defibrillator on non- arrhythmic death, misclassification of the adjudicated cause of death may have contributed since it is difficult to determine an arrhythmic cause of death accurately for unwitnessed deaths or deaths with limited documentation.(7,8) In VEST where WCD data were not used for adjudication, 5 of 9 participants with adjudicated arrhythmic death who were wearing the device had no arrhythmias.(1) Such misclassification has no effect on the total mortality outcome.

There are some important distinctions when comparing compliance data in this open-label randomized trial compared to previously published registry studies.(9–12) 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 and wore the WCD as part of clinical practice. In addition, compliance in VEST is based on wearing the WCD from the time of randomization to the end of the full 90 days of the study, whereas the "end-point" for registry and case series is based on when the WCD was first worn to the last day it was worn, regardless of the intent. Thus, in VEST, when the WCD was removed before 90 days or not worn for any day after randomization, those days counted as 0 hour-wear days. Another important distinction between clinical practice (including the reported registries) and an open-label randomized trial is that there is both expressed and implied equipoise when presenting a randomized trial option to a patient that may not exist to the same extent as part of clinical care. This may create a lower participant decision threshold to not wear the WCD compared to clinical practice, in which a patient is often only told the necessity of the treatment without equipoise presented.

In multivariate analysis, we found that being from a Polish enrolling site, being married, having had a cardiac arrest during the index MI, and an elevated Cr all independently predicted higher WCD wear-time, while being divorced and having a prior PCI (prior to index MI) independently predicted lower WCD wear-time. In multivariate analysis of early discontinuation of the WCD, being Asian, divorced, having diabetes, or prior diagnosis of heart failure independently predicted early discontinuation of the WCD, while being from Poland or having an EF 25% during the index MI hospitalization independently predicted continuation of WCD use. One can speculate that some of these factors have to do with

implicit (or explicit) mention of risk of sudden death by either the treating physician and/or patient. For example, one can speculate that physicians and patients may think that they are at higher risk of an event if they had a history of cardiac arrest, elevated Cr, or very low EF; this concern may be subtly (or not so subtly) communicated to the patient, and thus may improve WCD compliance. On the other hand, being divorced or not married may have resulted in not having a support structure that would encourage WCD compliance or help to understand the risk of sudden death post-MI. The fact that being Asian also predicted early discontinuation suggests that either cultural or language differences may play a role, either in adequately explaining the risk of sudden death or describing how to use the WCD properly. It is interesting to note that being from Poland was independently predictive of better WCD wear-time and less WCD discontinuation; the WCD was not commercially available in Poland during the study (the only way to receive the WCD was to be in the VEST study), while it was available commercially (outside of the study) in the US and Germany (of note, Hungary had only 9 VEST participants). One can speculate that the difference in wear-time may be due to either cultural differences or perhaps due to differences in implicit or explicit equipoise when the WCD is not available outside of the study.

The behavior of the WCD also independently influenced WCD wear-time and early discontinuation. Surprisingly, having alarms seems to improve WCD wear-time, perhaps suggesting that these alarms may be a reminder that the device is "doing something important." In contrast, having any shock both lowered WCD wear-time and promoted early discontinuation of the WCD; perhaps the pain and discomfort of the shock demotivated WCD use. Although it did not remain an independent predictor in multivariate analysis, aborted shocks predicted better WCD wear-times in univariate analysis, supporting the idea that the pain and discomfort of an actual shock may have had important negative impact on the decision to continue to wear the WCD.

In addition to identifying those patients most likely to wear the WCD, being able to identify those at highest risk and those who might benefit most from the WCD in the post-MI period may also help to select appropriate patients for this therapy. In the current study, we performed an analysis to determine whether there was any effect modification from factors likely to affect outcome in order to potentially identify those at highest risk of death and who might benefit most from the WCD. However, because outcomes were limited, exhaustive analyses or subgroup analyses were not possible. Instead, we looked at those variables that were plausible effect modifiers. We did not find any variables that demonstrated a statistically significant interaction with any of the outcome variables. However, there were trends toward improved survival with the WCD in patients with a cardiac arrest, pulmonary edema requiring intubation or elevated Cr during their index MI, all of which are likely to portend higher mortality and arrhythmic death risk.(13,14)

In conclusion, robust sensitivity analyses of our as-treated analyses and per-protocol analyses suggest that the WCD is protective (i.e., reducing mortality and arrhythmic death) in immediate post-MI patients with LVEF 35% who wear the WCD during the first 3 months post-MI. Emphasizing the importance of wearing the WCD in these patients may improve the efficacy of the therapy. Those without significant family support, language

or cultural barriers may require additional efforts to assess or promote compliance with wearing the WCD.

