OEM Online First, published on May 25, 2017 as 10.1136/oemed-2016-104248

ORIGINAL ARTICLE

Effect on return to work or education of Individual Placement and Support modified for people with mood and anxiety disorders: results of a randomised clinical trial

Lone Hellström,[1] Per Bech,[2] Carsten Hjorthøj,[1] Merete Nordentoft,[1] Jane Lindschou,[3] Lene Falgaard Eplov[1]

[1]Copenhagen University Hospital, Mental Health Center Copenhagen, Hellerup, Denmark
[2]Psychiatric Research Unit, Mental Health Centre North Zealand, University of Copenhagen, Hellerup, Denmark
[3]Copenhagen Trial Unit, Centre for Clinical Intervention Research, Copenhagen, Denmark

Correspondence to
Lone Hellström, Copenhagen University Hospital, Research Unit, Mental Health Center Copenhagen, Kildegårdsvej 28, DK-2900 Hellerup, Denmark; lone.hellstroem@regionh.dk

Received 9 December 2016
Revised 27 March 2017
Accepted 13 April 2017

ABSTRACT

Objectives The effect of Individual Placement and Support (IPS) on return to work or education among people with mood or anxiety disorders is unclear, while IPS increases return to work for people with severe mental illness. We examined the effect of IPS modified for people with mood and anxiety disorders (IPS-MA) on return to work and education compared with services as usual (SAU).

Methods In a randomised clinical superiority trial, 326 participants with mood and anxiety disorders were centrally randomised to IPS-MA, consisting of individual mentor support and career counselling (n=162) or SAU (n=164). The primary outcome was competitive employment or education at 24 months, while weeks of competitive employment or education, illness symptoms and level of functioning, and well-being were secondary outcomes.

Results After 24 months, 44.4% (72/162) of the participants receiving IPS-MA had returned to work or education compared with 37.8% (62/164) following SAU (OR=1.34, 95% CI: 0.86 to 2.10, p=0.20). We found no difference in mean number of weeks in employment or education (IPS-MA 32.4 weeks vs SAU 26.7 weeks, p=0.14), level of depression (Hamilton Depression 6-Item Scale score IPS-MA 5.7 points vs SAU 5.0 points, p=0.12), level of anxiety (Hamilton Anxiety 6-Item Scale score IPS-MA 5.8 points vs SAU 5.1 points, p=0.17), level of functioning (Global Assessment of Functioning IPS-MA 59.1 points vs SAU 59.5 points, p=0.81) or well-being measured by WHO-Five Well-being Index (IPS-MA 49.6 points vs SAU 48.5 points, p=0.83) at 24 months.

Conclusion The modified version of IPS, IPS-MA, was not superior to SAU in supporting people with mood or anxiety disorders in return to work at 24 months.

Trial registration number NCT01721824.

What this paper adds

- Individual Placement and Support (IPS) increases return to work for people with severe mental illness; however, the effect of IPS among people with mood or anxiety disorders is still unclear. The few existing randomised trials investigating the effect of return-to-work interventions for people with mood and anxiety were underpowered and included people with stress and burn-out.
- The version of IPS modified for people with mood and anxiety disorders - the IPS-MA method- was not superior to services as usual in supporting people with mood or anxiety disorders in their return to work.
- Implications for future research could be to integrate vocational services with mental health services to a higher extent, and to focus on regular discussions of disclosure in order to be able to provide sufficient workplace support.

INTRODUCTION

Mood and anxiety are highly prevalent disorders,[1] substantially impacting people's lives.[2] Moreover, considerable economic burden is imposed on societies,[2] mainly due to reduced working capacity and early retirement.[3] In Denmark, mood and anxiety disorders are among the five most frequent reasons for being granted a disability pension.[4] Consequently, increased attention has been on how to support people with mental illness in return to work, revealing a shortage of evidence concerning vocational rehabilitation for people with mood and anxiety disorders.[2]

Several randomised trials have found supported employment (place-train) to be more effective than prevocational training (train-place) regarding return to work of people with severe mental illness.[5] The most intensively studied intervention is Individual Placement and Support (IPS). IPS is based on eight principles: eligibility based on client choice, focus on competitive employment, integration of mental health and employment services, attention to client preferences, work incentives planning, rapid job search, systematic job development and individualised job supports.[6] A systematic review investigating IPS compared with usual vocational services for people with severe mental illness included 15 randomised trials and found that 59% returned to work following IPS compared with 23% following control conditions.[5] Consequently, strong evidence support IPS as an evidence-based approach to support people with severe mental illness in their return to work.[6]

To cite: Hellström L, Bech P, Hjorthøj C, *et al*. *Occup Environ Med* Published Online First: [please include Day Month Year]. doi:10.1136/oemed-2016-104248

At the time we planned our trial, the effect of IPS for people with mood and anxiety disorders had not to our knowledge been investigated. Only three randomised trials were found evaluating return-to-work interventions for people with mood and anxiety disorders.[7–9] One small trial (n=62) investigated occupational therapy and usual care versus usual care alone[7] and found time to return to work to be significantly reduced (207 days vs 299 days for the usual care group, RR=2.71, 93% CI: 1.16 to 6.29, p=0.01). A larger trial (n=240)[8] compared guideline-based care by occupational physicians with care as usual and found an effect on partial return to work (69% vs 54%, p=0.01) but not on time to return to work (HR=0.96, 95% CI: 0.73 to 1.27, p=0.78). A third trial (n=60) also included patients with stress and burn-out[9] and found an effect on return to work after 3 months (CAU: 11/25 (44%) vs intervention: 11/26 (58%), p=0.009) but not after 6 months (CAU: 21/25 (84%) vs intervention: 22/26% (85%), p=0.057) of training of occupational therapists and supportive psychiatric consultations.

On this background, we created the early supported employment intervention IPS modified for people with recently diagnosed mood or anxiety disorder (IPS-MA).[10]

METHODS AND MATERIALS

In an investigator-initiated, randomised clinical superiority trial, we aimed to evaluate the effect of the IPS-MA method on return to work or education, compared with services as usual (SAU). A detailed protocol of the randomised clinical trial has previously been published.[10] Slight changes to the trial protocol were made due to difficulties recruiting participants. Changes are presented in the section below and have been registered at ClinicalTrials.gov: NCT01721824.

