REVIEW



Vocational Outcomes of the Individual Placement and Support Model in Subgroups of Diagnoses, Substance Abuse, and Forensic Conditions: A Systematic Review and Analysis of Pooled Original Data

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Accepted: 8 January 2021

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Abstract

Purpose To investigate the effect of Individual Placement and Support (IPS) according to diagnoses of schizophrenia, bipolar disorder, major depression, substance use disorders, or forensic psychiatric conditions.

Methods A systematic search of the literature was conducted in June 2017 and repeated in December 2020. The systematic review included 13 studies. Analyses of pooled original data were based on the six studies providing data (n=1594). No studies on forensic psychiatric conditions were eligible. Hours and weeks worked were analyzed using linear regression. Employment, and time to employment was analyzed using logistic regression, and cox-regression, respectively.

Results The effects on hours and weeks in employment after 18 months were comparable for participants with schizophrenia, and bipolar disorder but only statistically significant for participants with schizophrenia compared to services as usual (SAU) (EMD 109.1 h (95% CI 60.5–157.7), 6.1 weeks (95% CI 3.9–8.4)). The effect was also significant for participants with any drug use disorder (121.2 h (95% CI 23.6–218.7), 6.8 weeks (95% CI 1.8–11.8)). Participants with schizophrenia, bipolar disorder, and any drug use disorder had higher odds of being competitively employed (OR 2.1 (95% CI 1.6–2.7); 2.4 (95% CI 1.3–4.4); 3.0 (95% CI 1.5–5.8)) and returned to work faster than SAU (HR 2.1 (95% CI 1.6–2.6); 1.8 (95% CI 1.1–3.1); 3.0 (95% CI 1.6–5.7)). No statistically significant effects were found regarding depression.

Conclusions IPS was effective regarding schizophrenia, bipolar disorder, and substance use disorder; however, the effect on hours, and weeks worked was not statistically significant regarding bipolar disorder. For people with depression the impact of IPS remains inconclusive. Non-significant results may be due to lack of power.

Trial Registration: PROSPERO protocol nr. CRD42017060524

Keywords Supported employment · Vocational rehabilitation · Mental disorders · Substance-related disorders

Introduction

Severe mental illnesses (SMI) such as schizophrenia, bipolar disorder, and major depression are associated with higher rates of unemployment than any other groups with disabilities [1]. However, most people with SMI want to work [2] and interventions have been developed to support their return to work [1, 3, 4]. Supported employment, which focuses on a rapid return to work with ongoing

than traditional vocational rehabilitation, where people are trained in supported environments before seeking employment ("train-place") [1, 4]. Individual Placement and Support (IPS) is the most widely studied model of supported employment and is considered an evidence-based practice for helping people with SMI to gain and maintain employment [1, 4–7]. IPS is based on eight principles: (1) focus is on competitive employment; (2) eligibility is based on client choice; (3) rapid job search; (4) attention to client preferences; (5) integration of mental health and employment services; (6) time-unlimited and individualized support; (7) systematic job development; and (8) personalized benefits counseling [7].

support ("place-train"), has shown to be more effective

Published online: 04 March 2021

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People with a schizophrenia spectrum diagnosis comprise the majority of participants in studies of IPS, whereas people diagnosed with bipolar disorder, major depression, and other psychiatric diagnoses are included to a lesser extent [8–10]. Given the very different courses of schizophrenia, bipolar disorder, and major depression, one could speculate that the effect of IPS might differ according to diagnosis; however, there has been a lack of attention to possible diagnostic differences in IPS studies. Across eight studies of different models of "supported employment", participants with bipolar, and depressive disorders were more likely to be competitively employed than participants with psychotic disorders, and substance use disorders [11]. However, only three of the eight included models were IPS programs.

A considerable number of people with SMI have dualdiagnosis (i.e., severe mental illness, and substance use disorder), which have severe consequences for the course of their illness, their health, and level of functioning [13], and may lead to multiple obstacles to obtaining employment. Even though most studies on IPS include participants with substance use problems [7], few studies have reported the effectiveness of IPS for participants with dual disorders [14]. Across four randomized trials IPS was found to be more effective in supporting the return to work of participants with dual-diagnosis than traditional vocational rehabilitation [14]. Criminal justice involvement is also high in people with SMI [15], especially in people with a dual-diagnosis, and many experience additional barriers to employment due to the stigma attributed to being an offender [16]. A study included participants with SMI (i.e. schizophrenia spectrum diagnosis, bipolar disorder, or depressive disorder) as well as forensic psychiatric conditions, that is a history of criminal justice involvement, or people who were involved in community forensic services, and found that more participants obtained competitive employment in IPS compared to the control group [17].

Although some studies have found IPS to have different impact on people with different diagnoses, substance use disorders, and forensic psychiatric conditions, the evidence is still quite equivocal, and most studies have been underpowered to detect differences. To sum up the evidence, a systematic review is needed.

