SAMLET SLUTRAPPORT FOR PROJEKT INKLUSION

Resumé af alle inkluderede studier

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Indholdsfortegnelse

Projekt Inklusion

Projekt inklusion blev gennemført i perioden 2011-2023, og består af to individuelle kliniske randomiserede forsøg, som har undersøgt beskæftigelseseffekter af indsatserne Individuel Planlagt job med Støtte (IPS), som er en indsats rettet mod personer med alvorlige sindslidelser, og IPS-MA, som er IPS modificeret til personer med angst og depression. Resultaterne af forsøgene er tidligere udgivet i rapporter til STAR, men ud over effekterne af indsatserne, er der i projektet udført en lang række posthoc studier vedrørende prædiktorer for beskæftigelse, trajectory studier, metaanalyser, systematiske reviews, registerstudier og kvalitative undersøgelser, hvor målet er at give et større samlet billede af psykisk sygdom og beskæftigelse i Danmark. Nærværende rapport er en opsamling af alle de enkelte studier i projektet, som alle bliver resumeret med yderligere henvisning til den publicerede artikel.

IPS – resultater fra et klinisk randomiseret forsøg

Baggrund: Individuelt Planlagt Job med Støtte (IPS) er en beskæftigelsesindsats, der internationalt har vist gode resultater i forhold til at støtte personer med alvorlig psykisk sygdom til at opnå og fastholde ordinær beskæftigelse eller uddannelse[1,2]. Den overordnede filosofi er, at personer med svære sindslidelser kan arbejde eller tage en uddannelse, når der opnås et godt match mellem kandidaten og arbejds- eller uddannelsesstedet og vedkommende sideløbende modtager intensiv støtte. IPS er integreret i den psykiatriske behandling og har fokus på kandidaternes egne valg og præferencer. Derudover arbejder IPS-konsulenterne opsøgende med henblik på at skabe relationer på det lokale arbejdsmarked og matche deltagerne til ledige stillinger. IPS-indsatsen tager afsæt i borgernes erfaringer, interesser og kompetencer, og det gode match er hovednøglen til et succesfuldt forløb for alle parter. Selvom uddannelse er det primære mål for mange mennesker med alvorlig psykisk sygdom, især unge patienter der nyligt er debuteret med sygdommen, har de fleste tidligere IPS-forsøg hovedsagelig fokuseret på, at støtte deltagerne til ordinær beskæftigelse[3]. Støttet uddannelse er dog beskrevet som en del af interventionen i den originale IPS-manual og tidligere studier har vist, at IPS-principperne med succes kan udvides til at omfatte støtte til uddannelse[4].

Baseret på positive resultater fra internationale randomiserede kliniske forsøg (RCT), har IPS vist sig at være en effektiv indsats sammenlignet med andre typer beskæftigelsesindsatser. En meta-analyse, der inkluderer 17 IPS-forsøg viser, at der er over dobbelt så stor sandsynlighed for ordinær beskæftigelse blandt IPS-deltagere sammenlignet med deltagere, der får en traditionel beskæftigelsesindsats ((RR=2,40 (95% CI 1,99-2,90))[5]. Andre outcomes, som tid til beskæftigelse og indtjening, favoriserer også IPS og der er ikke fundet nogen skadelige virkninger ved metoden[6–8]. Studier, der inkluderer uddannelse som et primært effektmål, har også fundet overbevisende effekt[9].

De seneste års international forskning med IPS-metoden har yderligere vist, at effekterne kan forstærkes ved at tilbyde et tillæg af træning i kognitive og sociale færdigheder[10,11]. Denne træning består af computertræning, hvor der trænes specifikke kognitive domæner som hukommelse, opmærksomhed og problemløsningsstrategier, samt af gruppesessioner hvor der undervises og

trænes i kognitive coping-strategier og sociale færdigheder. Et randomiseret forsøg, som inkluderede 107 personer med alvorlige sindslidelser, der ikke fik arbejde på trods af at de modtog IPS viste, at deltagerne, som modtog IPS med computerbaseret kognitive træning og undervisning i kognitive coping-strategier, havde betydeligt højere beskæftigelsesfrekvenser ved 24 måneders follow-up sammenlignet med deltagere, der kun fik IPS (60% mod 36%)[10]. I et andet RCT-studie, der inkluderede social færdighedstræning, var der også bedre effekt af at tilføje dette til IPS[11].

