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Return-to-work intervention for sick-listed employees with common mental disorders versus usual psychiatric care: cost-benefit analysis alongside a cluster randomised trial

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TITLE PAGE

Return-to-work intervention for sick-listed employees with common mental disorders versus usual psychiatric care: cost-benefit analysis alongside a cluster randomised trial

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Return-to-work intervention for sick-listed employees with common mental disorders versus usual care: cost-benefit analysis alongside a cluster randomised trial

ABSTRACT

OBJECTIVE: To evaluate the economic costs and benefits of a guided eHealth intervention (ECO) encouraging sick-listed employees to make an early return to work.

DESIGN: Data of a 2-armed cluster randomised trial were analysed to conduct a cost-benefit analysis from different perspectives. Online self-reported data were collected from the employees at baseline and after 3, 6, 9 and 12 months.

SETTINGS: 62 occupational physicians (OPs) in the Netherlands. OPs working in the same region were clustered and randomised into an experimental and a control group.

PARTICIPANTS: Employees working at small-sized and medium-sized companies (≥18 years) and sick-listed between 4 and 26 weeks with common mental disorders visiting their OP.

INTERVENTIONS: Employees in the intervention group (N=131) received an eHealth module aimed at changing cognitions regarding return to work, while the OPs were supported by a decision aid for treatment and referral options. Employees in the control condition (N=89) received usual sickness guidance.

OUTCOMES MEASURES: The number of days absent, resource use, and quality adjusted life years (QALYs) gained.

RESULTS: From the employer's perspective, the incremental net-benefits were €3,187 per employee over a single year, representing a return of investment of €11 per invested Euro, with a break-even point at six months. The economic case was also favourable from the employee's perspective, in part because of QALY health gains. However, the intervention was costing €213 per employee from a health service financier's perspective. The incremental net-benefits from a social perspective were €3,537. This amount dropped to €2,928 in the sensitivity analysis trimming the 5% highest costs.

CONCLUSIONS: The data suggest that the ECO intervention offers good value for money for virtually all stakeholders involved, because initial investments were more than recouped within a single year, but the wide 95% confidence intervals require careful interpretation.

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STRENGHTS AND LIMITATIONS OF THIS STUDY

- The analysis was based on the results of a randomised controlled trail, comparing the intervention to usual care.
- This study adds to the only few available studies that present a trial-based investment appraisal of the economic costs and benefits of a return to work intervention for sick-listed employees
- The trial was only powered to test a difference in sickness absence duration and not for testing economic hypotheses.
- The follow-up time is limited to 12 months.

INTRODUCTION

Long-term sickness absence has a significant economic impact, largely due to the substantial productivity losses.[1, 2] Mental disorders are a leading cause of sickness absence,[3-6] which is not without economic ramifications.[7] Common mental disorders, specifically depression and anxiety, are the most prevalent in the workforce.[8]

For the treatment of common mental disorders a range of psychological and pharmaceutical interventions have been shown to be effective and cost-effective.[9, 10] However, symptomatic recovery does not automatically reduce sickness absence.[10-12] To improve occupational outcomes it is also important to pay attention to return to work during treatment.

In the Netherlands, occupational physicians (OPs) provide sickness guidance.[13] A guideline has been developed to suggest directions to OPs to better assist employees with mental health problems in the return to work process. According to this guideline, the OPs need to closely monitor both the mental health problems and the level of functioning. When recovery is slow or hampered, they can consult or refer to a psychiatrist, a psychologist or a social worker.[14] A study of Rebergen and colleagues suggested that better adherence to the guideline is associated with earlier return to work.[15] However, in practice, adherence appears to be far from optimal,[16, 17] and there is often a lack of cooperation between the OPs and treatment providers in the mental health sector. Several attempts have been made to bridge this gap.

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One study about the effect of psychiatric consultation for OPs assisting sick-listed employees did provide results in terms of earlier return to work.[18] However, this study was small. Another study evaluating active treatment by an OP within a collaborative care arrangement did improve depressive symptoms, but failed to speed up return to work.[19] It appeared that OPs need support in helping sick-listed employees change their attitude towards resuming work and should monitor symptom improvement and work performance in a more systematic manner.

To overcome these problems and to better manage the return to work of sick-listed employees with common mental disorders, the "E-health module embedded in Collaborative Occupational health care" (ECO) intervention was developed. The ECO intervention was designed to promote return to work by improving work functioning in employees, providing a decision aid for the OP who gives guidance to the employee, and by including the opportunity for psychiatric consultation to the OP.[20]

The results of a recent trial showed that ECO led to an earlier first return to work than usual care (mean duration of 77 days in the ECO group versus 50 days in the CAU group) and higher remission rates of common mental disorder after 9 months in a group of sick-listed employees with common mental disorders.[21]

Taking the economic perspective, we expect that the ECO intervention is cost-effective as seen from the employer's viewpoint, because ECO is a low cost self-help intervention with a limited amount of support from the OP and appears to be effective in reducing absenteeism. There is less certainty how cost-effective the intervention would be as seen from the perspective of the sick-listed employees and the health care financier (i.e. health care insurance company in the Dutch context). Therefore, this study conducts a costs-benefit analysis of the ECO intervention from all three stakeholders' viewpoints, and combines these in an overarching societal perspective. These analyses are important because very few trial-based economic evaluations have been conducted with regard to return-to-work interventions for sick-listed employees with common mental disorders.[12, 22]

METHOD

Study design

The ECO study was designed as a 2-armed cluster randomised controlled trial, with randomisation at the level of the OP and sick-listed employees either randomised to usual care or usual care plus the ECO intervention. The Netherlands Organization for Health Research and Development funded the study (grant number 171002403 ZonMw Doelmatigheid) together

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with Achmea, a Dutch insurance company. The Medical Ethics Committee of the University Medical Center Utrecht approved the study protocol in 2011, and the trial was registered at the Netherlands Trial Register (NTR) under number 2108. The design of the study is described in detail elsewhere.[20, 21] Here, we provide a brief summary of the main characteristics and focus on the economic aspects.

Randomisation

To prevent contamination cluster randomisation took place at the level of the OPs working in the same region across a total of twelve regions. An independent statistician randomised six regions to the ECO condition and the remainder to the control condition using computer-generated randomisation. Since the OPs had to offer the intervention, they could not be blinded for randomisation. The researchers and participants were informed about the allocation after the randomisation procedure.

Participants

Participants were recruited from July 2011 to January 2013 from all-cause sick-listed employees working at small-sized and medium-sized companies in the Netherlands who visited an OP. To be eligible for inclusion the employees had to be at least 18 years of age and on sickness absence between 4 and 26 weeks. In addition, they needed to have a score ≥10 on either the depression or the somatization scale of the Patient Health Questionnaire (PHQ-9),[23, 24] or the Generalized Anxiety Disorder questionnaire (GAD-7).[25] Exclusion criteria were (1) poor command of the Dutch language, (2) pregnancy, (3) not having access to the Internet, (4) being involved in a legal action against the employer.

Procedure

Initially an independent statistician randomised 12 regions to either CAU (6 regions with 30 OPs) or ECO (6 regions with 32 OPs) by using a computer algorithm. Within the cluster of CAU regions 5,875 sick-listed employees were screened for eligibility resulting in 326 screen-positives. In the cluster of ECO regions, 537 screen-positives were obtained from 8740 sick-listed employees. Next, 89 and 131 consenting participants were randomised to CAU and ECO, respectively. The unequal distribution of participants over the conditions was due to cluster randomisation. Participants received measurements at baseline and at 3, 6, 9 and 12 months, which amounted to dropout in both conditions (see figure 1).

Figure 1. Flowchart of the participants

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Intervention

ECO consists of 2 components: (1) the eHealth module Return@Work for the employee and (2) an email-based decision-aid to support the OP. Return@Work is aimed at improving the self-efficacy of employees and promoting the employee's intention to return to work. Recent studies have shown that these factors are predictors of actual work resumption.[26-28] The decision-aid provides the OPs with advice regarding treatment and referral options based on the employee's outcome monitoring in Return@Work.

The eHealth module starts with an assessment questionnaire. Depending on the results of the questionnaire regarding symptoms and cognitions about return to work of the individual employee, Return@Work presented specific modules and sessions. As a consequence, the amount of modules and sessions offered to the employees differed. In total, Return@Work included 5 modules composed of 16 sessions, covering: 1) psycho-education, 2) cognitions regarding return to work while having symptoms (based on principles of cognitive behavioural therapy), 3) problem solving skills, 4) pain and fatigue management and reactivation, and 5) relapse prevention. The employees went through the modules independently, but had the possibility to discuss Return@Work modules and assignments with the OP. The OPs were requested to inquire about the employee's progress in the eHealth module and to provide support if necessary during their regular face-to-face contacts with the employee. Periodic visits between the employee and the OP are part of the guidelines of the Dutch Board for Occupational Medicine (NVAB),[14] which all OPs were required to adhere.

Besides the modules, Return@Work also contained a monitor of functioning and symptoms on a regular basis. This monitor was used for the second component of ECO, a decision aid to support OPs in the sickness guidance of employees. Based on the outcomes of the monitor in Return@Work the OPs received automated email messages with advice for next steps in collaborative care. In addition, the decision aid gave OPs the option to consult a psychiatrist in case insufficient progress was made. The OPs in the experimental condition received a 4-hour training about ECO.

In the control condition the employees received usual sickness guidance. The guidelines of the NVAB were used as a protocol.[14] As there is a lack of adherence to the guidelines,[16,17] actual care was assessed with a questionnaire by all of the participating employees.

Outcome measures

Participants filled in the Medical Technology Assessment Cost Questionnaire for Psychiatry (TiC-P),[29] which amongst health care use also measures absenteeism from work, which is the main outcome variable of this study. The TiC-P is based on self-report and to crosscheck

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the number of work days lost to absenteeism we compared the self-reports with administrative data (see Sensitivity Analysis below). Total follow-up time was 12 months with measurements at baseline and after 3, 6, 9 and 12 months. Finally, health gains in terms of quality adjusted life years (QALYs) were assessed using the EuroQoL-5D-3L,[30] with the Dutch tariff.[31]

Resource use and costing

Cost data were collected using the TiC-P, including (1) direct medical costs, including the costs of medication, (2) direct non-medical costs (patients' out-of-pocket costs for trips to health services), (3) costs stemming from productivity losses owing to absenteeism and presenteeism, and (4) costs that occurred in the domestic realm (help for housekeeping from family, friends or hired people). Standard costs, expressed in euro (€), were indexed for the reference year 2011 using the consumer price index from Statistics Netherlands. Costs were not discounted because the follow-up period did not exceed one year.

Computation of costs

The set costs of the ECO intervention are €300 per user, which is its current (post trial) rate. Direct medical costs are limited to mental health service use. The medical costs were computed by multiplying the number of health service units (sessions, visits, hospital days) with their standard full economic cost price.[32] Only medication costs for mental problems were included in the economic analysis. For every type of drug (e.g. antidepressants, benzodiazepines, antipsychotics, problems sleeping) an average cost price was calculated based on the cost prices per standard daily dose of three drugs most often prescribed to the participants as reported in the Pharmaceutical Compass,[33] while taking into account the GP's prescription costs, the pharmacist's dispensing costs and the pharmacist's claw back as per the guideline for cost computations in health care.[32]

The direct non-medical costs consisted of the travel costs that participants had to make to visit OPs and health services. These costs were calculated as the average distance to the specific health service provider multiplied by the costs per km (€0.21) plus parking costs (€3.11) per hour. To the direct non-medical costs we added the costs in the domestic realm, computed by multiplying €12.96 by the number of hours that others (family and friends) took over cleaning and running domestic errands.

In the Netherlands QALY health gains are valued at €50,000 per QALY with a range between €20,000 and €80,000.[34] We used the conservative threshold of €20,000 for our analysis.

Productivity losses comprised the costs of lost workdays due to absenteeism and the costs of inefficiency while at work (presenteeism). We used the human capital method to value the

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productivity costs.[35] In the case of absenteeism, this method multiplies the number of days absent by the gender and age-specific average gross wages per employee, as per the Dutch guideline for health economic evaluation.[32] To assess the costs of presenteeism we used the number of days actually worked when ill multiplied by a self-reported inefficiency score. This score ranged from 0 (as effective as in good health) to 1 (totally ineffective). Again, the gender and age-specific average gross wages were used to compute the costs of presenteeism.

Analyses

Following recommendations from the CONSORT and CHEERS statements,[36-38] analyses were conducted in agreement with the intention to treat principle. Therefore all participants as randomised were retained in the analysis and missing observations due to dropout were imputed. For imputation we used both the estimation-maximisation (EM) algorithm as implemented in SPSS for the main analysis, and regression imputation (RI) as implemented in Stata for the sensitivity analysis (see below). In both imputation strategies we used predictors of outcomes (costs and QALYs) and predictors of dropout (age, gender, partner status, country of birth, number of work loss days). Predictors of the outcomes were included to increase precision in the imputed values, predictors of dropout were incorporated to tackle selection-bias, if any, and to meet the missing at random (MAR) assumption underlying most imputation techniques.

The economic evaluation was conducted as an incremental cost-benefit analysis, because the primary outcome (duration of sick leave) could directly be expressed in terms of monetary benefits. The costs and benefits were calculated at baseline, 3, 6, 9 and 12 months in the ECO and CAU conditions. The costs in the intermediate months were linearly interpolated. This allowed mapping the monthly cash flows of costs and benefits over the full 12-month period. The cash flows were computed from four perspectives: (1) the employer's perspective focussing on the net-benefits from greater productivity via lesser absenteeism and lesser presenteeism; (2) the health care perspective focussing on the direct medical costs due to health service use, including the costs of medication, (3) the employee's perspective focussing on QALY health gains, fewer out-of-pockets costs and fewer costs in de domestic realm. Finally, we included a societal perspective (4), including all costs and benefits, regardless of who incurs costs or receives benefits.

The monthly cash flows were used to compute the cumulative costs and cumulative monetary benefits over the full twelve months. Incremental costs, incremental benefits and incremental net-benefits were obtained by comparing ECO intervention with CAU. These are the main outcomes of the economic analysis alongside metrics such as the break-even point and the return on investment (ROI).