The aim of the present systematic review was to investigate the effectiveness of IPS on return to competitive employment in subgroups of SMI: schizophrenia, bipolar disorder, and major depression, as well as on people with SMI, and substance use disorders, or who are involved with the criminal justice system.

Hypotheses were:

1. IPS is superior to services as usual (SAU) in improving hours and weeks worked over 18 months for participants

- with schizophrenia, bipolar disorders, and major depression as well as participants with substance use disorder, and forensic psychiatric involvement.
- Participants with schizophrenia, bipolar disorders, and major depression, as well as participants with substance use disorders, and forensic psychiatric involvement receiving IPS are more likely to be competitively employed, find work faster, and earn more wages over 18 months than participants receiving SAU.

Methods

Protocol and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [18], and a predefined protocol has been published online on PROSPERO [19], protocol nr. CRD42017060524.

A comprehensive literature search was originally performed in August 2017 and updated in January 2019 and December 2020 by two librarians employed at the library of University of Southern Denmark. Searches were conducted in the electronic databases Medline, Embase, PsycInfo, Scopus, Web of Science, Cochrane, Cinahl, Sociological abstracts and OT seeker. Furthermore, ClinicalTrials.gov and WHO-trial registration were searched for unpublished material. A combination of search terms and synonyms covering 'severe mental illness', 'Individual Placement and Support ', and 'Randomized trial' were used. There were no limitations regarding year of publication or language. Bibliographies from primary studies and review articles were hand searched. The full search strategy is presented in Table A in the appendix.

Eligible studies had to:

- (1) be randomized clinical trials (RCTs)
- (2) include unemployed participants of either gender, aged 18–65, with SMI defined as schizophrenia spectrum disorders, bipolar disorder, or severe depression according to the WHO International Classification of Diseases version 10 [20] or the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5th edition [21].
- (3) compare IPS to either SAU or other interventions not using IPS or modified IPS (referred to as SAU).
- (4) perform fidelity reviews with the IPS fidelity scale [22] with a minimum score of fair fidelity (corresponding to \geq 73 on the IPS-25 scale, and \geq 56 on the IPS-15 scale).
- (5) include one or more of the following outcome measures at 18 months of follow-up: employment status, weeks



and hours of employment, income, or time to employ-

Selection of Studies and Data Extraction

Using the online software program Covidence [23], two reviewers (PP and LH) independently screened titles and abstracts. Any disagreements were discussed to reach consensus. If this was not possible a third reviewer (TC) was consulted. Full text articles were obtained for the remaining articles and were examined independently by the same two reviewers to confirm eligibility. Again, a third reviewer was consulted in case of disagreement.

Information regarding study population (e.g. gender, age, diagnoses, substance use disorder, forensic conditions and follow-up period), intervention and control conditions, vocational outcomes (e.g. employment rate, hours and weeks worked, as well as time to employment) was extracted. If information was not available, authors for included studies were contacted by email and requested to provide either rawdata or the necessary analyses.

Risk of Bias in Studies

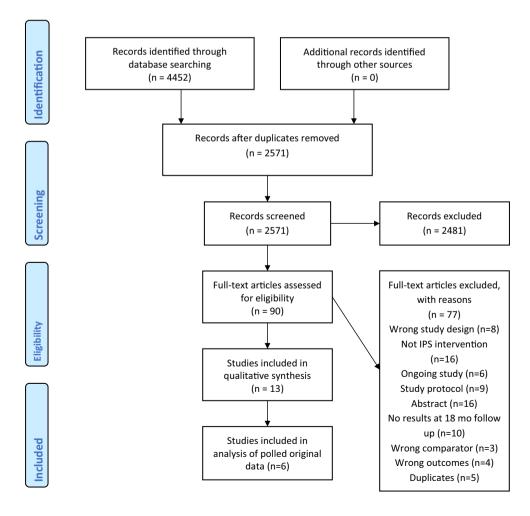
The Cochrane Risk of Bias Tool [24] was used to assess risk of bias in individual studies. The two reviewers independently assessed the included studies, and consensus was reached through discussion. It was not possible to blind participants and personnel to allocation due to the nature of the interventions; therefore, this item was not included in the assessment. Other sources of bias were limited to 'Vested financial interests bias', that is, whether any of the authors had any financial conflicts of interests. 'Appropriateness of statistical test' was also investigated for all included studies.

Studies were judged "Overall low risk of bias" if all domains were answered "Low risk of bias" and "Overall high risk of bias" if one or more domains were marked as "High risk" or "Unclear".

Study Selection

After duplicates were removed, the electronic searches resulted in 2571 unique records (Fig. 1). Titles and abstract were screened, and 2481 records were excluded, leaving 90 full text articles. Of these 77 were excluded, primarily due







to the intervention not being IPS, or the record being a conference abstract. This left us with 13 studies based on 13 trials including 3406 participants (see Appendix Table B for characteristic of studies).