Participants were recruited from mental health centres (inpatients and outpatients) and private practising psychiatrists within the Capital Region of Denmark, from 1 October 2011 until February 2013 (inclusion period was extended with 5 months). Inclusion criteria were as follows: (1) age 18–60 years; (2) diagnosis of affective disorder (International Classification of Diseases, 10th Revision (ICD-10): F30-39) or anxiety (ICD-10: F40-41); (3) no contact with mental health services for more than the past 3 years; (4) employed or enrolled in education at some time during the past 3 years (this criterion was changed during the trial from originally 2 years); (5) motivated to return to work or education; (6) not ready to return to work within 3 months after inclusion (equal to match group 2 or 3[11]; used by the job centres in Denmark to estimate how far from the labour market people are. Match group 2: able to participate in prevocational training but not able to work and be off public benefits within 3 months. Match group 3: severe long-term problems; cannot work or participate in prevocational training); (7) able to read and understand Danish and (8) give informed consent. Exclusion criteria were as follows: (1) somatic comorbidity causing reduced ability to work; (2) primary large-scale alcohol or substance abuse and (3) legal guardian or forensic psychiatric arrangements.

Participants were informed about the trial and referred by mental health professionals, who provided information on employment and education status, previous contact with mental health services and abuse or somatic comorbidity at referral; information was checked in hospital registers and was confirmed by the MINI International Neuropsychiatric Interview[12] and by asking the participants at the inclusion interview. A mentor and a researcher always participated in these interviews, and after obtaining informed consent, eligible participants went through a thorough baseline interview.

After the interview, the researcher, who had to remain blinded, left and the mentor called Copenhagen Trial Unit who carried out the randomisation. The mentor informed the participant of allocation group. A total of 326 participants on sick leave due to mood or anxiety disorder were included in the IPS-MA trial.

Register data on benefits received (employment or education status) were not available until the end of a 2-year follow-up. When we received these data, 43 of the included participants were registered as receiving state education grant or not receiving any benefits at baseline. Consequently, since data from the Danish Register for Evaluation of Marginalisation (DREAM) database were used to compute outcome variables, we had to exclude these 43 participants in the time-to-event analyses, since they would erroneously seem to be employed or studying at baseline.

Randomisation

Copenhagen Trial Unit generated the computer-generated allocation sequence with varying block sizes of 4, 6 and 8, concealed from the investigators. Randomisation was stratified by four diagnosis groups (bipolar disorder (F31); affective disorder (F30, F32–39); phobic anxiety (F40) or other anxiety disorders (F41)) and two match groups (match groups 2 and 3).

Interventions

Services as usual

Participants all received SAU as offered by the job centres in Denmark, for instance, courses, company internship programs, wage subsidy jobs, skill development and guidance, mentor support or gradual return to employment. Normally, benefits can be received for a maximum of 52 weeks.[13] Municipalities have economic incentives to implement an 'active and employment-oriented' policy.[14] If, after participating in prevocational rehabilitation, a person is not able to return to ordinary employment, he/she may be referred to a permanent wage-subsidised job where job demands and working hours are adjusted to his/her capacity. If the person cannot manage this job, he/she is eligible to receive disability benefits.[13]

IPS-MA method

Participants randomised to the intervention group received support according to the IPS-MA method, described in details elsewhere.[10] The method was tested and implemented by a private company, Sherpa.[15]

Briefly, the intervention consisted of mentor support and career counselling, providing five basic services: individualised mentor support based on psychiatric knowledge; coordination of services provided; career counselling; impartial help to clarify private economy; and contact with employers to help participants obtain jobs and keep them. Focus was on competitive employment and support was time unlimited.[10]

A plan of action was created based on goals, resources and challenges related to work/education, social relations and leisure activities, and the plan was evaluated regularly. Participants had the same mentor throughout the intervention, and support continued for as long as needed. The number and duration of contacts depended on the individual needs; most met with their mentor once a week for 1–1 ½ hours. Each mentor had a maximum caseload of 20 participants in order to secure the flexibility of the support.

Mentors had a minimum of 10 years' experience from mental health services, as nurses, social workers or occupational therapists. Career counsellors had many years of experience from

career counselling or human resources in the private sector. Mentors and career counsellors worked closely together.

Newly appointed mentors and career counsellors had a 2-week introduction to working routines and the IPS-MA method. Team members received monthly supervision provided by a trained psychologist.

The intervention was modified according to IPS with respect to the integration of services, since people with mood and anxiety disorders are treated in many different settings in Denmark, either by their general practitioner, private practising psychiatrist or psychologist, or in mental health centres, which hampered the integration of IPS-MA with mental health services. Instead, a coordinating approach was assumed to be adequate regarding this population. Furthermore, participants had to find jobs themselves through ordinary job-seeking channels but got support in choice of career, writing curriculum vitae, job applications and so on. Lastly, benefits counselling was not part of the IPS-MA method, but it would be part of the support in clarifying private economy if necessary.

Fidelity

To ensure implementation of the IPS-MA method, four fidelity measures were conducted by an independent investigator. Data were collected through multiple sources and focus was on core elements of the method.[10] The fidelity scale is a 21-item scale (scores ranging: 0–5 points) with a possible maximum score of 105 points. An organisational index was also developed: a 6-item scale (scores ranging: 0–5 points) with a maximum score of 30 points.

Data collection and outcomes

Participants were interviewed using clinician-administered scales, and patient-reported outcomes were scored at baseline and after

