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Complete List of Authors:	Suman, Arnela; Amsterdam UMC - Locatie VUMC Schaafsma, F; Amsterdam UMC - Locatie VUMC van Dongen, Johanna M.; Vrije Universiteit Amsterdam Elders, Petra; Amsterdam UMC - Locatie VUMC Buchbinder, Rachelle; Monash University Tulder, Maurits; Vrije Universiteit Amsterdam Anema, Johannes; Amsterdam UMC - Locatie VUMC
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Effectiveness and cost-effectiveness of a multifaceted eHealth strategy to improve back pain beliefs of patients with non-specific low back pain: a cluster randomised trial

Arnela Suman, Frederieke G. Schaafsma, Johanna M van Dongen, Petra JM Elders, Rachelle Buchbinder, Maurits W van Tulder, Johannes R Anema

Corresponding author: Arnela Suman, Amsterdam UMC, VU University Amsterdam, department of Public and Occupational Health, Amsterdam Public Health research institute, De Boelelaan 1117, 1081HV Amsterdam, The Netherlands; a.suman@vumc.nl; 0031-20-4445685

Frederieke G Schaafsma, Amsterdam UMC, VU University Amsterdam, department of Public and Occupational Health, Amsterdam Public Health research institute, Amsterdam, The Netherlands

Johanna M van Dongen, VU University Amsterdam, department of Health Sciences, Amsterdam Public Health research institute, Amsterdam, The Netherlands

Petra JM Elders, Amsterdam UMC, VU University Amsterdam, department of General Practice and Elderly Care, Amsterdam Public Health research institute, Amsterdam, The Netherlands

Rachelle Buchbinder, Monash Department of Clinical Epidemiology, Cabrini Institute and Department of Epidemiology and Preventive Medicine, School of Public Health & Preventive Medicine, Monash University, Victoria, Australia

Maurits W van Tulder, VU University Amsterdam, department of Health Sciences Amsterdam Public Health research institute, Amsterdam, The Netherlands

Johannes R Anema, Amsterdam UMC, VU University Amsterdam, department of Public and Occupational Health, Amsterdam Public Health research institute, Amsterdam, The Netherlands

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ABSTRACT

Background Low back pain is the world's leading cause of disability and has a high burden on individuals and societies. Many guidelines recommend self-management for patients with low back pain. The current study aims to assess whether a multifaceted eHealth strategy is effective and cost-effective compared to usual care in improving patients' back pain beliefs and quality of life, and in decreasing their disability and absenteeism.

Methods This study was a stepped wedge cluster randomised controlled trial with a parallel economic evaluation performed from a societal perspective. Four clusters of general and physiotherapy practices and occupational physicians were randomised and recruited patients with low back pain for this study. 779 patients participated in this study, of which 331 were randomised to the intervention group (multifaceted eHealth strategy), and 448 were randomised to the control group (usual care). All patients were followed up at 3, 6, and 12 months.

Results There were no between-group differences in back pain beliefs or other health outcomes at any time point. While the intervention group had lower costs due to absenteeism, presenteeism, and unpaid productivity losses, none of the costs were significantly different to the control group. At baseline, 37% of participants did not have back pain anymore.

Conclusion The study results show that the multifaceted eHealth strategy was not effective or cost-effective in improving patients' back pain beliefs and quality of life, and in decreasing their disability and absenteeism.

Trial registration Netherlands Trial Register (NTR), number: NTR4329.

Strengths and limitations of this study

- Robust study design: stepped-wedge cluster randomised controlled trial
- Comprehensive, multifaceted e-Health strategy for low back pain
- Effectiveness and cost-effectiveness evaluated
- High rate of loss to follow-up in intervention group (40%) compared to control group (23%)

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Competing Interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work (other than funding agency); no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Authors Statement

AS collected, prepared, and analysed data and prepared the manuscript. JMvD assisted in cost-effectiveness analyses, interpreted data, and revised the manuscript. FGS, PJME, RB,

MWvT, and JRA were all involved in design of the study, interpretation of data, and revising the manuscript for intellectual content.

Data sharing

Relevant data are available upon reasonable request.

BACKGROUND

Low back pain (LBP) is a major medical problem throughout the world. The global 1-month point prevalence is estimated to be 23.2%.[1] LBP is the leading cause of musculoskeletal and work disability, and years lived with disability (YLDs) worldwide.[2-3] Recent estimates from the Global Burden of Disease Study indicate that LBP accounts for 57 million YLDs, and that over 250 million people develop LBP annually.[2] The economic burden of LBP is high. Estimates of the annual economic burden of LBP vary from between AU$9.17 billion in Australia, £12.3 billion in the UK, and US$91 billion in the United States.[4-6] In the Netherlands, recent estimates report the costs of LBP to be around €1.3 billion, a quarter of all healthcare costs due to musculoskeletal disorders.[7] However, indirect costs due to absenteeism, and productivity losses due to disability are not included in this estimate. Previous research has shown that indirect costs make up 88% of all societal costs due to LBP.[8] Since LBP leads to a high proportion of work absence, the costs of LBP in the Netherlands are much higher than suggested.[7] Besides the burden on society, LBP has a high burden on the lives of individuals. Over the past decades, several studies have shown that people with negative back pain beliefs have more pain, disability, negative work-related outcomes (i.e. productivity loss and sickness absence), and higher health care utilization.[9-12]

Many guidelines for LBP recommend self-management for patients, which is a reflection of a newly proposed definition of health, i.e. “health as the ability to adapt and self-manage.[13-14] A systematic review on the effectiveness of education programmes designed to improve self-management suggested that these programmes are effective in improving pain intensity and disability, but did not measure actual self-management.[15]

Underlined by the high economic, societal, and individual burden of LBP, no highly effective treatment for LBP has yet been found. However, eHealth, which is the provision of (personalised) health care at a distance (e.g. through internet and thus digital), has shown

promise with regards to its' effectiveness and cost-effectiveness in improving outcomes such as patient health, patient satisfaction, self-management and healthcare costs in patients with physical diseases.[16-17] Therefore, the current study aimed to assess whether a multifaceted eHealth strategy to improve belief, knowledge, and self-management of LBP is effective and cost-effective compared to usual care in improving patients' back pain beliefs and quality of life, and in decreasing their disability and absenteeism.

METHODS

Study design

This study was part of a cluster-randomised controlled trial that was registered in 2013 with the Netherlands Trial Register (NTR) under number NTR4329.[18] The Medical Ethics Committee of the VU University medical centre assessed this study's design and procedures, and in accordance with the local regulatory guidelines and standards for human subjects protection in the Netherlands (Medical Research Involving Human Subjects Act [WMO], 2005), this study proved to be exempt from further medical ethical review. A detailed description of the design of this study has been published elsewhere.[18]

Participants

Twenty-five general practices, 19 physiotherapy practices, and 29 occupational physicians in the Amsterdam area participated in this study and recruited patients for this trial. Patients were aged 18-75 years and were diagnosed with nonspecific LBP by their general practitioner (GP) or physiotherapist (PT), whom they had visited due to back complaints no longer than 3 months prior to inclusion in the study. Nonspecific LBP was defined as LBP with or without motor and/or sensory deficits in one or both legs, including sciatica and radiculopathy, that is not caused by underlying specific pathology (red flags), i.e. a tumour, (osteoporotic) vertebral fracture, ankylosing spondylitis, and cauda equina syndrome. Exclusion criteria were: serious comorbidities including Alzheimer's disease, multiple sclerosis, Parkinson's disease, amyotrophic lateral sclerosis, cerebrovascular accident in the last year, confirmed pregnancy in the last year, malignancy in the last five years, and severe psychiatric disorders, i.e. schizophrenia and bipolar disorder.

Randomisation

This study was a stepped-wedge cluster randomised controlled trial. The participating general practices, physiotherapy practices, and occupational physicians were assigned to one of four clusters based on their geographic proximity to each other. The clusters sequentially received a multifaceted continuing medical education training (see Figure 1). This clustering allowed for minimisation of contamination between the participants. Patients were allocated according to the group their general practitioner, physiotherapist or occupational physician were assigned, i.e., patients registered within a practice that was in the control group at time of enrolment were allocated to the control group for patients. Randomisation was performed by means of computer-generated allocation. An independent research assistant performed the concealed allocation, enrolling of participants, and assignment of participants to groups.

Intervention and control

The intervention was provided to patients on an individual level. Patients in the cluster whose GP or PT was randomised into the intervention group received access to a multifaceted eHealth strategy that aimed to reduce patients' negative back pain beliefs and improve their knowledge and self-management of LBP. The campaign included an informative website, digital monthly newsletters, and social media platforms. The website provided comprehensive information about LBP, such as practical advice (e.g. on self-management), working and returning to work with LBP, exercise tips, and short video messages. In these videos, actors and healthcare professionals shared their experiences with LBP and provided tips on self-management, coping, and working with LBP. The videos were inspired by the effective Australian mass media campaign 'Back Pain: Don't Take It Lying Down'.[19] Social media platforms included a forum on the website, and a Facebook page where patients could contact researchers, healthcare providers, and other patients. All parts of the intervention were also available in a mobile version that was adaptive to any electronic device. The patient intervention was supported by continuing medical education for GPs, PTs, and occupational

physicians (OPs). More detailed descriptions of the patient and professional based interventions are published elsewhere.[20-21] Patients in the control group received a digital patient information letter and had no access to the intervention website, materials or social media platforms. Results of the professional based intervention will be published elsewhere.

Sample size and outcomes

The primary outcome measure was back pain beliefs, assessed using the Back Beliefs Questionnaire (BBQ). The BBQ is designed to measure the inevitable consequences of LBP (e.g. there is no real treatment for back trouble, back trouble must be rested). It is a validated questionnaire consisting of 14 items, and rates back pain beliefs on a scale of 9 to 45, with higher scores indicating more positive (better) back pain beliefs (e.g. exercising through LBP is good).[22-23]

The sample size calculation was based on a hypothesized 10% improvement in back pain beliefs as measured by the BBQ, based on an observed mean improvement of 9.6% between three successive surveys in the Australian campaign.[19] An intra-class correlation coefficient (ICC) of 0.05 was applied to adjust for the cluster randomisation design. Assuming a 10 % improvement from a mean score of 26.5 (95% Confidence Interval (CI) 26.1-26.8, SD 6) on the BBQ, and applying an ICC of 0.05, the necessary sample size was estimated to be 500 patients. This calculation takes into account a dropout-rate of 20%, power (1-beta) of 0.90 and an alpha of 0.05.

The secondary outcomes included disability, measured with the Roland Disability Questionnaire (RDQ-24), which has been shown to be a valid and reliable instrument for patients with LBP.[24] The RDQ-24 consists of 24 items, rating disability on a scale of 0 to 24, with higher scores indicating more disability. The EQ-5D-3L was used to measure quality of life.[25] Health care use, absenteeism, presenteeism and unpaid productivity losses were

measured with the generic PROductivity and DIsease Questionnaire (PRODISQ) and the Healthcare Utilization and Productivity Losses Questionnaire (TIC-P).[26-27] All outcomes were measured at baseline and after 3, 6, and 12 months follow-up.