The study by Christensen et al [25] was among the 13 studies included. Since the reviewing authors were involved in this trial, it was evaluated by two independent reviewers.

Risk of Bias in Selected Studies

Three of the included studies were of high quality with an 'Overall low risk of bias [8, 25, 26], whereas the remaining nine had an 'Overall high risk of bias', primarily due to lack of blinding of outcome assessors [9, 10, 12, 27–32] (Table 1).

All studies but one reported to use computer generated randomization lists [31]. Viering et al. reported to use a binomial probability distribution list to randomize participants, but it was not clearly stated how this list was generated or used to randomize participants. All studies except Viering et al. [31] reported satisfactory details on allocation concealment.

Three of the 13 included studies reported that outcome assessors were blinded to allocation [8, 25, 26], in two studies it was not clear whether assessors were blinded or not [31, 32], and in the remaining eight studies assessors were not blinded to allocation. The preponderance of un-blinded assessors may have led to an overestimation of the effect-sizes in the respective studies [33].

Table 1 The Cochrane Risk of Bias assessment of 13 included RCT's

Studies reported loss to follow-up ranging from 2 [28] to 32% [31], and reported no differences in attrition rates between groups. The study with an attrition rate of 32% used last observation carried forward (LOCF) to handle missing data [31].

Five studies reported outcomes according to a published protocol [8, 9, 25, 26, 31]. One study did not report educational activity as an outcome as stated in an a priori protocol [32]. The remaining 7 studies reported all vocational outcomes as stated in their aims.

None of the studies included were assessed to have high risk of vested financial interests. One study was assessed to have unclear risk of bias, since the authors did not include a conflict of interests statement [28].

Other Potential Sources of Bias: Appropriateness of Statistical Test

Reviewing the statistical procedures of the included studies showed only minor issues in three publications, where parametric methods (ANOVA, mixed effects regression) were used on potentially skewed or zero-inflated secondary outcomes [26, 28, 29].

Study Population of Pooled Original Data

Since none of the 13 included studies presented results stratified by diagnosis, substance use disorder or forensic psychiatric involvement, the authors were contacted and asked if they could provide these data. Six authors provided

	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors	Incomplete outcome reporting	Selective outcome reporting	Vested financial interests bias	Method fidelity
Bejerholm 2014								
Bond 2007								
Burns 2007								
Chiu 2008 /Wong								
Christensen 2018								
Mueser 2004				•				
Drake 1999								
Hoffmann 2012								
Lehman 2002						•		
Michon 2014								
Reme 2019								
Viering 2015								
Wong 2007								

Low risk of biasUnclear risk of bias

High risk of bias



data, hence, a total of six studies were included in the final pooled analysis of original data [8, 9, 25, 26, 29, 32], with a total of 1896 participants from 18 different sites [8, 9, 25, 26, 29, 32]. Participants were excluded if they had a diagnosis other than schizophrenia, bipolar disorder or depression (n=259), missing diagnosis (n=8), or incomplete outcome data (n=35), leaving 1594 participants in the final analysis.

Outcome Measures from Pooled Original Data

Primary outcomes were number of hours and weeks worked during the 18 months of follow-up. Secondary outcomes were employment status at 18 months, income during the 18 months as well as time to employment.

Employment referred to competitive employment, which was defined as any employment in the regular labor market on ordinary terms during the 18 months of follow-up. Time to employment was defined as time to any first competitive employment. Data for time until employment was unavailable in one study [32].

Income data was only available in two out of six studies, and as these data was not clearly defined, we excluded income in the analyses.

Exposure Measures from Pooled Original Data

A binary indicator of IPS was the exposure variable, and the effect of IPS compared to SAU was tested with diagnosis groups as strata, as well as an overall effect estimate for all three diagnosis groups combined.

Diagnoses were recoded based on the provided original data and grouped into schizophrenia, bipolar disorder and depression. Diagnoses were all based on validated clinical diagnostic instruments or clinical diagnoses using ICD-10 or DSM codes. The group with schizophrenia included a broader group of patients with psychosis in two studies [8, 32]. In two studies overlaps were accepted in diagnostic groups [8, 32]. This implies that some patients are included in the group with depression and also in either schizophrenia or bipolar disorder. Estimates are adjusted for this overlap.

Substance use disorder was recoded into alcohol use disorder, any drug use disorder, and hard drug use disorder. Alcohol use disorder was dichotomized as alcohol abuse (≥ five days with five drinks/day per month) and no alcohol abuse (< 5 days with five drinks per month) in the study by Christensen et al [25]. Alcohol use disorder was defined as abuse, dependence, or dependence with institutionalization and no alcohol abuse as abstinent, and use without impairment in the study by Mueser et al. [29] This category included alcohol abuse or alcohol dependence in Reme et al [32].