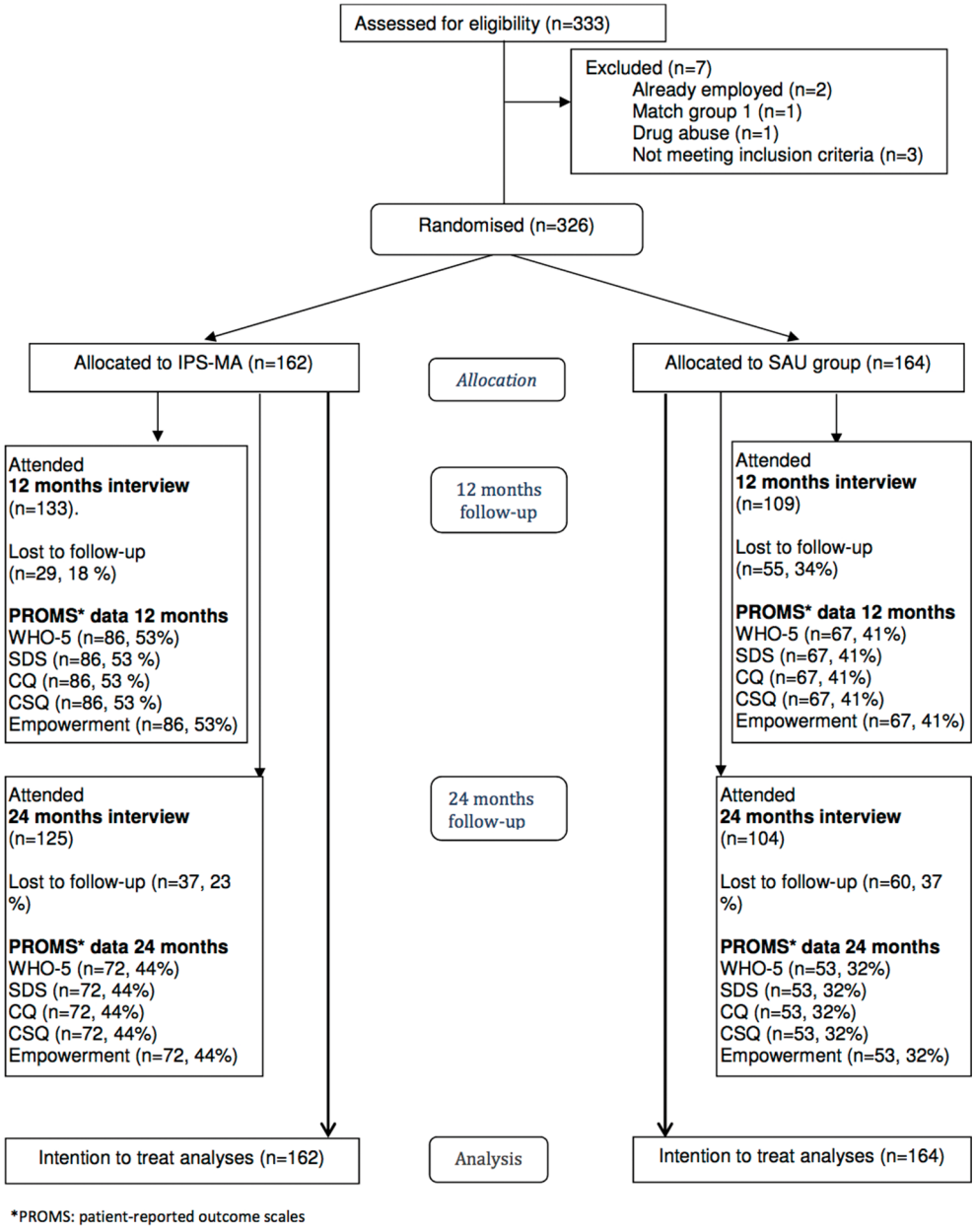

Figure 1 Flow chart of participants in the IPS-MA trial. CSQ, Client Satisfaction Questionnaire; CQ, Changes Questionnaire; IPS-MA, Individual Placement and Support modified for people with mood and anxiety disorders; MAS, Bech-Rafaelsen Mania Scale; PSP, Personal and Social Performance; ; SAU, services as usual; SDS, Sheehan Disability Scale; WHO-5, WHO-Five Well-being Index.

Table 1 Baseline characteristics of 326 participants in the IPS-MA trial, randomised to intervention (IPS-MA) or control group (SAU)

	IPS-MA (n=162)	SAU (n=164)
Gender, n (%)		
Female	115 (71)	106 (65)
Age, mean (SD)	34 (10)	36 (11)
Diagnosis, n (%)		
Depression (F30, F32-39)	112 (69)	113 (69)
Phobic anxiety (F40)	13 (8)	12 (7)
Other anxiety (F41)	19 (12)	20 (12)
Bipolar disorder (F31)	18 (11)	19 (12)
Match group*, n (%)		
Match group 2	106 (65)	108 (66)
Match group 3	56 (35)	56 (34)
Education, n (%)		
Primary school	29 (18)	23 (14)
High school	34 (21)	26 (16)
Vocational education	47 (29)	47 (29)
Bachelor degree	39 (24)	50 (31)
University degree or higher	13 (8)	17 (10)
Other	0	1 (1)
Civil status, n (%)		
Married/civil partnership/cohabitant	61 (38)	59 (36)
Single/separated/divorced/widow	101 (62)	105 (64)
Income support, n (%)		
Sickness benefit	87 (54)	101 (61)
State education grant (not active)	19 (12)	14 (8)
Social security	43 (26)	40 (25)
Other (inheritance, savings, spouse)	5 (3)	3 (2)
None	8 (5)	6 (4)
HAM-D6, mean (SD) (range)	10.1 (3.2) (0–17)	10.0 (3.3)(0–19)
HAM-A6, mean (SD) (range)	8.3 (3.8) (0–17)	8.1 (3.6)(0–18)
MAS, mean (SD) (range)	0.8 (1.9) (0–14)	0.7 (2.1)(0–19)
GAF-F, mean (SD) (range)	42.2 (6.2) (22–65)	42.7 (6.0)(32–70)
PSP, mean (SD) (range)	43.8 (7.1)(21–66)	44.2 (7.1)(30–71)
SDS, mean (SD)†	20.4 (5.2)	19.6 (5.3)
WHO-5, mean (SD)†	31.9 (19.4)	34.1 (18.2)
Empowerment, mean (SD)†	2.6 (0.3)	2.7 (0.2)
CQ, mean (SD)†	96.5 (18.8)	98.1 (16.8)
CSQ, mean (SD)†‡	22.1 (5.1)	23.5 (4.6)

*Match group 2: able to participate in prevocational training, but not able to work and be off public benefits within 3 months. Match group 3: severe long-term problems, cannot work or participate in prevocational training.
†% completed (IPS-MA; SAU): SDS (86; 84); WHO-5: (81; 80); Empowerment: (80; 79); CQ: (79; 77); CSQ: (83; 80).
CSQ, Client Satisfaction Questionnaire; CQ, Changes Questionnaire; GAF-F, Global Assessment of Functioning; HAM-A6, Hamilton Anxiety 6-Item Scale; HAM-D6, Hamilton Depression 6-Item Scale; IPS-MA, Individual Placement and Support modified for people with mood and anxiety disorders; MAS, Bech-Rafaelsen Mania Scale; PSP, Personal and Social Performance Scale; SAU, services as usual; SDS, Sheehan Disability Scale; WHO-5, The WHO-Five Well-being Index.

12 and 24 months after randomisation.[10] The patient-reported outcomes were answered online.

The primary outcome was competitive employment or education at 24 months, extracted from the DREAM database,[16] a register administered by the Danish Agency for Labour Market and Recruitment.

Secondary outcomes were weeks of competitive employment or education extracted from DREAM; level of symptoms and functioning assessed at the interview by the Hamilton Depression Scale (HAM-D6),[17] the Hamilton Anxiety Scale (HAM-A6)[17] and the Global Assessment of Functioning (GAF-F)[18] ; and self-reported quality of life by the WHO-Five Well-being Index (WHO-5),[17] measured at 24 months.

