

## Comparative cost-effectiveness of two interventions to promote work functioning by targeting mental health complaints among nurses: Pragmatic cluster randomised trial



Cindy Noben<sup>a,b,\*</sup>, Filip Smit<sup>a,c</sup>, Karen Nieuwenhuijsen<sup>d</sup>, Sarah Ketelaar<sup>d</sup>,  
Fania Gärtner<sup>d</sup>, Brigitte Boon<sup>a</sup>, Judith Sluiter<sup>d</sup>, Silvia Evers<sup>a,b</sup>

<sup>a</sup> Department of Public Mental Health, Trimbos Institute, Netherlands Institute of Mental Health and Addiction, Utrecht, Netherlands

<sup>b</sup> Department of Health Services Research, CAPHRI School of Public Health and Primary Care, Maastricht University, Maastricht, Netherlands

<sup>c</sup> Department of Epidemiology and Biostatistics, EMGO+ Institute of Health and Care Research, VU University Medical Centre, Amsterdam, Netherlands

<sup>d</sup> Coronel Institute of Occupational and Environmental Health, Academic Medical Centre, Amsterdam, Netherlands

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### ABSTRACT

**Background:** The specific job demands of working in a hospital may place nurses at elevated risk for developing distress, anxiety and depression. Screening followed by referral to early interventions may reduce the incidence of these health problems and promote work functioning.

**Objective:** To evaluate the comparative cost-effectiveness of two strategies to promote work functioning among nurses by reducing symptoms of mental health complaints. Three conditions were compared: the control condition consisted of online screening for mental health problems without feedback about the screening results. The occupational physician condition consisted of screening, feedback and referral to the occupational physician for screen-positive nurses. The third condition included screening, feedback, and referral to e-mental health.

**Design:** The study was designed as an economic evaluation alongside a pragmatic cluster randomised controlled trial with randomisation at hospital-ward level.

**Setting and participants:** The study included 617 nurses in one academic medical centre in the Netherlands.

**Methods:** Treatment response was defined as an improvement on the Nurses Work Functioning Questionnaire of at least 40% between baseline and follow-up. Total per-participant costs encompassed intervention costs, direct medical and non-medical costs, and indirect costs stemming from lost productivity due to absenteeism and presenteeism. All costs were indexed for the year 2011.

**Results:** At 6 months follow-up, significant improvement in work functioning occurred in 20%, 24% and 16% of the participating nurses in the control condition, the occupational physician condition and the e-mental health condition, respectively. In these conditions the total average annualised costs were €1752, €1266 and €1375 per nurse. The median incremental cost-effectiveness ratio for the occupational physician condition versus the control condition was dominant, suggesting cost savings of €5049 per treatment responder. The incremental cost-effectiveness ratio for the e-mental health condition versus the control condition was estimated at €4054 (added costs) per treatment responder. Sensitivity analyses attested to the robustness of these findings.

\* Corresponding author at: P.O. Box 616, 6200 MD Maastricht, Netherlands. Tel.: +31 43 38 81834; fax: +31 43 38 84162.

E-mail address: [c.noben@maastrichtuniversity.nl](mailto:c.noben@maastrichtuniversity.nl) (C. Noben).

*Conclusions:* The occupational physician condition resulted in greater treatment responses for less costs relative to the control condition and can therefore be recommended. The e-mental health condition produced less treatment response than the control condition and cannot be recommended as an intervention to improve work functioning among nurses.

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### What is already known about the topic?

- Nurses are at elevated risk for distress, anxiety and depression due to work characteristics such as high job demands and a lack of autonomy.
- Nurses with poor mental health experience significantly more medical errors.
- Worker Health Surveillance is a preventive strategy that aims at the early detection of negative health effects at work.

### What this paper adds

- Screening and feedback followed by e-health was not a success due to low uptake rates.
- Screening and feedback followed by referral to the occupational physician for nurses at risk improved work functioning in a cost-effective way.
- The intervention costs for screening and feedback followed by referral to the occupational physician for nurses at risk were more than recouped within 6 months.

## 1. Introduction

Nurses are at elevated risk for mental distress, anxiety and depression (Campo et al., 2009; Gartner et al., 2010; Magnavita and Heponiemi, 2012; Suresh et al., 2013). Possible explanations for this increased risk are found in work characteristics such as high job demands and a lack of autonomy (Gartner et al., 2010; Tayler, 1992). Poor mental health is not only undesirable in its own right, but will likely also have an adverse impact on the nurses' job functioning and may thus jeopardise the health and safety of the patients in their care. After all, nurses with poor mental health experience significantly more medical errors (Gartner et al., 2010; Karsh et al., 2006; Suzuki et al., 2004). For these reasons it is imperative to protect and promote mental health in nurses, and to monitor and safeguard the quality of their functioning at work (Gartner et al., 2010).

Mental disorders carry substantial disease and economic burdens. Preventive interventions for mental disorders exist; however, what interventions should be financed and implemented is an issue that needs to be addressed by decision makers. Moreover, the number of health-economic evaluations that were conducted in the work setting is very limited. Likewise, information to aid in the transferability of available results to different contexts and settings is limited (Zechmeister et al., 2008). Economic evaluations can provide answers, select interventions that are cost-effective and avoid wasting limited resources. An approach to priority setting is largely based on economic techniques to assess the cost-effectiveness to answer questions regarding the economic value for money of

competing interventions (Drummond et al., 1993; Tompa et al., 2006).