Limitations

Though our analyses suggests that propensity to adhere to WCD wear-time based on known factors measured in VEST did not confound the as-treated analysis, we cannot exclude confounding by other factors. In addition, our stratified analyses to identify those groups most likely to benefit from the WCD was limited by the small number of events.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosures

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SH, EHC, FL, TFH: None

ABBREVIATIONS

MI	myocardial infarction
WCD	wearable cardioverter-defibrillator
BMI	body mass index
PCI	percutaneous coronary intervention
CABG	coronary artery bypass grafting
EF	ejection fraction
VEST	Vest Prevention of Early Sudden Death Trial

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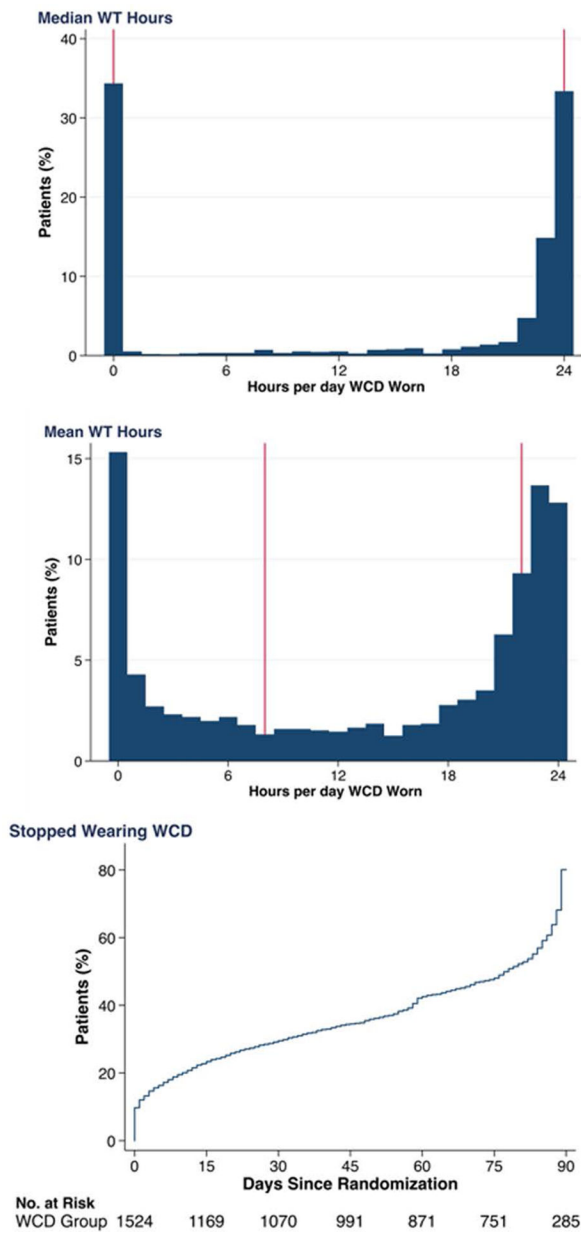
Figure 1:
