Aalborg Universitet

AALBORG UNIVERSITY
DENMARK

Efficacy of a web-based healthcare innovation to advance the quality of life and care of patients with an implantable cardioverter defibrillator (ACQUIRE-ICD): a randomized controlled trial

Skov, Ole; Johansen, Jens Brock; Nielsen, Jens Cosedis; Larroudé, Charlotte E.; Riahi, Sam; Melchior, Thomas M.; Vinther, Michael; Skovbakke, Søren Jensen; Rottmann, Nina; Wiil, Uffe Kock; Brandt, Carl Joakim; Smolderen, Kim G.; Spertus, John A.; Pedersen, Susanne S.

Published in:
Europace

DOI (link to publication from Publisher):
10.1093/europace/euad253

Creative Commons License
CC BY-NC 4.0

Publication date:
2023

Document Version
Publisher's PDF, also known as Version of record

Link to publication from Aalborg University

Citation for published version (APA):
Skov, O., Johansen, J. B., Nielsen, J. C., Larroudé, C. E., Riahi, S., Melchior, T. M., Vinther, M., Skovbakke, S. J., Rottmann, N., Wiil, U. K., Brandt, C. J., Smolderen, K. G., Spertus, J. A., & Pedersen, S. S. (2023). Efficacy of a web-based healthcare innovation to advance the quality of life and care of patients with an implantable cardioverter defibrillator (ACQUIRE-ICD): a randomized controlled trial. *Europace*, *25*(12), Article euad253. https://doi.org/10.1093/europace/euad253

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

ESC European Society of Cardiology

Europace (2023) **25**, 1–9
https://doi.org/10.1093/europace/euad253

CLINICAL RESEARCH

Efficacy of a web-based healthcare innovation to advance the quality of life and care of patients with an implantable cardioverter defibrillator (ACQUIRE-ICD): a randomized controlled trial

Ole Skov [1]*, Jens Brock Johansen [2], Jens Cosedis Nielsen [3,4], Charlotte E. Larroudé[5], Sam Riahi [6,7], Thomas M. Melchior [8], Michael Vinther [9], Søren Jensen Skovbakke [1], Nina Rottmann [1], Uffe Kock Wiil [10], Carl Joakim Brandt[11], Kim G. Smolderen [12,13], John A. Spertus [14], and Susanne S. Pedersen [1,2]

[1]Department of Psychology, University of Southern Denmark, Campusvej 55, DK-5230 Odense, Denmark; [2]Department of Cardiology, Odense University Hospital, Odense, Denmark; [3]Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; [4]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark; [5]Department of Cardiology, Herlev-Gentofte Hospital, Copenhagen, Denmark; [6]Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark; [7]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark; [8]Department of Cardiology, Zealand University Hospital, Roskilde, Denmark; [9]Department of Cardiology B, Rigshospitalet, Copenhagen, Denmark; [10]SDU Health Informatics and Technology, The Maersk Mc-Kinney Moller Institute, University of Southern Denmark, Odense, Denmark; [11]Research Unit for General Practice, Department of Public Health, University of Southern Denmark, Odense, Denmark; [12]Department of Internal Medicine, Vascular Medicine Outcomes Program, Yale School of Medicine, New Haven, CT, USA; [13]Department of Psychiatry, Yale School of Medicine, New Haven, CT, USA; and [14]Kansas City's Healthcare Institute for Innovations in Quality and Saint Luke's Mid America Heart Institute, University of Missouri, Kansas City, MO, USA

Received 7 June 2023; accepted after revision 8 August 2023; online publish-ahead-of-print 21 August 2023

Aims

Modern clinical management of patients with an implantable cardioverter defibrillator (ICD) largely consists of remote device monitoring, although a subset is at risk of mental health issues post-implantation. We compared a 12-month web-based intervention consisting of goal setting, monitoring of patients' mental health—with a psychological intervention if needed—psychoeducational support from a nurse, and an online patient forum, with usual care on participants' device acceptance 12 months after implantation.

Methods and results

This national, multi-site, two-arm, non-blinded, randomized, controlled, superiority trial enrolled 478 first-time ICD recipients from all 6 implantation centres in Denmark. The primary endpoint was patient device acceptance measured by the Florida Patient Acceptance Survey (FPAS; general score range = 0–100, with higher scores indicating higher device acceptance) 12 months after implantation. Secondary endpoints included symptoms of depression and anxiety. The primary endpoint of device acceptance was not different between groups at 12 months [$B = -2.67$, 95% confidence interval (CI) (−5.62, 0.29), $P = 0.08$]. Furthermore, the secondary endpoint analyses showed no significant treatment effect on either depressive [$B = -0.49$, 95% CI (−1.19; 0.21), $P = 0.17$] or anxiety symptoms [$B = -0.39$, 95% CI (−0.96; 0.18), $P = 0.18$].