På denne baggrund blev det danske randomiserede IPS-forsøg initieret i 2012 med det overordnede formål at evaluere effekten af IPS og IPS med et tillæg af kognitiv træning og arbejdsrelateret social færdighedstræning (IPSE) sammenlignet med den traditionelle jobcenterindsats. Den primære hypotese var, at deltagere der modtog IPS-indsatsen (gruppe 1), ville være flere timer i arbejde eller uddannelse over en 18 måneders periode sammenlignet med deltagere, der modtog standardindsatsen (gruppe 3). Desuden forventede vi, at et tillæg af IPS med kognitiv træning og arbejdsrelateret social færdighedstræning ville øge effekterne yderligere (gruppe 2)

Metode: I alt blev 720 deltagere med alvorlig sindslidelse, herunder skizofreni og andre psykoselidelser, bipolar sindslidelse og tilbagevendende depression, tilfældigt randomiseret til tre grupper: 1) IPS 2) IPS plus træning i kognitiv og sociale færdigheder (IPSE) eller 3) Standardindsatsen, som den traditionelt tilbydes i jobcenteret. Deltagerne blev rekrutteret fra distriktspsykiatriske centre og OPUS teams i København, Frederiksberg, Odense eller Silkeborg, og havde alle et ønske om at komme i beskæftigelse eller i gang med en uddannelse[12].

Resultater: Det kliniske randomiserede forsøg viste, at der i løbet af den 18 måneders opfølgningsperiode var 13% flere deltagere i IPS-gruppen (59,9%) og IPSE-gruppen (59.1%), der kom i ordinært arbejde eller uddannelse sammenlignet med deltagerne i standardindsatsen (46,5%). IPSE-deltagerne arbejdede eller studerede i gennemsnit 488 timer sammenlignet med 340 timer i standardindsatsen, hvilket gav en gennemsnitlig forskel på 148 timer (p=0.005). IPS-deltagerne arbejdede eller studerede i gennemsnit 410 timer og sammenlignet med standardindsatsen var forskellen 71 timer (p=0.018), og når de to IPS-grupper blev slået sammen og sammenlignet med standardindsatsen, var der ligeledes en statistisk signifikant forskel (p= 0.001). Deltagerne i begge IPS-grupper var derudover signifikant mere tilfrede med den behandling de havde modtaget målt med *client satisfaction scale* (P=0.000). Der var ikke forskel mellem grupperne i forhold til

depressive, psykotiske eller negative symptomer, samt kognitiv funktion eller helbredsrelateret livskvalitet, og dermed ingen indikation af at IPS leder til forværring af symptomer eller har andre negative konsekvenser[13].

Ved 30 måneders opfølgning var deltagere der modtog IPS eller IPSE, ligeledes mere tilbøjelige til at opnå ordinær beskæftigelse eller uddannelse sammenlignet med dem, der modtog Standardindsatsen (IPS 65%, IPSE 65%, SAU 53%, p = 0:006), og de arbejdede i gennemsnit flere uger (IPS 25 uger, IPSE 21 uger, SAU 17 uger; IPS vs. SAU p = 0:004 og IPSE vs. SAU p = 0:007). Desuden havde deltagerne i de to IPS-grupper færre ambulante besøg i løbet af den 30-måneders opfølgning. Dette var dog kun statistisk signifikant, når man sammenligner IPSE med Standardindsatsen p = 0:017[14].

Konklusion. Med udgangspunkt disse resultater og den eksisterende forskning, synes IPS og IPS suppleret med kognitiv og social træning (IPSE), at være farbare metoder til at øge beskæftigelses- og uddannelsesgraden blandt personer med alvorlig psykisk sygdom, der har et ønske om at komme i arbejde eller uddannelse. Deltagerne i IPS-grupperne var signifikant mere tilfredse med indsatsen, og sammenholdt med de positive resultater i forhold til beskæftigelse og uddannelse anbefales det, at IPS-indsatsen implementeres og udbredes til flest mulige.