Exploratory outcomes included all outcomes above measured at 12 months, in addition to being ready to work, weeks of competitive employment or education and time until returning to employment or education. Level of symptoms of mania (Bech-Rafaelsen Mania Scale[19]), level of function (Personal and Social Performance,[20] Sheehan Disability Scale[21]), empowerment (Empowerment Scale[22]), readiness to seeking employment or education (Changes Questionnaire[23]) and satisfaction with treatment (Client Satisfaction Questionnaire[24]) measured at 12 and 24 months.

Blinding

It was not possible to blind participants, mentors, career counsellors or care providers. Outcome assessors and research team were blinded to allocation throughout the trial period, data collection and statistical analysis. Self-reported online surveys were answered using an identification number enabling the research team to remain blinded. The randomisation code was broken when all analyses were completed, and two conclusions had been drawn.

Statistical methods

We hypothesised that 45% would return to work or education in the IPS-MA group, compared with 30% in the control group.[10] With a power of 0.80 and a type-I error probability of 5%, 162 participants would be required in each group (a total of 324).[25] Power calculations for secondary outcomes have been reported previously.[10]

Logistic regression[26 27] was used to analyse the primary outcome. Only allocation status and stratification variables (diagnosis and match group) were included in the model.

Continuous outcomes were analysed using analysis of covariance[27] adjusted for stratification variables. Skewed data were transformed (log10), or the non-parametric Kruskal-Wallis test[26] was performed.

Time until returning to work or education is presented descriptively by a Kaplan–Meier plot.[26] Hazard ratios are calculated using Cox regression, unadjusted and adjusted for stratification variables.

All analyses were conducted according to the intention-to-treat (ITT) principles. According to the protocol,[10] we would use mixed model with repeated measurements to handle missing data, but we chose to use multiple imputations, since we believed that this would give us a better estimate of the missing values.[28] Predictions were based on variables with full information indicative of missing values; 100 imputations were made. If more than 50% was missing, we chose to report results based on the actual data, but compared these with results based on multiple imputations, both being prone to bias, results did not differ. We had complete data on all register data.

We described[10] that results of a 12-month follow-up would be reported as secondary outcomes. In order to avoid multiplicity, we changed results of the 12-month follow-up to exploratory.

Ethical considerations

On the basis of written and verbal information, all participants gave informed consent prior to inclusion. The trial was approved by The Regional Ethics Committees of the Capital Region (journal number: H-2–2011-FSP20), reported to the

Table 2 Return to work or education after 12 and 24 months of 326 participants included in IPS-MA trial

	n (%)	OR (exp(B))	95% CI	p Value	OR (exp(B))	95% CI	p Value
Return to work or education at 24 months							
Randomised to							
SAU	62 (37.8 %)						
IPS-MA	72 (44.2 %)	1.34*	0.86 to 2.10	0.20	1.32†	0.85 to 2.05	0.22
Return to work or education at 12 months							
Randomised to							
SAU	46 (28.0 %)						
IPS-MA	51 (32.5 %)	1.19*	0.74 to 1.92	0.48	1.18†	0.73 to 1.90	0.50

*Adjusted for diagnosis and match group at baseline.
†Unadjusted OR.
IPS-MA, Individual Placement and Support modified for people with mood and anxiety disorders.

Danish Data Protection Agency (journal number: 2007-58-0015, local journal number: RHP-2011-20). The trial was registered at www.clinicaltrials.gov (identifier: NCT01721824) after recruitment had started, but before a 1-year follow-up.

RESULTS

Of 326 eligible participants, 162 were randomised to IPS-MA[10] in addition to SAU, and 164 were randomised to SAU alone. CONSORT flow chart and characteristics of participants are presented in figure 1 and table 1, respectively. The two groups were comparable at baseline.

Primary outcome

In the IPS-MA group, 44.4% (72/162) had returned to work or education after 24 months compared with 37.8% (62/162) in the SAU group (OR=1.34, 95% CI: 0.86 to 2.10, p=0.20) (table 2).

Secondary and exploratory outcomes

No statistically significant difference was found on any employment outcomes (tables 2 and 3), and there was no difference on adjusted and unadjusted estimates. Participants regarded ready for work after 1 year was 72.8% (118/162) in IPS-MA versus 72.0% (118/164) in SAU (OR=1.06, 95% CI: 0.65 to 1.74, p=0.82), and 80.9% (131/162) in the IPS-MA group versus 75.0% (123/164) in SAU after 24 months (OR=1.44, 95% CI: 0.84 to 2.45, p=0.18).

At baseline, 43 participants were registered as either studying or without benefits; 33 received educational grant (none was actively studying); another 10 had been fired but were on payed sick leave, supported by parents, lived from savings or did not report their income support. Since they would be categorised as employed or studying at baseline, we had to exclude the 43 participants from the analysis of time to return to employment or education. Time until return to work was 71 (SE: 3.0) weeks in the IPS-MA group and 70 (SE: 3.0) weeks in the SAU group (HR=0.99, 95% CI: 0.73 to 1.35, p=0.96) (figure 2). We made subgroup analyses on return to work and education, respectively; no difference between groups was found (data not shown).

We found no difference in level of symptoms, functioning, well-being or empowerment between groups after 12 or 24 months, as shown in table 3. However, the patient-reported outcome scales were at baseline completed by only 81.9% of the participants. At 24 months follow-up, approximately 40% had completed the scales (figure 1).

Participants in the IPS-MA group reported to be more satisfied with the treatment at 12 and 24 months, and at 1-year follow-up, participants in the IPS-MA group reported a lower level of disability and more readiness to return to employment or education compared with the SAU group, but the difference was not present at 24 months follow-up (table 3).

During the follow-up period, no difference was seen between groups according to severity of symptoms, number of inpatient and outpatient admissions, lengths of admissions, emergency visits or deaths.

Fidelity

Overall, fidelity results indicated that the method was well implemented, with fidelity scores of 100, 102, 103 and 103, respectively (maximum score is 105) and a general organisational index score of 30 (maximum score is 30) at all four measurements.[10] A reason not to reach maximum fidelity score was that comments were made concerning the service of contact to employers (the workplace intervention). All participants were offered this service, but very few agreed to let their employer know about their mental illness; consequently, the workplace intervention was not practised sufficiently.

DISCUSSION

This is the first randomised trial investigating the effect of IPS-MA on return to work or education for people with mood or anxiety disorder. Against our primary hypothesis, we did not find IPS-MA to be superior to SAU regarding return to work or education.