(**A**) Median and (**B**) mean WCD weartimes throughout the study and (**C**) Kaplan-Meier curve of stopping WCD wear (a 0 hour wear day with no further wear following). Red lines denote tertiles.
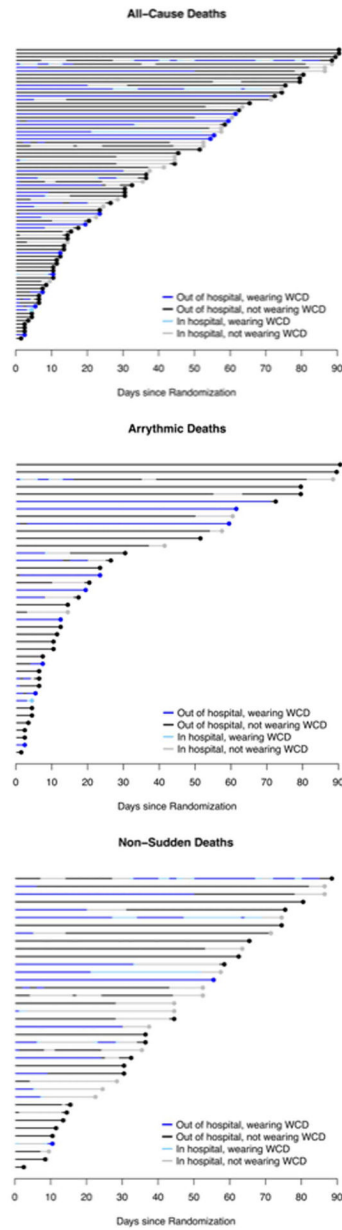
Figure 2:
Timing of events (**A**: total mortality; **B**: arrhythmic death; **C**: non-sudden death) in relation to wearing WCD and hospitalization. Out of hospital events leading to in hospital death (such as an out of hospital cardiac arrest) are categorized as out of hospital events.
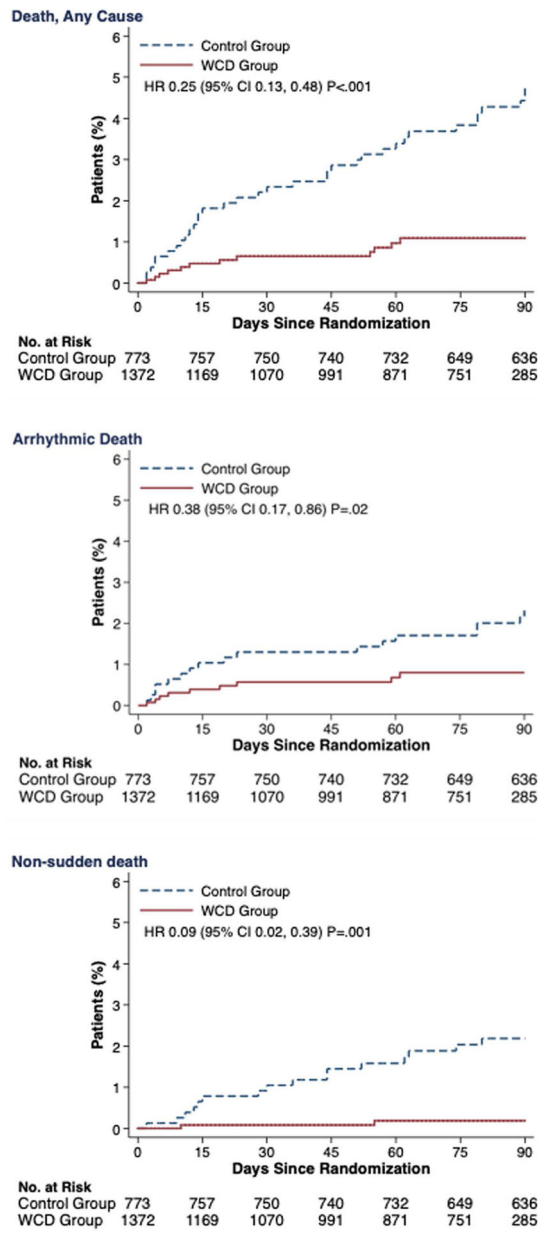
Figure 3:
Kaplan-Meier curves of time to events (**A**: total mortality; **B**: arrhythmic death; **C**: non-sudden death), with those stopping WCD wearing censored at the time of last WCD wear.

Table 1:

Characteristics of compliant and non-compliant participants based on mean wear time (WT) and time of stopping WCD wear.