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For statistical analysis we relied on non-parametric bootstrapping (2,500 replications) since costs are non-normally distributed. Statistics such as mean costs, 95% confidence intervals, standard errors and p-values are all based on non-parametric bootstrapping to increase the robustness of our findings. The data were analysed in SPSS (version 22) and Stata (version 13.1).

Sensitivity analysis

The main analysis (using the overarching societal perspective and based on EM imputation) was repeated three times in a series of sensitivity analyses. Firstly, the analysis was conducted again, but now based on regression imputation (RI) to assess the robustness of the findings under a different imputation technique. Secondly, we crosschecked the self-reported absenteeism against administrative data derived from the registers of the occupational health service or the employer, because the main analysis was based on self-reports and some recall bias (underreporting) could have occurred. Finally, we recalculated the incremental net-benefits after trimming the highest 5% of total cumulative costs per employee, because the participants with the extremely high costs were only a small minority but may have exercised a disproportional influence on the cost estimates and pushed outcomes to a more favourable outcomes for the ECO intervention. By excluding these participants, primarily from the CAU condition, the net-benefits were re-estimated but now under conservative assumptions.

RESULTS

Sample characteristics and baseline costs

Baseline characteristics of the sample (including baseline costs) are presented in table 1. The mean age of the 220 participants was 44 years and 59% was women. No important differences were observed at baseline in demographic characteristics and quality of life, but baseline costs were somewhat higher in the ECO condition, suggesting that the ECO group had a slightly disadvantageous start. We will return to this issue in the Discussion. As described by Volker and colleagues,[21] job characteristics and sickness absence duration at baseline were also comparable between the intervention condition and control condition, indicating that the randomisation was generally well balanced.

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Table 1. Baseline characteristics in the care as usual (CAU) and the ECO intervention group

	CAU (n=89)	ECO (n=131)
Age, mean (SD)	45.5 (10.7)	43.3 (9.5)
Female, N (%)	53 (59.6)	77 (58.8)
Married/living together, N (%)	62 (69.7)	91 (69.5)
Educational level, N (%)		
Low	32 (36.0)	48 (36.6)
Average	31 (34.8)	47 (35.9)
High	26 (29.2)	36 (27.5)
Country of birth: The Netherlands, N (%)	83 (93.3)	123 (93.9)
Direct medical costs, mean (SD)	645 (58)	602 (49)
Direct non-medical costs, mean (SD)	35 (2)	33 (2)
Absenteeism, mean (SD)	2850 (146)	3078 (125)
Presenteeism, mean (SD)	34 (16)	20 (14)
Costs in the domestic realm, mean (SD)	143 (26)	133 (20)
Medication, mean (SD)	8 (2)	12 (3)
Total costs, mean (SD)	3716 (154)	3879 (141)
Quality of life, mean (SD)	0.57 (0.027)	0.54 (0.024)

Loss to follow-up

The measurements at 3, 6, 9 and 12 months were completed by 155 (70.5%), 157 (71.4%), 134 (60.9%) and 128 (58.2%) of the participants. The dropout rate over the 12-month trial period was higher in the ECO condition (45.0%) than the control condition (37.1%), but this difference was statistically insignificant (χ^2=1.38; df=1; p=0.240). As indicated, we looked for variables that predict dropout and included these as predictors in the EM and IR imputations. This was done to counter selection-bias (if any) and to better meet the MAR assumption underpinning the imputation strategies.

Costs and QALYs at 3, 6, 9 and 12 months

The next step of the cost benefit analyses was to ascertain costs and quality of life at the follow-up measurements (Table 2). Cost differences were highest for absenteeism. At 12 months all the cost differences were statistically significant and in favour of the ECO condition. The total costs difference at the 12 month follow-up amounted to €919 (SE=205; z=4.48; p<0.001), mainly due to reduced absenteeism.

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Table 2. Average monthly costs in the care as usual (CAU) and the ECO intervention group at 3, 6, 9 and months (in 2011 Euro)[1, 2]

	3 months	6 months	9 months	12 months
Direct medical costs				
CAU	474	298	383	296
ECO	460	473	311	144
Cost difference	14	-175	71	*153*
Direct non-medical costs				
CAU	135	74	102	98
ECO	104	89	67	45
Cost difference	31	-15	35	*53*
Productivity losses				
Absenteeism				
CAU	2120	1699	1276	1118
ECO	1887	1264	725	572
Cost difference	233	435	*551*	*546*
Presenteeism				
CAU	166	233	269	493
ECO	357	408	322	325
Cost difference	*-191*	*-175*	-53	*168*
Total costs				
CAU	2895	2305	2029	2005
ECO	2808	2234	1425	1085
Cost difference	87	70	*605*	*919*
Quality of life (utility)				
CAU	0.65	0.68	0.68	0.73
ECO	0.65	0.72	0.76	0.77
Difference in utilities	0	0.04	*0.08*	0.04

1 Between-group differences in italics are statistically significant at p<0.05.

2 Numbers may not add due to rounding

Cost-benefit analysis: employer's perspective

For the employer's perspective only the intervention costs and costs stemming from absenteeism and presenteeism were included, thus assuming that the employer would be interested to know the pay out of this investment when paying for the intervention. Cumulated over the 12-months period the incremental benefits were €3,487 in favour of the ECO condition (Bootstrapped 95% CI= -418~7,390; SE=1,992; z=1.75; p=0.080), which was mainly due to a larger reduction in absenteeism over 12 months compared to care as usual (bootstrapped M=4,291; 95% CI= 290~8,292; SE=2,041; z=2.10; p=0.036). Next, we calculated incremental net-benefits, by subtracting the intervention costs (€300) from the incremental benefits. As shown in table 3 the incremental net-benefits over twelve months were €3,187 per employee in favour of the ECO condition, but there is significant uncertainty

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in the estimate (Bootstrapped 95% CI=-656~7,029; SE=1,961; z=1.63; p=0.104). We return to this issue in the Discussion. The break-even point for the employer, the moment in time where the investment of €300 is recouped, is around six months. The return of investment (ROI) is 3,187 / 300 = 10.62, indicating that for every euro invested the pay-out is €10.62.

Table 3. Monthly per patient costs in the care as usual (CAU) and the ECO intervention group from an employer's perspective (in 2011 Euro)

Month	1	2	3	4	5	6	7	8	9	10	11	12	Cumulative
CAU													
Absenteeism	2850	2485	2120	1910	1910	1699	1487	1487	1276	1197	1197	1118	20736
Presenteeism	34	100	166	199	199	233	251	251	269	380	380	493	2955
Total costs	2884	2585	2286	2109	2109	1932	1738	1738	1545	1577	1577	1611	23691
ECO													
Absenteeism	3078	2483	1887	1576	1576	1264	994	994	725	648	648	572	16445
Presenteeism	20	188	357	382	382	408	365	365	322	323	323	325	3760
Total costs	3098	2671	2244	1958	1958	1672	1359	1359	1047	971	971	897	20205
Incremental benefits	-214	-86	42	151	151	260	379	379	498	606	606	714	3486
Intervention costs	-300												
Incremental net-benefits	-514	-600	-558	-407	-256	4	383	762	1260	1866	2472	3186	
Return on investment	10,6												

Cost-benefit analysis: health care payer's perspective

For the perspective of the health care financier (in the Netherlands: health care insurers) we looked at the direct medical costs including the costs for medication. We computed the monthly cash flows and compared these between the ECO and CAU conditions as before. The cumulative costs over twelve months were more or less the same for each condition with a small difference of €87 in favour of the ECO condition. Assuming that the health insurer would pay for the intervention, the intervention costs of €300 have to be subtracted from these benefits in order to obtain the net-benefits. This generated a negative value of €213, implying that the ECO intervention is not cost saving from a health care insurer's perspective (bootstrapped 95% CI=-1,384~959; SE=598; z=-0.36; p=0.722).

Cost-benefit analysis: employee's perspective

Employee's costs and benefits included direct non-medical costs (i.e. the patient's out-of-pocket costs and costs in the domestic realm) and QALY health gains. Cumulated over twelve months the incremental benefits for the ECO group were €263 regarding non-medical costs and €696 due to QALY gains (0.035*€20,000). When solely focussing on the employee's out-of-pocket costs, then the incremental net-benefits of €263 are close the interventions cost of

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€300, but this break-even is surrounded by uncertainty (bootstrapped M=-37; 95% CI= -403~330; SE=187; z=-0.20; p=0.845). The benefits increase to a total of €959 when including the value of QALY gains. Then the incremental net-benefits become €959-€300= 659, which is again surrounded by uncertainty (bootstrapped 95% CI=287~1,031; SE=190; z=3.47; p=0.001).

Cost-benefit analysis: societal perspective

For the societal perspective we only included real economy euros, thus ignoring the value of QALY gains. The difference between conditions of the cumulative benefits was €29,822-€25,985=€3,837 in favour of the intervention condition (bootstrapped 95% CI= -541~8,216; SE=2,233; z=1.72; p=0.086). Subtraction of the intervention costs of €300 yielded incremental net-benefits from a social perspective of €3,537 (bootstrapped 95% CI= -875~7,950; SE=2,222; z=1.57; p=0.116). Break-even was achieved at seven months and the return on investment was 3537/300=11,8.

Sensitivity analyses

For the main analysis we used EM imputation; now we recomputed the estimates under regression imputation (RI). Taking the societal perspective, the incremental net-benefits became €3,423 (Bootstrapped 95% CI= -921~7,767; SE=2,216; z=1.54; p=0.122), which is close to the EM-based analysis where the incremental net-benefits were estimated at a mean of €3,537.

The incremental net-benefits in the main analyses were dominated by the costs offsets due to reduced absenteeism, but these were based on self-reported data. Crosschecking the self-reported data against administrative data derived from the registers of the occupational health service or employer showed that the self-report data were more conservative than the estimates based on administrative data (72 work days absent based on self-reported data versus an average of 101 work days absent based on administrative data). When basing the analysis on administrative data, the total cumulative incremental net-benefits became €5,758 (Bootstrapped 95% CI=-3,569~15,085; SE=4,759; z=1.21; p=0.226), which is higher by a factor 1.63 than the corresponding estimate presented in the main analysis. The main analysis thus represents a safer (lower) estimate.

Finally, we repeated the main analysis by replacing the total costs of the respondents with the top 5% highest total costs due to absenteeism by the highest amount witnessed in the other 95% respondents. The top 5% outliers were mainly situated in the CAU condition, raising the average costs for this group. The incremental net-benefits based on the trimmed costs

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dropped from €3,537 to €2,928 (SE 95% CI= -1,143~7,000; SE=2,077; z=1.41; p=0.159), which can be regarded as a more conservative lower bound.

DISCUSSION

Principal findings

This study was set out to evaluate the cost-effectiveness of an intervention that encourages sick-listed employees with common mental disorders to make an early return to their work. The economic evaluation was conducted as an incremental cost-benefit analysis and reports on the incremental cost to benefit ratio, the return on investment, the break-even point, and the incremental monetary net-benefits, as customary seen in business cases and investment appraisals. These metrics were computed from various perspectives, such as the employer's perspective, and those of the employee and the health care financier. The main findings can now be summarised as follows:

- Taking the employer's perspective, the focus of the economic evaluation was placed on the intervention costs and changes in productivity owing to changes in absenteeism and presenteeism. Assuming that the employer would make the investment in the ECO intervention of €300 per employee, the incremental net-benefits were €3,187 per employee over a year. This was equivalent to a return on investment of €11 per invested Euro. Benefits were largely stemming from reduced absenteeism and exceeded the investment costs after six months.
- From the perspective of the health care payer the incremental net-benefits were negative, amounting to additional costs of €213 per employee on average.
- As seen from the employee the net-benefits exceeded the costs by €659 when also valuing the employee's QALY health gains. When excluding the QALY benefits, the incremental net-benefits were slightly negative (€37).

From the societal perspective, the initial investment was also more than recouped. Considering all costs and benefits, but ignoring the value of QALY gains, the incremental net-benefits were €3,537, with a break-even point at 7 months. Every euro invested yielded €12. Trimming the 5% highest costs, mostly from the care as usual condition, reduced the incremental net-benefits to €2,928.

Limitations

This study has several limitations, which are reported and discussed here.

- First, cost data are often non-normally distribution with a few people generating very high costs. This results in large standard deviations in the costs estimates and less stable estimates of average costs. In such a context it would require a very large sample size to power the trial for testing economic hypotheses. However, our study was only powered to

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test a difference in sickness absence duration. As a consequence, the wide 95% confidence intervals indicate that the cost estimates are subject to much uncertainty. More specifically, when trimming the highest 5% of the costs in one of our sensitivity analysis showed that the incremental net-benefits became €2,928, which is 83% of the original estimate of €3,537. This suggests that our study needs replication, preferably in a larger study.

- Second, loss-to follow up was substantial. To handle dropouts, missing data were imputed using estimation maximization (EM). To ascertain the robustness of our findings we also used regression imputation (RI). With RI we arrived at similar conclusions: €3,423 (versus €3,537 under EM), attesting to the robustness in our findings. Nevertheless, selection bias introduced by (selective) dropout cannot be ruled out completely and could have influenced the outcomes that we obtained.
- Third, costs at baseline were higher in the ECO condition. We could have adjusted for the baseline differences, but this would have led to even better outcomes in favour of the ECO condition. Ignoring the baseline differences has therefore put our main analyses on a more conservative footing.
- Fourth, the main driver of costs and benefits was absenteeism and in the main analysis these were based on self-report. This may have introduced some recall bias, but self-reports of absenteeism usually involve underreporting thus leading to conservative outcomes. Nevertheless, we crosschecked the data with administrative data from the registers of the occupational health service and employer. As expected, the benefits were lower when based on self-reports than on administrative data.
- Fifth, it should be noted that the cost-benefit analysis did not include the future costs of implementing the ECO intervention on a wider scale. As the main component is a low cost self-help intervention (Return@Work) and the training of OPs only lasts a few hours, the implementation costs are expected to be low, but should be considered when the intervention is disseminated on a wider scale.
- Finally, the follow-up time is limited to 12 months. We do not know what the net-benefits would be over a longer time span. However, costs differences were highest in the last months. This may imply that a longer follow-up period would have seen more profitable outcomes.