For yderligere information se de tre videnskabelige artikler under bilag:

1: Christensen TN, Nielsen IG, Stenager E, *et al.* Individual Placement and Support supplemented with cognitive remediation and work-related social skills training in Denmark: Study protocol for a randomized controlled trial. *Trials* 2015; **16**: 1–10.

2: Christensen TN, Wallstrøm IG, Stenager E, *et al.* Effects of Individual Placement and Support Supplemented With Cognitive Remediation and Work-Focused Social Skills Training for People With Severe Mental Illness. *JAMA Psychiatry* 2019; **76**: 1232.

3: Christensen TN, Wallstrøm IG, Stenager E, *et al.* 30-Month Follow-Up of Individual Placement and Support (IPS) and Cognitive Remediation for People with Severe Mental Illness: Results from a Randomized Clinical Trial. *Psychiatry J* 2023; **2023**:

Sundhedsøkonomiske analyser af IPS-indsatsen:

Baggrund: Effekterne af IPS (individuelt planlagt job med støtte) og IPSE (IPS suppleret med kognitiv og social træning) blev i perioden 2012-2018 undersøgt i et klinisk randomiseret multicenter-studie. I alt blev 720 deltagere med alvorlig sindslidelse tilfældigt randomiseret til tre grupper: 1) IPS, 2) IPSE eller 3) standardindsatsen i jobcenteret (SI). I løbet af den 18 måneders opfølgningsperiode var der signifikant flere deltagere i IPS-gruppen (59,9%) og IPSE-gruppen (59.1%), der kom i ordinært arbejde eller uddannelse sammenlignet med deltagerne i standardindsatsen (46,5%), og deltagerne var signifikant mere tilfredse med den støtte, de havde fået sammenlignet med standardindsatsen. Formålet med nærværende studie er at undersøge omkostningseffektiviteten af IPS og IPSE-indsatserne i forhold til helbredsrelateret livskvalitet og beskæftigelseseffekter sammenlignet med standardindsatsen.

Metode: Via registerbaseret data og data indhentet fra det randomiserede forsøg blev omkostningerne i sundhedsvæsenet, beskæftigelses- og socialsektoren samt interventionsomkostningerne beregnet for opfølgningsperioden på 18 måneder, og forskellen testet med et t-test. Kvalitetsjusterede leveår (QALY) blev udregnet på baggrund af det generiske spørgeskema, EQ-5D, ved hjælp af danske præferencevægte. Derefter blev incremental cost-effectiveness ratioer (ICER) beregnet for gevinst i QALY og antal timer i beskæftigelse eller uddannelse. ICER blev fremstillet visuelt i scatterplot efter bootstrappping.

Resultater: Resultaterne viser at der i IPS og IPSE er en samfundsøkonomisk besparelse samt bedre effekter målt i QALY's og timer i arbejde eller uddannelse. Deltagerne i IPS og IPSE opnåede en statistisk signifikant samfundsøkonomisk besparelse over den 18 måneders opfølgningsperiode på 71.562 kr. (IPS vs. SI) og 54.660 kr. (IPSE vs. SI) per deltager. De lavere udgifter i de to IPS-grupper var primært på grund af færre udgifter til indsatser i jobcenteret og socialcenteret samt færre psykiatriske kontakter og højere produktivitetsgevinst. Der var også en forbedring i kvalitetsjusterede leveår efter 18 måneder i de to IPS- grupper, dog kun statistisk signifikant ved IPSE. ICER tyder på at IPS og IPSE var både bedre (målt i QALY) og billigere sammenlignet med standardindsatsen i jobcenteret. De to IPS-indsatser var omkostningseffektive i forhold til timer i arbejde eller uddannelse. Deltagerne i begge IPS-grupper arbejdede eller studerede flere timer i gennemsnit over den 18 måneders

opfølgningsperiode med en samfundsøkonomisk besparelse sammenlignet med standard-indsatsen.[15]

Konklusion: Resultaterne fra denne sundhedsøkonomiske analyse underbygger, på samme måde som resultaterne fra effektanalysen, at der er baggrund for en national implementering af IPS-indsatsen.