For the economic evaluation, the scores on the EQ-5D-3L were converted into utility scores using the Dutch tariff.[28] These utility scores range from 0 (death) to 1 (maximum health. Quality adjusted life years (QALYs) were calculated using linear interpolation between measurement points. Societal costs included intervention costs, costs for the use of healthcare, and costs for informal care (e.g. care by family and other volunteers), work absenteeism, and paid and unpaid productivity losses. The intervention costs comprised all costs for the development and implementation of the intervention, including costs for materials and personnel (Appendix 1). There were no costs for the intervention for the control group. Healthcare utilization included primary healthcare (e.g. GP, PT), secondary healthcare (e.g. diagnostic imaging, medical specialist), alternative healthcare (e.g. acupuncture or massage), and medication (both prescribed and over-the-counter).

To value healthcare utilization, prices from the Dutch Manual for Costing (DMC) were used.[29] Where standard costs were unavailable, we used prices provided by professional organizations. Medication use was valued using the prices of the Royal Dutch Society of Pharmacy.[30] Informal care was valued using a recommended Dutch shadow price according to the DMC.[29] Absenteeism was calculated and valued using patient data collected with the PRODISQ and TIC-P. In accordance with the DMC, patients' daily absenteeism cost was calculated by dividing their self-reported gross annual salary by their total number of workable days per year. Using the Friction Cost Approach (FCA, friction period 23 weeks), absenteeism costs were estimated by multiplying the total number of sick leave days during follow-up by their associated costs. Presenteeism was calculated using patient data collected with the TIC-P questionnaire, where patients indicated how many days they went to work

while having LBP. To obtain workday equivalents lost to presenteeism, this number of days was multiplied by a self-reported inefficiency score ranging between 0 (could not perform any tasks) and 1 (could perform all tasks as efficient as without LBP). Presenteeism costs were subsequently calculated by multiplying the total number of presenteeism days by their associated costs.

Statistical analyses

Analyses were performed according to the intention-to-treat principle. Descriptive statistics were used to compare baseline characteristics between intervention and control group participants as well as between participants with complete and incomplete data. Missing values for costs and effects were imputed using multiple imputation, and imputations were performed separately for the intervention and control group.[31-32] Effectiveness analyses were performed using maximum likelihood estimation longitudinal mixed-effects models with multilevel structure and 'missing at random' assumptions.[33] The mixed-effects models adjusted for the effect of clustering. Analyses of effect and cost data were performed in Stata 14, and the statistical significance level was set at $p<0.05$. Regression coefficients or odds ratios (ORs) were calculated with 95%-confidence intervals (CIs).

Cost-effectiveness analysis (CEA) and cost-utility analysis (CUA) were performed from a societal perspective. Imputation models included intervention costs, age, gender, educational level, nationality, being employed, performing physically demanding work, physical activity (minutes per week), and available cost and effect measure values. Using predictive mean matching, 10 complete data sets were created (loss-of-efficiency 5%).[34] Pooled estimates were calculated using Rubin's rules.[35] Cost and effect difference estimates between intervention and control group were analysed using seemingly unrelated regression (SUR), while simultaneously adjusting for the possible correlation between costs and effects.[36]

Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the adjusted mean cost differences by those in effects. Uncertainty surrounding the cost differences and ICERs was estimated using Bias Corrected and Accelerated bootstrapping (BCA) with 5000 replications, and presented by 95%-CIs and plotted on cost-effectiveness planes.[37] Cost-effectiveness acceptability curves (CEACs) presented the probability of the intervention being cost-effectiveness at different values of willingness to pay.[38]

Patient involvement

The Dutch patient association for spinal disorders ("NVV De Wervelkolom") was involved in the design of this study and provided advice about the content of the intervention.

RESULTS

Participants

In total, 5181 eligible patients were invited to participate in this study. Of these patients, 779 (response rate of 15%) agreed to participate and were randomised to the intervention (n=331) and control (n=448) groups (Figure 2). Follow-up responses in the intervention group were 69.8% at 3 months follow-up, 70.1% at 6 months follow-up, and 60.4% at 12 months follow-up. The follow-up responses in the control group were higher than in the intervention group at 3 months follow-up (77%) and 12 months follow-up (77.5%). At 6 months follow up the responses in the control group were similar to those in the intervention group (69.6%).

At baseline, characteristics of patients in the intervention group were similar to those in the control group. Table 1 shows that a high percentage of participants were female, 60% (intervention group) and 57% (control group) had a high educational level, and over half of the participants were employed. They performed about 3 hours of physical activity per week. Table 1 also shows the baseline scores on the BBQ, RDQ-24, absenteeism, and quality of life for both groups. At baseline, there was a lower absenteeism rate in the intervention group compared to the control group.

263 *Table 1. Baseline characteristics of patients*

	Intervention (n=331)	Control (n=448)
Mean age (SD)	55.7 (13.9) (n=320)	56.6 (14.6) (n=439)
Female gender (%)	188 (59) (n=320)	252 (57) (n=439)
Back pain at baseline (%)	201 (63) (n=320)	275 (63) (n=439)
Nationality (%) - Dutch - Western countries immigrant - Non-western countries immigrant	(n=320) 298 (93) 16 (5) 6 (2)	(n=439) 409 (93) 23 (5) 7 (2)
Educational level (%) - None (never attended school): - Lower - Vocational - Higher	(n=320) 9 (3) 25 (8) 92 (29) 194 (60)	(n=439) 12 (3) 42 (10) 134 (30) 251 (57)
Activity minutes/week (SD)	161 (109) (n=196)	166 (104) (n=254)
Employed (paid work) (%)	183 (57) (n=320)	232 (53) (n=439)
Physically demanding work (%)	88 (28) (n=320)	121 (28) (n=439)
Back pain beliefs *(measured by BBQ, range 9-45; higher score means more positive back pain beliefs)*	24.7 (6.0) (n=295)	24.8 (6.2) (n=394)
Disability (*measured by RDQ-24, range 0-24; higher score means more disability)*	5.1 (4.7) (n=317)	5.9 (5.3) (n=434)
Absenteeism *(self-reported number of days over past three months)*	2.2 (7.0) (n=187)	4.0 (13.2) (n=246)
Quality of life *(utility score measured by EQ-5D; range 0 to 1; higher score means better quality of life)*	0.79 (0.22) (n=331)	0.75 (0.25) (n=448)

264

Intention-to-treat effectiveness analysis

Table 2 shows the mean scores on the BBQ, RDQ-24, absenteeism, and quality of life of the intervention group compared to the control group. Table 3 shows the results of the intention-to-treat analysis. There were no significant differences in back pain beliefs, disability and absenteeism between groups at any time point. The interaction term with gender was significant for disability, showing that the effect for males was larger than that for females.

Table 2. Mean scores (SD) on BBQ, RDQ-24, EQ-5D and absenteeism

	Mean (SD) back pain beliefs *(measured by BBQ, range 9-45; higher score means more positive back pain beliefs)*		
	3 months follow-up	**6 months follow-up**	**12 months follow-up**
Intervention group	24.4 (5.8)	24.0 (5.9)	24.1 (5.8)
Control group	24.9 (6.2)	24.6 (6.0)	24.1 (6.3)
	Mean (SD) disability *(measured by RDQ-24, range 0-24; higher score means more disability)*		
	3 months follow-up	**6 months follow-up**	**12 months follow-up**
Intervention group	4.4 (4.7)	3.9 (4.3)	3.9 (4.3)
Control group	5.2 (5.1)	4.8 (4.8)	4.5 (4.7)
	Mean (SD) absenteeism *(self-reported number of days over past three months)*		
	3 months follow-up	**6 months follow-up**	**12 months follow-up**

Intervention group	1.2 (6.5)	0.9 (4.8)	0.7 (2.7)
Control group	2.6 (9.8)	0.7 (4.1)	0.7 (4.4)
	Mean (SD) quality of life *(utility score measured by EQ-5D; range 0 to 1; higher score means better quality of life)*		
	3 months follow-up	**6 months follow-up**	**12 months follow-up**
Intervention group	0.86 (0.21)	0.90 (0.16)	0.91 (0.15)
Control group	0.82 (0.24)	0.86 (0.21)	0.87 (0.19)

Table 3. Adjusted effects of the intervention based on intention-to-treat analyses

Outcome		**Difference between intervention and control**	**95%-CI**
Back beliefs[1]		-0.13	-0.90;0.65
Disability	M	-1.13	0.93;1.37
	F	-0.79	0.68;0.93
Absenteeism[2;3]		-0.94	0.69;1.29

1: Adjusted for educational level, physical activity, having back pain, being employed, comorbidity; 2:Adjusted for age, physical activity, having back pain; 3: Only for participants who were employed at baseline (intervention group n=183; control group n=232)

Cost-effectiveness analysis

Intervention costs per patient were € 70. Direct costs for primary care and medication were lower in the intervention than in the control group, while direct costs for secondary and alternative care were higher in the intervention than in the control group. Indirect costs due to

absenteeism, presenteeism, and unpaid productivity loss were lower in the intervention than in the control group. The crude total cost differences were not significant (Table 4).

Table 4. Crude costs per cost category in euros (€)

Cost category	**Mean costs (SEM) in €**		**Δ Costs (95%-CI) in €**
	Intervention	Control	
Direct costs			
Primary care	340 (26)	405 (26)	-65 (-134;-2)
Secondary care	478 (228)	229 (42)	249 (58;515)
Alternative care	742 (218)	322 (55)	421 (182;722)
Medication	29 (7)	44 (9)	-15 (-45;-0.70)
Intervention	70	0	70 (N/A)
Indirect costs			
Absenteeism	1034 (242)	1547 (235)	-513 (-941;-77)
Presenteeism	5735 (681)	6342 (537)	-607 (-2076;-831)
Unpaid productivity	4000 (887)	5047 (616)	-1047 (-1954;-203)
Total societal costs	8444 (820)	8979 (619)	-535 (-2230;1172)

There was no statistically significant difference in QALYs (adjusted for age, gender, educational level, nationality, employment, and physically demanding work) over the 12-month follow-up period between the control and intervention group (adjusted ΔE 0.04; 95%-CI 0.02;0.06). The intervention did not yield significant cost savings (adjusted for age, gender, educational level, nationality, employment, and physically demanding work ΔC € -748 per patient; 95%-CI € -2341;878). The ICER for QALYs was -18,353, which indicates

that one QALY gained was associated with a societal cost saving of € 18,353. The majority (79%) of incremental cost-effectiveness pairs was located in the southeast quadrant of the cost-effectiveness plane (Figure 3), indicating that the intervention was on average more effective and less costly. The uncertainty around the cost-effectiveness estimate was large. Figure 4 shows that the intervention has probability of 0.88 of being cost-effective on a willingness-to-pay of €10.000 per QALY gained, increasing to a probability of 1.00 on a willingness-to-pay of € 80.000 per QALY gained.

DISCUSSION

This study evaluated whether a multifaceted eHealth strategy is effective and cost-effective compared to usual care in improving patients' back pain beliefs and quality of life, and in decreasing their disability and absenteeism. The study results show that the campaign was not effective on these outcomes. The probability of cost-effectiveness was high: 0.88 per QALY gained at a willingness-to-pay threshold of € 10.000, and increased to a maximum probability of 1 per QALY gained at a willingness-to-pay threshold of € 80.000.