Drug use disorder included two categories: soft drugs (cannabis, etc.) and hard drugs. Substance use disorder was

defined in Burns et al [9] as use of non-prescribed drugs with hard drugs including use of heroin and cocaine. Christensen et al [25] defined drug use as self-reported use of drugs within 30 days prior to inclusion. Hard drugs excluded cannabis-based drugs for all studies. Michon et al [26] used binary classifications of drug use for both hard drugs and soft drugs. For Mueser et al [29] drug use disorder included patients with drug abuse, dependence or dependence with institutionalization. Drug use disorder in Reme [32] included patients with substance abuse or dependence.

None of the studies provided information about forensic psychiatric involvement, and therefore this subgroup was omitted from further analysis.

Statistical Analysis of Pooled Data

Baseline characteristics were presented for each included study and the pooled sample using means and standard deviation (SD) for continuous variables and n and percentages for categorical variables.

Number of hours and weeks worked were analyzed using linear regression with robust standard errors. All non-missing observations are included in the analysis, including a substantial number of zeros. Estimated mean differences (EMD), which correspond to the difference between group means, were reported. Crude results as well as results adjusted for age, gender, study, and site were presented. Diagnostic groups were also introduced as control variables as diagnostic groups overlapped for 37 patients. This way the effect of IPS was isolated for the group with depression when this group also contain patients with schizophrenia (n=2) or bipolar disorder (n=2). The remaining 33 were classified with both bipolar disorder and psychosis.

Competitive employment was analyzed using logistic regression. Time to competitive employment was analyzed using proportional hazard (Cox) regression. Significant hazard ratio estimates assume proportionality of the hazards compared over time. Proportionality in this context means that the ratio between hazards is constant over time. For one hazard ratio estimate this assumption was violated, but the estimate was robust when interacting the treatment effect with time. This interaction allows for violations of the proportionality assumption as the interaction between time and treatment effect allows the treatment effect to increase or decrease over time. In contrast, the standard proportionality assumptions imply that the ratio between the hazards of the comparison groups is constant over time. Estimates were adjusted for age, gender, study, and site as fixed effects. Diagnostic groups were also introduced as control variables in cases with overlapping categories.

All point estimates are presented with 95% confidence intervals. A two-sided probability of p < 0.05 was considered



statistically significant. All analyses were performed in R 3.6.0.

Results

Participants in the six studies included in the present review were similar regarding age, and gender; participants were mostly younger than 40 years of age, and 59.5% were men. Most participants had schizophrenia (74.4%), while people with bipolar disorder and depression comprised 14.1% and 14.1% respectively (Table 2). Across the studies providing information on alcohol or drug use disorder, 9.8% of participants were reported to have alcohol use disorder, 16.2% were reported to have any drug use disorder (hard and soft drugs), while 3% had a hard drug use disorder only (Table 2).

Hours and Weeks Worked

On average, participants in IPS worked more hours (221.5 vs 116.8) and weeks (14.6 vs 8.8) than the SAU group, with adjusted estimated mean differences (EMDs) of 98.4 h (95% CI 53.2–143.7) and 5.3 weeks (95% CI (3.2–7.4)) within the 18-month follow-up. Differences with similar magnitudes were observed for the subgroup of participants with

schizophrenia (adj. EMDs: 109.1 h (95% CI 60.5–157.7), 6.1 weeks (95% CI 3.9–8.4)). The magnitude was similar for participants with bipolar disorder (adj. EMDs: of 108 h (95% CI – 80.6–297.4) and 6.7 weeks (95% CI – 0.3–13.7)), which suggest a substantial positive treatment effect; however, this difference was not statistically significant. For participants with major depression no significant differences were observed in hours (adj. EMDs: – 32.7 (– 159.8–94.5) and weeks of employment (0.95 (– 5.56–7.47) compared to SAU. Participants with any drug use disorder (soft and hard drugs) in IPS worked significantly more hours and weeks compared to SAU (adj. EMDs: 121.2 h (95% CI 23.6–218.7), 6.8 weeks (95% CI 1.8–11.8)). No differences were observed between IPS and SAU for participants with alcohol or hard drug use disorder (Table 3).