For yderligere information se den videnskabelige artikel under bilag

4: Christensen TN, Kruse M, Hellström L, Eplov LF. Cost-utility and cost-effectiveness of individual placement support and cognitive remediation in people with severe mental illness: Results from a randomized clinical trial. *European Psychiatry* 2021; **64**. DOI:10.1192/j.eurpsy.2020.111

Prædiktorer for beskæftigelse

Baggrund: Mennesker med alvorlig psykisk sygdom oplever uforholdsmæssigt høj arbejdsløshed. Ikke desto mindre har forskning vist gode beskæftigelseseffekter ved metoden Individuel Planlagt job med Støtte (IPS) og IPS suppleret med kognitiv remediering (IPSE). Formålet med nærværende undersøgelse er at undersøge demografiske og kliniske prædiktorer for beskæftigelse eller uddannelse blandt mennesker med svær psykisk sygdom, der deltog i det danske randomiserede IPS-forsøg og at undersøge, om IPS eller IPSE kan kompensere for risikofaktorer for arbejdsløshed.

Metode: 720 deltagere blev tilfældigt randomiseret til IPS, IPSE eller Standardindsats. I løbet af den 18 måneders opfølgningsperioden opnåede deltagere i de to forsøgsgrupper væsentligt mere arbejde eller uddannelse. En række univariate og multiple logistiske regressionsanalyser blev udført for at undersøge i hvor høj grad demografiske og kliniske faktorer prædikterer beskæftigelse eller uddannelse. Både for den samlede population og for de tre indsatsgrupper individuelt.

Resultater: Den stærkeste prædiktor for beskæftigelse, udover interventionsgruppe, var tidligere arbejdshistorik (OR=1,78; 95%CI=1,28-2,47). Mænd havde en lavere sandsynlighed for beskæftigelse sammenlignet med kvinder (OR= 0,71; 95%CI= 0,50–0,99) og højere alder var negativt forbundet med arbejde eller uddannelse (OR= 0,79; 95% CI= 0,67-0,93). Derudover blev beskæftigelse prædikteret af højere motivation for forandring, målt på *readiness for change scale* (OR= 1,42; 95 % CI= 1,19-1,70). Deltagelse i IPS eller IPSE kunne ikke kompensere for negative risikofaktorer såsom lav kognitiv funktion eller negative symptomer[16].

Konklusion: I en multipel logistisk regressionsanalyse var alder, tidligere arbejdshistorik og motivation for forandring statistiske signifikante prædiktorer for at få arbejde eller uddannelse blandt personer med svær psykisk sygdom, som deltog i det Danske IPS-forsøg

For yderligere information se den videnskabelige artikel under bilag

5: Christensen TN, Wallstrøm IG, Bojesen AB, Nordentoft M, Eplov LF. Predictors of work and education among people with severe mental illness who participated in the Danish individual placement and support study: findings from a randomized clinical trial. *Soc Psychiatry Psychiatr Epidemiol* 2021; **56**: 1669–77.

Trajectories og prædiktorer for beskæftigelse

Baggrund: Tilbagevenden til arbejde er en proces, der sker i forskellige tempi for mennesker med alvorlig sindslidelse. Formålet med dette studie var at identificere mønstre (trajectories) i tilbagevenden til arbejde blandt deltagerne i IPS-studiet og undersøge, om IPS-interventionen, sociodemografiske eller kliniske faktorer, prædikterer medlemskab af en specifik trajectory-gruppe.

Metode: Vi anvendte det tidligere indsamlede data fra det danske IPS-forsøg (N=720). Beskæftigelse var defineret som 'uger i ordinær beskæftigelse eller uddannelse inden for de seneste 6 måneder' og blev målt efter 0,5, 1, 1,5, 2 og 2,5 år, ved brug af data fra Dansk Register for Evaluering af Marginalisering (DREAM) database. Latent growth mixture modelling blev anvendt til at identificere trajectories for beskæftigelse, og logistisk regression blev brugt til at estimere prædiktorer for trajcetory medlemskab.