A possible explanation for the lack of effectiveness might be that in this study, almost 40% of participants did not have back pain anymore at the start of the actual intervention (i.e. baseline moment). Patients who had visited their general practitioner or physiotherapist no longer than 3 months prior to recruitment could participate in this study. As a consequence, some patients may have agreed to participate while they had already recovered from their LBP at the start of the intervention. With the recruitment protocol used it was not possible to select only the chronic LBP cases. Therefore, the intervention may no longer have been necessary for the participants that did not have LBP at the start of the intervention, and for them effectiveness was not to be expected. The back beliefs of the study population were quite low at baseline compared to those of the Australian mass media campaign by which the current study was inspired. Mean BBQ scores in the Australian study were 26.5 at the start of the campaign and increased significantly to 29.7, while in the current study the BBQ scores were 24.7 and 24.8 in the intervention and control groups, respectively. This indicates that there was room for improvement in back pain beliefs in the current study.[39] Another study that assessed factors that were associated with beliefs and attitudes of elderly (mean age 69) also found low back pain beliefs scores (mean 23.7).[40] In the current study disability scores measured with the RDQ-24 showed low levels of disability, and absenteeism rates were also low. Quality of life scores were relatively high and similar between groups with no further improvement over

time. It is arguable that the participating patients were in good health states from the start and gaining much improvement on these functional outcomes was not realistic. Process evaluations among participating patients and professionals alongside the present study showed that compliance with the intervention was very low. Most patients did not comply to the full e-health intervention: 31% of the participants had not used the campaign materials at all, and 42.9% had only used it once, and professionals almost never discussed the intervention with their patients. Probably most participants did not need the intervention to improve their functional ability, but improvement in back pain beliefs could have been possible had the compliance rates in this study have been higher.[20-21]

Self-management is recommended for the management of LBP, and healthcare professionals are advised to provide advice and information, tailored to needs and capabilities, to help patients self-manage their LBP.[41] One possible way to help patients self-manage their LBP is through an eHealth strategy, but evidence regarding the most effective content and mode of delivery for self-management options is lacking.[42] eHealth is easy to deliver, safe, and usually inexpensive (e.g. in the current study, the intervention costs were less than € 70,- per patient), a recent systematic review on digital support intervention for LBP could not find significant beneficial effects of digital self-management interventions.[43] However, most of the participants in the included studies were Caucasian, highly educated, middle-aged females, meaning that the findings of the current study are comparable to similar studies. The results of the current study are in line with other studies that have attempted to improve patient outcomes and costs in LBP by using multifaceted strategies. A systematic review of the effectiveness of multifaceted strategies for guideline implementation in LBP and neck pain did not find that multifaceted strategies changed patient outcomes or costs of care.[44] However, the majority of the studies included in the review did not provide insight into the implementation process, raising the question whether the lack of effectiveness is caused by

the failure of the theory (multifaceted strategy) or by failure of the implementation process, making it difficult to compare the current study to others. It is important to evaluate the implementation processes in order to truly understand the effectiveness of multifaceted strategies.

Another interesting thing to note is the fact that the costs for secondary care and alternative care are higher in the intervention group than in the control group. This is in line with a very similar recent implementation study for the management of LBP. In that study, patients in the intervention group had higher LBP-related costs for inpatient secondary care.[45] Studies within and outside the field of LBP research have shown similar results, where patients and participants in intervention groups show higher costs due to secondary care and/or alternative care.[46-50] The literature does not provide explanations for this fact. One explanation could lie, again, in the low compliance rate of patients in this study.[20] On the other hand, the use of alternative care could be seen as self-management, because patients decide what they want, when they want it, and how much they are willing to pay for it. It could very well be that patients try self-management through alternative care for a while, and then get referred to secondary care when and because self-management (through alternative care) did not work for them. It would be interesting to explore the reasons for the higher costs for secondary care further.

While the strategy evaluated in this study did not yield (cost)effective results, it might still be worthwhile considering the possibilities of eHealth interventions from the perspective of outcomes that were not measured in this study but might have improved, for example actual self-management. A systematic review of randomised controlled trials that have assessed self-management education programmes for osteoarthritis found a mismatch between the aims of such programmes (education and advice about how to self-manage their condition despite their pain and fears) and how the success of the programmes were assessed.[51] Many studies

have measured health-related outcomes such as pain and function but have not specifically determined whether the programmes have improved participants' ability to self-manage. Outcomes such as knowledge about the condition and self-management skills may give more insight into the value of self-management education programmes and should be considered essential to measure in future studies evaluating these types of programmes.[51] Looking at the cost savings on absenteeism, presenteeism and unpaid productivity losses in the intervention group compared to the control group, future studies could also benefit from evaluating the effects and cost-effectiveness of eHealth strategies from employer's perspective.

Study limitations

The findings of this study must be interpreted with caution. In this study, the loss-to-follow-up rate was higher for the intervention group (40%) compared to the control group (23%). A possible explanation could be that the strategy provided too much information and participants were contacted too often, making them less willing to comply with completion of the questionnaires over time. The high percentage of loss to follow up may have resulted in a loss of power and in attrition bias. Furthermore the majority of participants did not need or use the intervention, and had minimal disability and impaired quality of life at baseline impacting upon our ability to test the value of our intervention.

Conclusion

Based on this study, a multifaceted eHealth strategy for patients who had presented to primary care (i.e. general practice and physiotherapy) with LBP was not effective or cost-effective in improving back pain beliefs, disability, absenteeism, or quality of life. The multifaceted eHealth strategy should be studied in a different population, i.e. a more mixed group of participants in terms of background (e.g. education, nationality), and participants with LBP and poorer health states at start of the intervention.

FIGURE LEGENDS

Figure 1. Design of the stepped-wedge cluster randomised controlled trial

Figure 2. Flow-chart of patient inclusion

Figure 3. Cost-effectiveness plane for QALYs

Figure 4. CEAC for QALYs

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	T0	T1	T2	T3	T4
Cluster 1	Control	Intervention	Intervention	Intervention	Intervention
Cluster 2	Control	Control	Intervention	Intervention	Intervention
Cluster 3	Control	Control	Control	Intervention	Intervention
Cluster 4	Control	Control	Control	Control	Intervention