Competitive Employment

Overall, participants in IPS had 1.92 times higher odds of being competitively employed at any time during follow-up compared to SAU (95% CI 1.53–2.42); this pattern was the same for the two subgroups of people with a diagnosis of schizophrenia (OR: 2.07 (1.58–2.73)) and a diagnosis of bipolar diagnosis (OR: 2.37 (1.27–4.43)). For participants with depression the magnitude was smaller and not

Table 2 Baseline characteristics of participants from the six studies included in the pooled analysis

	Bejerholm (n=69)		Burns (n = 281)		Christense $(n=720)$		Michon (n=98)		Mueser $(n=197)$		Reme (n=229)		Total (n = 1594)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Gender														
Male	36	52.2	168	59.8	444	61.7	70	71.4	121	61.4	109	47.6	948	59.5
Female	33	47.8	113	40.2	276	38.3	28	28.6	76	38.6	120	52.4	646	40.5
Age														
17–24	3	4.3	25	8.9	204	28.3	9	9.2	13	6.6	50	21.8	304	19.1
25-34	13	18.8	102	36.3	247	34.3	49	50	67	34	85	37.1	563	35.3
35–44	40	58	82	29.2	174	24.2	18	18.4	80	40.6	49	21.4	443	27.8
45–54	12	17.4	57	20.3	76	10.6	19	19.4	28	14.2	37	16.2	229	14.4
55–65	1	1.4	15	5.3	19	2.6	3	3.1	9	4.6	8	3.5	55	3.5
Diagnosis														
Schizophrenia	58	84.1	230	81.9	551	76.5	82	83.7	152	77.2	111	49.1	1184	74.4
Bipolar	6	8.7	51	18.1	87	12.1	8	8.2	10	5.1	61	27.6	223	14.1
Depression	9	13	0	0	82	11.4	8	8.2	35	17.8	90	39.3	224	14.1
Alcohol														
No					656	91.1			174	88.3	198	88.8	1028	90.2
Yes					64	8.9			23	11.7	25	11.2	112	9.8
Any drug use														
No			258	92.1	602	83.6	66	71.7	160	81.2	180	81.4	1266	83.8
Yes			22	7.9	118	16.4	26	28.3	37	18.8	41	18.6	244	16.2
Hard drug use														
No			258	98.9	698	96.9	85	92.4					1041	97
Yes			3	1.1	22	3.1	7	7.6					32	3



Table 3 Competitive employment and hours and weeks worked in strata of diagnoses and substance abuse

	IPS	SAU	Crude p-va OR/EMD (95% CI)		Adjusted OR/EMD (95% CI)	p-value	
All (n = 1594)		1					
Competitively employed (n, %)	395 (43.2)	192 (28.2)	1.93 (1.56-2.39) ^a	0.000	1.92 (1.53–2.42) ^a	0.000	
Hours (mean, SD)	221.51 (475.76)	116.79 (325.15)	104.73 (62.17-147.28) ^b	0.000	98.44 (53.21-143.67) ^b	0.000	
Weeks (mean, SD)	14.57 (22.50)	8.77 (19.34)	5.80 (3.74–7.86) ^b	0.000	5.33 (3.22–7.44) ^b	0.000	
Schizophrenia (n = 1184)							
Competitively employed (n, %)	267 (40.0)	130 (25.1)	1.98 (1.54–2.55) ^a	0.000	2.07 (1.58-2.73) ^a	0.000	
Hours (mean, SD)	212.45 (468.87)	102.35 (301.65)	110.10 (63.76–156.44) ^b	0.000	109.10 (60.49–157.71) ^b	0.000	
Weeks (mean, SD)	12.93 (21.57)	6.87 (17.01)	6.07 (3.87-8.26) ^b	0.000	6.12 (3.87-8.38) ^b	0.000	
Bipolar $(n=223)$							
Competitively employed (n, %)	81 (55.9)	28 (35.9)	2.26 (1.29-4.02) ^a	0.005	2.37 (1.27–4.43) ^a	0.007	
Hours (mean, SD)	336.41 (582.11)	214.40 (445.98)	122.01 (- 37.13-281.14) ^b	0.133	108.40 (- 80.63-297.44) ^b	0.261	
Weeks (mean, SD)	19.93 (24.02)	12.15 (22.01)	7.77 (1.52–14.03) ^b	0.019	6.71 (- 0.30-13.72) ^b	0.053	
Depression $(n=224)$							
Competitively employed (n, %)	58 (45.7)	37 (38.1)	1.36 (0.80-2.34) ^a	0.259	1.24 (0.69–2.23) ^a	0.463	
Hours (mean, SD)	140.09 (329.57)	125.98 (340.82)	14.11 (- 101.24-129.46) ^b	0.810	- 32.67 (- 159.84-94.50) ^b	0.615	
Weeks (mean, SD)	16.99 (24.18)	15.63 (25.28)	$1.35 (-5.21-7.91)^{b}$	0.685	0.95 (- 5.56-7.47) ^b	0.765	
Alcohol $(n=112)$							
Competitively employed (n, %)	26 (43.3)	16 (30.8)	1.72 (0.79-3.80) ^a	0.172	1.20 (0.50-2.86) ^a	0.678	
Hours (mean, SD)	199.10 (414.25)	98.94 (307.39)	100.17 (- 52.46-252.79) ^b	0.198	50.18 (- 104.04-204.40) ^b	0.524	
Weeks (mean, SD)	15.66 (22.88)	10.95 (21.98)	$4.72 (-3.60-13.03)^{b}$	0.270	1.66 (- 7.40-10.73) ^b	0.705	
Any drugs $(n=244)$							
Competitively employed (n, %)	55 (39.6)	21 (20.0)	2.59 (1.46-4.73)	0.002	2.95 (1.51-5.78) ^a	0.002	
Hours (mean, SD)	197.27 (458.43)	52.18 (173.34)	145.09 (54.26-235.91) ^b	0.002	121.16 (23.59-218.73) ^b	0.015	
Weeks (mean, SD)	12.30 (20.50)	6.39 (16.58)	5.91 (1.26–10.57) ^b	0.016	6.79 (1.83–11.76) ^b	0.005	
Hard drugs $(n=32)$							
Competitively employed (n, %)	4 (21.1)	3 (23.1)	0.80 (0.14-4.84) ^a	0.798	0.74 (0.11-5.19) ^a	0.766	
Hours (mean, SD)	23.41 (60.88)	38.72 (92.45)	- 15.31 (- 72.26-41.65) ^b	0.598	4.10 (- 43.73-51.94) ^b	0.866	
Weeks (mean, SD)	3.92 (9.77)	6.51 (15.57)	- 2.58 (- 12.07-6.91) ^b	0.568	- 1.31 (- 10.40-7.79) ^b	0.733	