Periodic screening might be useful to identify nurses with signs of mental health problems and encourage help-seeking behaviour. To that end a Worker Health Surveillance was developed. The Worker Health Surveillance is a preventive strategy that aims at the early detection of negative health effects at work (Gartner et al., 2010, 2012a; ILO, 1998). A Worker Health Surveillance with personalised feedback and referral to dedicated early interventions for screen positives might be a successful strategy to prevent the onset and further deterioration of mental health problems and to reduce impairments in work functioning (Gartner et al., 2010; Koh and Aw, 2003). In this study we compare a control condition consisting of screening without feedback versus Worker Health Surveillance screening with feedback plus referral for a consultation with an occupational physician or referral to preventive e-mental health interventions. These approaches have not been evaluated from a health-economic perspective.

Therefore, the aim of this study is to assess the comparative cost-effectiveness of the occupational physician condition and the e-mental health condition versus the control condition, with a view to protecting mental health and improving and sustaining work functioning in nurses.

## 2. Methods

### 2.1. Design

The *Mental Vitality @ Work* study (Gartner et al., 2011a) was designed as a pragmatic cluster randomised controlled trial, with randomisation at the level of hospital wards to three conditions:

- 1 Screening and feedback followed by referral to the occupational physician for screen-positives (the occupational physician condition),
- 2 Screening and feedback followed by referral and access to preventive e-mental health interventions (the e-mental health condition),
- 3 Screening without feedback and without referral to either the occupational physician or the e-mental health interventions (the control condition).

Data were recorded at baseline and after three and 6 months. In the economic evaluation, we assessed the comparative cost-effectiveness in two contrasting scenarios: (1) the occupational physician condition versus the control condition, and (2) the e-mental health condition versus the control condition. A medical ethics committee approved the study.

## 2.2. Randomisation

Cluster randomisation was performed at the ward level to prevent contamination between participants working in the same ward. A pre-randomisation procedure with incomplete-double-consent design was applied (Schellings et al., 2008, 2009) meaning that individuals were only informed about their own group. This further minimised the possibility of contamination.

Randomisation was conducted using the computer software programme Nquery Advisor in blocks of three wards. After randomisation, 28 wards with 591 employees were assigned to the occupational physician condition, 29 wards with 579 employees to the e-mental health condition, and 29 wards with 561 employees to the control-condition.

## 2.3. Sample

The study population of the complete trial included all nurses with similar work demands and work conditions; including surgical nurses, anaesthetic nurses, and allied health professionals (henceforth: 'nurses') working in one Dutch academic medical centre. Nurses who were sick-listed at the start of the study and expected to be on sick leave for more than 2 weeks were excluded from the study. All eligible employees were invited to take part in the study, which for the complete trial added up to 1731 employees working in 86 wards. Cost-effectiveness analyses were performed according to the intention-to-treat principle for the whole sample. However, participation rates of the nurses in the interventions at baseline were 34% in the control condition; 32% in the occupational physician condition; and 31% in the e-mental health condition.

After randomisation, 212 nurses were assigned to the e-mental health condition, 210 to the occupational physician condition and 211 to the control condition. Sixteen nurses (three in the occupational physician condition, eight in the e-mental health condition and five in the control condition) were sick-listed for more than 2 weeks at the start of the trial, did not contribute to the data and were excluded from the analysis. Thus, the study population comprised a total of 617 nurses: 207 in the occupational physician condition, 204 in the e-mental health condition and 206 in the control condition.

## 2.4. Interventions

All participants were screened for work functioning impairments and six types of mental health complaints: distress, work-related fatigue, risky drinking, depression, anxiety, and post-traumatic stress disorder. Nurses in the control condition filled out the questionnaires and no further steps were taken. After completing the screening, the occupational physician condition and the e-mental health condition immediately received personalised feedback about their screening results.

In the occupational physician condition, screening and feedback were followed by an invitation for the screen-positives to attend the occupational physician. The nurses

consulted the occupational physician or not at their own discretion. In order to structure the consultation of the occupational physician, a seven-step protocol was applied, with the focus on identifying impairments in work functioning and providing advice on how to improve wellbeing and work functioning.

In the e-mental health condition, screening and feedback were followed by referral to e-mental health interventions. The e-mental health interventions offered in the e-mental health condition were *Psyfit*, aimed at promoting mental fitness and wellbeing; *Strong at Work*, aimed at learning skills to cope better with work-related stress; *Colour your Life*, for coping with depressive symptoms; *Don't Panic Online*, to reduce symptoms of panic disorder; and *Drinking Less*, aimed at reducing risky alcohol consumption. Nurses who screened positive on one of these health problems were offered access to the corresponding e-mental health intervention. Nurses screening negative on mental health complaints, but positive on work functioning impairments were offered *Psyfit* and an onscreen psycho-educational leaflet about dealing with these impairments. Nurses screening negative on both mental health complaints and on work functioning impairments were only offered free access to *Psyfit*. The onscreen psycho-educational leaflet was also offered when nurses screened positive on mental health complaints and on work functioning impairments. In any case, making use of the e-mental health interventions was strictly voluntary and nurses were free to reject the offer of using the interventions (Gartner et al., 2011a).