Results in context

Reviews about the effectiveness of psychological return to work interventions for employees with mental health problems show mixed outcomes in reducing sickness absence and promoting an earlier return to work.[12, 22] Moreover, only a few of the reviewed studies that appeared to be effective report a full economic evaluation. Of these, none evaluated a guided eHealth intervention for return to work. One study that is somewhat comparable with our study is from Schene and colleagues. Schene et al describe the economic evaluation of an

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intervention for employees with major depression, who were sick-listed for 10 weeks up to 2 years.[39] The experimental condition received occupational therapy in addition to usual outpatient treatment for depression. Their intervention increased the number of hours worked accumulating in a median economic gain of US$4000–5000 per patient per year, which is in line with our findings regarding the reduction in absenteeism. The study of Schene et al was smaller (n=62), was directed at a more severely depressed population, and the intervention was not delivered online but as an intensive face-to-face therapy consisting of 24 group sessions and 15 individual sessions.

Lerner and colleagues evaluated a brief telephonic program to improve work functioning for employees with major depressive disorder or dysthymia with an at-work productivity loss of at least 5% in the past two weeks.[40] Compared to usual care, annualised cost savings averaged at $6042 per participant but these savings were extrapolated from a shorter (4 months) follow-up. These cost savings are higher than the cost-savings observed in our study. Nonetheless, Lerner's et al. extrapolation from 4 to 12 months might have overstated the savings if the treatment effect was not sustained.

Arends and colleagues evaluated the costs and benefits of a problem-solving intervention provided by OPs to prevent recurrent sickness absence in workers with common mental disorders.[41] Compared to care as usual the intervention was more effective but also more expensive. From an employer's perspective the intervention showed no economic benefits, which is in contrast to our study.

Finally, Noben and colleagues conducted a cost-benefit analysis from the employer's perspective of a preventive intervention in the work setting among nurses with an elevated-risk of mental complaints.[42] The authors concluded that the intervention was a good investment as the net-benefits (stemming from reduced absenteeism and presenteeism) were positive (€651) and the return on investment was €11. This return on investment is comparable with ours. However, the results of our study are related to a preventive intervention and can only be generalised to employees who have been sick-listed for 4-26 weeks, working in small- to medium-sized companies.

Conclusions and implications

In the Netherlands, employers have an incentive to invest in sickness management as they have the responsibility to pay 70-100% of the salary of sick-listed employees for up to two years. Employees who are on sickness absence have to visit an occupational physician, paid by the employer within the first six weeks. Both the employee and employer have to agree on an action plan. In this plan the responsibilities of both parties are defined to ensure a quick return to work of the employee. In this context the ECO-intervention can be seen as an effective intervention that, in addition, has a high probability of offering good value for money because the initial investment (of €300) is more than recouped within a single year as seen from the

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employer's perspective, while the employee derives benefits in the form of increased quality of life when returning to work sooner rather than later. However, the wide 95% confidence intervals require careful interpretation. This suggests that our study needs replication in a larger study and preferably over a longer time span.

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Contributors

CFC initiated the collaborative clinical trial project. MZV, AB and CFC contributed to the design of the study and obtained the funding. DV, MZV and CFC were responsible for the acquisition of the data. SL and FS conducted the statistical analysis and drafted the manuscript, which all authors critically revised. All authors read and approved the final manuscript. SL, FS and CFC are guarantors.

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: financial support for the submitted work from The Netherlands Organisation for Health Research and Development (ZonMw) and from Achmea SZ; SL, DV, MZV, BB, FS report personal fees from employment at the Trimbos institute, the Netherlands institute of mental health and addiction, a not-for-profit organisation, CFC has received research grants from Eli Lilly outside the submitted work.

Ethical approval

The study protocol was approved by the Medical Ethics Committee of the University Medical Center Utrecht, The Netherlands, in February 2011. All participants provided written informed consent before taking part.

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Transparancy

The lead author affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that and discrepancies from the study as planned (and if relevant, registered) have been explained.

Data sharing: No additional data

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Legends of figures

Figure 1. Flowchart of the clusters and participants

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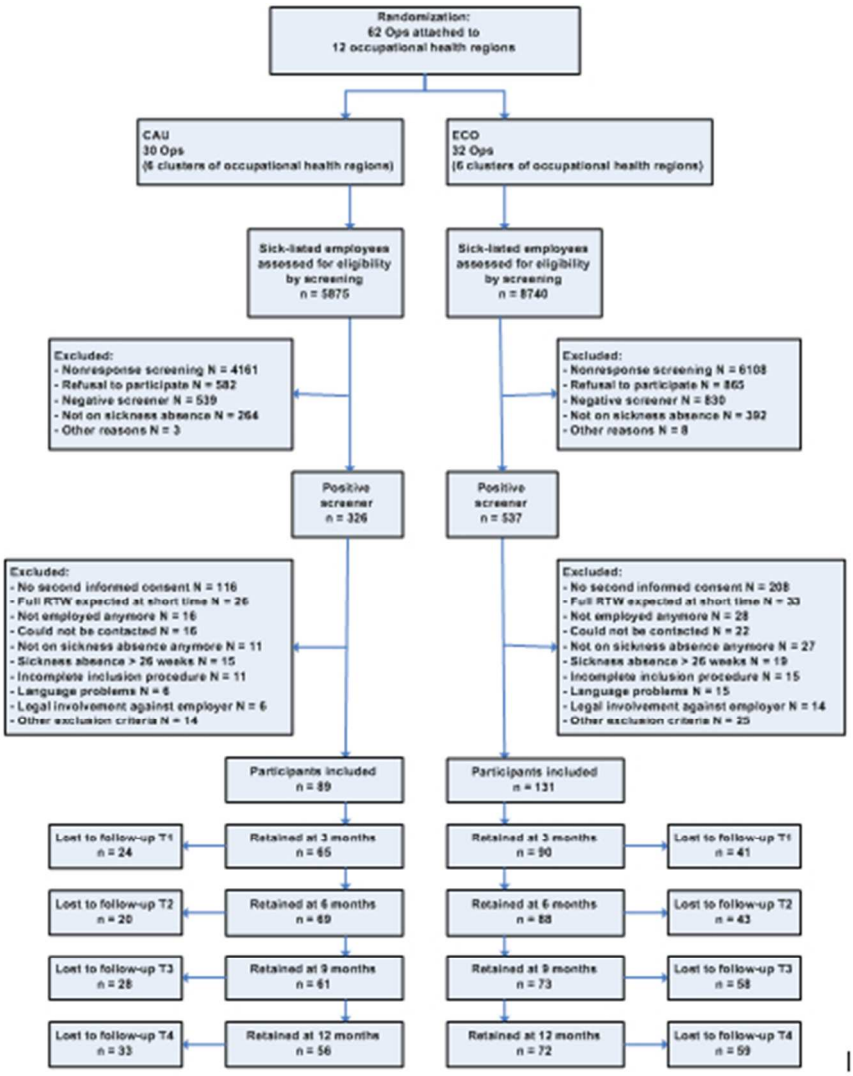

Flowchart of the participants

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

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.	3
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
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	4,5
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	6
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	6
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	9
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	7
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	8
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	8
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.	8/9
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.	5-7

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	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.	7,8
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate 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.	N.A.
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.	8
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.	9,10
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.	10-15
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.	10-15
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	12-14

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		of methodological assumptions (such as discount rate, study perspective).	
	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.	15-18
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	18
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.	18

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

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

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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	3
	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	4,5
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	5
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	5
	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	6
	4b	Settings and locations where the data were collected		6
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	7
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	7/8

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		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	N/A
	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		6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	5/6
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	5/6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	6
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete	

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			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	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		6
	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	9/10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		10
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	6/10/11
	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	10/11
Recruitment	14a	Dates defining the periods of recruitment and follow-up		**6**
	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	Table 1

		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	6/9
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	11-14
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		14/15
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		15/16
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	17
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		16/17
Other information				
Registration	23	Registration number and		5/6

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

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

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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

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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.

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Return-to-work intervention versus usual care for sick-listed employees: health-economic investment appraisal alongside a cluster randomised trial

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TITLE PAGE

Return-to-work intervention versus usual care for sick-listed employees: health-economic investment appraisal alongside a cluster randomised trial

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Return-to-work intervention versus usual care for sick-listed employees: health-economic investment appraisal alongside a cluster randomised trial

ABSTRACT

OBJECTIVE: To evaluate the health-economic costs and benefits of a guided eHealth intervention (ECO) encouraging sick-listed employees to a faster return to work.

DESIGN: A 2-armed cluster randomised trial with occupational physicians (OPs) (n=62), clustered and randomised by region into an experimental and a control group, to conduct a health-economic investment appraisal. Online self-reported data were collected from employees at baseline, after 3, 6, 9 and 12 months.

SETTINGS: Occupational health care in the Netherlands.

PARTICIPANTS: Employees from small-sized and medium-sized companies (≥18 years), sick-listed between 4 and 26 weeks with (symptoms of) common mental disorders visiting their OP.

INTERVENTIONS: In the intervention group, employees (N=131) received an eHealth module aimed at changing cognitions regarding return to work, while OPs were supported by a decision aid for treatment and referral options. Employees in the control condition (N=89) received usual sickness guidance.

OUTCOMES MEASURES: Net-benefits and return on investment based on absenteeism, presenteeism, health care use, and quality adjusted life years (QALYs) gained.

RESULTS: From the employer's perspective, the incremental net-benefits were €3,187 per employee over a single year, representing a return of investment of €11 per invested Euro, with a break-even point at six months. The economic case was also favourable from the employee's perspective, partly because of QALY health gains. The intervention was costing €213 per employee from a health service financier's perspective. The incremental net-benefits from a social perspective were €4,233. This amount dropped to €3,616 in the sensitivity analysis trimming the 5% highest costs.

CONCLUSIONS: The data suggest that the ECO intervention offers good value for money for virtually all stakeholders involved, because initial investments were more than recouped within a single year. The sometimes wide 95% confidence intervals suggest that the costs and benefits are not always very precise estimates and real benefits could vary considerably.

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TRIAL REGISTRATION: Netherlands Trial Register NTR2108

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study adds to the only few available studies that present a trial-based investment appraisal of the economic costs and benefits of a return to work intervention for sick-listed employees
- The trial was only powered to test a difference in sickness absence duration and not for testing economic hypotheses.
- The follow-up time is limited to 12 months.

INTRODUCTION

Long-term sickness absence has a significant economic impact, largely due to the substantial productivity losses.[1, 2] Mental disorders are a leading cause of sickness absence,[3-6] which is not without economic ramifications.[7] Common mental disorders, specifically depression and anxiety, are the most prevalent in the workforce.[8]

For the treatment of common mental disorders a range of psychological and pharmaceutical interventions have been shown to be effective and cost-effective.[9, 10] However, symptomatic recovery does not automatically reduce sickness absence.[10-12] To improve occupational outcomes it is also important to pay attention to return to work during treatment.

In the Netherlands, treatment and sickness certification are separated from each other in social security legislation. Occupational physicians (OPs) play a central role in the sickness guidance of workers by making a problem analysis and giving advice on a return to work plan, whereas treatment is provided by the mental health sector. The legislation was introduced to protect the worker's privacy and to the possibility for the worker to maintain a confidential relationship with the curative physician.[13, 14] A guideline has been developed to suggest directions to OPs to better assist employees with mental health problems in the return to work process. According to this guideline, the OPs need to closely monitor both the mental health problems and the level of functioning. When recovery is slow or hampered, they can consult or refer to a psychiatrist, a psychologist or a social worker.[15] A study of Rebergen and colleagues suggested that better adherence to the guideline is associated with earlier return to work.[16] However, in practice, adherence appears to be far from optimal,[17, 18] and there is often a lack of cooperation between the OPs and treatment providers in the mental health

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sector. Several attempts have been made to bridge this gap. One study about the effect of psychiatric consultation for OPs assisting sick-listed employees did provide results in terms of earlier return to work.[19] However, this study was small. Another study evaluating active treatment by an OP within a collaborative care arrangement did improve depressive symptoms, but failed to speed up return to work.[20] It appeared that OPs need support in helping sick-listed employees change their attitude towards resuming work and that OPs should monitor symptom improvement and work performance in a more systematic manner.

To overcome these problems and to better manage the return to work of sick-listed employees with (symptoms of) common mental disorders, the "E-health module embedded in Collaborative Occupational health care" (ECO) intervention was developed. The ECO intervention was designed to promote return to work by improving work functioning in employees, providing a decision aid for the OP who gives guidance to the employee, and by including the opportunity for psychiatric consultation to the OP.[21]

The results of a recent trial showed that ECO led to an earlier return to work than usual care (mean duration of 50 days in the ECO group versus 77 days in the CAU group) and higher remission rates of common mental disorder after 9 months in a group of sick-listed employees with (symptoms of) mental disorders.[22]

Taking the economic perspective, we expect that the ECO intervention is cost-effective as seen from the employer's viewpoint, because ECO is a low cost self-help intervention with a limited amount of support from the OP and appears to be effective in reducing absenteeism. There is less certainty how cost-effective the intervention would be as seen from the perspective of the sick-listed employees and the health care financier (i.e. health care insurance company in the Dutch context). Therefore, this study conducts a costs-benefit analysis of the ECO intervention from all three stakeholders' viewpoints, and combines these in an overarching societal perspective. These analyses are important because very few trial-based economic evaluations have been conducted with regard to return-to-work interventions for sick-listed employees with (symptoms of) common mental disorders.[12, 23]

METHOD

Study design

The ECO study was designed as a 2-armed cluster randomised controlled trial, with randomisation at the level of the OP. OPs were either randomised to usual care alone or usual care plus the ECO intervention. The Netherlands Organization for Health Research and Development funded the study (grant number 171002403 ZonMw Doelmatigheid) together

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with Achmea, a Dutch insurance company. The Medical Ethics Committee of the University Medical Center Utrecht approved the study protocol in 2011, and the trial was registered at the Netherlands Trial Register (NTR) under number 2108. The design of the study is described in detail elsewhere.[21, 22] Here, we provide a brief summary of the main characteristics and focus on the economic aspects.