As mentioned in the introduction, only three smaller randomised trials investigating return-to-work interventions to patients less severely ill than our target group had been carried out when we planned the present trial.[7–9] Four trials have been published since then[29–32]: three of which found no effect on return to work,[30–32] whereas one large trial (n=1193) by Reme *et al*[29] found an effect on work participation. This trial[29] compared usual care to integrated work-focused cognitive–behavioural therapy (CBT) and individual job support based on IPS for people with mood and anxiety disorders. In the trial by Reme *et al*, participants had baseline levels of depression and anxiety of approximately 8 (mild) and 11 (moderate), respectively, as measured by the Hospital Anxiety and Depression Questionnaire. In our trial, the participants had baseline mean levels of depression and anxiety of approximately 10 (moderate) and 8 (mild), measured by the HAM-D6 and HAM-A6, respectively (table 1). Altogether, the target groups in the two trials are similar but not identical when it comes to illness severity. Rather similar to our finding of a 6.6% points difference between IPS-MA and SAU (44.4% vs 37.8%), Reme *et al* found a significant difference of 7% points (44.2% vs 37.2%)[29] after 1 year, in favour of the intervention. However, p values are not able to provide an answer to a 'how much?' estimation question.[33] We

Table 3 Employment, symptoms, level of function, quality of life and other secondary and exploratory outcomes at 12 and 24 months

		12 months					24 months				
		ANCOVA				Kruskal-Wallis*	ANCOVA				Kruskal-Wallis*
		n (%)	Mean (SE)	Mean difference (SE)	p Value	p Value	n (%)	Mean (SE)	Mean difference (SE)	p Value	p Value
Employment											
Weeks worked	Control	164 (100)	9.9 (1.34)	1.68 (1.90)			164 (100)	26.7 (2.74)	5.72 (3.89)		
	IPS-MA	162 (100)	11.6 (1.35)	(−2.06 to 5.42)	0.38†	0.74	162 (100)	32.4 (2.76)	(−1.93 to 13.37)	0.14†	0.22
Symptoms‡											
HAM-D6	Control	109 (67)	6.7 (0.41)	−0.27 (0.45)			104 (63)	5.0 (0.44)	0.77 (0.48)		
	IPS-MA	133 (82)	6.5 (0.38)	(−1.15 to 0.61)	0.71†	0.74	125 (77)	5.7 (0.43)	(−0.17 to 1.71)	0.13†	0.23
HAM-A6	Control	109 (67)	6.6 (0.45)	0.15 (0.50)			104 (63)	5.1 (0.42)	0.66 (0.48)		
	IPS-MA	133 (82)	6.8 (0.42)	(−0.83 to 1.13)	0.77†	0.60	125 (77)	5.8 (0.42)	(−0.28 to 1.60)	0.14†	0.13
MAS	Control	109 (67)	0.3 (0.14)	0.21 (0.17)			104 (63)	0.5 (0.13)	−0.12 (0.14)		
	IPS-MA	133 (82)	0.5 (0.14)	(−0.12 to 0.54)	0.32†	0.25	125 (77)	0.4 (0.11)	(−0.39 to 0.15)	0.36†	0.74
Level of function‡											
GAF-F	Control	109 (67)	56.8 (1.38)	0.20 (1.51)			104 (63)	59.5 (1.38)	−0.36 (1.54)		
	IPS-MA	133 (82)	57.0 (1.27)	(−2.75 to 3.16)	0.76†	0.94	125 (77)	59.1 (1.30)	(−3.33 to 2.61)	0.71†	0.93
PSP	Control	109 (67)	60.2 (1.30)	−0.56 (1.46)			104 (63)	62.6 (1.42)	−1.29 (1.56)		
	IPS-MA	133 (82)	59.7 (1.19)	(−3.42 to 2.30)	0.94†		125 (77)	61.3 (1.34)	(−4.35 to 1.77)	0.44†	
SDS§	**Control**	70 (43)	15.7 (1.01)	−2.53 (1.10)			56 (34)	10.5 (1.25)	1.6 (1.41)		
	IPS-MA	86 (53)	13.2 (0.89)	(−4.70 to −0.35)	0.02†	0.08	73 (45)	12.1 (1.23)	(−1.17 to 4.41)	0.25†	0.20
Other‡											
WHO-5§	Control	69 (42)	42.1 (3.27)	5.34 (3.58)			53 (32)	47.7 (3.70)	2.48 (4.14)		
	IPS-MA	86 (53)	47.4 (2.90)	(−1.73 to 12.41)	0.14†	0.42	73 (45)	50.2 (3.60)	(−5.71 to 10.67)	0.55†	
Empowerment§	Control	68 (42)	2.7 (0.03)	−0.01 (0.04)			53 (32)	2.7 (0.04)	−0.04 (0.05)		
	IPS-MA	86 (53)	2.7 (0.03)	(−0.06 to 0.08)	0.77†		72 (44)	2.7 (0.04)	(−0.13 to 0.05)	0.38†	
CSQ§	Control	69 (42)	21.4 (0.87)	3.72 (0.95)			54 (33)	21.7 (0.92)	−3.59 (1.05)		
	IPS-MA	86 (53)	25.2 (0.77)	(1.85–5.60)	0.00†	0.00	73 (45)	25.3 (0.90)	(1.52–5.66)	0.00†	0.001
CQ§	Control	67 (41)	99.8 (3.03)	8.05 (3.32)			53 (32)	103.1 (3.66)	5.52 (4.10)		
	IPS-MA	86 (53)	107.8 (2.66)	(1.50–14.60)	0.02†	0.006	72 (44)	108.6 (3.61)	(−2.60 to 13.63)	0.18†	0.23

*When residuals were not normally distributed, and transformation did not result in normal distribution, non-parametric Kruskal-Wallis test was performed. It did not change the results.

†Adjusted for diagnosis and match group at baseline.

‡Multiple imputations were made to account for missing data. Missing data for each outcome (% control/IPS-MA): interview data: HAM-D6, HAM-A6, MAS, GAF-F and PSP: 12 months: 34/18; 24 months: 37/23. Survey data: SDS, WHO-5, Empowerment, CSQ, CQ: 12 months: 59/47; 24 months: 68/56. Since multiple imputations were made, n=164 for controls and n=162 for IPS-MA in the analyses.

§Results based on multiple imputations were not reported for SDS, WHO-5, Empowerment, CSQ and CQ since more than 50% data were missing. Imputed results did not differ from the reported results based on the actual number of respondents though. Still, results should be interpreted with caution.