Conclusion

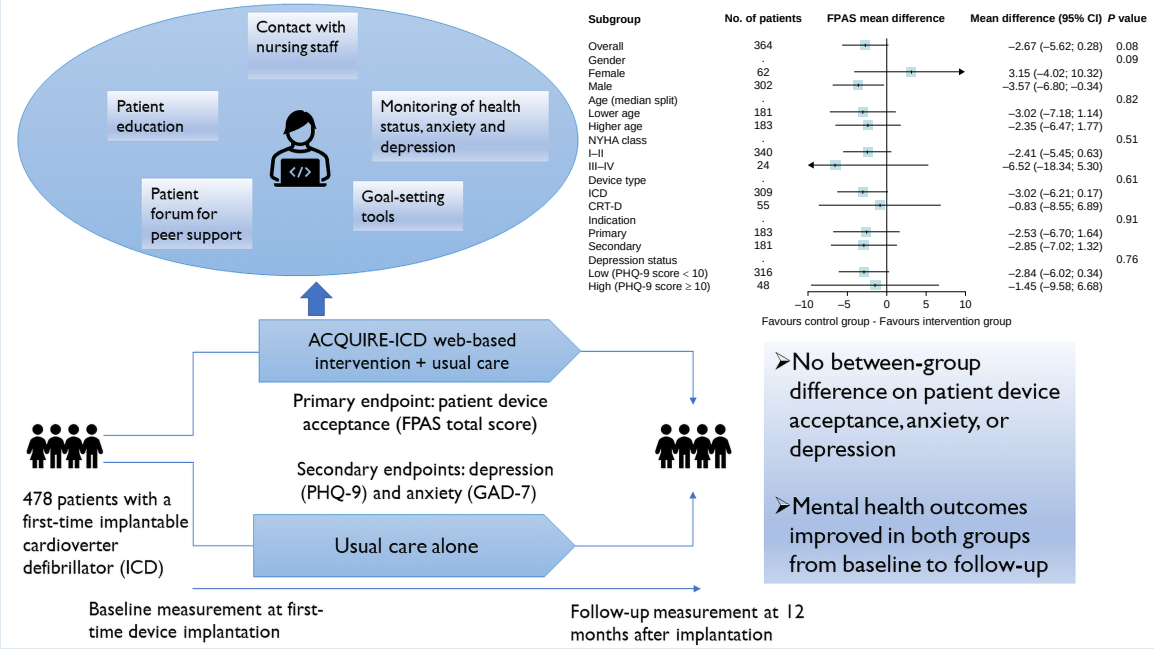
The web-based intervention as supplement to usual care did not improve patient device acceptance nor symptoms of anxiety and depression compared with usual care. This specific web-based intervention thus cannot be recommended as a standardized intervention in ICD patients.

* Corresponding author. Tel : +4565503091. *E-mail address*: olskov@health.sdu.dk

© The Author(s) 2023. Published by Oxford University Press on behalf of the European Society of Cardiology.
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024

Graphical Abstract



Keywords Implantable cardioverter defibrillator • Web-based intervention • Patient device acceptance • Depression • Anxiety • Randomized controlled trial

What's new?

- The purpose of the study was to develop and examine if a comprehensive 12-month web-based intervention (ACQUIRE-ICD) as supplement to usual care improve patient device acceptance, depression, and anxiety in ICD patients.
- The web-based intervention was designed to improve device acceptance of ICD patients by offering psychoeducational support from a nurse, an online patient forum, goal-setting tools, monthly monitoring of patients' mental health and health status, and providing psychological treatment when needed.
- The ACQUIRE-ICD web-based intervention as supplement to usual care did not improve patient device acceptance nor symptoms of anxiety and depression compared with usual care at one-year post-implantation.
- Patient device acceptance, symptoms of anxiety and depression improved significantly from ICD implantation to one-year follow-up in both the intervention and control group.
- Overall, we found no effect of the comprehensive web-based intervention on patient device acceptance at one year follow-up.

Introduction

The implantable cardioverter defibrillator (ICD) is the firstline treatment for prevention of sudden cardiac death and is used for both primary and secondary prevention.[1] In Europe alone, more than 100 000 ICD implantations were performed in 2016.[2] Adjusting to life with an ICD can be challenging for some patients due to concerns about shocks, fear of dying, limitations in daily functioning, worries about the future, body image concerns, and reduced quality of life.[3,4] Implantable cardioverter defibrillator patients are also at risk for mental health issues after implantation with a recent meta-analysis estimating prevalence rates of clinically relevant anxiety and depression at 23% and 15%, respectively.[5] The importance of managing psychosocial risk factors is highlighted in the 2021 European Society of Cardiology (ESC) guidelines on cardiovascular disease prevention in clinical practice with psychosocial stress being independently associated with development and progression of atherosclerotic cardiovascular disease.[6] Furthermore, a recent systematic literature review found that anxiety and depression are associated with increased risk of mortality in ICD patients.[7]

In many countries, modern clinical management of ICD patients has moved from frequent outpatient follow-ups to more remote device monitoring,[8] which may impede identification and support for the subset of patients struggling with device acceptance defined as 'the psychological accommodation and understanding of the advantages and disadvantages of the device, the recommendation of the device to others, and the derivation of benefit in terms of biomedical, psychological, and social functioning'.[9,10] Data from a Danish cohort study found that patients without psychological distress at the time of implantation have a cumulative incidence rate of developing anxiety and depression of 14.5% and 11.3%, respectively, emphasizing the need for a continuous approach in assessing the mental health status of patients receiving ICDs.[11] Studies on ICD patients' needs and preferences also point towards the need for increased focus on psychological support, regular feedback, and continuity in care.[12,13] This calls for a comprehensive care solution for ICD patients with a stepped education and care approach containing psychoeducation for all and therapy for some, suggested as a promising avenue to pursue.[14] Telemedicine solutions have the potential to be a cost-effective way of providing improved care to patients with cardiovascular disease.[15,16] A recent meta-analysis found that web-based health interventions in cardiac patients have beneficial effects on depression.[17]

The ACQUIRE-ICD intervention seeks to address these needs by delivering a web-based intervention that include monthly monitoring of patients' mental health and health status, offering additional support

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024

when needed by the individual patient. We tested the hypothesis that the ACQUIRE-ICD web-based intervention as a supplement to usual care increases device acceptance and mental health 12 months post-implantation as compared with usual care alone.

Methods

Trial design

The ACQUIRE-ICD trial is a national, multi-site, open-label, prospective, two-arm, randomized, controlled, superiority trial (NCT02976961) designed to evaluate the efficacy of a 12-month comprehensive web-based intervention with usual care on clinical and patient-reported outcomes in patients implanted with a first-time ICD with or without cardiac resynchronization therapy (CRT-D) as compared with usual care alone. A detailed description of the study design has been previously published.[10] All trial participants were required to give written informed consent.