Randomisation

To prevent contamination, cluster randomisation took place at the level of the OPs working in the same region across a total of twelve regions. An independent statistician randomised six regions to the ECO condition and the remainder to the control condition using computer-generated randomisation. Since the OPs had to offer the intervention, they could not be blinded for randomisation. The researchers and participants were informed about the allocation after the randomisation procedure.

Participants

Participants were recruited from July 2011 to January 2013 from all-cause sick-listed employees working at small-sized and medium-sized companies in the Netherlands who visited an OP. To be eligible for inclusion the employees had to be at least 18 years of age and on sickness absence between 4 and 26 weeks. This time window was chosen to avoid including employees with spontaneous recovery and to increase the probability of employees ever returning to work.[24] In addition, the employees needed to have a score ≥10 on either the depression or the somatization scale of the Patient Health Questionnaire (PHQ-9),[25, 26] or the Generalized Anxiety Disorder questionnaire (GAD-7).[27] Exclusion criteria were (1) poor command of the Dutch language, (2) pregnancy, (3) not having access to the Internet, (4) being involved in a legal action against the employer.

Procedure

Initially an independent statistician randomised 12 regions to either CAU (6 regions with 30 OPs) or ECO (6 regions with 32 OPs) by using a computer algorithm. Within the cluster of CAU regions 5,875 sick-listed employees were screened for eligibility resulting in 326 screen-positives. In the cluster of ECO regions, 537 screen-positives were obtained from 8740 sick-listed employees. Of these, 89 consenting participants received sickness guidance from OPs who were randomised to CAU and 131 participants from OPs in the ECO cluster. The unequal distribution of participants over the conditions was due to the cluster randomisation of the OPs. Participants received measurements at baseline and at 3, 6, 9 and 12 months post baseline. Dropout occurred in both conditions (see figure 1).

Figure 1. Flowchart of the participants

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Intervention

ECO consists of 2 components: (1) the eHealth module Return@Work for the employee and (2) an email-based decision-aid to support the OP. Return@Work is aimed at improving the self-efficacy of employees and promoting the employee's intention to return to work. Recent studies have shown that these factors are predictors of actual work resumption.[28-30] The decision-aid provides the OPs with advice regarding treatment and referral options based on the employee's outcome monitoring in Return@Work.

The eHealth module starts with an assessment questionnaire. Depending on the results of the questionnaire regarding symptoms and cognitions about return to work of the individual employee, Return@Work presented specific modules and sessions. As a consequence, the amount of modules and sessions offered to the employees differed. In total, Return@Work included 5 modules composed of 16 sessions, covering: 1) psycho-education, 2) cognitions regarding return to work while having symptoms (based on principles of cognitive behavioural therapy), 3) problem solving skills, 4) pain and fatigue management and reactivation, and 5) relapse prevention. The employees went through the modules independently, but had the possibility to discuss Return@Work modules and assignments with the OP. The OPs were requested to inquire about the employee's progress in the eHealth module and to provide support if necessary during their regular face-to-face contacts with the employee. Periodic visits between the employee and the OP are part of the guidelines of the Dutch Board for Occupational Medicine (NVAB),[15] to which all OPs were required to adhere.

Besides the modules, Return@Work also contained a monitor of functioning and symptoms on a regular basis. This monitor was used for the second component of ECO, a decision aid to support OPs in the sickness guidance of employees. Based on the outcomes of the monitor in Return@Work the OPs received automated email messages with advice for next steps in collaborative care. In addition, the decision aid gave OPs the option to consult a psychiatrist in case insufficient progress was made. The OPs in the experimental condition received a 4-hour training about ECO.

In the control condition the employees received usual sickness guidance. The guidelines of the NVAB were used as a protocol.[15] As there is a lack of adherence to the guidelines,[17,18] actual care was assessed with a questionnaire by all of the participating employees.

Outcome measures

Participants filled in the Medical Technology Assessment Cost Questionnaire for Psychiatry (TiC-P),[31] which amongst health care use also measures absenteeism from work, which is

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the main outcome variable of this study. The TiC-P is based on self-report and to crosscheck the number of work days lost to absenteeism we compared the self-reports with administrative data (see Sensitivity Analysis below). Total follow-up time was 12 months with measurements at baseline and after 3, 6, 9 and 12 months. Finally, health gains in terms of quality adjusted life years (QALYs) were assessed using the EuroQoL-5D-3L,[32] with the Dutch tariff.[33]

Resource use and costing

Cost data were collected using the TiC-P, including (1) direct medical costs, including the costs of medication, (2) direct non-medical costs (patients' out-of-pocket costs for trips to health services), (3) costs stemming from productivity losses owing to absenteeism and presenteeism, and (4) costs that occurred in the domestic realm (help for housekeeping from family, friends or hired people). Standard costs, expressed in euro (€), were indexed for the reference year 2011 using the consumer price index from Statistics Netherlands. Costs were not discounted because the follow-up period did not exceed one year.

Computation of costs

The set costs of the ECO intervention are €300 per user, which is its current (post trial) rate. Direct medical costs are limited to mental health service use. The medical costs were computed by multiplying the number of health service units (sessions, visits, hospital days) with their standard full economic cost price.[34] Only medication costs for mental problems were included in the economic analysis. For every type of drug (e.g. antidepressants, benzodiazepines, antipsychotics, hypnotics) an average cost price was calculated based on the cost prices per standard daily dose of three drugs most often prescribed to the participants as reported in the Pharmaceutical Compass,[35] while taking into account the GP's prescription costs, the pharmacist's dispensing costs and the pharmacist's claw back as per the guideline for cost computations in health care.[34]

The direct non-medical costs consisted of the travel costs that participants had to make to visit OPs and health services. These costs were calculated as the average distance to the specific health service provider multiplied by the costs per km (€0.21) plus parking costs (€3.11) per hour. To the direct non-medical costs we added the costs of (informal) caregivers (e.g. family and friends) due to the employee's reduced functionality at home, computed by multiplying the number of hours by €12.96.

In the Netherlands QALY health gains are valued at €50,000 per QALY with a range between €20,000 and €80,000.[36] We used the lower bound of €20,000 to conduct our analysis under conservative assumptions.

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Productivity losses comprised the costs of lost workdays due to absenteeism and the costs of inefficiency while at work (presenteeism). We used the human capital method to value the productivity costs.[37] In the case of absenteeism, this method multiplies the number of days absent by the gender and age-specific average gross wages per employee, as per the Dutch guideline for health economic evaluation.[34] To assess the costs of presenteeism we used the number of days actually worked when ill multiplied by a self-reported inefficiency score. This score ranged from 0 (as effective as in good health) to 1 (totally ineffective). Again, the gender and age-specific average gross wages were used to compute the costs of presenteeism. To illustrate, if an employee reported and inefficiency score of 0.50 for 7 working days then we assumed that 3.5 working days have been lost due to presenteeism.

Analyses

Following recommendations from the CONSORT and CHEERS statements,[38-40] analyses were conducted in agreement with the intention to treat principle. Therefore all participants as randomised were retained in the analysis and missing observations due to dropout were imputed. For imputation we used both the estimation-maximisation (EM) algorithm as implemented in SPSS for the main analysis, and regression imputation (RI) as implemented in Stata for the sensitivity analysis (see below). In both imputation strategies we used predictors of outcomes (costs and QALYs) and predictors of dropout (age, gender, partner status, country of birth, number of work loss days). Predictors of the outcomes were included to increase precision in the imputed values, predictors of dropout were incorporated to tackle selection-bias, if any, and to meet the missing at random (MAR) assumption underlying most imputation techniques.

The economic evaluation was conducted as an incremental cost-benefit analysis, because the primary outcome (duration of sick leave) could directly be expressed in terms of monetary benefits. The costs and benefits were calculated at baseline, 3, 6, 9 and 12 months in the ECO and CAU conditions. The costs in the intermediate months were linearly interpolated. This allowed mapping the monthly cash flows of costs and benefits over the full 12-month period. The cash flows were computed from four perspectives: (1) the employer's perspective focussing on the net-benefits from greater productivity via lesser absenteeism and lesser presenteeism; (2) the health care payer's perspective (in the Netherlands: health care insurers) focussing on the direct medical costs due to health service use, including the costs of medication, (3) the employee's perspective focussing on QALY health gains, fewer out-of-pockets costs and less informal care from family members or friends. Finally, we included the societal perspective (4), including all costs and benefits, regardless of who incurs costs or receives benefits.

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The monthly cash flows were used to compute the cumulative costs and cumulative monetary benefits over the full twelve months. Incremental costs, incremental benefits and incremental net-benefits were obtained by comparing ECO intervention with CAU. These are the main outcomes of the economic analysis alongside metrics such as the break-even point and the return on investment (ROI).

For assessing the incremental net-benefits we relied on non-parametric bootstrapping (2,500 replications) since costs are non-normally distributed. Statistics such as mean costs, 95% confidence intervals, standard errors and p-values are all based on non-parametric bootstrapping to increase the robustness of our findings. The data were analysed in SPSS (version 22) and Stata (version 13.1).

Sensitivity analysis

The main analysis (using the overarching societal perspective and based on EM imputation) was repeated three times in a series of sensitivity analyses. Firstly, the analysis was conducted again, but now based on regression imputation (RI) to assess the robustness of the findings under a different imputation technique. Secondly, we crosschecked the self-reported absenteeism against administrative data derived from the registers of the occupational health service or the employer, because the main analysis was based on self-reports and some recall bias (underreporting) could have occurred. Finally, we recalculated the incremental net-benefits after trimming the highest 5% of total cumulative costs per employee, because the participants with the extremely high costs were only a small minority but may have exercised a disproportional influence on the cost estimates and pushed outcomes to a more favourable outcomes for the ECO intervention. By excluding these participants, primarily from the CAU condition, the net-benefits were re-estimated but now under conservative assumptions.

RESULTS

Sample characteristics and baseline costs

Baseline characteristics of the sample (including baseline costs) are presented in table 1. The mean age of the 220 participants was 44 years and 59% was women. No important differences were observed at baseline in demographic characteristics and quality of life, but baseline costs were somewhat higher in the ECO condition, suggesting that the ECO group had a slightly disadvantageous start. We will return to this issue in the Discussion. As described by Volker and colleagues,[22] job characteristics and sickness absence duration at baseline were also comparable between the intervention condition and control condition, indicating that the randomisation was generally well balanced.

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Table 1. Baseline characteristics in the care as usual (CAU) and the ECO intervention group

	CAU (n=89)	ECO (n=131)
Age, mean (SD)	45.5 (10.7)	43.3 (9.5)
Female, N (%)	53 (59.6)	77 (58.8)
Married/living together, N (%)	62 (69.7)	91 (69.5)
Educational level, N (%)		
Low	32 (36.0)	48 (36.6)
Average	31 (34.8)	47 (35.9)
High	26 (29.2)	36 (27.5)
Country of birth: The Netherlands, N (%)	83 (93.3)	123 (93.9)
Direct medical costs, mean (SD)	645 (58)	602 (49)
Direct non-medical costs, mean (SD)	35 (2)	33 (2)
Absenteeism, mean (SD)	2850 (146)	3078 (125)
Presenteeism, mean (SD)	34 (16)	20 (14)
Costs in the domestic realm, mean (SD)	143 (26)	133 (20)
Medication, mean (SD)	8 (2)	12 (3)
Total costs, mean (SD)	3716 (154)	3879 (141)
Quality of life, mean (SD)	0.57 (0.027)	0.54 (0.024)

Loss to follow-up

The measurements at 3, 6, 9 and 12 months were completed by 155 (70.5%), 157 (71.4%), 134 (60.9%) and 128 (58.2%) of the participants. The dropout rate over the 12-month trial period was higher in the ECO condition (45.0%) than the control condition (37.1%), but this difference was not statistically significant (χ^2=1.38; df=1; p=0.240). As indicated, we looked for variables that predict dropout and included these as predictors in the EM and IR imputations. This was done to counter selection-bias (if any) and to better meet the MAR assumption underpinning the imputation strategies.

On the topic of treatment adherence, 90 of the 131 participants in the ECO condition (69%) finished the introduction and started with the intervention. These participants had a mean-number of total log-ins of 7.8. Forty percent (36/90) completed at least half of the modules.[22]

Costs and QALYs at 3, 6, 9 and 12 months

The next step of the cost benefit analyses was to ascertain costs and quality of life at the follow-up measurements (Table 2). Cost differences were highest for absenteeism. At 12 months all the cost differences were statistically significant and in favour of the ECO condition.

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The total costs difference at the 12 month follow-up amounted to €919 (SE=205; z=4.48; p<0.001), mainly due to reduced absenteeism.

Table 2. Average monthly costs in the care as usual (CAU) and the ECO intervention group at 3, 6, 9 and months (in 2011 Euro)[1, 2]

	3 months	6 months	9 months	12 months
Direct medical costs				
CAU	474	298	383	296
ECO	460	473	311	144
Cost difference	14	-175	71	*153*
Direct non-medical costs				
CAU	135	74	102	98
ECO	104	89	67	45
Cost difference	31	-15	35	*53*
Productivity losses				
Absenteeism				
CAU	2120	1699	1276	1118
ECO	1887	1264	725	572
Cost difference	233	435	*551*	*546*
Presenteeism				
CAU	166	233	269	493
ECO	357	408	322	325
Cost difference	*-191*	*-175*	-53	*168*
Total costs				
CAU	2895	2305	2029	2005
ECO	2808	2234	1425	1085
Cost difference	87	70	*605*	*919*
Quality of life (utility)				
CAU	0.65	0.68	0.68	0.73
ECO	0.65	0.72	0.76	0.77
Difference in utilities	0	0.04	*0.08*	0.04

1 Between-group differences in italics are statistically significant at p<0.05.

2 Numbers may not add due to rounding

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Cost-benefit analysis: employer's perspective

For the employer's perspective only the intervention costs and costs stemming from absenteeism and presenteeism were included, thus assuming that the employer would be interested to know the pay out of this investment when paying for the intervention. Cumulated over the 12-months period the incremental benefits were €3,487 in favour of the ECO condition (Bootstrapped 95% CI= -418~7,390; SE=1,992; z=1.75; p=0.080), which was mainly due to a larger reduction in absenteeism over 12 months compared to care as usual (bootstrapped M=4,291; 95% CI= 290~8,292; SE=2,041; z=2.10; p=0.036). Next, we calculated incremental net-benefits, by subtracting the intervention costs (€300) from the incremental benefits. As shown in table 3 the incremental net-benefits over twelve months were €3,187 per employee in favour of the ECO condition, but there is significant uncertainty in the estimate (Bootstrapped 95% CI=-656~7,029; SE=1,961; z=1.63; p=0.104). We return to this issue in the Discussion. The break-even point for the employer, the moment in time where the investment of €300 is recouped, is around six months. The return of investment (ROI) is 3,187/300=10.62, indicating that for every euro invested the pay-out is €10.6.