Figure 1. Design of the stepped-wedge cluster randomised controlled trial

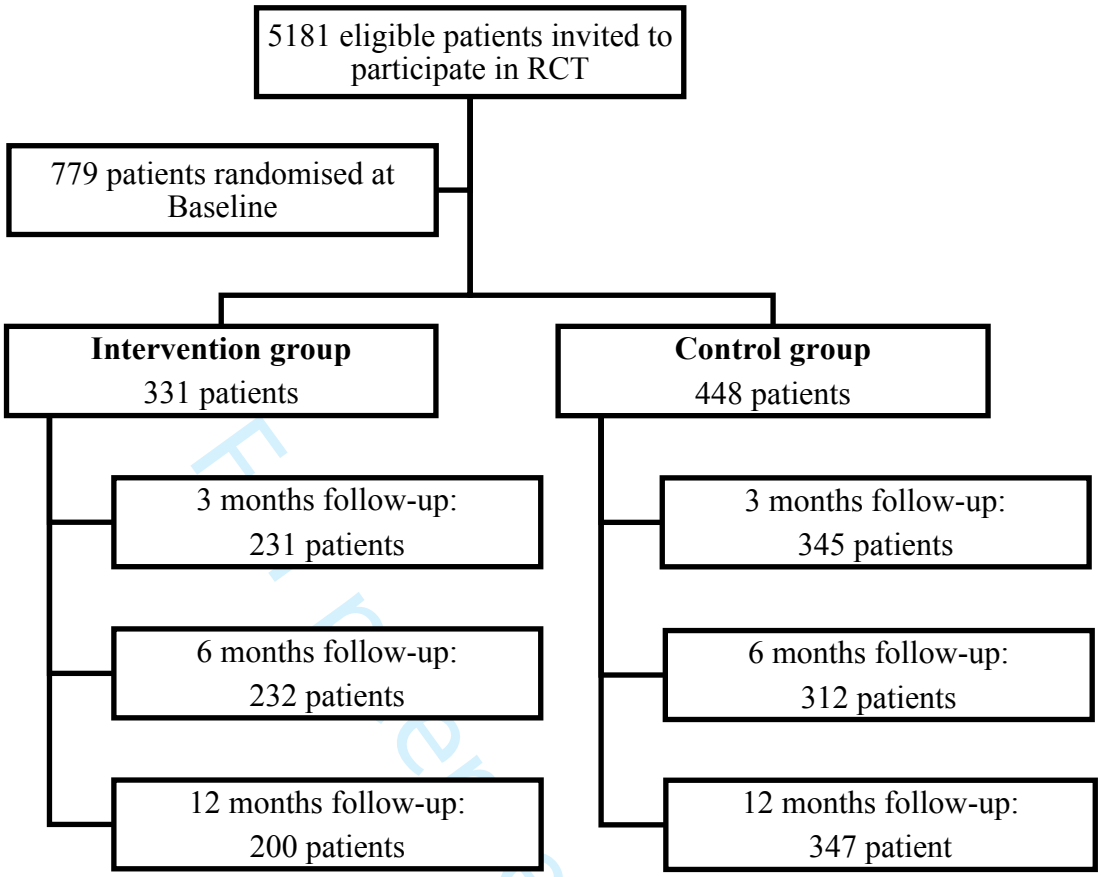

Figure 2. Flow-chart of patient inclusion

Figure 3. Cost-effectiveness plane for QALYs

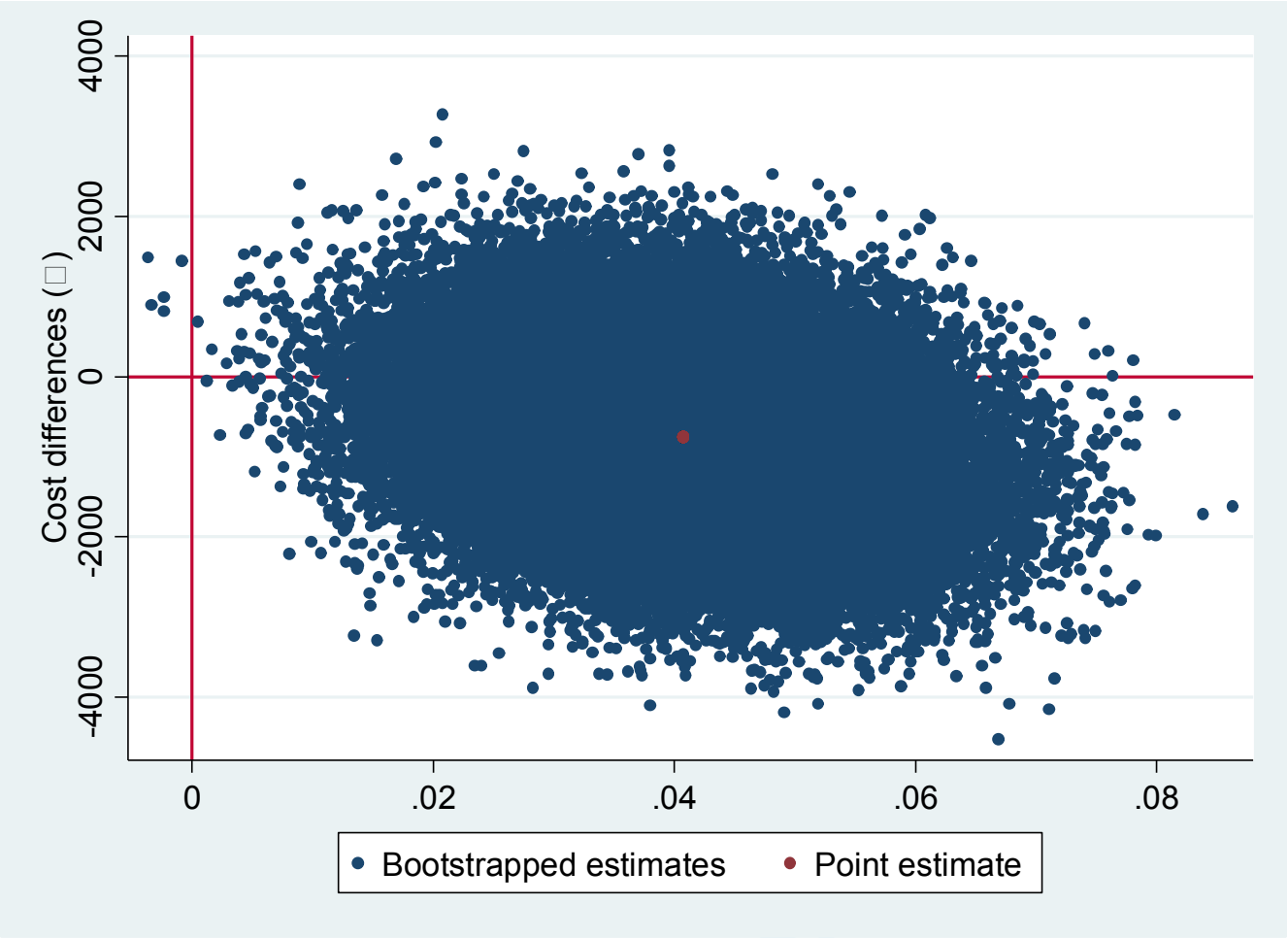

Figure 4. CEAC for QALYs

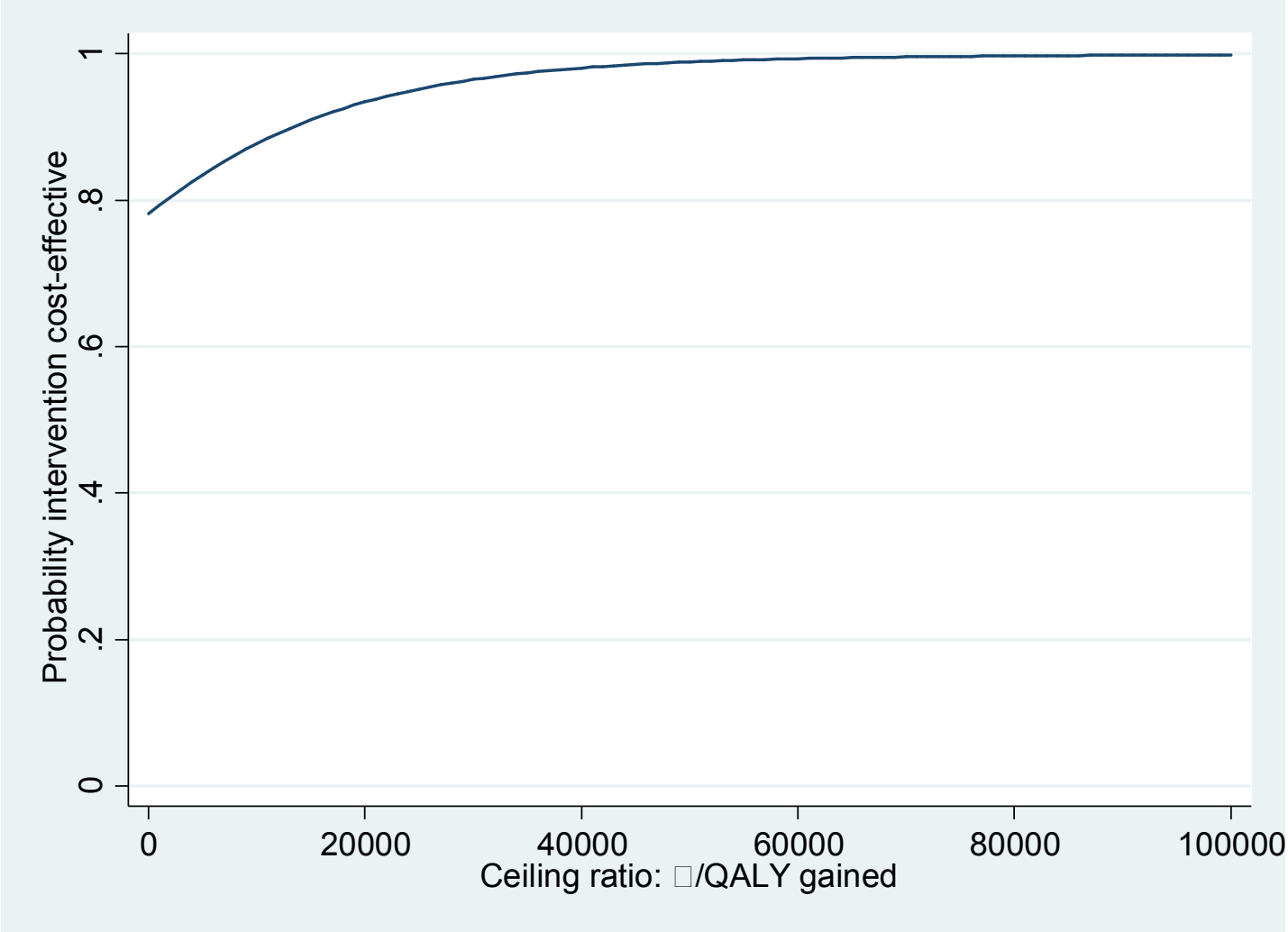

Table 1: CONSORT 2010 checklist of information to include when reporting a cluster randomised trial

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No *
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[1,2]	See table 2	3
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	5-6
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	6
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		N/A
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	7
	4b	Settings and locations where the data were collected		7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	8-9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and	Whether outcome measures pertain to the cluster level, the individual participant level or both	9-11

		when they were assessed		
	6b	Any changes to trial outcomes after the trial commenced, with reasons		N/A
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	10
	7b	When applicable, explanation of any interim analyses and stopping guidelines		N/A
Randomisation:				
Sequence generation	8a	Method used to generate the random allocation sequence		8
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	8
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	8
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	N/A
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	8
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete	8

			enumeration, random sampling)	
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	8
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		N/A
	11b	If relevant, description of the similarity of interventions		N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	11-12
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		11-12
Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	13-14
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	13-19
Recruitment	14a	Dates defining the periods of recruitment and follow-up		13
	14b	Why the trial ended or was stopped		N/A
Baseline data	15	A table showing baseline demographic and clinical	Baseline characteristics for the individual and cluster levels as	15-17

		characteristics for each group	applicable for each group	
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	15-17
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	15-17
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		15-17
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		17-19
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[3])		N/A
Discussion				
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		20-23
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	20-23
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		2-23
Other information				
Registration	23	Registration number and		7

		name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	25

** Note: page numbers optional depending on journal requirements*

Table 2: Extension of CONSORT for abstracts[1,2] to reports of cluster randomised trials

Item	Standard Checklist item	Extension for cluster trials
Title	Identification of study as randomised	**Identification of study as cluster randomised**
Trial design	Description of the trial design (e.g. parallel, cluster, non-inferiority)	
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	**Eligibility criteria for clusters**
Interventions	Interventions intended for each group	
Objective	Specific objective or hypothesis	**Whether objective or hypothesis pertains to the cluster level, the individual participant level or both**
Outcome	Clearly defined primary outcome for this report	**Whether the primary outcome pertains to the cluster level, the individual participant level or both**
Randomization	How participants were allocated to interventions	**How clusters were allocated to interventions**
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	
Results		
Numbers randomized	Number of participants randomized to each group	**Number of clusters randomized to each group**
Recruitment	Trial status[1]	
Numbers analysed	Number of participants analysed in each group	**Number of clusters analysed in each group**
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	**Results at the cluster or individual participant level as applicable for each primary outcome**
Harms	Important adverse events or side effects	
Conclusions	General interpretation of the results	
Trial registration	Registration number and name of trial register	
Funding	Source of funding	

[1] Relevant to Conference Abstracts

REFERENCES

1 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet* 2008, 371:281-283

2 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG at al (2008) CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med* 5(1): e20

3 Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; 141(10):781-788.

CHEERS checklist—Items to include when reporting economic evaluations of health interventions

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	P. 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	P. 3
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	P. 5 - 6
		Present the study question and its relevance for health policy or practice decisions.	P. 5 - 6
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	P. 7
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	P. 7
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	P. 7 - 12
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	P. 8 - 9
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	P. 7 - 12
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	N/A
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	P. 9 - 11
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	P. 9 - 12
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation:*Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	P. 10 – 12
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate	N/A

Section/item	Item No	Recommendation	Reported on page No/ line No
		resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	P. 10 – 12
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	P. 10 – 12
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	P. 10 – 12
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	P. 11 – 12
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	P. 17 – 19
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	P. 18 – 19
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	P. 18 – 19
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	N/A
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	N/A
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	P. 20 – 23
Other			
Source of funding	23	Describe how the study was funded and the role of	P. 25

Section/item	Item No	Recommendation	Reported on page No/ line No
		the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	P. 24

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist

BMJ Open

Effectiveness and cost-utility of a multifaceted eHealth strategy to improve back pain beliefs of patients with nonspecific low back pain: a cluster randomised trial

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology, General practice / Family practice, Health economics
Keywords:	LOW BACK PAIN, RANDOMIZED CONTROLLED TRIAL, E-HEALTH, PUBLIC HEALTH, HEALTH ECONOMICS

Effectiveness and cost-utility of a multifaceted eHealth strategy to improve back pain beliefs of patients with nonspecific low back pain: a cluster randomised trial

Arnela Suman, Frederieke G. Schaafsma, Johanna M van Dongen, Petra JM Elders, Rachelle Buchbinder, Maurits W van Tulder, Johannes R Anema

Arnela Suman, Amsterdam UMC, VU University Amsterdam, department of Public and Occupational Health, Amsterdam Public Health research institute, De Boelelaan 1117, 1081HV Amsterdam, The Netherlands

Corresponding author: Frederieke G Schaafsma, Amsterdam UMC, VU University Amsterdam, department of Public and Occupational Health, Amsterdam Public Health research institute, De Boelelaan 1117, 1081HV Amsterdam, The Netherlands; f.schaafsma@vumc.nl; 0031-20-4445685

Johanna M van Dongen, VU University Amsterdam, department of Health Sciences, Amsterdam Public Health research institute, Amsterdam, The Netherlands

Petra JM Elders, Amsterdam UMC, VU University Amsterdam, department of General Practice and Elderly Care, Amsterdam Public Health research institute, Amsterdam, The Netherlands

Rachelle Buchbinder, Monash Department of Clinical Epidemiology, Cabrini Institute and Department of Epidemiology and Preventive Medicine, School of Public Health & Preventive Medicine, Monash University, Victoria, Australia

Maurits W van Tulder, VU University Amsterdam, department of Health Sciences Amsterdam Public Health research institute, Amsterdam, The Netherlands

Johannes R Anema, Amsterdam UMC, VU University Amsterdam, department of Public and Occupational Health, Amsterdam Public Health research institute, Amsterdam, The Netherlands

Word count: 4356

ABSTRACT

Objectives To assess the effectiveness and cost-utility of a multifaceted eHealth strategy compared to usual care in improving patients' back pain beliefs, and in decreasing disability and absenteeism.