Characteristic	CTNRL GROUP	WCD GROUP[*]						
		Mean Weartime			WCD Stopped			
		<90% (21.6 hrs)	90% (21.6 hrs)[**]	P	1st month	2nd month	3rd month	P
n	778	989	525		439	242	833	
DEMOGRAPHICS								
Age, mean ± SD	61.1±11.8	60.3±11.8	61.5±11.5	**0.056**	61.8 (11.9)	59.9 (11.4)	60.4 (11.6)	**0.064**
Male, n (%)	577 (74.7%)	713 (72.3%)	387 (73.7%)	**0.56**	306 (70.0%)	165 (68.2%)	629 (75.6%)	**0.022**
Race/Ethnicity, n (%)				**0.001**				**0.12**
White	625 (81.5%)	780 (79.9%)	451 (86.1%)		348 (80.7%)	194 (80.8%)	689 (83.1%)	
Black	75 (9.8%)	95 (9.7%)	39 (7.4%)		34 (7.9%)	23 (9.6%)	77 (9.3%)	
Hispanic	34 (4.4%)	67 (6.9%)	18 (3.4%)		31 (7.2%)	17 (7.1%)	37 (4.5%)	
Asian	14 (1.8%)	20 (2.0%)	3 (0.6%)		12 (2.8%)	2 (0.8%)	9 (1.1%)	
Other	19 (2.5%)	14 (1.4%)	13 (2.5%)		6 (1.4%)	4 (1.7%)	17 (2.1%)	
Marital Status, n (%)				**<0.001**				**<0.001**
Single	114 (14.8%)	154 (15.6%)	65 (12.4%)		65 (14.9%)	39 (16.1%)	115 (13.8%)	
Married	495 (64.1%)	580 (58.9%)	369 (70.3%)		242 (55.5%)	147 (60.7%)	560 (67.3%)	
Widowed	70 (9.1%)	102 (10.4%)	52 (9.9%)		56 (12.8%)	19 (7.9%)	79 (9.5%)	
Divorced	87 (11.3%)	144 (14.6%)	36 (6.9%)		71 (16.3%)	37 (15.3%)	72 (8.7%)	
Other	6 (0.8%)	5 (0.4%)	2 (0.4%)		2 (0.5%)	0 (0%)	6 (0.7%)	
Country, n (%)				**<0,001**				**<0.001**
US	516 (66.3%)	699 (70.7%)	298 (56.8%)		312 (71.1%)	205 (84.7%)	480 (57.6%)	
Poland	213 (27.4%	229 (23.2%)	189 (36.0%)		98 (22.3%)	25 (10.3%)	295 (35.4%)	
Germany	46 (5.9%)	57 (5.8%)	36 (6.9%)		27 (6.2%)	12 (5.0%)	54 (6.5%)	
Hungary	3 (0.4%)	4 (0.4%)	2 (0.4%)		2 (0.5%)	0 (0%)	4 (0.5%)	
BASELINE CONDITIONS PRIOR TO INDEX HOSPITALIZATION								
Body mass index, median [IQR]	27.7 [24.8,31.1]	28.1 [25.0, 31.7]	27.5 [24.4, 30.9]	**0.055**	28.3 [24.8, 32.2]	28.1 [25.7, 31.5]	27.7 [24.6, 31.0]	**0.091**
Smoker, n (%)				**0.22**				**0.19**
Never	232 (30.1%)	302 (30.7%)	161 (30.7%)		142 (32.6%)	75 (31.0%)	246 (29.6%)	
Former	265 (34.4%)	305 (31.0%)	183 (34.9%)		125 (28.7%)	89 (36.8%)	274 (32.9%)	
Current	273 (35.5%)	378 (38.4%)	181 (34.5%)		169 (38.8%)	78 (32.2%)	312 (37.5%)	
Diabetes mellitus, n (%)	246 (31.7%)	336 (34.1%)	154 (29.3%)	**0.061**	158 (36.2%)	95 (39.3%)	237 (28.5%)	**<0.001**
Hypertension, n (%)	501 (64.6%)	657 (66.6%)	329 (62.7%)	**0.12**	297 (68.0%)	167 (69.0%)	522 (62.7%)	**0.073**
Prior MI, n (%)	193 (24.9%)	257 (26.1%)	120 (23.0%)	**0.40**	114 (26.1%)	68 (28.1%)	195 (23.5%)	**0.52**