Table 3. Monthly per patient costs in the care as usual (CAU) and the ECO intervention group from an employer's perspective (in 2011 Euro)

Month	1	2	3	4	5	6	7	8	9	10	11	12	Cumulative
CAU													
Absenteeism	2850	2485	2120	1910	1910	1699	1487	1487	1276	1197	1197	1118	20736
Presenteeism	34	100	166	199	199	233	251	251	269	380	380	493	2955
Total costs	2884	2585	2286	2109	2109	1932	1738	1738	1545	1577	1577	1611	23691
ECO													
Absenteeism	3078	2483	1887	1576	1576	1264	994	994	725	648	648	572	16445
Presenteeism	20	188	357	382	382	408	365	365	322	323	323	325	3760
Total costs	3098	2671	2244	1958	1958	1672	1359	1359	1047	971	971	897	20205
Incremental benefits	-214	-86	42	151	151	260	379	379	498	606	606	714	3486
Intervention costs	-300												
Incremental net-benefits	-514	-600	-558	-407	-256	4	383	762	1260	1866	2472	3186	
Return on investment	10.6												

Cost-benefit analysis: health care payer's perspective

For the perspective of the health care financier we looked at the direct medical costs including the costs for medication. We computed the monthly cash flows and compared these between the ECO and CAU conditions as before. The cumulative costs over twelve months were more or less the same for each condition with a small difference of €87 in favour of the ECO condition. Assuming that the health insurer would pay for the intervention, the intervention costs of €300

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have to be subtracted from these benefits in order to obtain the net-benefits. This generated a negative value of €213, implying that the ECO intervention is not cost saving from a health care insurer's perspective (bootstrapped 95% CI=-1,384~959; SE=598; z=-0.36; p=0.722).

Cost-benefit analysis: employee's perspective

Employee's costs and benefits included direct non-medical costs (i.e. the patient's out-of-pocket costs and costs in the domestic realm) and QALY health gains. Cumulated over twelve months the incremental benefits for the ECO group were €263 regarding non-medical costs and €696 due to QALY gains (0.035*€20,000). The incremental net-benefits were €959-€300= 659 (bootstrapped 95% CI=287~1,031; SE=190; z=3.47; p=0.001). The break-even point occurred at eight months and the return on investment was 659/300=2.2.

Cost-benefit analysis: societal perspective

For the societal perspective we included the costs and benefits of all stakeholders. The difference between conditions of the cumulative benefits was €29,823-€25,290=€4,533 in favour of the intervention condition (bootstrapped 95% CI= 141~8,925; SE=2,241; z=2.02 p=0.043). Subtraction of the intervention costs of €300 yielded incremental net-benefits from a social perspective of €4,233 (bootstrapped 95% CI= -194~8,660; SE=2,259; z=1.87; p=0.061). Break-even was achieved at seven months and the return on investment was 4,233/300= 14.1.

Sensitivity analyses

For the main analysis we used EM imputation; now we recomputed the estimates under regression imputation (RI). Taking the societal perspective, the incremental net-benefits became €4,093 (Bootstrapped 95% CI= -279~8,465; SE=2,231; z=1.83; p=0.067) and the return on investment 4,093/300=13.6, which is close to the EM-based analysis (see table 4).

The incremental net-benefits in the main analyses were dominated by the costs offsets due to reduced absenteeism, but these were based on self-reported data. Crosschecking the self-reported data against administrative data derived from the registers of the occupational health service or employer showed that the estimates for days absent were lower in the analysis based on self-report data than on administrative data (72 work days absent based on self-reported data versus an average of 101 work days absent based on administrative data). When basing the analysis on administrative data, the total cumulative incremental net-benefits became €6,154 (Bootstrapped 95% CI=-3,352~15,660; SE=4,850; z=1.27; p=0.205), which is higher by a factor 1.5 than the corresponding estimate presented in the main analysis. The main analysis thus represents a safer (lower) estimate.

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Finally, we repeated the main analysis by replacing the total costs of the respondents with the top 5% highest total costs due to absenteeism by the highest amount witnessed in the other 95% respondents. The top 5% outliers were mainly situated in the CAU condition, raising the average costs for this group. The incremental net-benefits based on the trimmed costs dropped from €4,233 to €3,613 (SE 95% CI= -491~7,718; SE=2,094; z=1.73; p=0.084), which can be regarded as a more conservative lower bound.

Table 4. Incremental net-benefit and return on investment from societal perspective for base case and sensitivity analyses (in 2011 Euro)

	Incremental net-benefit	Return on investment
Base case analysis	4,233 (-194 to 8,660)	14.1
sensitivity analysis regression imputation	4,093 (-279 to 8,465)	13.6
sensitivity analysis administrative data	6,154 (-3.352 to 15,660)	20.5
sensitivity analysis trimming highest 5%	3,613 (-491 to 7,718)	12.0

DISCUSSION

Principal findings

This study was set out to evaluate the cost-effectiveness of an intervention that encourages sick-listed employees with (symptoms of) common mental disorders to make an early return to their work. The economic evaluation was conducted as an incremental cost-benefit analysis and reports on the incremental cost to benefit ratio, the return on investment, the break-even point, and the incremental monetary net-benefits, as customary seen in business cases and investment appraisals. These metrics were computed from various perspectives: the perspective of the employer, the employee, the health care financier and society. The main findings can now be summarised as follows:

- Taking the employer's perspective, the focus of the economic evaluation was placed on the intervention costs and changes in productivity owing to changes in absenteeism and presenteeism. Assuming that the employer would make the investment in the ECO intervention of €300 per employee, the incremental net-benefits were €3,187 per employee over a year. This was equivalent to a return on investment of €11 per invested Euro. Benefits largely stemmed from reduced absenteeism and exceeded the investment costs after six months.
- From the perspective of the health care payer the incremental net-benefits were negative, amounting to additional costs of €213 per employee on average.

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- As seen from the employee the net-benefits exceeded the costs by €659 when also valuing the employee's QALY health gains. When excluding the QALY benefits, the incremental net-benefits were slightly negative (€37).
- From the societal perspective, the initial investment was also more than recouped. Considering all costs and benefits, but ignoring the value of QALY gains, the incremental net-benefits were €4,233, with a break-even point at 7 months. Every euro invested yielded €14. Trimming the 5% highest costs, mostly from the care as usual condition, reduced the incremental net-benefits to €3,613.

Limitations

This study has several limitations, which are reported and discussed here.

- First, cost data are often non-normally distributed with a some people generating very high costs. This results in large standard deviations in the costs estimates and less precise estimates of average costs. In such a context it would require a very large sample size to power the trial for testing economic hypotheses. However, our study was only powered to test a difference in sickness absence duration. As a consequence, the wide 95% confidence intervals indicate that the cost estimates are subject to much uncertainty. More specifically, when trimming the highest 5% of the costs in one of our sensitivity analysis showed that the incremental net-benefits became €3,613, which is 85% of the original estimate of €4,233. This suggests that our study needs replication, preferably in a larger study.
- Second, loss-to follow up was substantial. To handle dropout, missing data were imputed using estimation maximization (EM). To ascertain the robustness of our findings we also used regression imputation (RI). With RI we arrived at similar conclusions: €4,093 (versus €4,233 under EM), attesting to the robustness in our findings. Nonetheless, selection bias introduced by (selective) dropout cannot be ruled out completely and could have influenced the outcomes that we obtained.
- Third, costs at baseline were higher in the ECO condition. We could have adjusted for the baseline differences, but this would have led to even better outcomes in favour of the ECO condition. Ignoring the baseline differences has therefore put our main analyses on a more conservative footing.
- Fourth, the main driver of costs and benefits was absenteeism and in the main analysis these were based on self-report. This may have introduced some recall bias, but self-reports of absenteeism usually involve underreporting thus leading to conservative outcomes. Still, we crosschecked the self-reports against administrative data from the registers of the occupational health service and the employer. As expected, the benefits were lower when based on self-reports than on administrative data.
- Fifth, it should be noted that the cost-benefit analysis did not include the future costs of implementing the ECO intervention on a wider scale. As the main component is a low cost

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self-help intervention (Return@Work) and the training of OPs only lasts a few hours, the implementation costs are expected to be low, but should be considered when the intervention is disseminated on a wider scale.

- Finally, the follow-up time is limited to 12 months. We do not know what the net-benefits would be over a longer time span. However, costs differences were highest in the last months. This may imply that a longer follow-up period would have seen more profitable outcomes.

Results in context

Reviews about the effectiveness of psychological return to work interventions for employees with mental health problems show mixed outcomes in reducing sickness absence and promoting an earlier return to work.[12, 23] Moreover, only a few of the reviewed studies that appeared to be effective report a full economic evaluation. Of these, none evaluated a guided eHealth intervention for return to work. One study that is somewhat comparable with our study is from Schene and colleagues. Schene et al describe the economic evaluation of an intervention for employees with major depression, who were sick-listed between 10 weeks and 2 years.[41] The experimental condition received occupational therapy in addition to usual outpatient treatment for depression. Their intervention increased the number of hours worked accumulating in a median economic gain of US$4000–5000 per patient per year, which is in line with our findings regarding the reduction in absenteeism. The study of Schene et al was smaller (n=62), was directed at a more severely depressed population, and the intervention was not delivered online but as an intensive face-to-face therapy consisting of 24 group sessions and 15 individual sessions.

Lerner and colleagues evaluated a brief telephonic program to improve work functioning for employees with major depressive disorder or dysthymia with an at-work productivity loss of at least 5% in the past two weeks.[42] Compared to usual care, annualised cost savings averaged at $6042 per participant but these savings were extrapolated from a shorter (4 months) follow-up. These cost savings are higher than the cost-savings observed in our study. Nonetheless, Lerner's et al. extrapolation from 4 to 12 months might have overstated the savings if the treatment effect was not sustained.

Arends and colleagues evaluated the costs and benefits of a problem-solving intervention provided by OPs to prevent recurrent sickness absence in workers with common mental disorders.[43] Compared to care as usual the intervention was more effective but also more expensive. From an employer's perspective the intervention showed no economic benefits, which is in contrast to our study.

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Noben and colleagues conducted a cost-benefit analysis from the employer's perspective of a preventive intervention in the work setting among nurses with an elevated-risk of mental complaints.[44] The authors concluded that the intervention was a good investment as the net-benefits (stemming from reduced absenteeism and presenteeism) were positive (€651) and the return on investment was €11 per Euro spent. This return on investment is comparable with ours.

In contrast to Noben and colleagues and several other studies [45] we found negative results for presenteeism in the short run (first nine months), but these were alleviated in the longer run (at the end of the year). An explanation for the initially negative results on presenteeism might be that employees who returned to work early were not completely fit and as productive as normally. In other words there was an initial trade-off between reduced absenteeism and increased presenteeism. However, after the first nine months the additional costs caused by presenteeism ceased to exist and were reversed into benefits. This change is possibly driven by an improvement in quality of life when people work.

The literature suggests that in terms of economic costs presenteeism often is a larger problem than absenteeism. Our results are not in line with these findings. This could be due to the Dutch system in which employees receive a substantial percentage of their wage during the first two years of their illness. In many other countries the fall in income is more acute when employees stay absent from their work, increasing the incentive to keep on working – even when work is then associated with greater levels of presenteeism.

The results of our study can only be generalised to employees who have been sick-listed for 4-26 weeks, working in small- to medium-sized companies.

Conclusions and implications

In the Netherlands, employers have an incentive to invest in sickness management as they have the responsibility to pay 70-100% of the salary of sick-listed employees for up to two years. Employees who are on sickness absence have to visit an occupational physician, paid by the employer within the first six weeks. Both the employee and employer have to agree on an action plan. In this plan the responsibilities of both parties are defined to ensure a quick return to work of the employee. In this context the ECO-intervention can be seen as an effective intervention that, in addition, has a high probability of offering good value for money because the initial investment (of €300) is more than recouped within a single year as seen from the employer's perspective, while the employee derives benefits in the form of increased quality of life when returning to work sooner rather than later. As noted, some 95% confidence intervals of our estimates are wide. By implication, one should not rely too much on the point estimates

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of net-benefits, return on investment ratios, break-even points, because they lack precision. In other words, our estimates, although conservative, have some degree of uncertainty and are therefore no substitute for one's own business judgement.

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Contributors

CFC initiated the collaborative clinical trial project. MZV, AB and CFC contributed to the design of the study and obtained the funding. DV, MZV and CFC were responsible for the acquisition of the data. SL and FS conducted the statistical analysis and drafted the manuscript, which all authors critically revised. All authors read and approved the final manuscript. SL, FS and CFC are guarantors.

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: financial support for the submitted work from The Netherlands Organisation for Health Research and Development (ZonMw) and from Achmea SZ; SL, DV, MZV, BB, FS report personal fees from employment at the Trimbos institute, the Netherlands institute of mental health and addiction, a not-for-profit organisation, CFC has received research grants from Eli Lilly outside the submitted work.

Ethical approval

The study protocol was approved by the Medical Ethics Committee of the University Medical Center Utrecht, The Netherlands, in February 2011. All participants provided written informed consent before taking part.

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The lead author affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that and discrepancies from the study as planned (and if relevant, registered) have been explained.