## 2.5. Outcome measure

The primary outcome was 'work functioning' as measured by the following subscales of the 'Nurses Work Functioning Questionnaire': *Cognitive aspects of task execution*, *Causing incidents at work*, *Avoidance behaviour*, *Conflicts and irritations with colleagues*, *Impaired contact with patients and their family*, *Lack of energy* and *Motivation*. The 'Nurses Work Functioning Questionnaire' is a 50-item self-report questionnaire with Likert-type response scales ranging from 0 (totally disagree) to 6 (totally agree); 0 (disagree) to 4 (agree); and 0 (no difficulty) to 6 (great difficulty) (Gartner et al., 2012a). Internal reliability of the 'Nurses Work Functioning Questionnaire' is high, with Cronbach's alphas varying between 0.70 and 0.94 (Gartner et al., 2011b).

The difference between the occupational physician condition and the e-mental health condition versus the control condition was examined as the percentage of individuals who improved at follow-up. The primary outcome of work functioning is operationalised as job-specific impairments in work functioning and were measured using a total score of the Nurses Work Functioning Questionnaire. The minimal important change value for improvement was based on the relative pre-post change scores, that is  $(T_0 - T_1/T_0) \times 100\%$ , indicating the percentage of change on impaired work functioning in relation to the baseline score. Individuals with a relative improvement on their Nurses Work Functioning Questionnaire total score of 40% or more (Gartner et al., 2012b),

which is the minimal important change (MIC) value, were defined as *relevantly improved*, and henceforth denoted as treatment responders.

### 3. Resource use and costing

Resource usage and costs entailed can be split into (a) intervention costs, (b) direct medical costs (due to health service uptake and pharmacy use), (c) direct non-medical costs (the nurses' out-of-pocket costs for travel and parking, incurred while making use of health services) and (d) indirect costs stemming from lost productivity in paid work due to absenteeism and presenteeism. All costs were in euro indexed for the reference year 2011 based on the price indices from Statistics Netherlands (CBS, 2012).

#### 3.1. Intervention costs

When calculating the intervention costs, a distinction was made between human and material resources. Material resources are divided into capital items that have a time span longer than one year, such as the equipment that was needed to build the screening module for the provision of the feedback and the interventions, and recurrent or revenue items that are consumed in less than one year, such as maintenance costs. For human resources, costs were based on the valuation of the personnel involved in the development and the application of the intervention. The corresponding calculations for the intervention costs can be obtained from the first author.

The per-participant costs for the online 'Worker Health Surveillance' were estimated to be €3.80. The costs of the occupational physician intervention consisted of the per-participant screening costs of €3.80 plus the costs of the occupational physician at €73.11 per contact. For the e-mental health intervention, the per-participant costs were the screening costs of €3.80 plus the costs of the specific e-mental health interventions. The costs of the e-mental health interventions were only charged when a participant logged in to an e-mental health intervention and thus became a user of that intervention. The e-mental health interventions have fixed per-participant cost prices that are based on their market values, which are subject to change over time. In the reference year of 2011, the per-user costs were as follows: *Psyfit* €30, *Strong at Work* €175, *Colour your Life* €195, *Don't Panic Online* €225 and *Drinking Less* €45.

#### 3.2. Direct medical costs

Health service costs were calculated by multiplying the health service units (contact, session, hour) with their standard full economic cost price. The standard costs were reported in the Dutch guideline for health economic evaluations (Hakkaart et al., 2010) and indexed for the year 2011 using the consumer price index from Statistics Netherlands (CBS, 2012). The costs of prescription drugs were calculated as the price per standard daily dose as reported in Dutch guidelines and multiplied by the number of days (CVZ, 2012). The pharmacist's dispensing costs of €5.99 and the general practitioners' prescription costs of

€14 were added (Hakkaart et al., 2010). Over the counter drugs were based on their market prices.

#### 3.3. Direct non-medical costs

The participants' travel and parking expenses incurred in receiving professional help were computed as the distance to a health service multiplied by the costs per kilometre (€0.21), with parking costs (€3 per hour) added (Hakkaart et al., 2010).

#### 3.4. Indirect non-medical costs

Finally, the costs stemming from production losses in paid work were calculated from the number of days absent from work (absenteeism) plus the number of workdays lost due to work cutback (presenteeism). Presenteeism was calculated by correcting for the degree of inefficiency, resulting in an inefficiency score used as point prevalence for the calculation of presenteeism costs. The inefficiency score for work quantity and work quality derived from items from the Productivity and Disease Questionnaire (ranging from 0 to 1, with 0 meaning not inefficient and 1 completely inefficient) was multiplied by the number of days at work while not feeling well in order to compute the costs of presenteeism (Koopmanschap, 2005).