Design A stepped-wedge cluster randomized trial with parallel economic evaluation.

Setting Dutch primary health care.

Participants Patients diagnosed with nonspecific low back pain by their general practitioner or physiotherapist. Patients with serious comorbidities or confirmed pregnancy were excluded. 779 patients were randomised into intervention group (n=331, 59% female; 60.4% completed study) or control group (n=448, 57% female; 77.5% completed study).

Interventions The intervention consisted of a multifaceted eHealth strategy that included a (mobile) website, digital monthly newsletters, and social media platforms. The website provided information about back pain, practical advice (e.g. on self-management), working and returning to work with back pain, exercise tips, and short video messages from healthcare providers and patients providing information and tips. The control consisted a digital patient information letter. Patients and outcome assessors were blinded to group allocation.

Primary and secondary outcome measures The primary outcome was back pain beliefs. Secondary outcome measures were disability and absenteeism, and for the pre-planned economic evaluation quality of life and societal costs were measured.

Results There were no between-group differences in back pain beliefs, disability, or absenteeism. Mean intervention costs were € 70,- and the societal cost difference was € 535,- in favour of the intervention group, but no significant cost savings were found. The ICER

indicated that the intervention dominated usual care and the probability of cost-effectiveness was 0.85 on a willingness-to-pay of € 10,000/QALY.

Conclusions A multifaceted eHealth strategy was not effective in improving patients' back pain beliefs or in decreasing disability and absenteeism, but showed promising cost-utility results based on QALYs.

Trial registration Netherlands Trial Register (NTR), number: NTR4329.

Strengths and limitations of this study

- Robust study design: stepped-wedge cluster randomised controlled trial
- Comprehensive, multifaceted e-Health strategy for low back pain
- Effectiveness and cost-utility evaluated
- High rate of loss to follow-up in intervention group (40%) compared to control group (23%)

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Competing Interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work (other than funding agency); no financial relationships with any organisations

that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Authors Statement

AS collected, prepared, and analysed data and prepared the manuscript. JMvD assisted in cost-utility analyses, interpreted data, and revised the manuscript. FGS, PJME, RB, MWvT, and JRA were all involved in design of the study, interpretation of data, and revising the manuscript for intellectual content.

Data sharing

Relevant data are available upon reasonable request.

BACKGROUND

Low back pain (LBP) is a major medical problem throughout the world. The global 1-month point prevalence is estimated to be 23.2%.[1] LBP is the leading cause of musculoskeletal and work disability, and years lived with disability (YLDs) worldwide.[2-3] Recent estimates from the Global Burden of Disease Study indicate that LBP accounts for 57 million YLDs, and that over 250 million people develop LBP annually.[2] The economic burden of LBP is high. Estimates of the annual economic burden of LBP vary from between AU$9.17 billion in Australia, £12.3 billion in the UK, and US$91 billion in the United States.[4-6] In the Netherlands, recent estimates report the costs of LBP to be around €1.3 billion, a quarter of all healthcare costs due to musculoskeletal disorders.[7] However, indirect costs due to absenteeism and to reduced productivity while at work are not included in this estimate. Previous research has shown that indirect costs make up 88% of all societal costs due to LBP.[8] Since LBP leads to a high proportion of work absence, the costs of LBP in the Netherlands are much higher than suggested.[7] Besides the burden on society, LBP has a high burden on the lives of individuals. Over the past decades, several studies have shown that people with negative back pain beliefs have more pain, disability, negative work-related outcomes (i.e. productivity loss and sickness absence), and higher health care utilization.[9-12]

Many guidelines for LBP recommend self-management for patients, which is a reflection of a newly proposed definition of health, i.e. “health as the ability to adapt and self-manage.[13-14] A systematic review on the effectiveness of education programmes designed to improve self-management suggested that these programmes are effective in improving pain intensity and disability, but did not measure actual self-management.[15]

Underlined by the high economic, societal, and individual burden of LBP, no highly effective treatment for LBP has yet been found. However, eHealth, which is the provision of (personalised) health care at a distance (e.g. through internet and thus digital), has shown

promise with regards to its' effectiveness and cost-effectiveness in improving outcomes such as patient health, patient satisfaction, self-management and healthcare costs in patients with physical diseases.[16-17] Therefore, the current study aimed to assess the effectiveness and cost-utility of a multifaceted eHealth strategy to improve beliefs, knowledge, and self-management of LBP compared to usual care in improving patients' back pain beliefs, and in decreasing their disability and absenteeism.

METHODS

Study design

This study was part of a cluster-randomised controlled trial with a pre-planned parallel economic evaluation, that was registered in 2013 with the Netherlands Trial Register (NTR) under number NTR4329.[18] The trial lasted from September 2013 to September 2017, with the actual intervention being provided between April 2014 and December 2016. The Medical Ethics Committee of the VU University medical centre assessed this study's design and procedures, and in accordance with the local regulatory guidelines and standards for human subjects protection in the Netherlands (Medical Research Involving Human Subjects Act [WMO], 2005), this study proved to be exempt from further medical ethical review. A detailed description of the design of this study has been published elsewhere.[18] This study is reported following the Consort statement (Supplementary file 1) and the Cheers statement (Supplementary file 2).

Participants

Twenty-five general practices, 19 physiotherapy practices, and 29 occupational physicians in the Amsterdam area participated in this study and recruited patients for this trial. Patients were aged 18-75 years and were diagnosed with nonspecific LBP by their general practitioner (GP) or physiotherapist (PT), whom they had visited due to back complaints no longer than 3 months prior to inclusion in the study. Nonspecific LBP was defined as LBP with or without motor and/or sensory deficits in one or both legs, including sciatica and radiculopathy, that is not caused by underlying specific pathology (red flags), i.e. a tumour, (osteoporotic) vertebral fracture, ankylosing spondylitis, and cauda equina syndrome. Exclusion criteria were: serious comorbidities including Alzheimer's disease, multiple sclerosis, Parkinson's disease, amyotrophic lateral sclerosis, cerebrovascular accident in the last year, malignancy in the last

five years, and severe psychiatric disorders, i.e. schizophrenia and bipolar disorder. Patients with confirmed pregnancy in the last year were also excluded. Assessment of exclusion criteria was done electronically using software, as well as manual assessment by the referring general practitioner or physiotherapist.

Randomisation

This study was a stepped-wedge cluster randomised controlled trial. The participating general practices, physiotherapy practices, and occupational physicians were assigned to one of four clusters based on their geographic proximity to each other. The clusters sequentially received a multifaceted continuing medical education training (illustrated by Figure 1). This clustering allowed for minimisation of contamination between the participants. Patients were allocated according to the group their general practitioner, physiotherapist or occupational physician were assigned, i.e., patients registered within a practice that was in the control group at time of enrolment were allocated to the control group for patients, thus randomisation and allocation were performed on cluster level. However, patients were blinded and not aware of group allocation, and thus concealment was on individual level. Randomisation was performed by means of computer-generated allocation, using specific software. An independent research assistant performed the concealed allocation, enrolling of participants, and assignment of participants to groups. Outcome assessors were blinded to individual patient allocation.

Intervention and control

The intervention was provided to patients on an individual level. Patients in the cluster whose GP or PT was randomised into the intervention group received access to a multifaceted eHealth strategy that aimed to reduce patients' negative back pain beliefs and improve their knowledge and self-management of LBP. The campaign included an informative website, digital monthly newsletters, and social media platforms. The website provided comprehensive information

about LBP, such as practical advice (e.g. on self-management), working and returning to work with LBP, exercise tips, and short video messages. In these videos, actors and healthcare professionals shared their experiences with LBP and provided tips on self-management, coping, and working with LBP. The videos were inspired by the effective Australian mass media campaign 'Back Pain: Don't Take It Lying Down'.[19] Social media platforms included a forum on the website, and a Facebook page where patients could contact researchers, healthcare providers, and other patients. All parts of the intervention were also available in a mobile version that was adaptive to any electronic device. Patients were required to use pre-set usernames and passwords to enter the intervention website. The patient intervention was supported by continuing medical education for GPs, PTs, and occupational physicians (OPs). More detailed descriptions of the patient and professional based interventions are published elsewhere.[20-21] Patients in the control group received a digital patient information letter and had no access to the intervention website, materials or social media platforms. Results of the professional based intervention have been published elsewhere.[22]

Sample size and outcomes

The primary outcome measure was back pain beliefs, assessed using the Back Beliefs Questionnaire (BBQ). The BBQ is designed to measure beliefs about the inevitable consequences of LBP (e.g. there is no real treatment for back trouble, back trouble must be rested). It is a validated questionnaire consisting of 14 items, and rates back pain beliefs on a scale of 9 to 45, with higher scores indicating more positive (better) back pain beliefs (e.g. exercising through LBP is good).[23-24]

The sample size calculation was based on a hypothesized 10% improvement in back pain beliefs as measured by the BBQ, based on an observed mean improvement of 9.6% between three successive surveys in the Australian campaign.[19] An intra-class correlation coefficient (ICC)

of 0.05 was applied to adjust for the cluster randomisation design. Assuming a 10% improvement from a mean score of 26.5 (95% Confidence Interval (CI) 26.1-26.8, SD 6) on the BBQ, and applying an ICC of 0.05, the necessary sample size was estimated to be 500 patients. This calculation takes into account a dropout-rate of 20%, power (1-beta) of 0.90 and an alpha of 0.05.

The secondary outcomes included disability, measured with the Roland Disability Questionnaire (RDQ-24), which has been shown to be a valid and reliable instrument for patients with LBP.[25] The RDQ-24 consists of 24 items, rating disability on a scale of 0 to 24, with higher scores indicating more disability. The EQ-5D-3L was used to measure quality of life for the purpose of the economic evaluation.[26] Health care use, absenteeism, presenteeism and unpaid productivity losses were measured with the generic PROductivity and DIsease Questionnaire (PRODISQ) and the Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness (TIC-P).[27-28] Resource use data was collected using 3-month recall periods. All outcomes were measured at baseline and after 3, 6, and 12 months follow-up. The study protocol initially included measuring the level of pain using the Pain Coping Inventory (PCI) questionnaire. However, as this questionnaire proved to put an unreasonable (time) burden on the patients, it was no longer used and measured. Instead, having back pain at baseline was measured and reported.

For the economic evaluation, the scores on the EQ-5D-3L were converted into utility scores using the Dutch tariff.[29] These utility scores range from 0 (death) to 1 (maximum health. Quality adjusted life years (QALYs) were calculated using linear interpolation between measurement points.