Data sharing: No additional data

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Legends of figures

Figure 1. Flowchart of the clusters and participants

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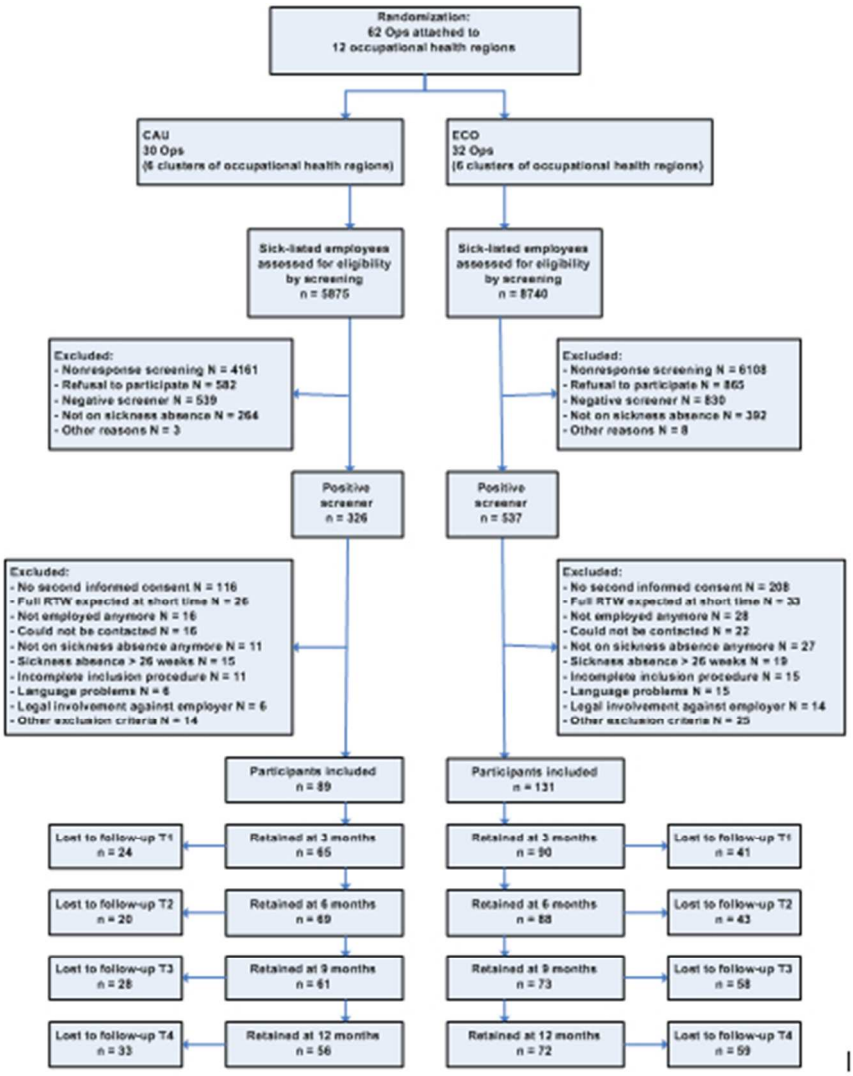

Flowchart of the participants

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	3
	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	4,5
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	5
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	5
	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	6
	4b	Settings and locations where the data were collected		6
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	7
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	7/8

		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	N/A
	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		6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	5/6
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	5/6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	6
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete	

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			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	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		6
	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	9/10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		10
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	6/10/11
	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	10/11
Recruitment	14a	Dates defining the periods of recruitment and follow-up		**6**
	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	Table 1

		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	6/9
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	11-15
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		14/15
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		16/17
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	17
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		17-19
Other information				
Registration	23	Registration number and		5/6

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

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

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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.

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CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

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.	3
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
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	4,5
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	6
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	6
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	9
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	7
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	8
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	8
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.	8/9
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.	5-7

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	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.	7,8
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate 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.	N.A.
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.	8
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.	9,10
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.	10-15
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.	10-15
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	12-14

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		of methodological assumptions (such as discount rate, study perspective).	
	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.	15-19
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	19
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.	19

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

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

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Return-to-work intervention versus usual care for sick-listed employees: health-economic investment appraisal alongside a cluster randomised trial

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TITLE PAGE

Return-to-work intervention versus usual care for sick-listed employees: health-economic investment appraisal alongside a cluster randomised trial

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Return-to-work intervention versus usual care for sick-listed employees: health-economic investment appraisal alongside a cluster randomised trial

ABSTRACT

OBJECTIVE: To evaluate the health-economic costs and benefits of a guided eHealth intervention (ECO) encouraging sick-listed employees to a faster return to work.

DESIGN: A 2-armed cluster randomised trial with occupational physicians (OPs) (n=62), clustered and randomised by region into an experimental and a control group, to conduct a health-economic investment appraisal. Online self-reported data were collected from employees at baseline, after 3, 6, 9 and 12 months.

SETTINGS: Occupational health care in the Netherlands.

PARTICIPANTS: Employees from small-sized and medium-sized companies (≥18 years), sick-listed between 4 and 26 weeks with (symptoms of) common mental disorders visiting their OP.

INTERVENTIONS: In the intervention group, employees (N=131) received an eHealth module aimed at changing cognitions regarding return to work, while OPs were supported by a decision aid for treatment and referral options. Employees in the control condition (N=89) received usual sickness guidance.

OUTCOMES MEASURES: Net-benefits and return on investment based on absenteeism, presenteeism, health care use, and quality adjusted life years (QALYs) gained.

RESULTS: From the employer's perspective, the incremental net-benefits were €3,187 per employee over a single year, representing a return of investment of €11 per invested Euro, with a break-even point at six months. The economic case was also favourable from the employee's perspective, partly because of QALY health gains. The intervention was costing €234 per employee from a health service financier's perspective. The incremental net-benefits from a social perspective were €4,210. This amount dropped to €3,559 in the sensitivity analysis trimming the 5% highest costs.

CONCLUSIONS: The data suggest that the ECO intervention offers good value for money for virtually all stakeholders involved, because initial investments were more than recouped within a single year. The sometimes wide 95% confidence intervals suggest that the costs and benefits are not always very precise estimates and real benefits could vary considerably.

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TRIAL REGISTRATION: Netherlands Trial Register NTR2108

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study adds to the few available studies that present a trial-based investment appraisal of the economic costs and benefits of a return to work intervention for sick-listed employees
- The trial was only powered to test a difference in sickness absence duration and not for testing economic hypotheses.
- The follow-up time is limited to 12 months.

INTRODUCTION

Long-term sickness absence has a significant economic impact, largely due to the substantial productivity losses.[1, 2] Mental disorders are a leading cause of sickness absence,[3-6] which is not without economic ramifications.[7] Common mental disorders, specifically depression and anxiety, are the most prevalent in the workforce.[8]

For the treatment of common mental disorders a range of psychological and pharmaceutical interventions have been shown to be effective and cost-effective.[9, 10] However, symptomatic recovery does not automatically reduce sickness absence.[10-12] To improve occupational outcomes it is also important to pay attention to return to work during treatment.

In the Netherlands, treatment and sickness certification are separated from each other in social security legislation. Occupational physicians (OPs) play a central role in the sickness guidance of workers by making a problem analysis and giving advice on a return to work plan, whereas treatment is provided by the mental health sector. The legislation was introduced to protect the worker's privacy and to the possibility for the worker to maintain a confidential relationship with the curative physician.[13, 14] A guideline has been developed to suggest directions to OPs to better assist employees with mental health problems in the return to work process. According to this guideline, the OPs need to closely monitor both the mental health problems and the level of functioning. When recovery is slow or hampered, they can consult or refer to a psychiatrist, a psychologist or a social worker.[15] A study of Rebergen and colleagues suggested that better adherence to the guideline is associated with earlier return to work.[16] However, in practice, adherence appears to be far from optimal,[17, 18] and there is often a lack of cooperation between the OPs and treatment providers in the mental health

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sector. Several attempts have been made to bridge this gap. One study about the effect of psychiatric consultation for OPs assisting sick-listed employees did provide results in terms of earlier return to work.[19] However, this study was small. Another study evaluating active treatment by an OP within a collaborative care arrangement did improve depressive symptoms, but failed to speed up return to work.[20] It appeared that OPs need support in helping sick-listed employees change their attitude towards resuming work and that OPs should monitor symptom improvement and work performance in a more systematic manner.

To overcome these problems and to better manage the return to work of sick-listed employees with (symptoms of) common mental disorders, the "E-health module embedded in Collaborative Occupational health care" (ECO) intervention was developed. The ECO intervention was designed to promote return to work by improving work functioning in employees, providing a decision aid for the OP who gives guidance to the employee, and by including the opportunity for psychiatric consultation to the OP.[21]

The results of a recent trial showed that ECO led to an earlier return to work than usual care (mean duration of 50 days in the ECO group versus 77 days in the CAU group) and higher remission rates of common mental disorder after 9 months in a group of sick-listed employees with (symptoms of) mental disorders.[22]

Taking the economic perspective, we expect that the ECO intervention is cost-effective as seen from the employer's viewpoint, because ECO is a low cost self-help intervention with a limited amount of support from the OP and appears to be effective in reducing absenteeism. There is less certainty how cost-effective the intervention would be as seen from the perspective of the sick-listed employees and the health care financier (i.e. health care insurance company in the Dutch context). Therefore, this study conducts a costs-benefit analysis of the ECO intervention from all three stakeholders' viewpoints, and combines these in an overarching societal perspective. These analyses are important because very few trial-based economic evaluations have been conducted with regard to return-to-work interventions for sick-listed employees with (symptoms of) common mental disorders.[12, 23]

METHOD

Study design

The ECO study was designed as a 2-armed cluster randomised controlled trial, with randomisation at the level of the OP. OPs were either randomised to usual care alone or usual care plus the ECO intervention. The Netherlands Organization for Health Research and Development funded the study (grant number 171002403 ZonMw Doelmatigheid) together

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with Achmea, a Dutch insurance company. The Medical Ethics Committee of the University Medical Center Utrecht approved the study protocol in 2011, and the trial was registered at the Netherlands Trial Register (NTR) under number 2108. The design of the study is described in detail elsewhere.[21, 22] Here, we provide a brief summary of the main characteristics and focus on the economic aspects.

Randomisation

To prevent contamination, cluster randomisation took place at the area level of the OPs working in the same region across a total of twelve regions. An independent statistician randomised six regions to the ECO condition and the remainder to the control condition using computer-generated randomisation. Since the OPs had to offer the intervention, they could not be blinded for randomisation. The researchers and participants were informed about the allocation after the randomisation procedure.

Participants

Participants were recruited from July 2011 to January 2013 from all-cause sick-listed employees working at small-sized and medium-sized companies in the Netherlands who visited an OP. To be eligible for inclusion the employees had to be at least 18 years of age and on sickness absence between 4 and 26 weeks. This time window was chosen to avoid including employees with spontaneous recovery and to increase the probability of employees ever returning to work.[24] In addition, the employees needed to have a score ≥10 on either the depression or the somatization scale of the Patient Health Questionnaire (PHQ-9),[25, 26] or the Generalized Anxiety Disorder questionnaire (GAD-7).[27] Exclusion criteria were (1) poor command of the Dutch language, (2) pregnancy, (3) not having access to the Internet, (4) being involved in a legal action against the employer.

Procedure

Initially an independent statistician randomised 12 regions to either CAU (6 regions with 30 OPs) or ECO (6 regions with 32 OPs) by using a computer algorithm. Within the cluster of CAU regions 5,875 sick-listed employees were screened for eligibility resulting in 326 screen-positives. In the cluster of ECO regions, 537 screen-positives were obtained from 8740 sick-listed employees. Of these, 89 consenting participants received sickness guidance from OPs who were randomised to CAU and 131 participants from OPs in the ECO cluster. The unequal distribution of participants over the conditions was due to the cluster randomisation of the OPs. Participants received measurements at baseline and at 3, 6, 9 and 12 months post baseline. Dropout occurred in both conditions (see figure 1).

Figure 1. Flowchart of the participants

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Intervention

ECO consists of 2 components: (1) the eHealth module Return@Work for the employee and (2) an email-based decision-aid to support the OP. Return@Work is aimed at improving the self-efficacy of employees and promoting the employee's intention to return to work. Recent studies have shown that these factors are predictors of actual work resumption.[28-30] The decision-aid provides the OPs with advice regarding treatment and referral options based on the employee's outcome monitoring in Return@Work.

The eHealth module starts with an assessment questionnaire. Depending on the results of the questionnaire regarding symptoms and cognitions about return to work of the individual employee, Return@Work presented specific modules and sessions. As a consequence, the amount of modules and sessions offered to the employees differed. In total, Return@Work included 5 modules composed of 16 sessions, covering: 1) psycho-education, 2) cognitions regarding return to work while having symptoms (based on principles of cognitive behavioural therapy), 3) problem solving skills, 4) pain and fatigue management and reactivation, and 5) relapse prevention. The employees went through the modules independently, but had the possibility to discuss Return@Work modules and assignments with the OP. The OPs were requested to inquire about the employee's progress in the eHealth module and to provide support if necessary during their regular face-to-face contacts with the employee. Periodic visits between the employee and the OP are part of the guidelines of the Dutch Board for Occupational Medicine (NVAB),[15] to which all OPs were required to adhere.

Besides the modules, Return@Work also contained a monitor of functioning and symptoms on a regular basis. This monitor was used for the second component of ECO, a decision aid to support OPs in the sickness guidance of employees. Based on the outcomes of the monitor in Return@Work the OPs received automated email messages with advice for next steps in collaborative care. In addition, the decision aid gave OPs the option to consult a psychiatrist in case insufficient progress was made. The OPs in the experimental condition received a 4-hour training about ECO.

In the control condition the employees received usual sickness guidance. The guidelines of the NVAB were used as a protocol.[15] As there is a lack of adherence to the guidelines,[17,18] actual care was assessed with a questionnaire by all of the participating employees.