ANCOVA, analysis of covariance; CSQ, Client Satisfaction Questionnaire; CQ, Changes Questionnaire; GAF-F, Global Assessment of Functioning; HAM-A6, Hamilton Anxiety 6-Item Scale; HAM-D6, Hamilton Depression 6-Item Scale; IPS-MA, Individual Placement and Support modified for people with mood and anxiety disorders; MAS, Bech-Rafaelsen Mania Scale; PSP, Personal and Social Performance Scale; SDS, Sheehan Disability Scale; WHO-5, The WHO-Five Well-being Index.

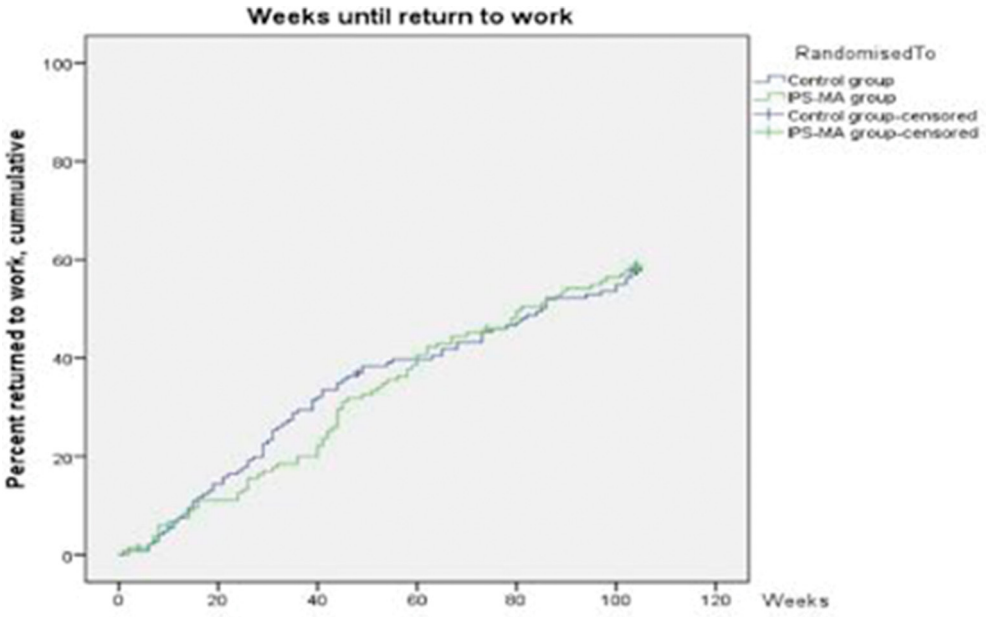

Figure 2 Time until return to work or education for 283 participants included in the analysis, randomised to IPS-MA (n=136) or SAU (n =147). IPS-MA, Individual Placement and Support modified for people with mood and anxiety disorders; SAU, services as usual.

may have been too optimistic when planning the present trial as we based the number of participants needed to include on a 15% points difference. Therefore, in contrast to Reme *et al*, we do not have the power to state if the observed difference of 6.6% points is in fact a true difference, but it is most likely not of any 'clinical' relevance in a socioeconomic perspective. The number needed to treat (NNT) in the trial by Reme *et al*[29] was 13, and a positive economic return of their intervention was not found. The difference of 6.6% in our trial equals an NNT of 15 (1/0.066), but since the IPS-MA intervention is very intensive, an ongoing health economic analysis will reveal whether this difference is in fact cost effective.

According to the sparse literature available when planning this trial, return-to-work interventions were recommended to have an outreach to the workplace and to be integrated with mental health services.[7–9] We based the IPS-MA method on this literature and the principles of IPS,[6] but IPS-MA differs in one important aspect: the integration of mental health and employment services, hampered by the many different treatment settings. Since Sherpa, who provided the IPS-MA method, already cooperated with mental health services and job centres, we chose to let Sherpa coordinate services; this deviation from IPS may have impacted our results. In accordance with our trial, the three recently published randomised trials[30–32] with similar patient groups compared adjuvant occupational therapy,[31] collaborative care aimed at return to work[32] or work-related CBT[30] with usual care and did not find enhanced clinical or vocational care separately to be superior concerning return to work.[30 32] They, too, did not integrate treatment with vocational support.[30–32] In contrast,[29] integrated mental healthcare and individual job support based on IPS had sufficient power to find an effect on work participation. Moreover, trials of IPS[6] and two recent OECD reports[34 35] conclude that integration of vocational rehabilitation and mental health services is highly recommended. Hence, growing evidence support that integration of services is vital; this may very well be a reason for not finding an effect in our trial.

Furthermore, the IPS-MA method was well implemented, yet remarks on the workplace intervention were made at all four fidelity measures. One fidelity report stated that: 'reaching out to the workplace, Sherpa being 'hotline' for employer and giving information to colleagues seem to have been deliberately deprioritized'. Sherpa argue that they focus on the participant's 'healthy self', and they do not wish to introduce the participant as a new colleague in need of support. This may indicate that disclosure has not been a priority in Sherpa, resulting in practically no participants in IPS-MA choosing to disclose, a fact that may have hindered sufficient workplace support. The lack of disclosure is surprising since a literature review[36] found rates of disclosure between 35% and 87%, people with mood disorders significantly less likely to disclose than people with severe mental illness[36] though, indicating that they could be more vulnerable relative to disclosure and may have an increased need for support in this matter. Disclosure is a process, and feasible tools have been developed to assist people considering disclosure in an employment setting.[37] 'To gain adjustments' at work is a common reason for disclosure of mental illness,[38] and once people realise that the workplace support is troubled by their lack of disclosure, they may change their mind regarding disclosure. In recent studies of IPS,[39 40] disclosure is regularly discussed, pros and cons are evaluated (which have been found to be strongly correlated with employment) and disclosure is found to have an impact on how support can be delivered.[40] Recent studies of people with mood and anxiety disorders support the importance of the workplace intervention[2 32 41] and thereby disclosure. A Cochrane review from 2014,[2] investigating interventions to improve return to work in depressed people, concludes that a workplace-directed intervention including support in modifying work tasks or working hours in addition to treatment reduces sickness leave compared with treatment alone. A recent Dutch trial,[32] comparing collaborative care with usual care, reports a poorly applied workplace intervention as one reason for not finding an effect on return to work. In our trial, the lack of disclosure may have hampered the workplace intervention since support could only be provided 'behind the scenes', and it could be another reason why we did not find an effect of the intervention.