Societal costs are the sum of intervention costs, costs for the use of healthcare, and costs for informal care (i.e. care provided by family and other volunteers), work absenteeism,

presenteeism (i.e. reduced productivity at work), and unpaid productivity losses (i.e. reduced productivity in unpaid activities, such as volunteer work). The intervention costs comprised all costs related to the development and implementation of the intervention (Supplementary file 3). Intervention costs were micro-costed, meaning that detailed data were collected on the number of resources consumed as well as their associated unit prices (Supplementary file 4 shows unit costs). Information on the costs of materials was collected from a detailed overview of project budget expenditures. The time investments of the intervention providers were costed using estimates of their gross hourly salaries. There were no costs for the intervention for the control group. Healthcare utilization included primary healthcare (e.g. GP, PT), secondary healthcare (e.g. diagnostic imaging, medical specialist), alternative healthcare (e.g. acupuncture or massage), and medication (both prescribed and over-the-counter medication related to LBP). To value healthcare utilization, prices from the Dutch Manual for Costing (DMC) were used.[30] Where standard costs were unavailable, prices provided by healthcare professionals' associations were used. Medication use was valued using the prices of the Royal Dutch Society of Pharmacy.[31] Informal care was valued using a recommended Dutch shadow price according to the DMC.[30] Absenteeism was calculated and valued using patient data collected with the PRODISQ and TIC-P. In accordance with the DMC, patients' daily absenteeism cost was calculated by dividing their self-reported gross annual salary by their total number of workable days per year. Using the Friction Cost Approach (FCA, friction period 23 weeks), absenteeism costs were estimated by multiplying the total number of sick leave days during follow-up by their associated costs. Presenteeism was calculated using patient data collected with the TIC-P, where patients indicated how many days they went to work while having LBP. To obtain workday equivalents lost to presenteeism, this number of days was multiplied by a self-reported inefficiency score ranging between 0 (could not perform any tasks) and 1 (could perform all tasks as efficient as without LBP). Presenteeism costs were subsequently calculated by

multiplying the total number of presenteeism days by their associated costs. All costs were transformed to 2016 Euros. As follow-up was 12 month, discounting was not necessary.

Statistical analyses

Analyses were performed according to the intention-to-treat principle. Descriptive statistics were used to compare baseline characteristics between intervention and control group participants as well as between participants with complete and incomplete data. Missing values for costs and effects were imputed using Multiple Imputation by Chained Equations, and imputations were performed separately for the intervention and control group.[32-33] Variables associated with the "missingness" of data, outcomes and potential confounders were included in the imputation model. Cost and effect measure values were imputed per time point, costs were imputed at the cost category level and effects were imputed at the outcome level. Using predictive mean matching, a total of 10 complete data sets were generated in order for the loss of efficiency to be below 5% and pooled estimated were calculated according to Rubin's rules.[32-35] Effectiveness analyses were performed using maximum likelihood estimation longitudinal mixed-effects models with multilevel structure to account for clustering effects, and 'missing at random' assumptions.[36] Analyses of effect and cost data were performed in Stata 14, and the statistical significance level was set at $p<0.05$. Regression coefficients or odds ratios (ORs) were calculated with 95%-confidence intervals (CIs).

A cost-utility analysis (CUA) was performed from a societal perspective. Imputation models included intervention costs, age, gender, educational level, nationality, being employed, performing physically demanding work, physical activity (minutes per week), and available cost and effect measure values. Cost and effect difference estimates between intervention and control group were analysed using seemingly unrelated regression (SUR), while simultaneously adjusting for the possible correlation between costs and effects.[37] Incremental cost-

effectiveness ratios (ICERs) were calculated by dividing the adjusted mean cost differences by those in effects. Uncertainty surrounding the cost differences and ICERs was estimated using Bias Corrected and Accelerated bootstrapping (BCA) with 5000 replications, and presented by 95%-CIs and plotted on cost-effectiveness planes.[38] Cost-effectiveness acceptability curves (CEACs) presented the probability of the intervention being cost-effectiveness at different values of willingness to pay.[39] A sensitivity analysis was performed, in which only patients with complete data on all measurement points were included.

Patient involvement

The Dutch patient association for spinal disorders ("NVV De Wervelkolom") was involved in the design of this study and provided advice about the content of the intervention.

RESULTS

Participants

In total, 5181 eligible patients were invited to participate in this study. Of these patients, 779 (response rate of 15%) agreed to participate and were randomised to the intervention (n=331) and control (n=448) groups (Figure 2). Follow-up responses in the intervention group were 69.8% at 3 months follow-up, 70.1% at 6 months follow-up, and 60.4% at 12 months follow-up. The follow-up responses in the control group were higher than in the intervention group at 3 months follow-up (77%) and 12 months follow-up (77.5%). At 6 months follow-up the responses in the control group were similar to those in the intervention group (69.6%).

At baseline, characteristics of patients in the intervention group were similar to those in the control group. Table 1 shows that a high percentage of participants were female, 60% (intervention group) and 57% (control group) had a high educational level, and over half of the participants were employed. They performed about 3 hours of physical activity per week. Table 1 also shows the baseline scores on the BBQ, RDQ-24, and absenteeism for both groups. At baseline, there was a lower absenteeism rate in the intervention group compared to the control group.

292 *Table 1. Baseline characteristics of patients*

	Intervention (n=331)	**Control (n=448)**
Mean age (SD*)	55.7 (13.9) (n=320)	56.6 (14.6) (n=439)
Female gender (%)	188 (59) (n=320)	252 (57) (n=439)
Back pain at baseline (%)	201 (63) (n=320)	275 (63) (n=439)
Nationality (%) - Dutch - Western countries immigrant - Non-western countries immigrant	(n=320) 298 (93) 16 (5) 6 (2)	(n=439) 409 (93) 23 (5) 7 (2)
Educational level (%) - None (never attended school): - Lower (primary school) - Vocational (college) - Higher (university and university of applied sciences)	(n=320) 9 (3) 25 (8) 92 (29) 194 (60)	(n=439) 12 (3) 42 (10) 134 (30) 251 (57)
Mean activity minutes/week (SD)	161 (109) (n=196)	166 (104) (n=254)
Employed (paid work) (%)	183 (57) (n=320)	232 (53) (n=439)
Physically demanding work (%)	88 (28) (n=320)	121 (28) (n=439)
Mean back pain beliefs score (SD) *(measured by BBQ, range 9-45; higher score means more positive back pain beliefs)*	24.7 (6.0) (n=295)	24.8 (6.2) (n=394)
Mean disability score (SD) (*measured by RDQ-24, range 0-24; higher score means more disability)*	5.1 (4.7) (n=317)	5.9 (5.3) (n=434)
Mean absenteeism days (SD) *(self-reported number of days over past three months)*	2.2 (7.0) (n=187)	4.0 (13.2) (n=246)
Mean quality of life score (SD) *(utility score measured by EQ-5D; range 0 to 1; higher score means better quality of life)*	0.79 (0.22) (n=331)	0.75 (0.25) (n=448)

293

294 * SD: Standard Deviation

Intention-to-treat effectiveness analysis

Table 2 shows the mean scores on the BBQ, RDQ-24, absenteeism, and quality of life of the intervention group compared to the control group. Table 3 shows the results of the intention-to-treat analysis. There were no significant differences in back pain beliefs, disability and absenteeism between groups at any time point. The interaction term with gender was significant for disability, showing that the effect for males was larger than that for females.

Table 2. Mean scores (SD) on BBQ, RDQ-24, EQ-5D and absenteeism

	Mean (SD) back pain beliefs *(measured by BBQ, range 9-45; higher score means more positive back pain beliefs)*		
	3 months follow-up	**6 months follow-up**	**12 months follow-up**
Intervention group	24.4 (5.8)	24.0 (5.9)	24.1 (5.8)
Control group	24.9 (6.2)	24.6 (6.0)	24.1 (6.3)
	Mean (SD) disability *(measured by RDQ-24, range 0-24; higher score means more disability)*		
	3 months follow-up	**6 months follow-up**	**12 months follow-up**
Intervention group	4.4 (4.7)	3.9 (4.3)	3.9 (4.3)
Control group	5.2 (5.1)	4.8 (4.8)	4.5 (4.7)
	Mean (SD) absenteeism *(self-reported number of days over past three months)*		
	3 months follow-up	**6 months follow-up**	**12 months follow-up**
Intervention group	1.2 (6.5)	0.9 (4.8)	0.7 (2.7)

Control group	2.6 (9.8)	0.7 (4.1)	0.7 (4.4)
	Mean (SD) quality of life *(utility score measured by EQ-5D; range 0 to 1; higher score means better quality of life)*		
	3 months follow-up	**6 months follow-up**	**12 months follow-up**
Intervention group	0,857 (0,209)	0,904 (0,163)	0,914 (0,152)
Control group	0,824 (0,236)	0,857 (0,214)	0,866 (0,191)

Table 3. Adjusted effects of the intervention based on intention-to-treat analyses

Outcome		**Difference between intervention and control**	**95%-CI**
Back pain beliefs[1]		-0.13	-0.90;0.65
Disability	Male	-1.13	0.93;1.37
	Female	-0.79	0.68;0.93
Absenteeism[2;3]		-0.94	0.69;1.29

1: Adjusted for educational level, physical activity, having back pain at baseline, being employed, comorbidity; 2:Adjusted for age, physical activity, having back pain at baseline; 3: Only for participants who were employed at baseline (intervention group n=183; control group n=232)

Cost-utility analysis

Intervention costs per patient were € 70. Direct costs for primary care and medication were lower in the intervention than in the control group, while direct costs for secondary and alternative care were higher in the intervention than in the control group. Indirect costs due to absenteeism, presenteeism, and unpaid productivity loss were lower in the intervention than in the control group. The crude total cost differences were not significant (Table 4).

Table 4. Crude costs per cost category in euros (€)

Cost category	**Mean costs (SEM*) in €**		**Cost difference (95%-CI) in €**
	Intervention	Control	
Direct costs			
Primary care	340 (26)	405 (26)	-65 (-134;-2)
Secondary care	478 (228)	229 (42)	249 (58;515)
Alternative care	742 (218)	322 (55)	421 (182;722)
Medication	29 (7)	44 (9)	-15 (-45;-0.70)
Intervention	70	0	70 (N/A)
Indirect costs			
Absenteeism	1034 (242)	1547 (235)	-513 (-941;-77)
Presenteeism	5735 (681)	6342 (537)	-607 (-2076;-831)
Unpaid productivity	4000 (887)	5047 (616)	-1047 (-1954;-203)
Total societal costs	8444 (820)	8979 (619)	-535 (-2230;1172)

* SEM: Standard Error of the Mean

During the 12-month follow-up, intervention and control group participants gained 0.881 (SEM=0.008) and 0.837 (SEM=0.008) QALYs, respectively. There was a statistically significant difference in QALYs (adjusted for age, gender, educational level, nationality, employment, and physically demanding work, and baseline utility value) over the 12-month follow-up period between the control and intervention group (adjusted effect difference 0.03; 95%-CI 0.001;0.042). The intervention did not yield significant cost savings (adjusted for age, gender, educational level, nationality, employment, and physically demanding work cost

difference € -748 per patient; 95%-CI € -2341;878). The ICER for QALYs indicated that the intervention dominated usual care. The majority (79%) of incremental cost-effectiveness pairs was located in the southeast quadrant of the cost-effectiveness plane (Figure 3), indicating that the intervention was on average more effective and less costly. Figure 4 shows that the intervention has probability of 0.85 of being cost-effective on a willingness-to-pay of €10.000 per QALY gained, increasing to a probability of 1.00 on a willingness-to-pay of € 80.000 per QALY gained. Results of the sensitivity analysis differed extensively from those of the main analysis (adjusted cost difference € 1780 per patient; 95%-CI € -1298 to 6945; adjusted effect difference -0.002; 95%-CI -0.079 to 0.075), suggesting that the "missingness" of data is likely related to various observed factors.