Outcome measures

Participants filled in the Medical Technology Assessment Cost Questionnaire for Psychiatry (TiC-P),[31] which amongst health care use also measures absenteeism from work, which is

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the main outcome variable of this study. The TiC-P is based on self-report and to crosscheck the number of work days lost to absenteeism we compared the self-reports with administrative data (see Sensitivity Analysis below). Total follow-up time was 12 months with measurements at baseline and after 3, 6, 9 and 12 months. Finally, health gains in terms of quality adjusted life years (QALYs) were assessed using the EuroQoL-5D-3L,[32] with the Dutch tariff.[33]

Resource use and costing

Cost data were collected using the TiC-P, including (1) direct medical costs, including the costs of medication, (2) direct non-medical costs (patients' out-of-pocket costs for trips to health services), (3) costs stemming from productivity losses owing to absenteeism and presenteeism, and (4) costs that occurred in the domestic realm (help for housekeeping from family, friends or hired people). Standard costs, expressed in euro (€), were indexed for the reference year 2011 using the consumer price index from Statistics Netherlands. Costs were not discounted because the follow-up period did not exceed one year.

Computation of costs

The set costs of the ECO intervention are €300 per user, which is its current (post trial) rate. Direct medical costs are limited to mental health service use. The medical costs were computed by multiplying the number of health service units (sessions, visits, hospital days) with their standard full economic cost price.[34] Only medication costs for mental problems were included in the economic analysis. For every type of drug (e.g. antidepressants, benzodiazepines, antipsychotics, hypnotics) an average cost price was calculated based on the cost prices per standard daily dose of three drugs most often prescribed to the participants as reported in the Pharmaceutical Compass,[35] while taking into account the GP's prescription costs, the pharmacist's dispensing costs and the pharmacist's claw back as per the guideline for cost computations in health care.[34]

The direct non-medical costs consisted of the travel costs that participants had to make to visit OPs and health services. These costs were calculated as the average distance to the specific health service provider multiplied by the costs per km (€0.21) plus parking costs (€3.11) per hour. To the direct non-medical costs we added the costs of (informal) caregivers (e.g. family and friends) due to the employee's reduced functionality at home, computed by multiplying the number of hours by €12.96.

In the Netherlands QALY health gains are valued at €50,000 per QALY with a range between €20,000 and €80,000.[36] We used the lower bound of €20,000 to conduct our analysis under conservative assumptions.

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Productivity losses comprised the costs of lost workdays due to absenteeism and the costs of inefficiency while at work (presenteeism). We used the human capital method to value the productivity costs.[37] In the case of absenteeism, this method multiplies the number of days absent by the gender and age-specific average gross wages per employee, as per the Dutch guideline for health economic evaluation.[34] To assess the costs of presenteeism we used the number of days actually worked when ill multiplied by a self-reported inefficiency score. This score ranged from 0 (as effective as in good health) to 1 (totally ineffective). Again, the gender and age-specific average gross wages were used to compute the costs of presenteeism. To illustrate, if an employee reported and inefficiency score of 0.50 for 7 working days then we assumed that 3.5 working days have been lost due to presenteeism.

Analyses

Following recommendations from the CONSORT and CHEERS statements,[38-40] analyses were conducted in agreement with the intention to treat principle. Therefore all participants as randomised were retained in the analysis and missing observations due to dropout were imputed. For imputation we used both the estimation-maximisation (EM) algorithm as implemented in SPSS for the main analysis, and regression imputation (RI) as implemented in Stata for the sensitivity analysis (see below). In both imputation strategies we used predictors of outcomes (costs and QALYs) and predictors of dropout (age, gender, partner status, country of birth, number of work loss days). Predictors of the outcomes were included to increase precision in the imputed values, predictors of dropout were incorporated to tackle selection-bias, if any, and to meet the missing at random (MAR) assumption underlying most imputation techniques.

The economic evaluation was conducted as an incremental cost-benefit analysis, because the primary outcome (duration of sick leave) could directly be expressed in terms of monetary benefits. The costs and benefits were calculated at baseline, 3, 6, 9 and 12 months in the ECO and CAU conditions. The costs in the intermediate months were linearly interpolated. This allowed mapping the monthly cash flows of costs and benefits over the full 12-month period. The cash flows were computed from four perspectives: (1) the employer's perspective focussing on the net-benefits from greater productivity via lesser absenteeism and lesser presenteeism; (2) the health care payer's perspective (in the Netherlands: health care insurers) focussing on the direct medical costs due to health service use, including the costs of medication, (3) the employee's perspective focussing on QALY health gains, fewer out-of-pockets costs and less informal care from family members or friends. Finally, we included the societal perspective (4), including all costs and benefits, regardless of who incurs costs or receives benefits.

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The monthly cash flows were used to compute the cumulative costs and cumulative monetary benefits over the full twelve months. Incremental costs, incremental benefits and incremental net-benefits were obtained by comparing ECO intervention with CAU. These are the main outcomes of the economic analysis alongside metrics such as the break-even point and the return on investment (ROI).

For assessing the incremental net-benefits we relied on non-parametric bootstrapping (2,500 replications) since costs are non-normally distributed. Statistics such as mean costs, 95% confidence intervals, standard errors and p-values are all based on non-parametric bootstrapping to increase the robustness of our findings. The data were analysed in SPSS (version 22) and Stata (version 13.1).

Sensitivity analysis

The main analysis (using the overarching societal perspective and based on EM imputation) was repeated three times in a series of sensitivity analyses. Firstly, the analysis was conducted again, but now based on regression imputation (RI) to assess the robustness of the findings under a different imputation technique. Secondly, we crosschecked the self-reported absenteeism against administrative data derived from the registers of the occupational health service or the employer, because the main analysis was based on self-reports and some recall bias (underreporting) could have occurred. Finally, we recalculated the incremental net-benefits after trimming the highest 5% of total cumulative costs per employee, because the participants with the extremely high costs were only a small minority but may have exercised a disproportional influence on the cost estimates and pushed outcomes to a more favourable outcomes for the ECO intervention. By excluding these participants, primarily from the CAU condition, the net-benefits were re-estimated but now under conservative assumptions.

RESULTS

Sample characteristics and baseline costs

Baseline characteristics of the sample (including baseline costs) are presented in table 1. The mean age of the 220 participants was 44 years and 59% was women. No important differences were observed at baseline in demographic characteristics and quality of life, but baseline costs were somewhat higher in the ECO condition, suggesting that the ECO group had a slightly disadvantageous start. We will return to this issue in the Discussion. As described by Volker and colleagues,[22] job characteristics and sickness absence duration at baseline were also comparable between the intervention condition and control condition, indicating that the randomisation was generally well balanced.

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Table 1. Baseline characteristics in the care as usual (CAU) and the ECO intervention group

	CAU (n=89)	ECO (n=131)
Age, mean (SD)	45.5 (10.7)	43.3 (9.5)
Female, N (%)	53 (59.6)	77 (58.8)
Married/living together, N (%)	62 (69.7)	91 (69.5)
Educational level, N (%)		
Low	32 (36.0)	48 (36.6)
Average	31 (34.8)	47 (35.9)
High	26 (29.2)	36 (27.5)
Country of birth: The Netherlands, N (%)	83 (93.3)	123 (93.9)
Direct medical costs, mean (SD)	645 (58)	602 (49)
Direct non-medical costs, mean (SD)	35 (2)	33 (2)
Absenteeism, mean (SD)	2850 (146)	3078 (125)
Presenteeism, mean (SD)	34 (16)	20 (14)
Costs in the domestic realm, mean (SD)	143 (26)	133 (20)
Medication, mean (SD)	8 (2)	12 (3)
Total costs, mean (SD)	3716 (154)	3879 (141)
Quality of life, mean (SD)	0.57 (0.027)	0.54 (0.024)

Loss to follow-up

The measurements at 3, 6, 9 and 12 months were completed by 155 (70.5%), 157 (71.4%), 134 (60.9%) and 128 (58.2%) of the participants. The dropout rate over the 12-month trial period was higher in the ECO condition (45.0%) than the control condition (37.1%), but this difference was not statistically significant (χ^2=1.38; df=1; p=0.240). As indicated, we looked for variables that predict dropout and included these as predictors in the EM and IR imputations. This was done to counter selection-bias (if any) and to better meet the MAR assumption underpinning the imputation strategies.

On the topic of treatment adherence, 90 of the 131 participants in the ECO condition (69%) finished the introduction and started with the intervention. These participants had a mean-number of total log-ins of 7.8. Forty percent (36/90) completed at least half of the modules and 23% (21/90) finished at least 70% of the prescribed number of sessions.[22]

Costs and QALYs at 3, 6, 9 and 12 months

The next step of the cost benefit analyses was to ascertain costs and quality of life at the follow-up measurements (Table 2). Cost differences were highest for absenteeism. At 12 months all the cost differences were statistically significant and in favour of the ECO condition.

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The total costs difference at the 12 month follow-up amounted to €919 (SE=205; z=4.48; p<0.001), mainly due to reduced absenteeism.

Table 2. Average monthly costs in the care as usual (CAU) and the ECO intervention group at 3, 6, 9 and months (in 2011 Euro)[1, 2]

	3 months	6 months	9 months	12 months
Direct medical costs				
CAU	474	321	383	296
ECO	463	476	333	148
Cost difference	11	-155	50	*148*
Direct non-medical costs				
CAU	135	74	102	98
ECO	104	89	67	45
Cost difference	31	-15	35	*53*
Productivity losses				
Absenteeism				
CAU	2120	1699	1276	1118
ECO	1887	1264	725	572
Cost difference	233	435	*551*	*546*
Presenteeism				
CAU	166	233	269	493
ECO	357	408	322	325
Cost difference	*-191*	*-175*	-53	*168*
Total costs				
CAU	2895	2328	2029	2005
ECO	2811	2238	1446	1090
Cost difference	84	90	*583*	*915*
Quality of life (utility)				
CAU	0.65	0.68	0.68	0.73
ECO	0.65	0.72	0.76	0.77
Difference in utilities	0	0.04	*0.08*	0.04

1 Between-group differences in italics are statistically significant at p<0.05.

2 Numbers may not add due to rounding

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Cost-benefit analysis: employer's perspective

For the employer's perspective only the intervention costs and costs stemming from absenteeism and presenteeism were included, thus assuming that the employer would be interested to know the pay out of this investment when paying for the intervention. Cumulated over the 12-months period the incremental benefits were €3,487 in favour of the ECO condition (Bootstrapped 95% CI= -418~7,390; SE=1,992; z=1.75; p=0.080), which was mainly due to a larger reduction in absenteeism over 12 months compared to care as usual (bootstrapped M=4,291; 95% CI= 290~8,292; SE=2,041; z=2.10; p=0.036). Next, we calculated incremental net-benefits, by subtracting the intervention costs (€300) from the incremental benefits. As shown in table 3 the incremental net-benefits over twelve months were €3,187 per employee in favour of the ECO condition, but there is significant uncertainty in the estimate (Bootstrapped 95% CI=-656~7,029; SE=1,961; z=1.63; p=0.104). We return to this issue in the Discussion. The break-even point for the employer, the moment in time where the investment of €300 is recouped, is around six months. The return of investment (ROI) is 3,187/300=10.62, indicating that for every euro invested the pay-out is €10.6.

Table 3. Monthly per patient costs in the care as usual (CAU) and the ECO intervention group from an employer's perspective (in 2011 Euro)

Month	1	2	3	4	5	6	7	8	9	10	11	12	Cumulative
CAU													
Absenteeism	2850	2485	2120	1910	1910	1699	1487	1487	1276	1197	1197	1118	20736
Presenteeism	34	100	166	199	199	233	251	251	269	380	380	493	2955
Total costs	2884	2585	2286	2109	2109	1932	1738	1738	1545	1577	1577	1611	23691
ECO													
Absenteeism	3078	2483	1887	1576	1576	1264	994	994	725	648	648	572	16445
Presenteeism	20	188	357	382	382	408	365	365	322	323	323	325	3760
Total costs	3098	2671	2244	1958	1958	1672	1359	1359	1047	971	971	897	20205
Incremental benefits	-214	-86	42	151	151	260	379	379	498	606	606	714	3486
Intervention costs	-300												
Incremental net-benefits	-514	-600	-558	-407	-256	4	383	762	1260	1866	2472	3186	
Return on investment	10.6												

Cost-benefit analysis: health care payer's perspective

For the perspective of the health care financier we looked at the direct medical costs including the costs for medication. We computed the monthly cash flows and compared these between the ECO and CAU conditions as before. The cumulative costs over twelve months were more or less the same for each condition with a small difference of €66 in favour of the ECO condition. Assuming that the health insurer would pay for the intervention, the intervention costs of €300

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have to be subtracted from these benefits in order to obtain the net-benefits. This generated a negative value of €234, implying that the ECO intervention is not cost saving from a health care insurer's perspective (bootstrapped 95% CI=-1,379~911; SE=584; z=-0.40; p=0.689).

Cost-benefit analysis: employee's perspective

Employee's costs and benefits included direct non-medical costs (i.e. the patient's out-of-pocket costs and costs in the domestic realm) and QALY health gains. Cumulated over twelve months the incremental benefits for the ECO group were €262 regarding non-medical costs and €696 due to QALY gains (0.035*€20,000). The incremental net-benefits were €958-€300= 658 (bootstrapped 95% CI=290~1,025; SE=187; z=3.51; p=0.000). The break-even point occurred at eight months and the return on investment was 658/300=2.2.

Cost-benefit analysis: societal perspective

For the societal perspective we included the costs and benefits of all stakeholders. The difference between conditions of the cumulative benefits was €29,893-€25,383=€4,510 in favour of the intervention condition (bootstrapped 95% CI= 103~8,918; SE=2,249; z=2.01 p=0.045). Subtraction of the intervention costs of €300 yielded incremental net-benefits from a social perspective of €4,210 (bootstrapped 95% CI= -259~8,674; SE=2,2277; z=1.85; p=0.064). Break-even was achieved at seven months and the return on investment was 4,233/300= 14.0.

Sensitivity analyses

For the main analysis we used EM imputation; now we recomputed the estimates under regression imputation (RI). Taking the societal perspective, the incremental net-benefits became €4,093 (Bootstrapped 95% CI= -279~8,465; SE=2,231; z=1.83; p=0.067) and the return on investment 4,093/300=13.6, which is close to the EM-based analysis (see table 4).