Notably, 23% of the participants in the IPS-MA group still had symptoms of moderate to severe depression after 2 years, and 19% had symptoms corresponding to moderate to severe anxiety. This is in accordance with the course of mood and anxiety disorders in a number of longitudinal studies,[42 43] reporting approximately 20% of participants still having symptoms of depression and only 59% of patients with anxiety[42] having remitted 2 years after inclusion, supporting that the courses of illnesses are heterogeneous and that some might be long lasting and hard to treat. Furthermore, the participants' level of functioning was surprisingly impaired; according to the GAF-F, 22% in IPS-MA and 28% in SAU were seriously impaired even after 2 years. Impairments both due to symptoms and level of function at follow-up bound to impact participants' ability to work indicate that neither treatment nor the workplace intervention may have been adequate. This could also be an explanation of our results; participants may have needed far more treatment in order to be ready to return to work and more support in managing employment and negotiating workplace accommodations.

In short, at least three possible explanations for not finding an effect of IPS-MA emerge: lack of integration of IPS-MA with mental health services; lack of disclosure, and thereby insufficiently applied workplace intervention; and lastly, the rather large proportion of participants still challenged with symptoms of depression and anxiety and low level of function after 2 years indicate that they may have needed further treatment in order to return to work.

Incentives, mostly economic, have been made in SAU to promote a faster return to work, and focus on return to work of our target group has increased during the trial period; one could argue that SAU is 'as good as it gets'? A systematic review[39] including 15 randomised clinical trials investigating IPS in patients with severe mental illness found that 59% returned to work following IPS; hence, 38% returning to work following SAU in our trial cannot be satisfying in a group of patients considered less severely ill. Furthermore, in our trial, 75% and 81% were regarded ready to work in the two groups, respectively, after 2 years, with only 38%–44% actually returning to work, and neither IPS-MA nor SAU can be said to have the desirable effect. Thus, it is crucial to continue the search for better interventions to support return to work.

This trial has several strengths: it has been designed in order to minimise the risks of systematic errors and the risks of random errors, by means of central randomisation stratified for prognostic factors. Assessors and research team were blinded to allocation, and data were analysed according to the ITT principle. Furthermore, the use of the DREAM database gave us the unique possibility of having complete data on all employment outcomes.

Some limitations have to be mentioned though. The follow-up rate for patient-reported outcome scales answered online was low. Thus, an algorithm to remind participants not completing the questionnaires was lacking in our online contact. Consequently, the trial may be underpowered for some outcomes, which may therefore only be viewed as hypothesis generating.

The DREAM database has some limitations. First, only one benefit can be recorded per week; consequently, some benefits overwrite others, and some participants may have been misclassified, but we have no reason to believe this to be different in the two groups.[16] Second, it is possible to receive state education grant for a long time without being actively studying, and participants who do not actively deactivate their grant will be registered as studying; in IPS-MA, they were encouraged to deactivate their grant, and we do not know if this was the case for the control group. In order to elucidate possible misclassification and to validate the database, we compared data from DREAM with interview data collected at 2-year follow-up. In total, four participants were registered as receiving state education grant but reported to be sick-listed; two reported to be studying but did not receive education grant according to DREAM. Overall, a kappa coefficient=0.83 was found, indicating sufficient correlation.

In conclusion, we failed to show superiority of the IPS-MA method compared with SAU. However, our results, which are in line with the robust, but non-socioeconomically relevant difference of 7% found by Reme *et al*, demonstrate a crucial need for continued research in order to develop effective vocational interventions for people with mood and anxiety, which are clinically relevant from an individual as well as a socioeconomic perspective.

Acknowledgements The authors thank Britt Reuter Morthorst, Christine Posselt and Marie Lønberg Hansen for excellent assistance in recruiting participants, conducting research interviews, and data assessment. They also thank Ann-Lis Gregersen for, among many other things, patiently contacting participants for follow-up.

Contributors LH participated in the planning and design of the trial and conducted the research interviews, data analysis and interpretation, drafting of the figures and writing of the manuscript. LFE conceived the trial and participated in the planning and design, data interpretation and co-writing of the manuscript. MN participated in the planning and design of the trial and in data interpretation. JL participated in the design of the trial and in the planning of analysis. PB participated in the planning and design of the trial and was responsible of the training of the assessors. CH took part in the data preparation, analysis and interpretation of data. All authors have read and critically revised the manuscript.

Funding The trial as a whole is funded by the Obel Family Foundation, the Tryg Foundation and the Danish Agency for Labour Market and Recruitment. No current or future sponsors of the trial will have any role in the trial design, collection of data, analysis of data, data interpretation or publication of data from the trial.

Competing interests Managerial responsibility and supervision lie with LFE, MN and PB. Sherpa has had no role in the trial design, collection, analysis or interpretation of data nor in publication of data from the trial. Due to administrative convenience, LH was formally employed by Sherpa from 1 June 2011 until 31 August 2013. LH's PhD has exclusively been funded by external funding, and LH has throughout the entire period been working at the Research Unit at Mental Health Centre Copenhagen, where she is now employed. None of the other authors has any competing interest.

Ethics approval The Regional Ethics Committees of the Capital Region (journal no: H-2-2011-FSP20).

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Vos T, Flaxman AD, Naghavi M, *et al*. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2163–96
2 Nieuwenhuijsen K, Faber B, Verbeek JH, *et al*. Interventions to improve return to work in depressed people. *Cochrane Database Syst Rev* 2014;(12):CD006237.
3 Borg V, Nexø MA KI. *Hvidbog om mentalt helbred, sygefravær og tilbagevenden til arbejde*. København, Arbejdstilsynet: Det Nationale Forskningscenter for Arbejdsmiljø, 2010.
4 Flachs EM, Eriksen L, Koch MB, *et al*. *Sygdomsbyrden i Danmark - sygdomme*. København: Sundhedsstyrelsen, 2015.
5 Bond GR, Drake RE, Becker DR. Generalizability of the Individual Placement and Support (IPS) model of supported employment outside the US. *World Psychiatry* 2012;11:32–9.
6 Drake RE, Bond GR, Becker DR, *et al*. *Individual Placement and Support: an evidence-based approach to supported employment*. Oxford: Oxford University Press, 2013:1–204.
7 Schene AH, Koeter MWJ, Kikkert MJ, *et al*. Adjuvant occupational therapy for work-related major depression works: randomized trial including economic evaluation. *Psychol Med* 2006;2007:351–62.