Study setting and participants

Patients were recruited from all six national ICD implanting centres in Denmark while hospitalized for their device implantation. Inclusion criteria were first-time ICD or CRT-D recipient and aged ≥ 18 years. Exclusion criteria were as follows: implanted with a totally subcutaneous ICD (S-ICD), received device upgrades, with a history of psychiatric illness other than affective/anxiety disorders, cognitive impairments (e.g. dementia), left ventricular assist device (LVAD) or upcoming implant, patients being considered for heart transplantation, patients without an email address or inability to manage computer technology, insufficient knowledge of the Danish language, participation not recommended according to good clinical practice (GCP), and participation in other randomized controlled trials (RCTs).[10]

Intervention

The ACQUIRE web-based intervention was originally developed for patients with heart failure[18] and subsequently adapted to ICD patients using a participatory design study.[19] The web-based intervention was delivered through the Liva Healthcare Platform,[20] an existing monitoring and communication platform designed to support behavioural change delivered by nursing staff at the implanting centres. The intervention lasted 12 months and consisted of a variety of features including goal-setting tools for facilitating behavioural changes; monthly monitoring of symptoms of anxiety, depression, and self-rated health status; and the possibility of a dialogue with and continuous feedback from nursing staff, referral to an online cognitive–behavioural psychological treatment module in case of elevated depression or anxiety symptoms [Patient Health Questionnaire-9 (PHQ-9) or General Anxiety Disorder-7 (GAD-7) score ≥ 10], and written interaction with nursing staff through the platform's messaging system. In addition, the platform provided a comprehensive archive of educational material, including patient relevant topics related to life with an ICD, psychoeducational content, relaxation exercises, quizzes and vodcasts, and access to an online forum for ICD patients. Usual care consisted of remote device monitoring and in-person consultation at 3 months post-implantation and then every 1 to 2 years depending on the implantation centres' standards of care.

Study flow and randomization

Patients were randomized 1:1 to the ACQUIRE intervention as an add-on to usual care or usual care alone by a permuted block randomization sequence generated by an independent statistician and stratified by implantation centre and severity of heart failure symptoms (New York Heart Association (NYHA) functional class I/II vs. III/IV). Block sizes varied randomly between four and six. Blinding patients to their condition was not possible due to the nature of the study design. Participants answered the baseline questionnaires between 48 h before and 2 weeks after implantation. Following completion of the questionnaire and ICD implantation, patients in the intervention group were given a 45 min introduction to the web-based eHealth platform by a nurse either face-to-face or via telephone. Patients in both groups received survey questionnaires via email at 6-, 12-, and 24-month follow-up. For 6- and 24-month follow-up, patients not returning the questionnaires were sent reminders by email three times with 7 day intervals. At 12-month follow-up, non-responders were contacted by phone as renewed consent was needed according to the General Data Protection Regulation (GDPR).

Data collection and measurements

Baseline assessment included demographic and clinical data (e.g. medication, comorbidity, and clinical events) obtained via electronic health records. Patient-reported outcomes were assessed with the following standardized and validated self-report questionnaires: the shortened 12-item version of the Florida Patient Acceptance Survey (FPAS)[21] for assessing patient device acceptance with a total score range of 0 to 100, with higher scores indicating higher device acceptance.[9] The PHQ-9 was used to assess symptoms of depression with total scores ranging from 0 to 27 and scores ≥ 10 indicating clinical depressive symptomatology.[22] The GAD-7 was used to measure symptoms of anxiety with total scores ranging from 0 to 21 and scores ≥ 10 indicating clinical anxiety levels.[23] Data were collected and stored in the Research Electronic Data Capture (REDCap) database.

Outcomes

The pre-specified primary endpoint was patient device acceptance (total FPAS score) 12 months after implantation. We chose the FPAS as the best proxy for a disease-specific quality of life measure for this population as no other disease-specific quality of life measure was available at the time of designing the trial. Anxiety and depression symptoms at 12 months post-implantation were secondary endpoints.

Sample size

Sample size calculations were based on the ability to detect a minimal clinically important difference defined as 3 points of mean difference between treatment groups on 12-month FPAS scores.[10] With a target power of 90%, a type I error rate of 0.05 (two-sided), and assumed attrition rate of 20%, a total of 478 patients were needed.[10]

Statistical analyses

Data analysis was performed using R (version 4.2.2) and IBM SPSS Statistics (version 28). Data were analysed according to a modified intention-to-treat principle with participants completing 12-month follow-up evaluation included in the analyses as randomized. Descriptive analyses were summarized as *n* (%) for categorical variables and min–max, mean, and standard deviation for continuous variables and reported for the entire sample as well as separately for each randomization group. Linear regression analyses were conducted to analyse the effect of the intervention on 12-month FPAS scores by regressing on treatment group and including baseline FPAS scores and strata (NYHA class and implantation centre) as covariates in the model. One implantation centre only included a single patient, and in the statistical analyses, this patient was added to the centre geographically nearest that implantation centre. Pre-specified sub-group analyses were conducted for device type (ICD vs. CRT-D), indication (primary vs. secondary), heart failure symptom severity (NYHA class I–II vs. NYHA class III–IV), sex, age (median split), and depression (PHQ score ≤ 9 vs. ≥ 10) and tested by adding an interaction term between the treatment group and each patient characteristic, one at a time.

As a secondary analysis, longitudinal changes over time in mean FPAS scores were modelled using a linear mixed effect model procedure incorporating participants as a random effect, thus modelling the nested data structure in the repeated measures design. The linear mixed effect models included all randomized participants in the analyses. Secondary endpoints of anxiety and depression were modelled similarly to the primary endpoint by linear regression analyses with 12-month scores regressed on treatment group including baseline scores and strata (NYHA class and implantation centre) as covariates in the models.