The incremental net-benefits in the main analyses were dominated by the costs offsets due to reduced absenteeism, but these were based on self-reported data. Crosschecking the self-reported data against administrative data derived from the registers of the occupational health service or employer showed that the estimates for days absent were lower in the analysis based on self-report data than on administrative data (72 work days absent based on self-reported data versus an average of 102 work days absent based on administrative data). When basing the analysis on administrative data, the total cumulative incremental net-benefits became €5,316 (Bootstrapped 95% CI=-2,590~13,222; SE=4,034; z=1.32; p=0.188), which is higher by a factor 1.3 than the corresponding estimate presented in the main analysis. The main analysis thus represents a safer (lower) estimate.

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Finally, we repeated the main analysis by replacing the total costs of the respondents with the top 5% highest total costs due to absenteeism by the highest amount witnessed in the other 95% respondents. The top 5% outliers were mainly situated in the CAU condition, raising the average costs for this group. The incremental net-benefits based on the trimmed costs dropped from €4,210 to €3,559 (SE 95% CI= -611~7,729; SE=2,128; z=1.67; p=0.094), which can be regarded as a more conservative lower bound.

Table 4. Incremental net-benefit and return on investment from societal perspective for base case and sensitivity analyses (in 2011 Euro)

	Incremental net-benefit	Return on investment
Base case analysis	4,210 (-259 to 8,674)	14.0
sensitivity analysis regression imputation	4,093 (-279 to 8,465)	13.6
sensitivity analysis administrative data	5,316 (-2,590 to 13,222)	17.7
sensitivity analysis trimming highest 5%	3,559 (-611 to 7,729)	11.9

DISCUSSION

Principal findings

This study was set out to evaluate the cost-effectiveness of an intervention that encourages sick-listed employees with (symptoms of) common mental disorders to make an early return to their work. The economic evaluation was conducted as an incremental cost-benefit analysis and reports on the incremental cost to benefit ratio, the return on investment, the break-even point, and the incremental monetary net-benefits, as customary seen in business cases and investment appraisals. These metrics were computed from various perspectives: the perspective of the employer, the employee, the health care financier and society. The main findings can now be summarised as follows:

- Taking the employer's perspective, the focus of the economic evaluation was placed on the intervention costs and changes in productivity owing to changes in absenteeism and presenteeism. Assuming that the employer would make the investment in the ECO intervention of €300 per employee, the incremental net-benefits were €3,187 per employee over a year. This was equivalent to a return on investment of €11 per invested Euro. Benefits largely stemmed from reduced absenteeism and exceeded the investment costs after six months.
- From the perspective of the health care payer the incremental net-benefits were negative, amounting to additional costs of €234 per employee on average.

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- As seen from the employee the net-benefits, including the value of the employee's QALY health gains, exceeded the costs by €658.
- From the societal perspective, the initial investment was also more than recouped. Considering all costs and benefits, but ignoring the value of QALY gains, the incremental net-benefits were €4,210, with a break-even point at 7 months. Every euro invested yielded €14. Trimming the 5% highest costs, mostly from the care as usual condition, reduced the incremental net-benefits to €3,559.

Limitations

This study has several limitations, which are reported and discussed here.

- First, cost data are often non-normally distributed with a some people generating very high costs. This results in large standard deviations in the costs estimates and less precise estimates of average costs. In such a context it would require a very large sample size to power the trial for testing economic hypotheses. However, our study was only powered to test a difference in sickness absence duration. As a consequence, the wide 95% confidence intervals indicate that the cost estimates are subject to much uncertainty. More specifically, when trimming the highest 5% of the costs in one of our sensitivity analysis showed that the incremental net-benefits became €3,559, which is 85% of the original estimate of €4,210. This suggests that our study needs replication, preferably in a larger study.
- Second, loss-to follow up was substantial. To handle dropout, missing data were imputed using estimation maximization (EM). To ascertain the robustness of our findings we also used regression imputation (RI). With RI we arrived at similar conclusions: €4,093 (versus €4,210 under EM), attesting to the robustness in our findings. Nonetheless, selection bias introduced by (selective) dropout cannot be ruled out completely and could have influenced the outcomes that we obtained.
- Third, costs at baseline were higher in the ECO condition. We could have adjusted for the baseline differences, but this would most likely have led to even better outcomes in favour of the ECO condition. Ignoring the baseline differences has therefore put our main analyses on a more conservative footing.
- Fourth, the main driver of costs and benefits was absenteeism and in the main analysis these were based on self-report. This may have introduced some recall bias, but self-reports of absenteeism usually involve underreporting thus leading to conservative outcomes. Still, we crosschecked the self-reports against administrative data from the registers of the occupational health service and the employer. As expected, the benefits were lower when based on self-reports than on administrative data.
- Fifth, it should be noted that the cost-benefit analysis did not include the future costs of implementing the ECO intervention on a wider scale. As the main component is a low cost self-help intervention (Return@Work) and the training of OPs only lasts a few hours, the

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implementation costs are expected to be low, but should be considered when the intervention is disseminated on a wider scale.

- Finally, the follow-up time is limited to 12 months. We do not know what the net-benefits would be over a longer time span. However, costs differences were highest in the last months. This may imply that a longer follow-up period would have seen more profitable outcomes.

Results in context

Reviews about the effectiveness of psychological return to work interventions for employees with mental health problems show mixed outcomes in reducing sickness absence and promoting an earlier return to work.[12, 23] Moreover, only a few of the reviewed studies that appeared to be effective report a full economic evaluation. Of these, none evaluated a guided eHealth intervention for return to work. One study that is somewhat comparable with our study is from Schene and colleagues. Schene et al describe the economic evaluation of an intervention for employees with major depression, who were sick-listed between 10 weeks and 2 years.[41] The experimental condition received occupational therapy in addition to usual outpatient treatment for depression. Their intervention increased the number of hours worked accumulating in a median economic gain of US$4000–5000 per patient per year, which is in line with our findings regarding the reduction in absenteeism. The study of Schene et al was smaller (n=62), was directed at a more severely depressed population, and the intervention was not delivered online but as an intensive face-to-face therapy consisting of 24 group sessions and 15 individual sessions.

Lerner and colleagues evaluated a brief telephonic program to improve work functioning for employees with major depressive disorder or dysthymia with an at-work productivity loss of at least 5% in the past two weeks.[42] Compared to usual care, annualised cost savings averaged at $6042 per participant but these savings were extrapolated from a shorter (4 months) follow-up. These cost savings are higher than the cost-savings observed in our study. Nonetheless, Lerner's et al. extrapolation from 4 to 12 months might have overstated the savings if the treatment effect was not sustained.

Arends and colleagues evaluated the costs and benefits of a problem-solving intervention provided by OPs to prevent recurrent sickness absence in workers with common mental disorders.[43] Compared to care as usual the intervention was more effective but also more expensive. From an employer's perspective the intervention showed no economic benefits, which is in contrast to our study.

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Noben and colleagues conducted a cost-benefit analysis from the employer's perspective of a preventive intervention in the work setting among nurses with an elevated-risk of mental complaints.[44] The authors concluded that the intervention was a good investment as the net-benefits (stemming from reduced absenteeism and presenteeism) were positive (€651) and the return on investment was €11 per Euro spent. This return on investment is comparable with ours.

In contrast to Noben and colleagues and several other studies [45] we found negative results for presenteeism in the short run (first nine months), but these were alleviated in the longer run (at the end of the year). An explanation for the initially negative results on presenteeism might be that employees who returned to work early were not completely fit and as productive as normally. In other words there was an initial trade-off between reduced absenteeism and increased presenteeism. However, after the first nine months the additional costs caused by presenteeism ceased to exist and were reversed into benefits. This change is possibly driven by an improvement in quality of life when people work.

The literature suggests that in terms of economic costs presenteeism often is a larger problem than absenteeism. Our results are not in line with these findings. This could be due to the Dutch system in which employees receive a substantial percentage of their wage during the first two years of their illness. In many other countries the fall in income is more acute when employees stay absent from their work, increasing the incentive to keep on working – even when work is then associated with greater levels of presenteeism.

The results of our study can only be generalised to employees who have been sick-listed for 4-26 weeks, working in small- to medium-sized companies.

Conclusions and implications

In the Netherlands, employers have an incentive to invest in sickness management as they have the responsibility to pay 70-100% of the salary of sick-listed employees for up to two years. Employees who are on sickness absence have to visit an occupational physician, paid by the employer within the first six weeks. Both the employee and employer have to agree on an action plan. In this plan the responsibilities of both parties are defined to ensure a quick return to work of the employee. In this context the ECO intervention can be seen as an effective intervention that, in addition, has a high probability of offering good value for money because the initial investment (of €300) is more than recouped within a single year as seen from the employer's perspective, while the employee derives benefits in the form of increased quality of life when returning to work sooner rather than later. As noted, some 95% confidence intervals of our estimates are wide. By implication, one should not rely too much on the point estimates

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of net-benefits, return on investment ratios, break-even points, because they lack precision. In other words, our estimates have some degree of uncertainty, but suggest that the ECO intervention has a high likelihood to be an appealing business case as seen from most stakeholder perspectives.

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Contributors

CFC initiated the collaborative clinical trial project. MZV, AB and CFC contributed to the design of the study and obtained the funding. DV, MZV and CFC were responsible for the acquisition of the data. SL and FS conducted the statistical analysis and drafted the first manuscript. DV, MZV, EB, BB, AB and CFC critically revised the manuscript. All authors read and approved the final manuscript. SL, FS and CFC are guarantors.

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: financial support for the submitted work from The Netherlands Organisation for Health Research and Development (ZonMw) and from Achmea SZ; SL, DV, MZV, BB, FS report personal fees from employment at the Trimbos institute, the Netherlands institute of mental health and addiction, a not-for-profit organisation, CFC has received research grants from Eli Lilly outside the submitted work.

Ethical approval

The study protocol was approved by the Medical Ethics Committee of the University Medical Center Utrecht, The Netherlands, in February 2011. All participants provided written informed consent before taking part.

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The lead author affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that and discrepancies from the study as planned (and if relevant, registered) have been explained.

Data sharing: No additional data

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Legends of figures

Figure 1. Flowchart of the clusters and participants

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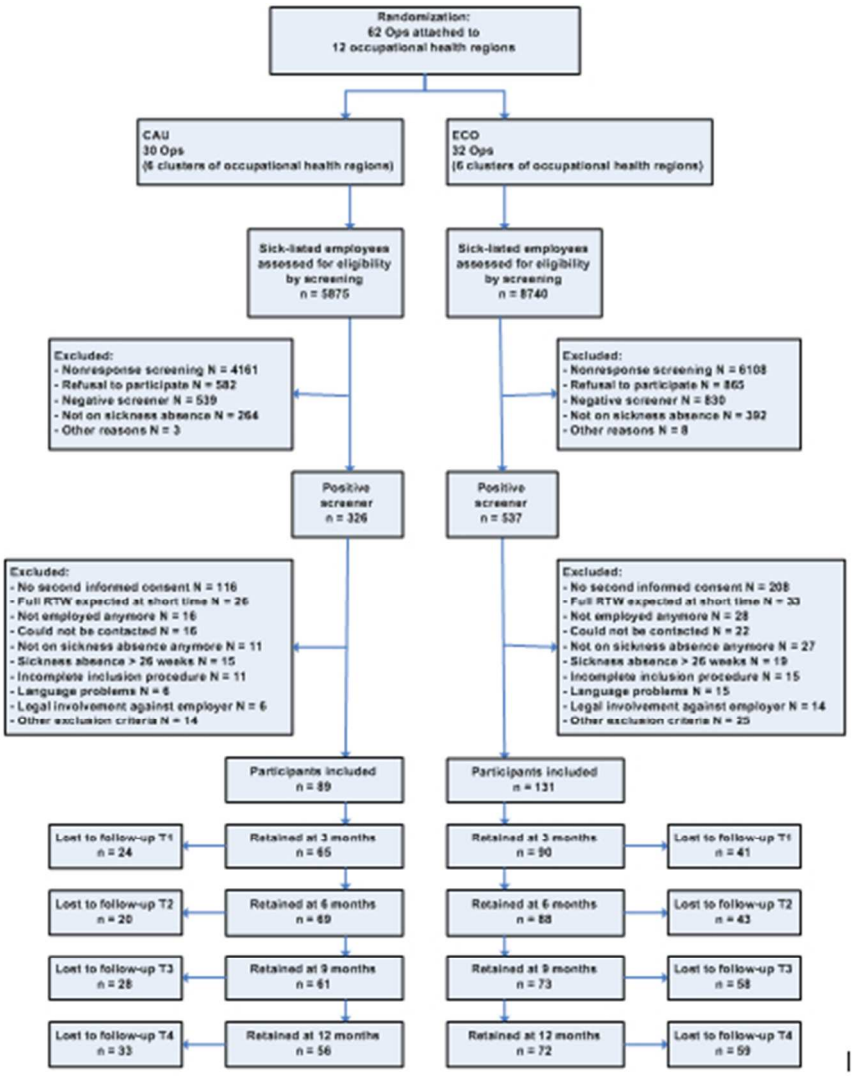

Flowchart of the participants

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	3
	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	4,5
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	5
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	5
	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	6
	4b	Settings and locations where the data were collected		6
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	7
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	7/8

		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	N/A
	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		6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	5/6
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	5/6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	6
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete	

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			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	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		6
	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	9/10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		10
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	6/10/11
	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	10/11
Recruitment	14a	Dates defining the periods of recruitment and follow-up		**6**
	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	Table 1

		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	6/9
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	11-15
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		14/15
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		16/17
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	17
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		17-19
Other information				
Registration	23	Registration number and		5/6

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

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

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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

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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.

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CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

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.	3
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
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	4,5
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	6
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	6
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	9
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	7
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	8
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	8
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.	8/9
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.	5-7

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	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.	7,8
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate 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.	N.A.
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.	8
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.	9,10
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.	10-15
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.	10-15
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	12-14

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		of methodological assumptions (such as discount rate, study perspective).	
	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.	15-19
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	19
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.	19

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

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

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