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Representativeness of participants in heart failure e-health trials: a report from the e-Vita heart failure study

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Research letter

Well-designed and properly executed randomized controlled trials (RCTs) provide the strongest evidence on the effects of interventions. However, eligibility criteria and the willingness to participate may result in differences between participants and non-participants. When participants differ considerably from non-participants, the participants will not be representative for the domain of study. As a consequence, the results of the trial may not be generalizable to that domain of patients. (1) However, this will only be the case if the characteristics (e.g. age) in which the groups differ, modify the effect of the intervention (e.g. that the effect is larger or smaller in older or younger patients). (2) Such ‘effect modifiers’ may differ per intervention. Selectivity of participants of RCTs in general is well known but representativeness of heart failure (HF) patients in e-health trials is lacking. Insight in representativeness in e-health is pivotal as the number of trials in this area increases. They might even be more sensitive to selectivity than device and drug trials in HF, as they require active participation and possible technical ‘savviness’. We aimed to compare characteristics of participants with non-participants in the e-Vita HF study that evaluates e-health in patients with HF and to compare characteristics of e-Vita HF participants with participants of previous e-health randomized studies in HF.

We used data from the Dutch multicenter e-Vita HF study, a randomized trial on the effectiveness of two e-health tools in patients with HF. (3) Eligibility criteria are reported elsewhere. (3) In total, 405 patients consented to participate. A random sample of non-participants (n=402) were taken as the comparison group. Demographic and disease-specific characteristics of the participants and the non-participants were collected at baseline. In addition, we collected potential effect modifiers for e-health interventions: age, comorbidities, and socio-

economic status (SES). (4) To define SES, the 4 digits of the Dutch postal codes were linked to a SES according to the Netherlands Institute for Social research database (SCP). (5) The SES was categorized for the present analysis as: <0= low SES, 0= middle SES, >0 =high SES.

Participants signed an informed consent, and the data of the non-participants was stored and analyzed anonymously. This strategy was approved by the Medical Ethical Committee of the University Medical Center Utrecht. Information about participants of previously performed e-health studies was retrieved from a recently published Cochrane review. (6)

Table 1 shows characteristics of participants and non-participants. Participants were younger (mean age 66.7 vs. 73.4 years), more often male (75% vs. 58%), and had fewer comorbidities. After adjustment for age anemia and angina pectoris were no longer significantly different, and SES became significantly higher in participants. From the Cochrane review we retrieved information on participants (data on non-participants was not presented) of 18 studies evaluating telemonitoring interventions, published between 2001 and 2014. The mean age was 68 years (range 54 to 78 years), 73% (range 35 to 85%) were men, 30% (4 to 43%) with diabetes and 43% (15 to 67%) with hypertension.

Table 1. Demographic and disease-specific characteristics of the participants and non-participants in the e-health e-Vita HF trial

	Participants(N=405)		Non-participants (N=402)	
<i>Demographics</i>	%		%	
				P-value¶ P-value (adjusted for age)§
Female sex	25.2		42.3	<0.001 <0.001
Mean age in years (SD)	66.7 (10.8)		73.4 (11.1)	<0.001 NA
SES*†				
Low	16.5		19.9	0.34 0.02
Middle	38.0		39.3	
High	44.9		40.8	
<i>Comorbidities</i>				
Angina pectoris	17.8		24.6	0.02 0.15
Prior MI‡	42.2		41.0	0.73 0.42
Hypertension	44.0		62.2	<0.001 <0.001
Hyperlipidemia	40.0		38.3	0.62 0.57
Anaemia	15.1		20.9	0.03 0.79
Diabetes	25.2		30.1	0.12 0.25
Renal insufficiency¥	15.6		40.3	<0.001 <0.001
COPD / Asthma	25.7		21.4	0.15 0.07
Cancer	18.0		21.4	0.23 0.62
Sleep disorders	9.6		8.7	0.65 0.70

*SES=socio-economic status, †0.5% missing among participants, ‡MI=myocardial infarction, ¥renal insufficiency = patients < 65 years, creatinine clearance < 45 ml/min; ≥ 65 years, creatinine clearance < 30 ml/min, ¶P-value calculated with chi-square test and T-test, §P-value calculated with multiple linear or (ordinal) logistic regression analysis.

The e-Vita HF trial participants were similar to the participants of previous e-health studies. This is the first study on representativeness of HF participants in an e-health RCT. In line with RCTs evaluating pharmaceutical interventions in chronic HF patients, participants in the e-Vita HF study were younger, more often male and had fewer comorbidities than non-participants. (7) However, importantly, the modifying effect of these characteristics may vary between pharmaceutical and e-health interventions. It has been suggested that gender may modify the effect of drug interventions in HF because women have more often HF with preserved ejection fraction, are older and have more comorbidities. (8) Such gender-related differences that may affect the outcomes have not yet been suggested in e-health interventions. (4) The SES between participants and non-participants differed after adjustment for age. This confirms previous studies showing an association between SES and the use of internet in elderly. (9, 10) A limitation of this study is that marital status and interest in new technical items as potential effect modifiers were not included. (9) Further research should address to what extent age, comorbidity and other patient characteristics actually modify the effect of e-health tools in HF. This requires detailed characteristics of non-participants to be reported in future trials and individual patient data analysis to assess subgroup effects (identify effect modifiers).

In conclusion, participants differ from non-participants in HF e-health studies. Differences between participating and non-participating HF patients should be taken into account in the interpretation of research findings and e-health trials should report patient's characteristics of non-participants.

Conflicts of interest

None declared.

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