Results

Patient characteristics

Between February 2017 and July 2020, 478 patients were randomized to either the intervention plus usual care ($n = 237$) or usual care alone ($n = 241$) out of the 1098 patients screened for study eligibility (see

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024

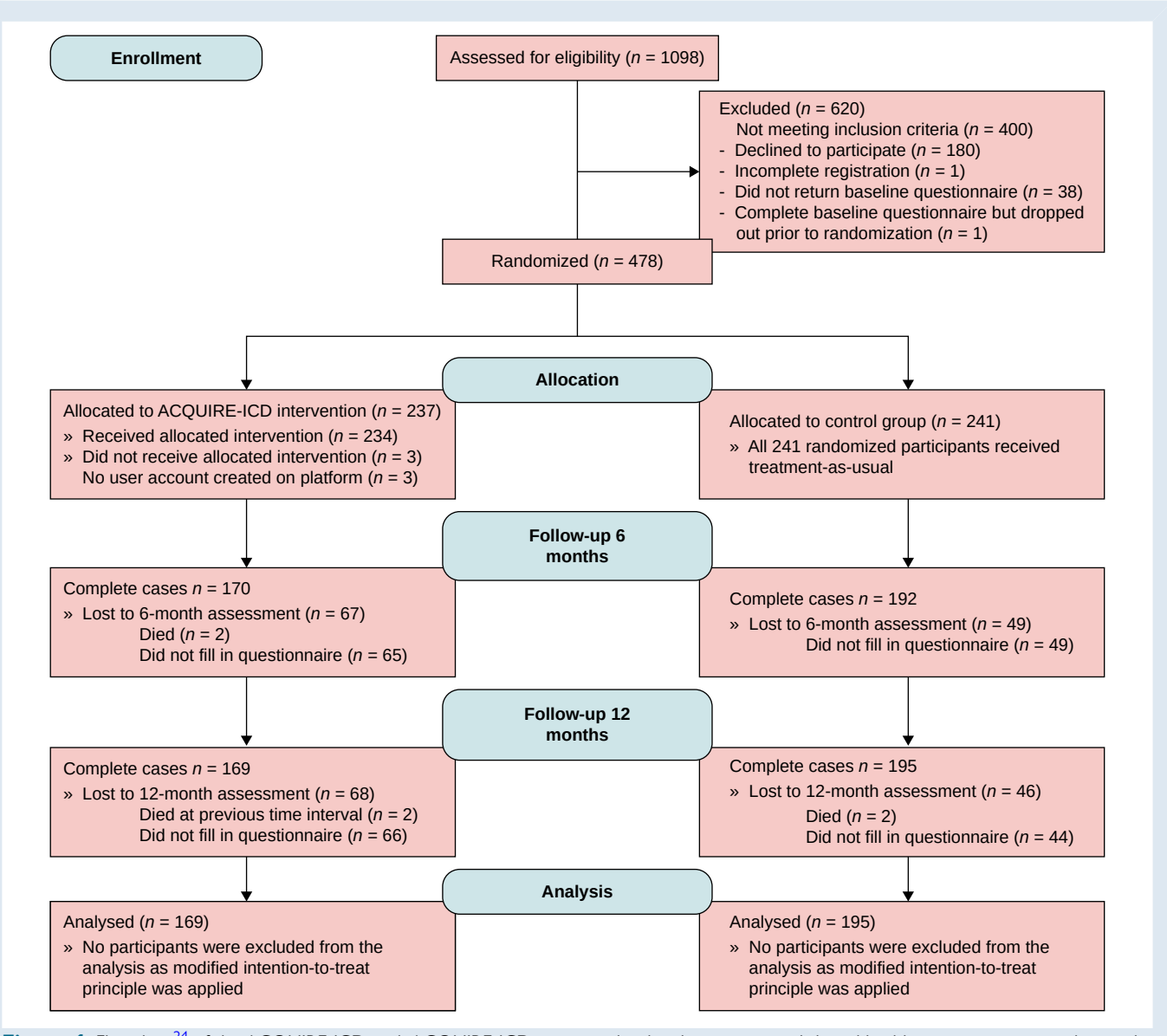


Figure 1 Flowchart[24] of the ACQUIRE-ICD trial. ACQUIRE-ICD: a personalized and interactive web-based healthcare innovation to advance the quality of life and care of patients with an implantable cardioverter defibrillator.

Figure 1). Patients in the intervention group did not differ in baseline characteristics compared with the usual care group (*Table 1*). Of 478 patients randomized (mean age 59.6 ± 11.6; 83% male), 4 deaths (2 in each group) occurred before 12-month follow-up, and 110 did not complete the FPAS at 12-month follow-up (66 in the intervention group and 44 in the control group), resulting in 364 patients eligible for the primary endpoint analysis, 169 in the intervention group and 195 in the control group (see Supplementary material online, *Table S2*). The three most frequently reported reasons for dropping out of the intervention were (i) dissatisfaction with the content of the intervention, (ii) lack of personal resources to engage in the intervention, and (iii) not experiencing mental health issues related to the ICD. Patients who were lost to 12-month follow-up were more likely to be in the intervention group (completers: 46.4% vs. lost to follow-up: 59.6%, $P = 0.014$) and to be smoking daily (completers: 11% vs. lost to follow-up: 18.4%, $P = 0.038$) but did not otherwise differ significantly from the patients who completed the follow-up on psychological or demographic characteristics (see Supplementary material online, *Table S1*). Significant differences were found on clinical variables with patients lost to 12-month follow-up being more likely to have the ICD for primary prevention (completers: 50.3% vs. lost to follow-up: 63.2%, $P = 0.016$) and having hypertension (completers: 35.1% vs. lost to follow-up: 46.5%, $P = 0.029$). From baseline to 12-month follow-up, 10 patients experienced at least 1 shock (4 in intervention group and 6 in control group).

