## Vocational outcomes of the individual placement and support model in subgroups of diagnosis, substance abuse and forensic conditions: a systematic review and analysis of pooled original data

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## Abstract

Objective

To investigate if Individual Placement and Support (IPS) was equally effective regarding obtaining employment for participants with schizophrenia, bipolar disorder, major depression, substance abuse disorders, or forensic psychiatric conditions.

Methods

The systematic review included 13 studies. Authors were contacted and analyses of pooled original data were based on the six studies providing data (n=1594). Effectiveness was measured after 18 months. Number of hours and weeks worked were analyzed using linear regression. Competitive employment and time to competitive employment were analyzed using logistic regression and proportional hazard (cox) regression, respectively. No studies provided data on criminal history; hence analysis of this subgroup was omitted.

Results

The effects on hours and weeks in competitive employment were comparable for participants with schizophrenia and bipolar disorder but were only statistically significant for participants with schizophrenia with an estimated mean difference of 109.1 hours (95% CI 60.5-157.7), and 6.1 weeks (95% CI 3.9-8.4) worked. No significant difference was found for participants with depression compared to services as usual (SAU). Participants with any drug use disorder worked significantly more hours and weeks in IPS compared to SAU (121.2 hours (95% CI 23.6-218.7), 6.8 weeks (95% CI 1.8-11.8).

Participants with schizophrenia had 2.1 times higher odds of being competitively employed (95% CI 1.6-2.7) and returned to work 2.1 times faster than SAU (95% CI 1.6-2.6). Participants with bipolar disorder were more often competitively employed (OR 2.4, 95%CI 1.3-4.4) and returned to work faster (HR 1.8, 95% CI 1.1-3.1) than SAU. No difference was found for participants with depression. Participants with any drug use disorder had 3.0 times higher odds of being competitively employed in IPS compared to SAU (95% CI 1.5-5.8).

Conclusion

Overall, IPS was more effective than SAU considering participants with schizophrenia, bipolar disorder and substance use disorder. For people with a diagnosis of depression the specific impact of IPS remains inconclusive as no statistically significant effects or clinically relevant effect size estimates were identified for this subgroup. Non-significant results for bipolar disorder, depression, alcohol-, and hard drug use disorders may be due to lack of power.

**Trial Registration:** PROSPERO protocol nr. CRD42017060524

**Keywords:** Supported employment, Individual placement and support, severe mental illness, employment, vocational rehabilitation, vocational outcomes, schizophrenia, bipolar disorder, depression, substance abuse, forensic conditions.

## Introduction

Severe mental illnesses (SMI) such as schizophrenia, bipolar disorder and major depression are associated with high rates of unemployment, higher than for any other groups with disabilities1. However, most people with SMI want to work2 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 support (“place-train”), has shown to be more effective 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 employment1,4–7. 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 counseling7.

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” Cook et al 2008 found that participants with bipolar and depressive disorders were more likely to be competitively employed than participants with psychotic disorders and substance use disorders11. However, only three of the eight included models of “supported employment” were IPS programs.

A considerable number of people with SMI have dual-diagnosis (i.e., severe mental illness and substance use disorder), which have severe consequences for the course of their illness, their health, and level of functioning13, 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 disorders14. In a study including the results of four randomized trials IPS was found to be more effective in supporting the return to work of participants with dual diagnosis than traditional vocational rehabilitation14. Moreover, criminal justice involvement is also high in people with SMI15, especially in people with a dual-diagnosis, and many experience additional barriers to employment due to the stigma attributed to being an offender16. 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 group17.

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 across three different 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 will be 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.
2. Participants with schizophrenia, bipolar disorders, and major depression as well as participants with alcohol or substance use disorders, and forensic psychiatric conditions receiving IPS will be more likely to be competitively employed, find work faster, and will 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) guidelines18, and a predefined protocol has been published online on PROSPERO19, protocol nr. CRD42017060524.

A comprehensive literature search was performed in August 2017 and updated in January 2019 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 1020 or the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5th edition21.
3. compare IPS to either service as usual or other interventions not using IPS or modified IPS (referred to as SAU).
4. perform fidelity reviews with the IPS fidelity scale22 with a minimum score of fair fidelity (corresponding to >73 on the IPS-25 scale and >56 on the IPS-15 scale), and
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 employment

### Selection of studies and data extraction

Two reviewers (PP and LH) independently screened titles and abstracts and excluded articles that did not meet the inclusion criteria. The online software program Covidence23 was used for handling the screening of articles. 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, 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 raw-data or the necessary analyses.

### Risk of bias in studies

The Cochrane Risk of Bias Tool24 in Covidence 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”, whereas studies with one or more domains marked as “High risk” or “Unclear” were categorized as “Overall high risk of bias”.

### Study selection

After duplicates were removed, the electronic search resulted in 2167 unique records (Figure 1). Titles and abstract were screened, and 2085 records were excluded, leaving 82 full text articles to be assessed for eligibility. Of these 69 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 etal25was among the 13 studies included. Since the reviewing authors were involved in this trial, it was evaluated by two independent reviewers.