The valuation method for productivity is rooted in the human capital theory whereby the production losses are assumed to equal the present value of all lost future earnings of the individual. That is, income (before tax) acts as a proxy for the production value of that individual and encompasses all productivity losses by this person (Krol et al., 2011; Weisbrod, 1961). The costs of productivity losses were then assessed by multiplying the number of workdays lost by the gender and age-specific productivity levels per paid employee, indexed for the year 2011 (CBS, 2012; Hakkaart et al., 2010).

## 4. Analyses

All analyses were performed in agreement with the intention-to-treat principle, thus including all participants as randomised. To that end, missing data were imputed. Since substantial dropout had occurred, sensitivity analyses were conducted to gauge the robustness of our findings across different imputation techniques. In the main analysis, missing data were replaced by their most likely value under the expectation maximisation algorithm in SPSS 19. In one sensitivity analysis, all analyses were repeated with last observation carried forward, as implemented in SPSS. In yet another sensitivity analysis, regression imputation as implemented in Stata (version 12.1) was used to impute missing data. As predictor variables we used baseline costs, baseline work functioning, age, gender, partner status and the Karasek factors job demands, control, support from colleagues and superiors (Karasek et al., 1981, 2007) Directing the sensitivity analyses towards the various imputation strategies was an a priori decision, because it was imperative to ascertain that the research findings did not solely hinge on the chosen imputation technique.

The cost-effectiveness analysis was conducted from the societal perspective in which all costs and benefits were included, irrespective of who bears the costs or receives the benefits (Drummond et al., 1993). Both the incremental costs and incremental effects were used to calculate the incremental cost-effectiveness ratio. The incremental cost-effectiveness ratio was calculated as  $(C_1 - C_0)/(E_1 - E_0)$ , where  $C$  denotes the average per-participant costs and  $E$  is the effect in the experimental and control conditions (subscripted 1 and 0, respectively). The incremental cost-effectiveness ratio can be interpreted as the net costs (or savings) per treatment responder.

To handle stochastic uncertainty in the cost and effect data, non-parametric bootstraps were used to simulate 5000 incremental cost-effectiveness ratios. The incremental cost-effectiveness ratios were plotted on the cost-effectiveness plane to capture the uncertainty in the incremental cost-effectiveness estimate (see Fig. 2). To be more precise, each simulated incremental cost-effectiveness ratio can be plotted on one of the four quadrants of the incremental cost-effectiveness plane. In the North East quadrant the intervention produces superior health gains at additional costs relative to the control condition. In the North West quadrant less health is produced for additional costs. Clearly, this is the worst possible outcome, and the intervention is then “dominated” by the control condition. In the South West quadrant less health is produced, but there are cost savings. Finally, in the South East quadrant the intervention generates superior health gains (relative to the comparator condition) and does so for lower costs. This is the best possible outcome and the intervention is then said to “dominate” the control condition. It is often seen that a new intervention falls in the North East quadrant, because better health is obtained for additional costs.

## 5. Results

### 5.1. Sample characteristics

Baseline characteristics of the groups are shown in Table 1. There were no differences across the conditions in

terms of demographics, baseline costs and work functioning. Therefore we concluded that randomisation had resulted in a balanced trial.

### 5.2. Missing data and dropout

At baseline, data on impaired work functioning were missing for 11/206 (5.3%) participants in the control condition, 10/207 (4.8%) in the occupational physician condition and 15/204 (7.4%) in the e-mental health condition. At 3 months follow-up, the dropout rates in the control condition, the occupational physician condition and the e-mental health condition were 61 (29.6%), 77 (37.2%) and 121 (59.3%), respectively. At 6 months follow-up, dropout rates had increased to 68 (33%), 94 (45.4%), 133 (65.2%). The flow of the participants through the trial is shown in Fig. 1.

Since loss to follow-up was substantial, we assessed if dropout was selective. A dropout dummy variable (1 = lost, 0 = retained) was computed and regressed on condition, baseline costs, baseline work functioning, age, gender, partner status, and the Karasek factors (job demands, control, support by colleagues and superiors). (Karasek et al., 2007, 1981) The analyses indicated that the occupational physician condition was associated with higher dropout than the control condition, and that poorer work functioning at baseline increased the risk of dropout, but having a partner was associated with a smaller likelihood for dropout. When comparing the e-mental health condition to the control condition, it was shown that the e-mental health condition was associated with greater dropout, as were poorer work functioning and higher job demands at baseline. Again, living together with a partner was associated with a reduced likelihood of dropping out.