In the intervention group, 41 patients were offered referral to an online cognitive–behavioural psychological treatment module due to elevated anxiety and/or depression symptoms with 20 patients accepting the offer. Reasons for rejecting treatment were (i) no or few ICD-related mental health issues ($n = 16$), (ii) already participating in or having planned psychological counselling elsewhere ($n = 4$), and (iii) unknown reason ($n = 1$). Out of the 20 patients accepting treatment, 13 patients completed the majority of the online psychological treatment modules. Patients dropping out of the intervention

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024

Table 1 Baseline characteristics for the total ACQUIRE-ICD cohort and stratified by intervention[a]

	Total (*N* = 478)	ACQUIRE-ICD (*N* = 237)	Usual care (*N* = 241)
Demographics			
Age	59.6 ± 11.6	59.9 ± 11.7	59.3 ± 11.5
Height	178 ± 10.2	178 ± 10.5	178 ± 9.9
Weight (*n* = 461)	89.7 ± 19.5	90.4 ± 20.1	88.9 ± 18.9
Gender			
Male	397 (83.1)	191 (80.6)	206 (85.5)
Female	81 (16.9)	46 (19.4)	35 (14.5)
Working			
Yes	241 (50.4)	118 (49.8)	123 (51.0)
No	237 (49.6)	119 (50.2)	118 (49.0)
Higher education[b]			
Yes	242 (50.6)	112 (47.3)	130 (53.9)
No	236 (49.4)	125 (52.7)	111 (46.1)
Married/partner			
Yes	378 (79.1)	187 (78.9)	191 (79.3)
No	100 (20.9)	50 (21.1)	50 (20.7)
Smoking daily			
Yes	61 (12.8)	26 (11.0)	35 (14.5)
No	417 (87.2)	211 (89.0)	206 (85.5)
Clinical			
Device type			
ICD	408 (85.4)	205 (86.5)	203 (84.2)
CRT-D	70 (14.6)	32 (13.5)	38 (15.8)
Indication			
Primary	255 (53.3)	125 (52.7)	130 (53.9)
Secondary	223 (46.7)	112 (47.3)	111 (46.1)
QRS duration (*n* = 475)	111 ± 25	110 ± 23.3	111 ± 26.7
QRS ≥ 120 ms (*n* = 475)			
Yes	137 (28.8)	72 (30.5)	65 (27.2)
No	338 (71.2)	164 (69.5)	174 (72.8)
NYHA			
NYHA class Ⅰ	192 (40.2)	96 (40.5)	96 (39.8)
NYHA class Ⅱ	249 (52.1)	124 (52.3)	125 (51.9)
NYHA class Ⅲ	34 (7.1)	16 (6.8)	18 (7.5)
NYHA class Ⅳ	3 (0.6)	1 (0.4)	2 (0.8)
Ischaemic heart disease (*n* = 473)			
Yes	267 (56.4)	137 (58.3)	130 (54.6)
No	206 (43.6)	98 (41.7)	108 (45.4)
CABG pre-implantation (*n* = 461)			
Yes	65 (14.1)	37 (16.2)	28 (12.0)
No	396 (85.9)	191 (83.8)	205 (88.0)
Medication			
Beta-blockers			
Yes	378 (79.1)	182 (76.8)	196 (81.3)
No	100 (20.9)	55 (23.2)	45 (18.7)
ACE inhibitors			
Yes	211 (44.1)	105 (44.3)	106 (44.0)

Continued

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024

Table 1 *Continued*

	Total (*N* = 478)	ACQUIRE-ICD (*N* = 237)	Usual care (*N* = 241)
No	267 (55.9)	132 (55.7)	135 (56.0)
Statins			
Yes	302 (63.2)	150 (63.3)	152 (63.1)
No	176 (36.8)	87 (36.7)	89 (36.9)
Digoxin			
Yes	8 (1.7)	4 (1.7)	4 (1.7)
No	470 (98.3)	233 (98.3)	237 (98.3)
Diuretics			
Yes	199 (41.6)	102 (43.0)	97 (40.2)
No	279 (58.4)	135 (57.0)	144 (59.8)
Amiodarone			
Yes	33 (6.9)	18 (7.6)	15 (6.2)
No	445 (93.1)	219 (92.4)	226 (93.8)
Comorbidity (*n* = 473)			
Diabetes			
Yes	82 (17.3)	37 (15.7)	45(18.9)
No	391 (82.7)	198 (84.3)	193(81.1)
Hypertension			
Yes	179 (37.8)	90 (38.3)	89 (37.4)
No	294 (62.2)	145 (61.7)	149 (62.6)
Psychological characteristics			
Device acceptance (FPAS total score)	74.1 ± 15.2	74.6 ± 15.3	73.5 ± 15.2
Depressive symptoms (PHQ-9 total score)	4.55 ± 4.43	4.56 ± 4.63	4.55 ± 4.24
Depressive symptoms above cut off (PHQ-9 total score ≥ 10)			
Yes	63 (13.2)	31 (13.1)	32 (13.3)
No	415 (86.8)	206 (86.9)	209 (86.7)
Anxiety symptoms (GAD-7 total score)	3.57 ± 4.19	3.37 ± 4.01	3.78 ± 4.36
Anxiety symptoms above cut off (GAD-7 total score ≥ 10)			
Yes	43 (9.0)	21 (8.9)	22 (9.1)
No	435 (91.0)	216 (91.1)	219 (90.9)

ACE inhibitors, angiotensin-converting enzyme inhibitors; ACQUIRE-ICD, a personalized and interactive web-based healthcare innovation to advance the quality of life and care of patients with an implantable cardioverter defibrillator; CABG, coronary artery bypass grafting; CRT-D, implantable cardioverter defibrillator with cardiac resynchronization therapy; FPAS, Florida Patient Acceptance Survey; GAD-7, General Anxiety Disorder-7; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.

[a]Categorical variables summarized as *n* (%); continuous variables summarized as means ± SD.

[b]Higher education refers to completion of a short-, medium-, or long-cycle higher education programme.

were mainly because of either a lack of personal resources to meet treatment demands or patient did not reply to messages from the therapist.