**(Figure 1)**

### Assessment of risk of bias in selected studies

Three of the included studies were assessed to be of high quality with an ‘Overall low risk of bias8,25,26, whereas the remaining nine were assessed to have an ‘Overall high risk of bias’, primarily due to lack of blinding of outcome assessors9,10,12,27–32 (Table 1).

**(Table 1)**

#### Sequence generation and allocation concealment

All studies but one reported to use computer generated randomization lists31. Viering at 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.

#### Blinding

Three of the 13 included studies reported that outcome assessors were blinded to allocation8,25,26, in two studies it was not clear whether assessors were blinded or not31,32, and in the remaining eight studies assessors were not blinded to allocated intervention group. The preponderance of un-blinded assessors may have led to an overestimation of the effect-sizes in the respective studies33.

#### Incomplete outcome data

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 data31.

#### Selective outcome reporting

Five studies reported outcomes according to a published protocol8,9,25,26,31. One study did not report educational activity as an outcome as stated in an a priori protocol32. The remaining 7 studies reported all vocational outcomes as stated in their aims.

#### Vested financial interests bias

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 statement28.

#### 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 outcomes26,28,29.

### 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 of all studies were contacted and asked if they could provide these data. Six authors provided data, hence, a total of six studies were included in the final pooled analysis of original data8,9,25,26,29,32

These studies included a total of 1896 participants from 18 different sites8,9,25,26,29,32 . 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 study32.

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 groups8,32. 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 al25. 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 al32.

Drug use disorder included two categories: soft drugs (cannabis, etc.) and hard drugs. Substance use disorder was defined in Burns et al9 as use of non-prescribed drugs with hard drugs including use of heroin and cocaine. Christensen et al25 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 al26 used binary classifications of drug use for both hard drugs and soft drugs. For Mueser et al29 drug use disorder included patients with drug abuse, dependence or dependence with institutionalization. Drug use disorder in Reme32 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 of the participants 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).

**(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 hours (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 hours (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 hours (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 hours (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).

**(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 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)(Figure 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).

**(Figure 2)**

## Discussion

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

Overall, we found that 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 were 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.

In contrast to the findings for participants with schizophrenia or bipolar disorder, 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 out-of-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 was competitively employed during the 24 months compared to 32.7 % in the control group (ref). 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 schizophrenia11, and have been found to predict sick leave in general34. 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 34. 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 (Lagerveld et al 2012). 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. For participants with alcohol or hard drug use disorder, on the other hand, no statistically significant impact of IPS was found. The benefit of IPS for people with any drug use disorder 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 the hard drugs group was very small (n=32) leading to large confidence intervals. However, as for depression, the observed difference between IPS and SAU is quite small and may 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 participants14.The evidence regarding vocational outcomes of people with substance use disorder is mixed14. In a study of 4 combined RCT’s, participants with dual diagnosis had significantly better work outcomes following IPS compared to the control group14, whereas a study included in the present review, found that an active substance abuse disorder was associated with worse employment outcomes among participants in the IPS group compared to participants without an active substance use disorder12. 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 benefits35. 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 the effectiveness of IPS in the different subgroups on 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 association12,28. 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 did not fulfill the inclusion criteria for the present review because it had only 12 months of follow-up, although 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 patients16.

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 al34.

### 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. Since the hypothesis could not be answered based on the literature found, 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. The smaller subgroups 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.

The diagnoses were coded using either DSM or ICD diagnostic criteria. Four studies used validated structured interviews (SCID29, SCAN25, OPCRIT9, MINI32), while two studies used clinical diagnosis based on DSM26 or ICD-108.

Vocational outcomes were self-reported (interviews, logbooks, or employment records) which could introduce non-differential misclassification as it can be difficult to recall detailed employment information for the past 18 months. If the assessor conducting the interview was not blinded this is a risk of bias, however in the majority of the six included studies the assessors were blinded for allocation8,25,26.

Two of the included 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 al25and Reme et al32, 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.

When competitive employment was obtained was not defined the same way in the six included studies. 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 day9,26 to at least one week8. 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. If both treatment groups are marked to a similar extent of this potential measurement error, it will not produce any bias in the treatment effect estimates.

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 alcohol25,29,32, five studies in the analysis of any drug use9,25,26,29,32, and three studies in the analysis of hard drugs9,25,29. 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.