### 5.3. Health care service use

The most frequently used health care services among all three conditions were the physiotherapist and GP services. At 3 months follow-up, consulting the occupational physician increased only in the occupational physician condition, most likely due to the intervention in which

**Table 1**  
Sample characteristics by condition at baseline.

	Control condition (n = 206)	OP condition (n = 207)	E-mental health condition (n = 204)
Age, mean (sd)	41.83 (11.305)	42.56 (11.357)	37.5 (12.16)
Female, N (%)	159 (77.2)	170 (82.1)	169 (82.8)
Working hours, mean (sd)	30.98 (5.964)	28.73 (8.045)	31.33 (5.23)
Living with a partner, N (%)	154 (74.8)	153 (73.9)	151 (74)
Born in the Netherlands, N (%)	176 (85.4)	167 (80.7)	174 (85.3)
Work experience, years (sd)	11.3 (10.078)	12.53 (10.416)	10.03 (10.03)
Turnover intention, N (%)	22 (10.7)	27 (13)	25 (12.3)
Baseline costs, <sup>a</sup> mean (sd)			
Medication costs	1.06 (6.59)	1.54 (1870)	1.68 (11.34)
Health care service use	116.97 (229.13)	121.84 (239.49)	211.85 (1090.35)
Absenteeism	491.62 (1689.34)	659.92 (2110.12)	376.98 (856.16)
Presenteeism	1068.93 (1862.79)	1125.04 (2429.29)	973.65 (1541.15)
irect non-medical costs	10.67 (19.87)	10.69 (19.68)	20.1 (104.82)
Work functioning, mean (sd)	14.11 (9.478)	12.56 (9.233)	13.41 (9.2)

<sup>a</sup> In €, time horizon of baseline costs was 3 months.

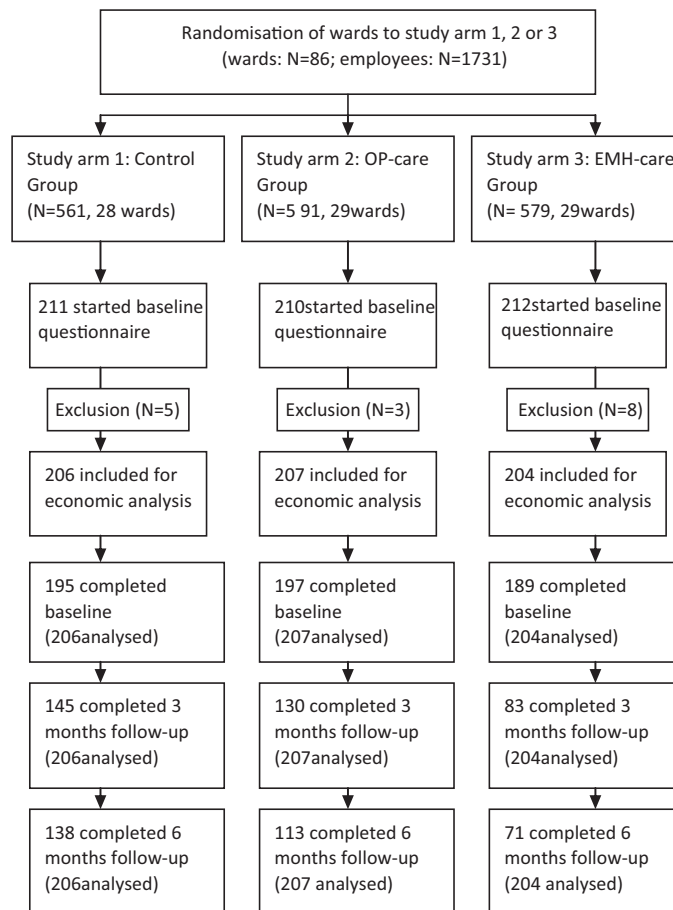


Fig. 1. Participants' flow through the study.

these visits were encouraged. Interestingly, the occupational physician condition visits showed a substantial decrease at 6 months follow-up. After 6 months a reduction in the average volumes of physiotherapist and GP visits is noticeable in all three conditions. Also, use of prescription drugs decreased over time in the three groups. Supplementary Table 1 lists the average volumes of resource use by treatment group and time.

Supplementary material related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ijnurstu.2014.01.017>.

#### 5.4. Incremental cost-effectiveness

##### 5.4.1. Costs

Table 2 presents the costs of health care uptake and the costs stemming from productivity losses by condition and time point. The most significant costs can be attributed to the productivity losses. In particular, the costs of presenteeism increased in the control condition between baseline and 6 months follow-up, but decreased in the occupational physician condition and the e-mental health condition.

Table 2  
Mean per-participant costs by condition and measurement (in €).

	Baseline			3 months			6 months		
	Control (n = 204)	OP (n = 206)	e-mental health (n = 204)	Control (n = 148)	OP (n = 132)	e-mental health (n = 89)	Control (n = 140)	OP (n = 115)	e-mental health (n = 73)
<i>Direct medical costs</i>									
Service use	116.97	121.84	211.85	102.09	117.71	101.93	97.96	98.5	100.39
Medication	1.06	1.54	1.69	0.94	1.52	2.14	0.99	2.21	2.37
<i>Indirect non-medical costs</i>									
Absenteeism	491.62	659.92	376.98	116.45	347.78	186.59	373.95	234.1	230.03
Presenteeism	1068.93	1125.04	973.65	1054.71	995.18	995.31	1266.78	916.09	1016.28
Direct non-medical costs	10.67	10.69	20.09	9.37	10.83	9.77	9.37	10.83	9.77