^aOR

statistically significant (OR: 1.24 (0.69–2.23)). Participants with any drug use disorder had 2.95 higher odds of obtaining employment following IPS compared to SAU (95% CI 1.51–5.78), although there was no difference between the groups when examining at participants with an alcohol or hard drug use disorder (Table 3).

Time to Work

Participants in IPS obtained employment 1.90 times faster than participants in SAU (95% CI 1.55–2.32). The pattern remained the same when looking at the subgroups of the specific diagnoses of schizophrenia (HR 2.06 (95% CI 1.63–2.61)) and bipolar disorder (1.80 (95% CI 1.05–3.08)); however, the hazard ratio was lower and not significant for participants with depression (1.07 (95% CI 0.56–2.03) (Fig. 2).

For participants with any drug use disorder IPS was associated with a faster return to work compared to SAU (HR 2.98 (95% CI 1.57–5.66)), whereas participants with alcohol or hard drug use disorder did not significantly differ from the SAU group (HR's 0.93 (95% CI 0.41–2.13) and 0.33 (95% CI 0.02–5.15) respectively).

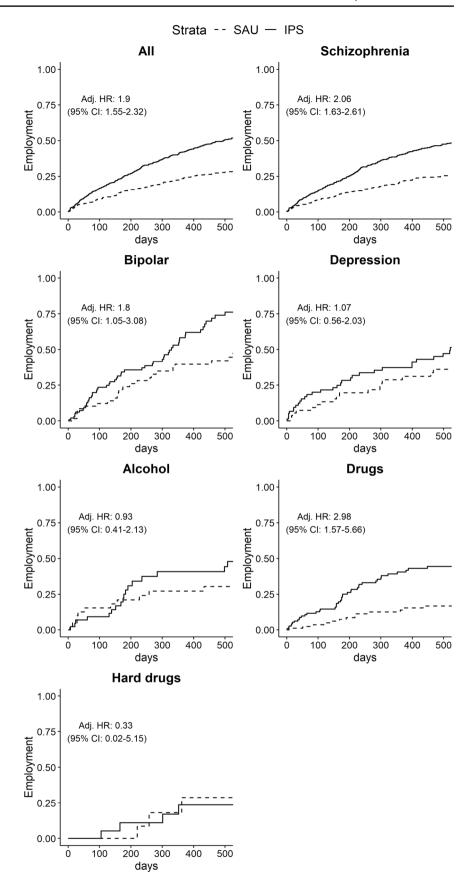
Discussion

The aim of the present systematic review was to investigate the effectiveness of IPS on return to competitive employment across three subgroups of SMI; schizophrenia, bipolar disorder, and major depression, as well as for participants with SMI, and substance use disorders or involvement with the criminal justice system.



^bEMD, adjusted for: age, gender, study and site

Fig. 2 Time until employment





Overall, IPS was more effective in helping participants obtain competitive employment, work more hours and weeks, and get work faster than SAU. The magnitude of these effects was similar in participants with schizophrenia and bipolar disorder but only statistically significant for those with schizophrenia. Participants with bipolar disorder were significantly more likely to obtain competitive employment and returned to work significantly faster than the SAU group. But the highly skewed distributions of hours and weeks employed resulted in quite large, but unstable treatment effect estimates for the group of patients with bipolar disorder. These estimates are not statistically significant as the high variance and zero-inflation for these outcomes generate correspondingly large standard errors. This is also reflected in small effect sizes when point estimates are standardized using the overall standard deviation: the 108.4 additional hours worked correspond to standardized mean difference of 0.26. This figure is 0.31 for the additional weeks worked among patients with bipolar disorder. A larger sample with bipolar disorder might have resulted in statistically significant effects for this subgroup as well.