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**Figure 1. PRISMA 2009 Flow Diagram**

Screening

Eligibility

Records after duplicates removed
(n = 2167)

Records screened
(n = 2167)

Records excluded
(n = 2085)

Full-text articles excluded, with reasons
(n = 69)

Wrong study design (n=5)

Not IPS intervention (n=14)

Ongoing study (n=6)

Study protocol (n=9)

Abstract (n=16)

No results at 18 mo follow up (n=9)

Wrong comparator (n=3)

Wrong outcomes (n=4)

Duplicates (n=3)

Identification

Included

Studies included in analysis of polled original data (n=6)

Studies included in qualitative synthesis
(n = 13)

Full-text articles assessed for eligibility
(n = 82)

Records identified through database searching
(n = 3774)

Additional records identified through other sources
(n = 0)

### Table 1. The Cochrane Risk of Bias assessment of 13 included RCT’s

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 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 bias

 Unclear risk of bias

 High risk of bias

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

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Bejerholm** (n=69) | **Burns** (n=281) | **Christensen** (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-value | Adjusted | p-value |
| **OR/EMD (95% CI)** | **OR/EMD (95% CI)** |
| All (n=1594) |
|  Competitively employed (n, %) | 395 (43.2) | 192 (28.2) | 1.93 (1.56-2.39) \* | 0.000 | 1.92 (1.53-2.42) \* | 0.000 |
|  Hours (mean, SD) | 221.51 (475.76) | 116.79 (325.15) | 104.73 (62.17-147.28) ¤ | 0.000 | 98.44 (53.21-143.67) ¤ | 0.000 |
|  Weeks (mean, SD) | 14.57 (22.50) | 8.77 (19.34) | 5.80 (3.74-7.86) ¤ | 0.000 | 5.33 (3.22-7.44) ¤ | 0.000 |
| Schizophrenia (n=1184) |
|  Competitively employed (n, %) | 267 (40.0) | 130 (25.1) | 1.98 (1.54-2.55) \* | 0.000 | 2.07 (1.58-2.73) \* | 0.000 |
|  Hours (mean, SD) | 212.45 (468.87) | 102.35 (301.65) | 110.10 (63.76-156.44) ¤ | 0.000 | 109.10 (60.49-157.71) ¤ | 0.000 |
|  Weeks (mean, SD) | 12.93 (21.57) | 6.87 (17.01) | 6.07 (3.87-8.26) ¤ | 0.000 | 6.12 (3.87-8.38) ¤ | 0.000 |
| Bipolar (n=223) |
|  Competitively employed (n, %) | 81 (55.9) | 28 (35.9) | 2.26 (1.29-4.02) \* | 0.005 | 2.37 (1.27-4.43) \* | 0.007 |
|  Hours (mean, SD) | 336.41 (582.11) | 214.40 (445.98) | 122.01 (-37.13-281.14) ¤ | 0.133 | 108.40 (-80.63-297.44) ¤ | 0.261 |
|  Weeks (mean, SD) | 19.93 (24.02) | 12.15 (22.01) | 7.77 (1.52-14.03) ¤ | 0.019 | 6.71 (-0.30-13.72) ¤ | 0.053 |
| Depression (n=224) |
|  Competitively employed (n, %) | 58 (45.7) | 37 (38.1) | 1.36 (0.80-2.34) \* | 0.259 | 1.24 (0.69-2.23) \* | 0.463 |
|  Hours (mean, SD) | 140.09 (329.57) | 125.98 (340.82) | 14.11 (-101.24-129.46) ¤ | 0.810 | -32.67 (-159.84-94.50) ¤ | 0.615 |
|  Weeks (mean, SD) | 16.99 (24.18) | 15.63 (25.28) | 1.35 (-5.21-7.91) ¤ | 0.685 | 0.95 (-5.56-7.47) ¤ | 0.765 |
| Alcohol (n=112) |
|  Competitively employed (n, %) | 26 (43.3) | 16 (30.8) | 1.72 (0.79-3.80) \* | 0.172 | 1.20 (0.50-2.86) \* | 0.678 |
|  Hours (mean, SD) | 199.10 (414.25) | 98.94 (307.39) | 100.17 (-52.46-252.79) ¤ | 0.198 | 50.18 (-104.04-204.40) ¤ | 0.524 |
|  Weeks (mean, SD) | 15.66 (22.88) | 10.95 (21.98) | 4.72 (-3.60-13.03) ¤ | 0.270 | 1.66 (-7.40-10.73) ¤ | 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) \* | 0.002 |
|  Hours (mean, SD) | 197.27 (458.43) | 52.18 (173.34) | 145.09 (54.26-235.91) ¤ | 0.002 | 121.16 (23.59-218.73) ¤ | 0.015 |
|  Weeks (mean, SD) | 12.30 (20.50) | 6.39 (16.58) | 5.91 (1.26-10.57) ¤ | 0.016 | 6.79 (1.83-11.76) ¤ | 0.005 |
| Hard drugs (n=32) |
|  Competitively employed (n, %) | 4 (21.1) | 3 (23.1) | 0.80 (0.14-4.84) \* | 0.798 | 0.74 (0.11-5.19) \* | 0.766 |
|  Hours (mean, SD) | 23.41 (60.88) | 38.72 (92.45) | -15.31 (-72.26-41.65) ¤ | 0.598 | 4.10 (-43.73-51.94) ¤ | 0.866 |
|  Weeks (mean, SD) | 3.92 (9.77) | 6.51 (15.57) | -2.58 (-12.07-6.91) ¤ | 0.568 | -1.31 (-10.40-7.79) ¤ | 0.733 |

\*=OR, ¤=EMD, adjusted for: age, gender, study and site.

## Figure 2. Time until employment