**Table 3**  
Summary statistics for each of the interventions under each imputation technique.

	Costs, € <sup>a</sup>	Effect <sup>b</sup>	ICER, <sup>c</sup> €	North East	North West (inferior)	South West	South East (dominant)
<b>Base-case scenario</b>							
<i>(Expectation maximisation)</i>							
Control	1752	0.20					
OP	1266	0.24	Dominant <sup>d</sup>	2%	1%	21%	75%
e-mental health	1375	0.16	4054	1%	8%	76%	16%
<b>Alternative scenario A</b>							
<i>(Last observation carried forward)</i>							
Control	1800	0.21					
OP	1421	0.27	Dominant <sup>d</sup>	10%	2%	9%	80%
e-mental health	1388	0.17	6303	1%	5%	75%	18%
<b>Alternative scenario B</b>							
<i>(Regression)</i>							
Control	1681	0.21					
OP	1214	0.25	Dominant <sup>d</sup>	1%	0%	17%	81%
e-mental health	1395	0.16	4022	1%	8%	74%	16%

<sup>a</sup> Cost per treatment responder at 2011 prices.

<sup>b</sup> Fraction treatment responders (differences in effect estimates in the text and the table are due to rounding).

<sup>c</sup> The presented median ICER is 50th percentile of 5000 bootstrap replications of the ICER.

<sup>d</sup> When the ICERs are negative (suggesting cost savings) then they are labelled as 'dominant', representing a situation where the intervention is superior to the control condition from a cost-effectiveness perspective.

#### 5.4.2. Incremental costs

Table 3 (upper panel) shows the costs per condition. The average total costs were calculated to be €1266 per participant in the occupational physician condition and €1752 in the control condition. The incremental costs were therefore €1266 – €1752 = –€486 per-participant (negative costs, hence a cost reduction). The incremental costs for the e-mental health condition were associated with a decrease in costs compared to the control condition: €1375 – €1752 = –€377.

#### 5.4.3. Incremental effects

Table 3 (upper panel) shows the effects per condition. At follow-up, 49/207 = 23.7% of the participating nurses met criteria for treatment response in the occupational physician condition compared with 45/206 = 20.4% in the control condition. In the e-mental health condition, this was 23/204 = 15.7%. The incremental effectiveness between the occupational physician condition and the control condition was therefore 0.237–0.204 = 0.033. This was 0.157–0.204 = –0.047 for the e-mental health condition versus the control condition.

#### 5.4.4. ICER occupational physician condition versus control condition

As noted for the occupational physician condition, the incremental costs were –€486 (savings) and the incremental effect was 0.033. We rely on the median incremental cost-effectiveness ratio (ICER) as estimated from the 5000 non-parametric bootstraps. The median incremental cost-effectiveness ratio for the occupational physician condition versus the control condition was estimated as a saving of –€5049 per treatment responder. Fig. 2a shows the scatter of bootstrapped incremental cost-effectiveness ratios on the incremental cost-effectiveness plane. Of the 5000 simulated incremental cost-effectiveness ratios, 75% fall into the South East-quadrant,

indicating that more treatment responses are generated for fewer costs by the occupational physician intervention relative to the control condition. Another 2% of the simulated incremental cost-effectiveness ratios fall in the North East-quadrant, indicating a probability of 2% that by applying the intervention an additional treatment response is produced, but at additional costs. The remainder of the stimulated incremental cost-effectiveness ratios showed up on the west side of the plane, indicating less effectiveness and less costs (21%), or less effectiveness and more costs (1%). In sum, the occupational physician condition is associated with a 75% probability that the intervention generates better outcomes for less money than the control condition.

#### 5.4.5. ICER e-mental health condition versus control condition

As noted, in the e-mental health condition the incremental costs were –€377 (negative costs, hence a cost saving), but the incremental effect was –0.047 (a small loss in effectiveness) relative to the control condition. The median incremental cost-effectiveness ratio could be estimated as €4054. Fig. 2b shows that 76% of the simulated incremental cost-effectiveness ratios fall in the South West-quadrant indicating a probability of 76% that by applying the e-mental health condition fewer treatment responses are produced, albeit at less additional costs. Another 16% of the simulated incremental cost-effectiveness ratios fell into the South East-quadrant, indicating that more treatment responses are generated for less additional costs by the e-mental health condition relative to the control condition. Finally, 1% indicates more effects at higher costs and 8% indicates less effect at higher costs.

#### 5.4.6. Sensitivity analysis

Sensitivity analyses were conducted by repeating all analyses under two alternative imputation strategies:

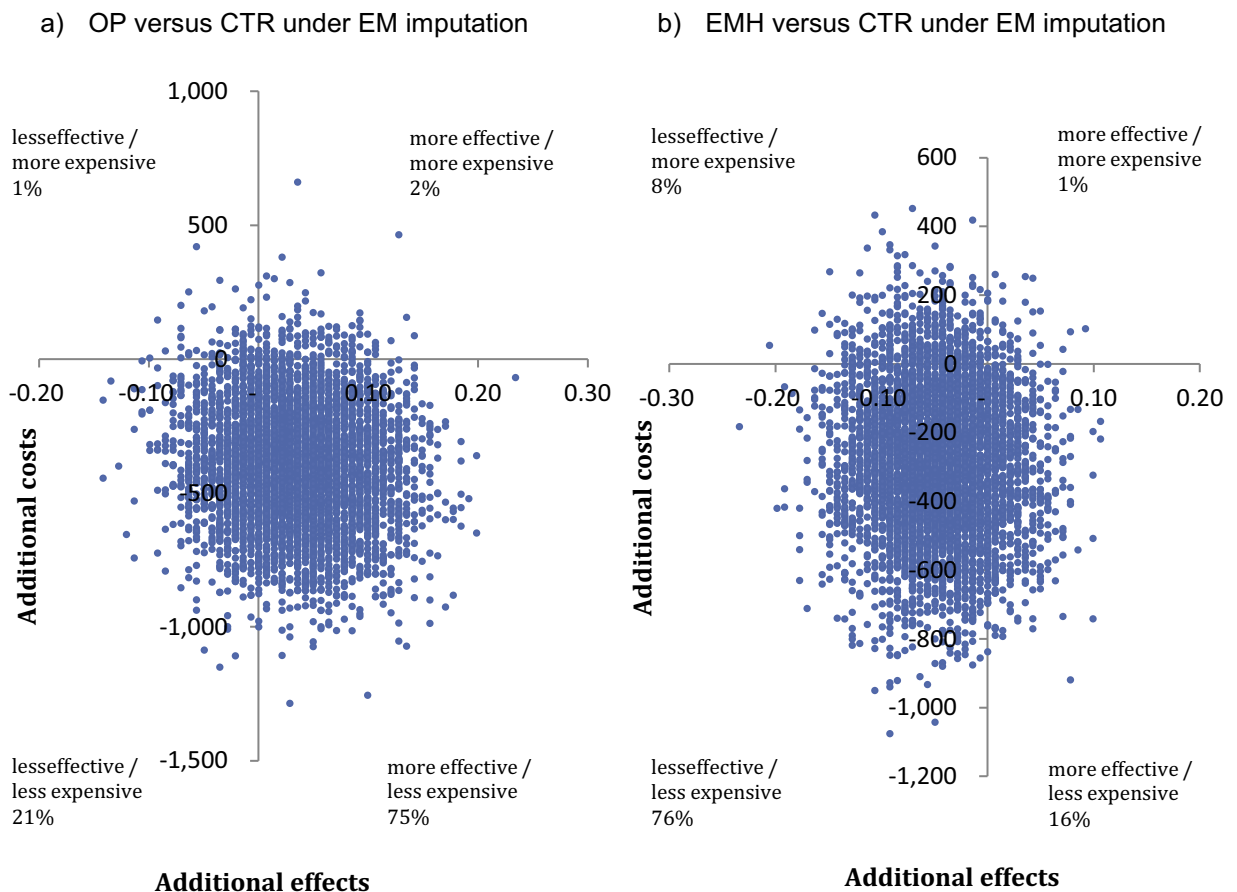


Fig. 2. Scatter of simulated incremental cost-effectiveness ratios ( $n = 5000$ ) on the cost-effectiveness plane. (a) OP versus CTR under EM imputation. (b) EMH versus CTR under EM imputation.

using last observation carried forward imputation (in SPSS 19) and under regression imputation (in Stata 12.1). Table 3 (lower panels) presents the summary statistics of the sensitivity analyses. As can be seen, the findings that were obtained under expectation maximisation imputation are consistent with the results produced under last observation carried forward and regression imputation. In fact, the results obtained under expectation maximisation imputation fall between last observation carried forward and regression imputation.

## 6. Discussion

### 6.1. Main findings

This study was conducted to assess the cost-effectiveness of two strategies (the occupational physician condition and the e-mental health condition) to improve work functioning compared to the control condition of screening alone. The proportion of participants that manifested with a reliable change in work functioning was higher, although non-significant, in the occupational physician condition: 23.7% against 20.4% in the control condition. The proportion of improved participants on work functioning in the e-mental health condition on the other hand was lower:

15.7% against 20.4% in the control condition. The average per-responder costs in the three conditions were €1266 in the occupational physician condition, €1375 in the e-mental health condition and €1752 in the control condition.

The median incremental cost-effectiveness ratio in the occupational physician condition versus the control condition comparison is dominant ( $-\text{€}5049$ ), hence a cost-saving per treatment responder. Therefore, the occupational physician condition can be recommended over the control condition, because the occupational physician condition is associated with a greater likelihood that beneficial effects are obtained for fewer costs.

The median incremental cost-effectiveness ratio in the e-mental health condition versus the control condition comparison is €4054 per treatment responder. The e-mental health intervention does not outperform the control condition, because the odds are that nurses derive fewer benefits from this intervention. Sensitivity analyses attested to the robustness of these findings.

### 6.2. Strengths and limitations

Some of the strengths of this study are its randomised design and its relatively large sample size. This is worth



mentioning, because the literature identifies several barriers to conducting randomised trials within the work setting such as the difficulties encountered when randomising employees while also trying to avoid the risk of contamination (Chapman and Combs, 2005; Chapman et al., 2011; Chau et al., 2008; Kajermo et al., 2008).

The design with cluster randomisation and pre-randomisation was a strength of this study because randomisation at the ward level reduces the contamination of study groups. Furthermore, pre-randomisation allowed the participants to be blinded with respect to the information related to the other study groups. This minimised contamination effect in the study.