Characteristic	CTNRL GROUP	WCD GROUP*						
		Mean Weartime			WCD Stopped			
		<90% (21.6 hrs)	90% (21.6 hrs)**	P	1st month	2nd month	3rd month	P
Prior CABG, n (%)	70 (9.0%)	89 (9.0%)	42 (8.0%)	0.50	45 (10.3%)	25 (10.3%)	61 (7.3%)	0.12
Prior PCI, n (%)	202 (26.0%)	262 (26.6%)	110 (21.0%)	0.015	121 (27.7%)	65 (26.9%)	186 (22.4%)	0.078
Prior congestive heart failure, n (%)	146 (18.9%)	166 (16.9%)	81 15.5%)	0.48	78 (17.9%)	37 (15.3%)	132 (15.9%)	0.58
NYHA classification, n (%)				0.10				0.19
I	326 (42.1%)	465 (47.2%)	221 (42.2%)		196 (44.9%)	115 (47.5%)	375 (45.1%)	
II	286 (36.9%)	324 (32.9%)	201 (38.4%)		138 (31.6%)	82 (33.9%)	305 (36.7%)	
III	116 (15.0%)	134 (13.6%)	76 (14.5%)		75 (17.2%)	34 (14.0%)	101 (12.2%)	
IV	47 (6.1%)	63 (6.4%(	26 (5.0%)		28 (6.4%)	11 (4.5%)	50 (6.0%)	
INDEX MI HOSPITALIZATION								
Left ventricular ejection fraction,** mean ± SD	28.2±5.8	28.3±6.2	28.1±5.8	0.39	28.2±6.2	28.4±6.0	28.2±6.0	0.88
PCI	650 (83.5%)	817 (82.6%)	444 (84.6%)	0.33	364 (82.9%)	203 (83.9%)	694 (83.3%)	0.95
Thrombolytics	71 (9.2%)	84 (8.6%)	34 (6.5%)	0.16	47 (10.9%)	22 (9.1%)	49 (5.9%)	0.006
CABG	15 (1.9%)	21 (2.1%)	13 (2.5%	0.66	10 (2.3%)	1 (0.4%)	23 (2.8%)	0.095
Cardiac arrest or ventricular fibrillation	70 (9.1%)	98 (10.0%)	70 (13.4%)	0.047	40 (9.3%)	31 (12.8%)	97 (11.7)%)	0.29
Pulmonary edema requiring intubation	88 (12.0%)	108 (11.0%)	52(9.9%)	0.52	58 (13.4%)	29 (12.0%)	73 (8.8%)	0.031
Intra-aortic balloon pump	93 (10.2%)	116 (11.8%)	54 (10.3%)	0.38	55 (12.7%)	36 (14.9%)	79 (9.5%)	0.038
Cardiogenic shock	79 (10.2%)	87 (8.9%)	46 (8.8%)	0.96	36 (8.3%)	25 (10.3%)	72 (8.7%)	0.66
Atrial fibrillation	91 (11.8%)	97 (9.9%)	54 (10.3%)	0.79	45 (10.4%)	27 (11.2%)	79 (9.5%)	0.73
Creatinine max (mean ± SD)	1.1±1.2	1.5±9.8	1.4±5.9	0.96	1.1±0.4	2.8 ±20.4	1.3±4.0	0.031

*
 Includes only 1514 of the 1524 randomized to the WCD since 10 participants in the WCD arm had no WCD wear-time data due never receiving the device (refused after randomization).

**
 Pre-specified WCD wear-time used for sample size calculation.

Table 2:

Predictors of WCD wear time (using daily wear time as a continuous variable) using a multi-variable linear model in 120,325 observation days in 1,472 participants.

Characteristic	MULTIVARIATE ANALYSIS		
	Difference (hrs)	95% CI	P value
Country			
US	*REF*		
Poland	2.38	1.29, 3.47	<0.0005
Germany	1.05	−0.94, 3.03	0.30
Hungary	3.21	−5.05, 11.47	0.45
Marital Status			
Single	REF		
Married	1.70	0.33, 3.07	0.015
Widowed	−0.06	−1.92, 2.04	0.95
Divorced	−2.55	−4.36, −0.74	0.006
Other	2.67	−2.73, 8.07	0.33
BMI, per kg/m2	−0.10	−0.19, −0.02	0.021
Prior PCI	−1.27	−2.38, −0.16	0.026
Index Hosp Cardiac Arrest or VF	2.04	0.62, 3.47	0.005
Index Hosp Cr Max	0.05	0.02, 0.07	<0.0005
In Hospital	−7.63	−8.85, −6.41	<0.0005
Mean Number of Alarms in previous 7 days, per alarm	0.68	0.5, 0.87	<0.0005
Any Appropriate Shock in previous 7 days	−9.77	−17.09, −2.45	0.009
Any Appropriate Shock in previous 8–90 days	−13.13	−16.27, −9.99	<0.0005
Any Inappropriate Shock in previous 7 days	−8.67	−15.39, −1.96	0.011
Any Inappropriate Shock in previous 8–90 days	−9.24	−13.23, −5.24	<0.0005
Days since randomization	0.01	−0.10, −0.02	0.39