Primary endpoint

No significant difference was found on total FPAS scores at 12 months post-implantation between the intervention and control groups [$B = -2.67$, 95% confidence interval (CI) (−5.62, 0.29), $P = 0.08$] with the direction of the point estimate being in favour of the control group. Pre-planned sub-group analyses showed no moderating effect of device type, ICD indication, heart failure severity, age, or depression status at implant (*Figure 2*). We found no statistically significant interaction effect between treatment and sex ($P = 0.10$). However, men in the intervention group reported lower levels of device acceptance 12 months post-implantation compared with men in the control group [$B = -3.57$, 95% CI (−6.80; −0.34), $P = 0.03$], while for women, a non-significant opposite trend was observed [$B = 3.15$, 95% CI (−4.02; 10.32), $P = 0.39$]. Linear mixed effect models of overall longitudinal changes in mean total FPAS scores (*Figure 3*) revealed a significant effect for time for both groups combined with patient device acceptance levels increasing from baseline to 6-month follow-up [$B = 4.13$, 95% CI (2.61; 5.65), $P < 0.001$] and 12-month follow-up [$B = 5.68$, 95% CI (4.16; 7.19), $P < 0.001$]. This time trend was present and statistically significant in both groups.

Secondary endpoints

The analyses of secondary endpoints showed no statistically significant treatment effect on either depression [$B = -0.49$, 95% CI (−1.19; 0.21), $P = 0.17$] or anxiety symptoms [$B = -0.39$, 95% CI (−0.96; 0.18),

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024

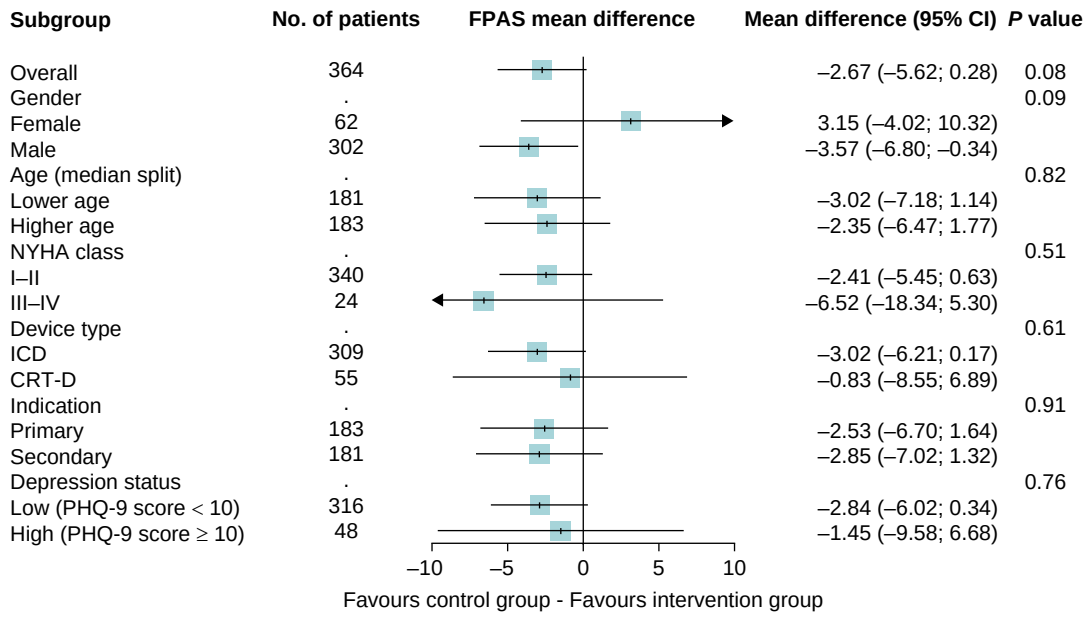


Figure 2 Forest plot of FPAS mean differences between intervention and control groups in pre-planned sub-group analyses. CI, confidence interval; CRT-D, implantable cardioverter defibrillator with cardiac resynchronization therapy; FPAS, Florida Patient Acceptance Survey; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; PHQ-9, Patient Health Questionnaire-9.

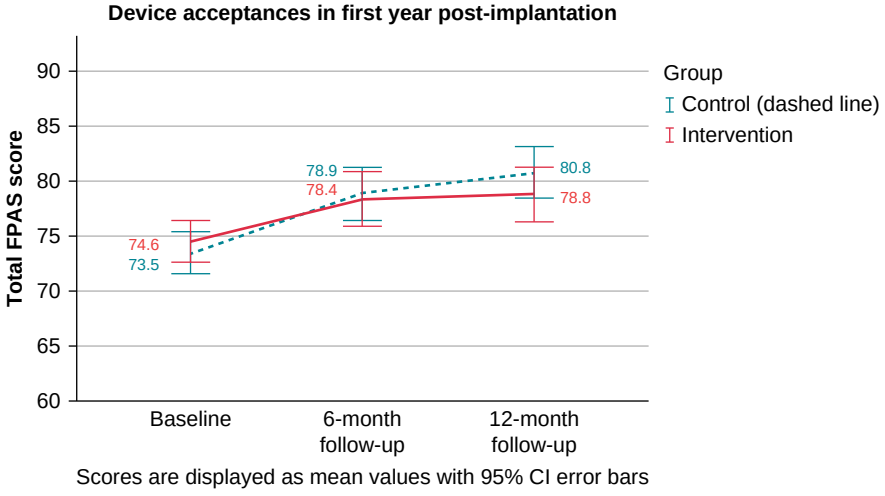


Figure 3 Device acceptance in first year post-implantation. CI, confidence interval; FPAS, Florida Patient Acceptance Survey.

$P = 0.18$]. Linear mixed effect models of overall longitudinal changes in depression symptoms showed significant decreases in depression symptoms from baseline to 6-month follow-up [$B = -0.75$, 95% CI (−1.13; −0.36), $P < 0.001$] and 12-month follow-up [$B = -1.04$, 95% CI (−1.42; −0.66), $P < 0.001$] (see Supplementary material online, *Figure S1*). A similar pattern of overall longitudinal changes was found for anxiety symptoms, which decreased significantly from baseline to 6-month follow-up [$B = -1.17$, 95% CI (−1.53; −0.81), $P < 0.001$] and 12-month follow-up [$B = -1.60$, 95% CI (−1.96; −1.24), $P < 0.001$] (see Supplementary material online, *Figure S2*).