Next, in an attempt to tie the results of this study to previous research, wherein a lack of economic workplace mental health promotion studies is prevailing (Mihalopoulos et al., 2011; Zechmeister et al., 2008), this mental health oriented intervention for nurses can be seen as a welcome addition to the literature strengthening the evidence base.

The findings of this study need to be placed in the context of the study's limitations. First, the trial suffered from dropout, and our own analysis indicated that dropout had not occurred randomly. Unfortunately we do not have data on reasons for non-responding to the interventions. However, we can speculate that the main reason for drop-out in this specific study population might be feelings of work overload and the inability to find the time to improve their self-management skills. Again, this remains speculative but might have distorted the findings. However, we conducted intention-to-treat analysis using expectation maximisation imputation to handle missing data. In addition, sensitivity analyses were conducted with different imputation techniques and these attested to the robustness of our findings.

Second, the follow-up period used in this trial was short and we do not know what the cost-effectiveness of the interventions would look like beyond 6 months.

Third, the per-participant intervention costs were partly based on assumptions. In particular, the assumption about the number of nurses that would engage in the online screening was important, because the number of participants affects economies-of-scale and ultimately determines the costs of online screening. It should be mentioned that whenever we had to make an assumption, we preferred to err on the conservative side, thus making a conscious choice to steer away from sketching too positive a picture of the cost-effectiveness of the interventions. It should also be noted that the costs for screening are low anyway and are therefore unlikely to have a substantial impact on the outcomes overall.

Fourth, the study's results are inevitably conditional on the central clinical end-point: work functioning. This was an a priori choice, but is also a limitation, because in this economic evaluation we did not report on secondary outcomes such as mental wellbeing, changes in symptom level of mental distress and so forth. Had we chosen other outcomes, we would have drawn different conclusions, because the nurses manifested with favourable response on some of these outcomes, even when they did not manifest with treatment response on work functioning. Thus, when we say that the e-mental health intervention is not to be recommended, we say this only with respect to

work functioning and our recommendations cannot be generalised towards other outcomes.

Fifth, the measurements of work functioning were based on self-report and this may have biased outcomes. However, it is difficult to say if this might have led to an upward or downward bias. Moreover, we are looking at relative change in work functioning over time and this may have cancelled out a constant bias in participants to exaggerate or diminish the level of their work functioning, while randomisation may have counteracted bias across conditions.

Sixth, it should be noted that all costs are computed for a situation in which the interventions have been fully implemented. Thus the initial investment required to implement the interventions is not part of our study. This was done in agreement with guidelines for economic evaluations (Drummond et al., 1993; Hakkaart et al., 2010; Krol et al., 2011), but we recognise that the costs required for implementing the interventions might be interesting in their own right. Estimates of these costs can therefore be obtained from the first author.

Seventh, although we complied with the guidelines for pharmacoeconomic evaluations carried out from the societal perspective whereby direct and indirect costs, inside and outside the healthcare system were included, we acknowledge the possibility of missing costs that might influence the results. Potentially, medical costs which may arise during life-years gained as a result of the treatment are lacking in this study. However, due to the preventive nature of the intervention, it is rather unlikely that these indirect costs within the health care system influence the cost-effectiveness results in a substantial manner.

Finally, this study was designed as a pragmatic trial that was conducted in the real-life context of one large academic medical centre in the Netherlands. The strength of this approach is that the trial has a good ecological (external) validity (Ramsey et al., 2005); its weakness is that the outcomes cannot be interpreted as evidence of the interventions' efficacy – only of the interventions' effectiveness under real-life conditions. The hospital in which this study was performed is an academic medical centre. Therefore, the findings are best generalised towards other teaching hospitals, while some caution must be applied when projecting the study's outcomes on hospitals that are not embedded in a university. In this context, it is important to note that the nurses were under constant pressure from their professional obligations and were free to make use of the interventions offered. We see that uptake rates and compliance rates are low, especially regarding the e-mental health interventions. While this may strengthen the level of realism of the trial's outcomes, the outcomes can now not be read as evidence for or against the efficacy of the interventions and are likely to differ from estimates that would have been obtained under tightly controlled conditions.

### 6.3. Recommendations

For improving work functioning in nurses, we recommend implementing the occupational physician condition over the control condition, because the occupational

physician condition is associated with better outcomes and cost savings. However, we must be careful recommending for or against implementing the e-mental health condition, because it is associated with a smaller likelihood of producing beneficial effects albeit for lesser costs than the control condition. We also note that had the e-mental health intervention been embedded more rigorously in the work setting, then uptake rates might have looked very different and the e-mental health condition might have yielded more favourable outcomes. At any rate, we recommend that e-health interventions be more fully integrated in the organisation before testing their effectiveness. These recommendations need to be viewed with some caution, because the economic evaluation was conducted with the specific, perhaps somewhat narrow, aim of improving work functioning. Moreover, the outcome was based on self-report, was extended over a brief follow-up period of 6 months, and was measured in the context of substantial, possibly selective, drop-out.

**Conflict of interest:** The e-mental health interventions evaluated in this study were developed by the Trimbos Institute. Trial registration: Netherlands Trial Register NTR2786.

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