DISCUSSION

This study evaluated the effectiveness and cost-utility of a multifaceted eHealth strategy compared to usual care in improving patients' back pain beliefs, and in decreasing their disability and absenteeism. The study results show that the campaign was not effective on these outcomes. The probability of cost-effectiveness was high: 0.85 per QALY gained at a willingness-to-pay threshold of € 10.000, and increased to a maximum probability of 1 per QALY gained at a willingness-to-pay threshold of € 80.000.

A possible explanation for the lack of effectiveness might be that in this study, almost 40% of participants did not have back pain anymore at the start of the actual intervention (i.e. baseline moment). Patients who had visited their general practitioner or physiotherapist no longer than 3 months prior to recruitment could participate in this study. As a consequence, some patients may have agreed to participate while they had already recovered from their LBP at the start of the intervention. With the recruitment protocol used it was not possible to select only the chronic LBP cases. Therefore, the intervention may no longer have been necessary for the participants that did not have LBP at the start of the intervention, and for them effectiveness was not to be expected. The back pain beliefs of the study population were quite low at baseline compared to those of the Australian mass media campaign by which the current study was inspired.[40] Mean BBQ scores in the Australian study were 26.5 at the start of the campaign and increased significantly to 29.7, while in the current study the BBQ scores were 24.7 and 24.8 in the intervention and control groups, respectively. This indicates that there was room for improvement in back pain beliefs in the current study.[40] Another study that assessed factors that were associated with beliefs and attitudes of elderly (mean age 69) also found low back pain beliefs scores (mean 23.7).[41] In the current study disability scores measured with the RDQ-24 showed low levels of disability, and absenteeism rates were also low. Quality of life scores were relatively high and similar between groups with no further improvement over time.

It is arguable that the participating patients were in good health states from the start and gaining much improvement on these functional outcomes was not realistic. Process evaluations among participating patients and professionals alongside the present study showed that compliance with the intervention was very low.[20-21] Most patients did not comply to the full e-health intervention: 31% of the participants had not used the campaign materials at all, and 42.9% had only used it once, and professionals almost never discussed the intervention with their patients. Probably most participants did not need the intervention to improve their functional ability, but improvement in back pain beliefs could have been possible had the compliance rates in this study been higher.[20-21]

Self-management is recommended for the management of LBP, and healthcare professionals are advised to provide advice and information, tailored to needs and capabilities, to help patients self-manage their LBP.[42] One possible way to help patients self-manage their LBP is through an eHealth strategy, but evidence regarding the most effective content and mode of delivery for self-management options is lacking.[43] eHealth is easy to deliver, safe, and usually inexpensive (e.g. in the current study, the intervention costs were less than € 70per patient), a recent systematic review on digital support intervention for LBP could not find significant beneficial effects of digital self-management interventions.[44] However, most of the participants in the included studies were Caucasian, highly educated, middle-aged females, meaning that the findings of the current study are comparable to similar studies. The results of the current study are in line with other studies that have attempted to improve patient outcomes and costs in LBP by using multifaceted strategies. A systematic review of the effectiveness of multifaceted strategies for guideline implementation in LBP and neck pain did not find that multifaceted strategies changed patient outcomes or costs of care.[45] However, the majority of the studies included in the review did not provide insight into the implementation process, raising the question whether the lack of effectiveness is caused by the failure of the theory (multifaceted

strategy) or by failure of the implementation process, making it difficult to compare the current study to others. It is important to evaluate the implementation processes in order to truly understand the effectiveness of multifaceted strategies.

Another interesting thing to note is the fact that the costs for secondary care and alternative care are higher in the intervention group than in the control group. This is in contrast with a very similar recent implementation study for the management of LBP. In that study, patients in the intervention group had higher LBP-related costs for primary care, but lower LBP-related costs for secondary care.[46] Other studies within and outside the field of LBP however have shown similar results to the current study, where patients and participants in intervention groups show higher total medical care costs due to secondary care and/or alternative care.[47-51] The literature does not provide explanations for this fact. One explanation could lie, again, in the low compliance rate of patients in this study.[20] On the other hand, the use of alternative care could be seen as self-management, because patients decide what they want, when they want it, and how much they are willing to pay for it. It could very well be that patients try self-management through alternative care for a while, and then get referred to secondary care when and because self-management (through alternative care) did not work for them. It would be interesting to explore the reasons for the higher costs for secondary care further.

While the strategy evaluated in this study did not yield effective results, it might still be worthwhile considering the possibilities of eHealth interventions from the perspective of outcomes that were not measured in this study but might have improved, for example actual self-management. A systematic review of randomised controlled trials that have assessed self-management education programmes for osteoarthritis found a mismatch between the aims of such programmes (education and advice about how to self-manage their condition despite their pain and fears) and how the success of the programmes were assessed.[52] Many studies have measured health-related outcomes such as pain and function but have not specifically

determined whether the programmes have improved participants' ability to self-manage. Outcomes such as knowledge about the condition and self-management skills may give more insight into the value of self-management education programmes and should be considered essential to measure in future studies evaluating these types of programmes.[52] Looking at the cost savings on absenteeism, presenteeism and unpaid productivity losses in the intervention group compared to the control group, future studies could also benefit from evaluating the effects and cost-effectiveness of eHealth strategies from employer's perspective.

Study limitations

The findings of this study must be interpreted with caution. In this study, the loss-to-follow-up rate was higher for the intervention group (40%) compared to the control group (23%). A possible explanation could be that the strategy provided too much information and participants were contacted too often, making them less willing to comply with completion of the questionnaires over time. A comparison between patients that completed the study and patients that were lost to follow-up showed that, in both the intervention and the control group, patients that completed the study were more likely to have a high educational background. Additionally, in the intervention group, patients that completed the study were more likely to not be employed (i.e. involved in paid work) than patients that were lost to follow-up. The high percentage of loss to follow-up may have resulted in a loss of power and in attrition bias. Additionally, it underlines the need to take educational backgrounds and daily activities of participants into account in designing studies and interventions. Furthermore, the majority of participants did not need or use the intervention, and had minimal disability and impaired quality of life at baseline impacting upon our ability to test the value of our intervention. Unfortunately, the eHealth strategy is no longer accessible, which makes repeating of this study difficult. As the strategy was financed through the funding for the trial, no financial resources were available to keep the eHealth strategy functioning after the trial ended and funding stopped. Materials and

screenshots are still available for future use. Lastly, as for the lack of significant cost differences in light of the cost-utility analysis, it is known that cost data are highly skewed and therefore require large sample sizes to detect statistically significant differences.[53] In this study, the sample size calculation was based on back pain beliefs, which may have underpowered it to detect significant cost differences.

Conclusion

Based on this study, a multifaceted eHealth strategy for patients who had presented to primary care (i.e. general practice and physiotherapy) with LBP was not effective in improving back pain beliefs, disability, or absenteeism. However, the cost-utility analysis based on QALYs showed promising results. The multifaceted eHealth strategy should be studied in a different population, i.e. a more mixed group of participants in terms of background (e.g. education, nationality), and participants with LBP and poorer health states at start of the intervention.

FIGURE LEGENDS

Figure 1. Design of the stepped-wedge cluster randomised controlled trial

Figure 2. Flow-chart of patient inclusion

Figure 3. Cost-effectiveness plane for QALYs

Figure 4. CEAC for QALYs

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	T0 (Baseline)	T1 (3 months)	T2 (6 months)	T3 (9 months)	T4 (12 months)
Cluster 1	Control	Intervention	Intervention	Intervention	Intervention
Cluster 2	Control	Control	Intervention	Intervention	Intervention
Cluster 3	Control	Control	Control	Intervention	Intervention
Cluster 4	Control	Control	Control	Control	Intervention