Discussion

Given the psychological burden of ICD implantation and the evolving trend for more remote follow-up, developing strategies to support patients receiving ICDs is increasingly important. In this RCT of a web-based intervention to supplement usual care, we found no differences in patient device acceptance at 12 months. The ACQUIRE-ICD was a well-powered randomized controlled web-based intervention trial targeting general well-being and mental health in the ICD population. Although the null finding related to the primary endpoint did not

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024

support our original hypothesis, this finding is in line with the results from other RCTs of web-based interventions in ICD patients that also found neutral primary endpoints albeit on anxiety and a composite outcome of psychosocial well-being, respectively.[25,26]

None of the pre-planned sub-group analyses showed significant moderation effects; however, men in the control group showed better patient device acceptance than men in the intervention group, while for women, a non-significant opposite trend in favour of the intervention group was observed. Women have been found to be more likely to use eHealth interventions as recommended,[27] which could explain an increased benefit from the intervention; however, the difference could also be a spurious finding due to multiple testing as the pre-planned treatment by sex interaction was not statistically significant.

The intervention also failed to improve the secondary endpoints anxiety and depression. The absence of intervention effects on anxiety and depression levels mimics the results from the WEBCARE trial,[26] but not from the ICD-FORUM trial,[25] which found that a web-based intervention reduced anxiety and depression symptoms at 1 year follow-up compared with usual care. Whereas the ICD-FORUM trial included only patients with distress, ACQUIRE-ICD and WEBCARE targeted a broad scope of ICD patients, regardless of pre-intervention distress. This may partly explain the differences across the three trials.

The longitudinal analyses revealed that ICD patients' mental health status improved significantly from ICD implantation to 1 year follow-up in both the intervention and control groups. The observed improvement over time suggests that most ICD patients find ways to mentally adjust to life with an ICD irrespectively of whether they are offered a comprehensive web-based intervention. The improvement in psychological well-being over time might explain why loss to follow-up was higher in the intervention group compared with the control group, as patients generally feeling well may be less motivated to use the resources in the web-based intervention. It is possible that the combination of a time-consuming web-based intervention implemented in a population with many non-distressed patients could be an explanation why a neutral result emerged. This also raises the question whether future eHealth interventions should target all ICD patients or perhaps rather allocate resources to the specific subset of patients showing signs of psychological distress or other challenges. For new interventions in the area, our recommendation would be to increase attention to involving patients in the development of the intervention through a patient and public involvement (PPI). In addition, it will be important to conduct a feasibility or pilot RCT prior to conducting the full trial and to continuously assess the needs and preferences of patients and deliver targeted interventions using a precision medicine approach.

Some limitations of the current study should be acknowledged. There is uncertainty concerning the extent to which the participants used the resources available in the web-based intervention; thus, we cannot rule out variation in the dosage of the intervention across participants in the intervention group. Patient-reported outcomes were measured in the interval between 2 days prior to ICD implantation and up to 2 weeks post-implantation, potentially generating heterogeneity in the psychological distress measures depending on the time of completion. In the intervention group, anxiety and depression were measured repeatedly once a month as part of monitoring patients' mental health, using the same questionnaires as the study endpoints, which could lead to test–retest bias. There was increased dropout in the intervention group; however, patients dropping out did not significantly differ on psychological characteristics from those remaining in the study.

Conclusion

The ACQUIRE-ICD web-based intervention as add-on to usual care did not improve device acceptance and mental health compared with usual care alone, as we found no significant effect on patient device acceptance, anxiety, or depression at 12 months post-implantation. This specific web-based intervention thus cannot be recommended as a standardized intervention in ICD patients.

Supplementary material

Supplementary material is available at *Europace* online.

Acknowledgements

We are grateful to the nursing staff at all six implantation centres for their involvement in the project and for the patients who participated in the trial.

Funding

This work was funded by the Lundbeck Foundation, grant # R198-2015-175; TrygFonden, Grant # 109704; and Patient@Home seeding grant.

Conflict of interest: J.C.N. received institutional grants from the Novo Nordisk Foundation and the Danish Heart Foundation. J.B.J. is a consultant for Medtronic. M.V. serves on conduction system pacing advisory boards for Medtronic and Abbott. K.G.S. reports unrestricted research grants from Philips, Abbott, Merck, and Johnson & Johnson, and she is a consultant for Optum Labs and Abbott, Happify, and Haemonetics. K.G.S. is supported by NIH grants 1R21AT012430-01 (NCCIH) and 1R01HL163640-01A1 (NHLBI). J.A.S. has no conflicts of interest for the study but discloses providing consultative services on patient-reported outcomes and evidence evaluation to Alnylam, AstraZeneca, Bayer, Merck, Janssen, Bristol Meyers Squibb, Edwards, Kineksia, 4DT Medical, Terumo, Cytokinetics, Imbria, and United Healthcare. He holds research grants from Bristol Meyers Squibb, Abbott Vascular, and Janssen. He owns the copyright to the Seattle Angina Questionnaire, Kansas City Cardiomyopathy Questionnaire, and Peripheral Artery Questionnaire and serves on the Board of Directors for Blue Cross Blue Shield of Kansas City. All remaining authors have declared no conflicts of interest.

Data availability

Given that we just started writing papers on the data set, we are not able to share data at this point in time.