Table 3:

Predictors of stopping WCD wear early using a multi-variable logistic regression model of 85,840 observation days prior to stopping in 1,494 participants and 837 events.

Characteristic	UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
	OR	95% CI	P value	OR	95% CI	P value
Country						
US	*REF*			*REF*		
Poland	0.64	0.54, 0.75	<0.001	0.60	0.50, 0.72	<0.001
Germany	0.84	0.62, 1.14	0.26	0.78	0.57, 1.07	0.12
Hungary	0.50	0.09, 2.72	0.13	0.48	0.09, 2.65	0.40
Race/Ethnicity						
White	*REF*			*REF*		
Black	0.97	0.77, 1.22	0.80	0.83	0.65, 1.06	0.13
Hispanic	1.35	1.00, 1.81	0.05	1.07	0.80, 1.44	0.63
Asian	2.09	1.29, 3.38	0.003	1.79	1.14, 2.814	0.011
Other	0.78	0.46, 1.33	0.36	0.590	0.34, 1.04	0.07
Marital Status						
Single	*REF*			REF		
Married	0.85	0.70, 1.04	0.11	0.92	0.74, 1.13	0.41
Widowed	1.18	0.89, 1.56	0.26	1.28	0.97, 1.71	0.08
Divorced	1.44	1.11, 1.87	0.006	1.40	1.080, 1.83	0.011
Other	0.74	0.32, 1.747	0.49	0.66	0.28, 1.53	0.33
Diabetes	1.22	1.05, 1.41	0.008	1.21	1.04, 1.41	0.013
Prior CHF	3.87	1.81, 8.28	<0.001	4.07	2.53, 6.55	<0.001
EF<25%	0.88	0.76, 1.02	0.09	0.78	0.67, 0.91	0.001
Any Appropriate Shock in previous 7 days	23.7	5.60, 100	<0.001	39.5	9.44, 165	<0.001
Any Inappropriate Shock in previous 7 days	8.39	2.24, 31.4	0.002	11.0	3.37, 35.7	<0.001

Table 4:

As treated analysis with and without in-hospital deaths.

| | ALL EVENTS | | | | | | | OUT OF HOSPITAL EVENTS ONLY | | | | | | |
| | | | | Unadjusted | | Adjusted** | | | | | Unadjusted | | Adjusted** | |
	Events	Person-Mos	Rate [CI]	RR*	P	RR*	P	Events	P-Mos	Rate [CI]	RR*	P	RR*	P
TOTAL MORTALITY														
Wearing WCD	12	2420	0.5 [0.26,0.87]	0.26	<0.0005	0.26	<0.0005	11	2407	0.46 [0.23,0.82]	0.33	<0.001	0.33	0.001
Not Wearing WCD	71	3724	1.91 [1.49,2.41]					50	3650	1.37 [1.02–1.81]				
ARRHYTHMIC DEATH														
Wearing WCD	9	2420	0.37 [0.17,0.71]	0.43	0.026	0.43	0.026	8	2407	0.33 [0.14,0.65]	0.45	0.046	0.44	0.043
Not Wearing WCD	32	3724	0.86 [0.59,1.21]					27	3650	0.74 [0.49, 1.08]				
NON-SUDDEN DEATH														
Wearing WCD	2	2420	0.08 [0.01,0.3]	0.09	0.001	0.09	<0.001	2	2407	0.08 [0.01,0.3]	0.15	0.011	0.16	0.012
Not Wearing WCD	36	3724	0.97 [0.68, 1.34]					20	3650	0.55 [0.33,0859]				

*
Poison model

**
adjusted for Diabetes and PCI, the only variables that remained after backwards stepwise variable deletion.

P values are unadjusted (not corrected for multiple hypothesis testing).