Figure 1. Design of the stepped-wedge cluster randomised controlled trial

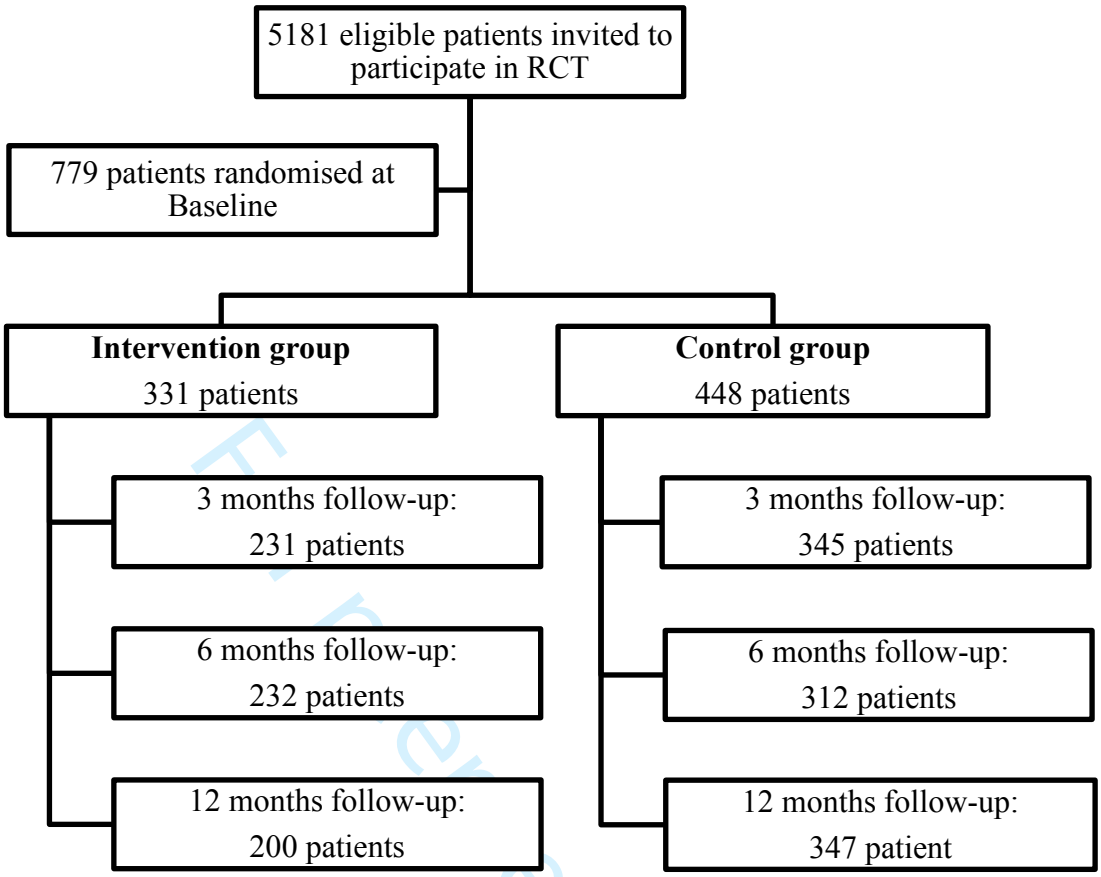
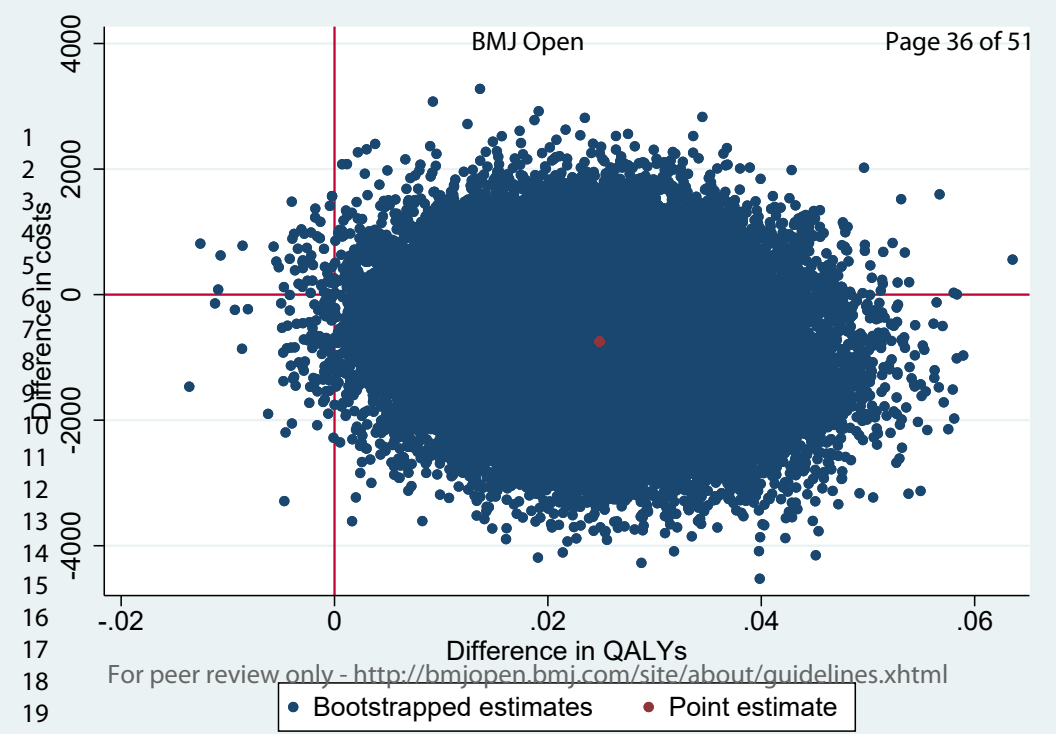


Figure 2. Flow-chart of patient inclusion



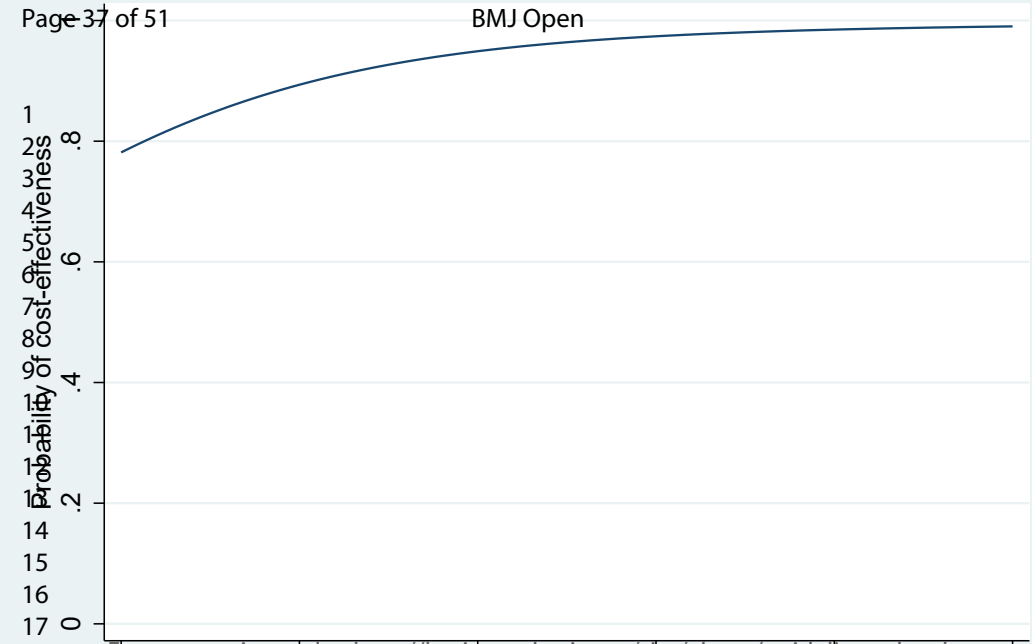


Table 1: CONSORT 2010 checklist of information to include when reporting a cluster randomised trial

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No *
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[1,2]	See table 2	3-4
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	6
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	7
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		N/A
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	8-9
	4b	Settings and locations where the data were collected		8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	9-10
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and	Whether outcome measures pertain to the cluster level, the individual participant level or both	10-13

		when they were assessed		
	6b	Any changes to trial outcomes after the trial commenced, with reasons		11
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	10-11
	7b	When applicable, explanation of any interim analyses and stopping guidelines		N/A
Randomisation:				
Sequence generation	8a	Method used to generate the random allocation sequence		9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	9
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	9
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	9
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	9
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete	9

			enumeration, random sampling)	
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	N/A
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		9
	11b	If relevant, description of the similarity of interventions		N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	13-14
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		13-14
Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	15
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	15
Recruitment	14a	Dates defining the periods of recruitment and follow-up		8
	14b	Why the trial ended or was stopped		N/A
Baseline data	15	A table showing baseline demographic and clinical	Baseline characteristics for the individual and cluster levels as	16-17

		characteristics for each group	applicable for each group	
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	15-19
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	15-19
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		15-19
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		15-21
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[3])		N/A
Discussion				
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		22-26
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	22-26
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		22-26
Other information				
Registration	23	Registration number and		4

		name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	4
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	4

** Note: page numbers optional depending on journal requirements*

Table 2: Extension of CONSORT for abstracts[1,2] to reports of cluster randomised trials

Item	Standard Checklist item	Extension for cluster trials
Title	Identification of study as randomised	**Identification of study as cluster randomised**
Trial design	Description of the trial design (e.g. parallel, cluster, non-inferiority)	
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	**Eligibility criteria for clusters**
Interventions	Interventions intended for each group	
Objective	Specific objective or hypothesis	**Whether objective or hypothesis pertains to the cluster level, the individual participant level or both**
Outcome	Clearly defined primary outcome for this report	**Whether the primary outcome pertains to the cluster level, the individual participant level or both**
Randomization	How participants were allocated to interventions	**How clusters were allocated to interventions**
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	
Results		
Numbers randomized	Number of participants randomized to each group	**Number of clusters randomized to each group**
Recruitment	Trial status[1]	
Numbers analysed	Number of participants analysed in each group	**Number of clusters analysed in each group**
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	**Results at the cluster or individual participant level as applicable for each primary outcome**
Harms	Important adverse events or side effects	
Conclusions	General interpretation of the results	
Trial registration	Registration number and name of trial register	
Funding	Source of funding	

[1] Relevant to Conference Abstracts

REFERENCES

1 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet* 2008, 371:281-283

2 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG at al (2008) CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med* 5(1): e20

3 Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; 141(10):781-788.

CHEERS checklist—Items to include when reporting economic evaluations of health interventions

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	3-4
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	6-7
		Present the study question and its relevance for health policy or practice decisions.	6-7
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	8-9
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	8
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	8-14
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	9-10
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	8-14
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	N/A
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	10-14
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	8-14
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	12-14
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate	N/A

Section/item	Item No	Recommendation	Reported on page No/ line No
		resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	10-14
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	N/A
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	N/A
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	10-14
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	19-21
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	19-21
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	19-21
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	N/A
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	19-21
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	22-26
Other			
Source of funding	23	Describe how the study was funded and the role of	4

Section/item	Item No	Recommendation	Reported on page No/ line No
		the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	4-5

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist

Intervention component	**Cost category**	**Units**	**Unit prices**	**Total costs (Euros 2016)**	**Costs per patient (Euros 2016)**
Professional intervention					
Development costs					
CME training material by Junior reseacher **	Labor costs	6 months	2.618,- per month	15.708,00	0,01
Training costs					
Accreditation by professional associations *	Capital costs	1	484,-	484,00	1,51
Training material *	Capital costs	96	9,03	866,26	2,71
Printing training material *	Capital costs	96	4,46	428,20	1,34
Training locations *	Capital costs	7	51,86	363,00	1,14
Catering during training *	Capital costs	7	164,91	1.154,35	3,61
Participation costs GPs *	Labor costs	31 GPs/3 hours per GP	81,75/hour	7.602,75	23,76
Participating costs OPs *	Labor costs	23 OPs/3 hours per OP	81,75/hour	5.640,75	17,63

Participating costs PTs *	Labor costs	42 PTs/3 hours per PT	22,22/hour	2.799,72	8,75
Participating costs Junior researcher *	Labor costs	18 hours	33,63/hour	605,34	1,89
Participating costs Senior researcher *	Labor costs	12 hours	68,49/hour	821,88	2,57
Participating costs Prinicpal Investigator *	Labor costs	12 hours	126,26/hour	1.515,12	4,74
Patient intervention					
Development costs					
Intervention material by Junior researcher **	Labor costs	6 months	2.618,- per month	15.708,00	0,01
Videomessages by professionals actors **	Labor costs	12 actors	139,67	1.675,98	0,01
Traveling expenses professional actors **	Capital costs	12 actors	7,56	90,62	0,01
Development of videomessages **	Capital costs	12 videos	610,78	7.329,41	0,01
Development of voice-over videomessages **	Capital costs	12 videos	58,38	700,60	0,01
Development of translations **	Capital costs	1	430,-	430,00	0,01
Intervention costs					

Website hosting **	Capital costs	3 years	193,92	581,75	0,01
Total intervention costs			**Total**	64.505,73	69,73
* Costs per patient					
** Costs per patient for all patients in the Netherlands (n=2 million)					

Unit	Price weight (€, 2016)
Intervention costs (per patient)	69,73
Medical costs	
General practitioner	
Office consultation	33,31
Telephone consultation	17,16
House call	50,46
Occupational physician	25,84
Physiotherapist	33,31
Occupational therapist	33,31
Dietician	29,95
Homeopath	67,08
Psychologist	93,17
Psychotherapist	84,74
Psychiatrist	94,87
Other medical specialists	91,84
Emergency room	261,40
Outpatient clinic visit	91,84
Hospitalization (per day)	480,41
Medication	Variable
Alternative care	Variable
Absenteeism costs	
Sick leave days	Variable, depended on gender and age
Presenteeism costs	
Presenteeism score	Variable, depended on gender and age