References

1. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J *et al.* 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC) Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Europace* 2015;**17**:1601–87.
2. Raatikainen MJP, Arnar DO, Merkely B, Nielsen JC, Hindricks G, Heidbuchel H *et al.* A decade of information on the use of cardiac implantable electronic devices and interventional electrophysiological procedures in the European Society of Cardiology countries: 2017 report from the European Heart Rhythm Association. *Europace* 2017;**19**:ii1–ii90.
3. Frydensberg VS, Skovbakke SJ, Pedersen SS, Kok RN. Body image concerns in patients with an implantable cardioverter defibrillator: a scoping review. *Pacing Clin Electrophysiol* 2018;**41**:1235–60.
4. Rottmann N, Skov O, Andersen CM, Theuns DAMJ, Pedersen SS. Psychological distress in patients with an implantable cardioverter defibrillator and their partners. *J Psychosom Res* 2018;**113**:16–21.
5. Ghezzi ES, Sharman RLS, Selvanayagam JB, Psaltis PJ, Sanders P, Astley JM *et al.* Burden of mood symptoms and disorders in implantable cardioverter defibrillator patients: a systematic review and meta-analysis of 39 954 patients. *Europace* 2023;**25**:euad130.
6. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M *et al.* 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2021;**42**:3227–337.
7. Lindekilde N, Skov O, Skovbakke SJ, Johansen JB, Nielsen JC, Pedersen SS. Anxiety and depression as risk factors for ICD shocks and mortality in patients with an implantable cardioverter defibrillator – a systematic review. *Gen Hosp Psychiat* 2022;**78**:96–107.
8. Bertini M, Marcantoni L, Toselli T, Ferrari R. Remote monitoring of implantable devices: should we continue to ignore it? *Int J Cardiol* 2016;**202**:368–77.
9. Burns JL, Serber ER, Keim S, Sears SF. Measuring patient acceptance of implantable cardiac device therapy:. *J Cardiovasc Electrophysiol* 2005;**16**:384–90.

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024

10. Pedersen SS, Skovbakke SJ, Wiil UK, Schmidt T, Depont Christensen R, Brandt CJ *et al.* Effectiveness of a comprehensive interactive eHealth intervention on patient-reported and clinical outcomes in patients with an implantable cardioverter defibrillator ACQUIRE-ICD trial.: study protocol of a national Danish randomised controlled trial. *BMC Cardiovasc Disord* 2018;**18**:136.
11. Pedersen SS, Nielsen JC, Wehberg S, Jørgensen OD, Riahi S, Haarbo J *et al.* New onset anxiety and depression in patients with an implantable cardioverter defibrillator during 24 months of follow-up (data from the national DEFIB-WOMEN study). *Gen Hosp Psychiat* 2021;**72**:59–65.
12. Pedersen SS, Knudsen C, Dilling K, Sandgaard NCF, Johansen JB. Living with an implantable cardioverter defibrillator: patients' preferences and needs for information provision and care options. *Europace* 2017;**19**:983–90.
13. Januszkiewicz L, Barra S, Marijon E, Providencia R, de Asmundis C, Chun JKR *et al.* Major gaps in the information provided to patients before implantation of cardioverter defibrillators: a prospective patient European evaluation. *Europace* 2023;**25**:1144–51.
14. Sears SF, Ford J. Seeking innovation in the delivery of psychosocial care for ICD patients. *Eur Heart J* 2020;**41**:1212–4.
15. Farabi H, Rezapour A, Jahangiri R, Jafari A, Rashki Kemmak A, Nikjoo S. Economic evaluation of the utilization of telemedicine for patients with cardiovascular disease: a systematic review. *Heart Fail Rev* 2020;**25**:1063–75.
16. Whitelaw S, Pellegrini DM, Mamas MA, Cowie M, Van Spall HGC. Barriers and facilitators of the uptake of digital health technology in cardiovascular care: a systematic scoping review. *Eur Heart J Digit Health* 2021;**2**:62–74.
17. Kaihara T, Scherrenberg M, Intan-Goey V, Falter M, Kindermans H, Frederix I *et al.* Efficacy of digital health interventions on depression and anxiety in patients with cardiac disease: a systematic review and meta-analysis. *Eur Heart J Digit Health* 2022;**3**:445–54.
18. Pedersen SS, Schmidt T, Skovbakke SJ, Wiil UK, Egstrup K, Smolderen KG *et al.* A personalized and interactive web-based health care innovation to advance the quality of life and care of patients with heart failure (ACQUIRE-HF): a mixed methods feasibility study. *JMIR Res Protoc* 2017;**6**:e96.
19. Noergaard B, Sandvei M, Rottmann N, Johannessen H, Wiil U, Schmidt T *et al.* Development of a web-based health care intervention for patients with heart disease: lessons learned from a participatory design study. *JMIR Res Protoc* 2017;**6**:e75.
20. Liva Healthcare Platform. Liva Healthcare Platform. https://livahealthcare.com (17 February 2023, date last accessed).
21. Versteeg H, Starrenburg A, Denollet J, Palen J, Sears SF, Pedersen SS. Monitoring device acceptance in implantable cardioverter defibrillator patients using the Florida Patient Acceptance Survey. *Pacing Clin Electrophysiol* 2012;**35**:283–93.
22. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. *J Gen Int Med* 2001;**16**:606–13.
23. Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006;**166**:1092–7.
24. Schulz Kenneth F, Altman Douglas G, Moher David. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Medicine* 2010;**8**:42.
25. Schulz SM, Ritter O, Zniva R, Nordbeck P, Wacker C, Jack M *et al.* Efficacy of a web-based intervention for improving psychosocial well-being in patients with implantable cardioverter-defibrillators: the randomized controlled ICD-FORUM trial. *Eur Heart J* 2020;**41**:1203–11.
26. Habibovic M, Denollet J, Cuijpers P, van der Voort PH, Herrman JP, Bouwels L *et al.* Web-based distress management for implantable cardioverter defibrillator patients: a randomized controlled trial. *Health Psychol* 2017;**36**:392–401.
27. Reinwand DA, Schulz DN, Crutzen R, Kremers SP, de Vries H. Who follows eHealth interventions as recommended? A study of participants' personal characteristics from the experimental arm of a randomized controlled trial. *J Med Internet Res* 2015;**17**:e115.

Downloaded from https://academic.oup.com/europace/article/25/12/euad253/7246543 by Aalborg University Library user on 05 January 2024