8 Rebergen DS, Bruinvels DJ, Bezemer PD, *et al*. Guideline-based care of Common Mental Disorders by Occupational Physicians (CO-OP study): a randomized controlled trial. *J Occup Environ Med*2009;51:305–12.
9 van der Feltz-Cornelis CM, Hoedeman R, de Jong FJ, *et al*. Faster return to work after psychiatric consultation for sicklisted employees with common mental disorders compared to care as usual. A randomized clinical trial. *Neuropsychiatr Dis Treat* 2010;6:375–85 http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2938286&tool=pmcentrez&rendertype=abstract
10 Hellström L, Bech P, Nordentoft M, *et al*. The effect of IPS-modified, an early intervention for people with mood and anxiety disorders: study protocol for a randomised clinical superiority trial. *Trials* 2013;14:442 http://www.trialsjournal.com/content/14/1/442\nhttp://www.scopus.com/inward/record.url?eid=2-s2.0-84890825750&partnerID=tZOtx3y1
11 The Danish Agency for Labour Market and Recruitment. The match model (match model, styrelsen for arbejdsmarked og rekruttering). *Retsinformation* 2016.
12 Sheehan DV, Lecrubier Y, Sheehan KH, *et al*. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59 Suppl 20:22–33.
13 The Danish Agency for Labour Market and Recruitment. Vocational rehabilitation, initiatives and arrangements (Internet). 2016 http://star.dk/da/Indsatser-og-ordninger.aspx
14 Ministry of Employment. Denmarks active labour market policy (lov om en aktiv beskæftigelsesindssats). 2015 https://www.retsinformation.dk/forms/r0710.aspx?id=173094
15 Sherpa. 2016 http://www.team-sherpa.dk/
16 The Danish Agency for Labour Market and Recruitment. *The DREAM database, statistics Denmark (DREAM databasen, Danmarks Statistik)*. Copenhagen, Denmark: The National Labour Market Authority, 2015. http://www.dst.dk/da/TilSalg/Forskningsservice/Data/Andre_Styrelser.aspx
17 Bech P. *Clinical psychometrics*. Oxford: Wiley-Blackwell, 2012.
18 Pedersen G, Karterud S. The symptom and function dimensions of the Global Assessment of Functioning (GAF) scale. *Compr Psychiatry* 2012;53:292–8.
19 Licht RW, Jensen J. Validation of the Bech-Rafaelsen Mania Scale using latent structure analysis. *Acta Psychiatr Scand* 1997;96:367–72.
20 Nafees B, van Hanswijck de Jonge P, Stull D, *et al*. Reliability and validity of the Personal and Social Performance scale in patients with schizophrenia. *Schizophr Res* 2012;140:71–6.
21 Sheehan DV, Harnett-Sheehan K, Raj BA. The measurement of disability. *Int Clin Psychopharmacol* 1996;11:89–95.
22 Rogers ES, Chamberlin J, Ellison ML, *et al*. A consumer-constructed scale to measure empowerment among users of mental health services. *Psychiatr Serv* 1997;48:1042–7.
23 Miller WR, Johnson WR. A natural language screening measure for motivation to change. *Addict Behav* 2008;33:1177–82.
24 Nguyen TD, Attkisson CC, Stegner BL. Assessment of patient satisfaction: development and refinement of a service evaluation questionnaire. *Eval Program Plann* 1983;6:299–313.
25 Dupont WD, Plummer WD. Power and sample size calculations. A review and computer program. *Control Clin Trials* 1990;11:116–28.
26 Altman DG. *Practical statistics for medical research.* 1st edn. London: Chapman & Hall, 1991.
27 Slt APK. *Regression with linear predictors*. New York, NY: Springer, 2010.
28 Schafer JL, Graham JW. Missing data: our view of the state of the art. *Psychol Methods* 2002;7:147–77.
29 Reme SE, Grasdal AL, Løvvik C, *et al*. Work-focused cognitive–behavioural therapy and individual job support to increase work participation in common mental disorders: a randomised controlled multicentre trial. *Occup Environ Med* 2015;72:745–52.
30 Himle JA, Bybee D, Steinberger E, *et al*. Work-related CBT versus vocational services as usual for unemployed persons with social anxiety disorder: A randomized controlled pilot trial. *Behav Res Ther* 2014;63:169–76.
31 Hees HL, de Vries G, Koeter MWJ, *et al*. Adjuvant occupational therapy improves long-term depression recovery and return-to-work in good health in sick-listed employees with Major depression: results of a randomised controlled trial. *Occup Environ Med* 2013;70:252–60.
32 Vlasveld MC, van der Feltz-Cornelis CM, Adèr HJ, *et al*. Collaborative care for sick-listed workers with Major depressive disorder: a randomised controlled trial from the Netherlands Depression Initiative aimed at return to work and depressive symptoms. *Occup Environ Med* 2013;70:223–30.
33 Cummings G. *Understanding the new statistics*. London: Routledge, 2012.
34 OECD. *Mental health and work: Denmark*. Paris: OECD Publishing, 2013.
35 OECD. *Sick on the job? Myths and realities about mental health and work*. Paris: OECD Publishing, 2012.
36 Jones AM. Disclosure of mental illness in the workplace: a literature review. *Am J Psychiatr Rehabil* 2011;14:212–29.
37 Henderson C, Brohan E, Clement S, *et al*. Decision aid on disclosure of mental health status to an employer: feasibility and outcomes of a randomised controlled trial. *Br J Psychiatry* 2013;203:350–7.
38 Brohan E, Henderson C, Wheat K, *et al*. Systematic review of beliefs, behaviours and influencing factors associated with disclosure of a mental health problem in the workplace. *BMC Psychiatry* 2012;12:11 http://www.biomedcentral.com/1471-244X/12/11http://discovery.ucl.ac.uk/1346898/.
39 Bond GR, Peterson AE, Becker DR, *et al*. Validation of the Revised Individual Placement and Support Fidelity Scale (IPS-25). *Psychiatr Serv* 2012;63:758–63.
40 Allott KA, Turner LR, Chinnery GL, *et al*. Managing disclosure following recent-onset psychosis: utilizing the individual placement and support model. *Early Interv Psychiatry* 2013;7:338–44.
41 Dewa CS, Loong D, Bonato S. Work outcomes of sickness absence related to mental disorders: a systematic literature review. *BMJ Open* 2014;4:e005533.
42 Penninx BW, Nolen WA, Lamers F, *et al*. Two-year course of depressive and anxiety disorders: results from the Netherlands Study of Depression and Anxiety (NESDA). *J Affect Disord* 2011;133:76–85.
43 Keller MB, Lavori PW, Mueller TI, *et al*. Time to recovery, chronicity, and levels of psychopathology in major depression. A 5-year prospective follow-up of 431 subjects. *Arch Gen Psychiatry* 1992;49:809–16.

Effect on return to work or education of Individual Placement and Support modified for people with mood and anxiety disorders: results of a randomised clinical trial

Lone Hellström, Per Bech, Carsten Hjorthøj, Merete Nordentoft, Jane Lindschou and Lene Falgaard Eplov

Occup Environ Med published online May 25, 2017