No effect of IPS was found for participants with depression regarding any vocational outcome. Although our overall findings are in line with the strong evidence already established for the effect of IPS for people with SMI, [1, 4, 5, 7] the lack of differences for participants with depression is a novel finding. Our findings could be due to lack of power, since the subgroups of participants with depression and bipolar disorders only comprised approximately 14% each of the population included in the present study.

In the Mental Health Treatment Study (MHTS) SAU was compared to IPS plus a comprehensive package of services and benefits (i.e., behavioral health and related services, comprehensive insurance to pay for needed services and outof-pocket expenses). Compared to other studies, the number of participants with affective disorders was rather high in this study (70%, n = 1574), and more than half of these had major depression. According to the final report, 53.7% with affective disorder were competitively employed during the 24 months compared to 32.7% in the control group [34, 35]. These numbers are generally in line with our findings, however, the MHTS lack data on specific outcomes for participants with depression. Depressive symptoms have been associated with a negative impact on employment for participants with and without schizophrenia [11], and have been found to predict sick leave in general [36]. Thus, as a supplement to IPS, participants with depressive symptoms may need additional support or treatment (e.g., strengthening motivation and coping strategies) in order to decrease depressive thoughts and avoidance behavior in relation to work [36]. Work-focused cognitive behavioral therapy, with a focus on return to work, and work-related aspects, has been found to decrease time to return to work, and to speed up functional recovery in work in a regular psychotherapeutic setting treating people with common mental disorders [37]. IPS may be better suited for people with more severe illness. Whether the lack of effect regarding people with depression is due to the content of IPS, or merely a question of power must be investigated further.

Participants with any drug use disorder appeared to benefit from IPS; they worked more hours and weeks than the SAU group, they obtained work faster, and had higher odds of being competitively employed after 18 months than participants in the SAU group. This is a unique finding, and somewhat counter-intuitive. However, one might speculate, that the emphasis on zero exclusion and rapid job search in IPS may be helpful in reducing delays or concerns among traditional vocational service providers about the readiness and ability of a person with a drug use disorder to get competitive work. The lack of association with hard drug use disorder may be due to lack of power, since this group was very small (n = 32). However, as for depression, the observed difference between IPS and SAU is quite small and might not be relevant, even if a larger sample would render a significant result. Patients with dual diagnoses may be additionally marginalized due to the stigma attributed to the substance abuse; however, few studies have conducted subgroup analysis on this group of participants [14]. The evidence regarding vocational outcomes of people with substance use disorder is mixed [14]. Across 4 RCT's, participants with dual diagnosis had significantly better work outcomes following IPS compared to the control group [14], whereas a study included in the present review, found that an active substance use disorder was associated with worse employment outcomes among participants in the IPS group compared to participants without an active substance use disorder [12]. In a pilot study on methadone treatment for opioid use disorder, IPS was found to enhance the chances of getting work, and to sustain employment within the 12 months follow-up. In both IPS and the control group employment was less likely to be competitive, and most worked for minimum wages without healthcare benefits [38]. Investigating the effect of IPS provided to participants with different kinds of substance use disorder may be important to be able to better support this subgroup of patients, which may have different needs according to type of disorder.

We intended to study if IPS had an effect in income, however, income data was only provided by two out of six studies, and as these data was not clearly defined, this outcome was omitted. We would have expected people in IPS to have had a higher income compared to SAU, since the goal of IPS is competitive employment. Studies have found IPS to be associated with higher wages earned [8, 10, 29], although others have not found this association [12, 28]. We also intended to study the effect of IPS in a subgroup of participants with SMI and forensic psychiatric involvement,



but found only one relevant study [17]. This study was not included since it only had 12 months of follow-up, however, it reported a significant effect of IPS on proportion of participants in competitive employment compared to SAU. A protocol for a randomized trial studying the feasibility of IPS for patients with offending histories in the community forensic services was also found. Results from this trial will add to the limited evidence regarding this group of patients [16].

The results of our review indicate that IPS is an effective intervention for participants with schizophrenia and suggest participants with bipolar disorder may experience similar benefits, although the differences were not statistically significant, presumably due to lower power. The results for participants with depression, on the other hand, indicated no effect of IPS; however, confidence intervals were wide, which could potentially mask an effect, and similar to bipolar disorder power to detect differences was low. The effect of IPS for these two groups of patients should be evaluated in either an RCT with sufficient power or in a meta – analyses including more data on participants with bipolar disorder and depression. Furthermore, it might be relevant to investigate whether participants with depression would benefit from support in strengthening motivation and functional cognitive strategies in order to decrease depressive thoughts and avoidance behavior prior to the IPS intervention, as proposed by Bejerholm et al [36].

Strengths and Limitations

This systematic review was based on a comprehensive review of the literature conducted by trained librarians. The included studies were of moderate to very good methodological quality. Authors of the included studies were contacted to obtain original raw-data. We only received data from six out of 13 studies; which could influence the external validity of our results. However, the six studies represent US, UK, Germany, Italy, Switzerland, Netherlands, Bulgaria, Sweden, Norway and Denmark, and our results should to some extent be representative of European and American society. Even though only six of 13 studies provided original raw-data, the total study population was rather large (n = 1594). However, participants with bipolar disorder or depression only comprised approximately 14% each of the total study population, which may induce wide confidence intervals and uncertainty of the results due to lack of power. Participants with mood disorders added up to a total of 287 participants in the 7 studies not providing data for the present review, being able to include these studies would probably have resulted in more robust results regarding the subgroups of depression.

We chose only to include studies with a follow-up of 18 months because this is the most commonly used follow-up period (n = 13 studies). Our results might have looked

different if we had chosen 12 or 24 months, however, this would have given us less power, since only 10 and 6 studies, respectively, used these time points. We could have reported vocational outcomes at 12 and 18 months in order to include more studies.

Two studies did not have blinded outcome assessors, introducing the possibility of rater bias, which may result in an overestimation of the effect. However, employment outcomes are quite objective and often information was gathered from several sources (interviews and logbooks).

The results might be influenced by drop-outs since the pooled data analysis is based on complete cases, except for Christensen et al [25] and Reme et al [32], where register data on employment was retrieved for all included patients. However, only one, out of the six studies was affected by dropout in the vocational outcome measurements.

All studies defined competitive employment as having a job in the regular labor market, paying at least minimum wages, contracted by clients and not set aside for persons with disability. However, when a participant was defined as being employed varied from having worked one day [9, 26] to at least one week [8]. Studies defining being employed as having worked one day may overestimate the effect of the intervention, since it is not a sustainable measure of employment. This potential measurement error will turn into biased effect estimates only if it occurs more often in one treatment group compared to the other.

The original data we received on alcohol and drug use disorders, were quite heterogeneous and the criteria for use disorder was not very well defined and often judged by the professional to be 'problematic use' or not, without any indications of amount, or frequency of use. Therefore, only data from three studies were included in the analysis of alcohol [25, 29, 32], five studies in the analysis of any drug use [9, 25, 26, 29, 32], and three studies in the analysis of hard drugsy [9, 25, 29]. A pragmatic and rather conservative definition was adapted to compute the variables. However, results may have been affected, but since abuse is known to be under reported in general, the results are most likely underestimated. Specifically, regarding the hard drugs only group, the number of participants included is rather low, which may have jeopardized the power.

The hazard ratio estimate assumes proportional hazards over time, which is not the case for the group of bipolar patients as the survival curves overlap in the first few days. When adding the interaction between IPS and time, the effect remained significant and of similar magnitude. By adding the interaction between time and treatment effect, we estimate the violation of the proportionality assumption. This means that any disproportionality over time in the hazards of the two groups compared is incorporated in the model and the proportionality assumption is relaxed.



Conclusion

Overall, IPS was more effective than SAU in supporting participants to obtain competitive employment, to work more hours, and weeks, and to return to work faster. This applied particularly for participants with schizophrenia, bipolar disorder, and substance abuse; however, even though the magnitude of the effect was similar to that of Schizophrenia. the effect on hours, and weeks worked was not statistically significant for participants with bipolar disorder, which is probably due to lack of power. Participants with any drug abuse seemed to benefit the most from IPS, whereas participants with alcohol or hard drug only abuse did not seem to benefit significantly. No statistically significant effect of IPS was found for participants with depression on any of the vocational outcomes, which could also be due to lack of power. However, differences were small and probably not relevant, hence, for people with depression the impact of IPS remains indecisive.

Supplementary Information The online version of this article (https://doi.org/10.1007/s10926-021-09960-z) contains supplementary material, which is available to authorized users.

Author contributions LFE, TNC, IGW, PP, ABB, ES, and LH participated in the planning and design of the study. TNC, IGW, UB, JvB, HM, KTM, SER, SW provided data for the review. PP and LH reviewed the literature. ABB conducted the analyses and drafting of figures and tables. ABB, PP and LH wrote the manuscript. All authors have participated in the interpretation of the results and have read and critically revised the manuscript.

Funding No funding was received for conducting this study.

Data Availability Data from the study is only available on request due to privacy/ethical restrictions.

Compliance with Ethical Standards

Conflicts of interest The authors declare no conflicts of interests.

Ethics Approval Included studies were all performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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