Resultater: Fire trajectories blev identificeret: 'Lav beskæftigelse' (61,3 %), 'Lav stigende beskæftigelse' (8,2 %), 'Øgende aftagende beskæftigelse' (7,2 %) og 'Høj beskæftigelse' (23,4 %). Modtagelse af IPS-interventionen øgede odds for medlemskab i 'Høj beskæftigelse' i forhold til 'Lav beskæftigelse' (OR=2,18; 95 % CI 1,37–3,48) og det samme gjorde videregående uddannelser (OR=2,25; 95 % CI 1,39–3,64), højere kognitiv funktion (OR=1,17; 95 % CI 1,02–1,35), højere motivation for forandring (OR=1,04; 95 % CI 1,02–1,05) og tidligere arbejde historik (OR=1,64; 95 % CI 1,09-2,46). Højere alder reducerede odds for medlemskab i 'Høj beskæftigelse' (OR=0,95; 95 % CI 0,93-0,98) sammenlignet med 'Lav beskæftigelse'[17].

Konklusion: Der var høj heterogenitet i de identificerede recovery trajectories, på trods af at alle deltagere udtrykte et ønske til arbejde og uddannelse ved baseline. Der er derfor behov for forbedringer af IPS-interventionen for at støtte specifikke grupper i at opnå effekter og bevare beskæftigelsen.

For yderligere information se den videnskabelige artikel under bilag

6: Poulsen CH, Christensen TN, Madsen T, Nordentoft M, Eplov LF. Trajectories of Vocational Recovery Among Persons with Severe Mental Illness Participating in a Randomized Three-Group Superiority Trial of Individual Placement and Support (IPS) in Denmark. *J Occup Rehabil* 2022; **32**: 260–71.

Borgerens perspektiv, IPS og recovery (Kvalitativ studie)

Baggrund: Individuel planlagt job med støtte (IPS) støtter personer med svær psykisk sygdom til at opnå ordinær beskæftigelse. Selvom IPS-interventionen betegnes som en recovery-orienteret intervention, eksistere der kun begrænset forskning om hvordan deltagerne oplever at IPS påvirker deres recovery proces. Formålet var at undersøge, hvordan IPS og beskæftigelse påvirke recovery hos personer med alvorlig psykisk sygdom

Metode: Studiet var et kvalitativt fænomenologisk hermeneutisk interview studie med 12 IPS-deltagere. Studiet undersøgte hvordan IPS og beskæftigelse påvirkede bedring hos personer med svær psykisk lidelse.

Resultater: IPS og beskæftigelse bidrog positivt til bedring hos personer med svær psykisk lidelse. IPS-deltagerne oplevede forholdet til IPS-konsulenten som tillidsvækkende, seriøst og anerkendende. Både beskæftigelse og IPS bidrog til et positivt ændret selv-billede, øgede deltagernes selvværdsfølelse og ledte til en normalisering og stabilisering af deltagernes hverdagsliv. Studiet fandt, at der var forskellige opfattelser af, hvordan IPS og beskæftigelse bidrog til bedring. Deltagere, der led af psykotiske symptomer, udtrykte, at hverken IPS eller beskæftigelse påvirkede sværhedsgraden af symptomer. Derfor oplevede deltagere med psykotiske symptomer ikke bedring som følge af IPS eller beskæftigelse. Modsat, oplevede deltagere, der var plaget af depression og negative symptomer, at IPS og beskæftigelse førte til mindre/lavere grad social tilbagetrækning og isolation[18].

Konklusion: IPS og ordinær beskæftigelse synes at have indflydelse på personlig recovery, at påvirke arbejdsfunktionen og mindske depressive symptomer, men synes ikke at have indflydelse på psykotiske symptomer

For yderligere information se den videnskabelige artikel under bilag

7: Gammelgaard I, Christensen TN, Eplov LF, Jensen SB, Stenager E, Petersen KS. 'I have potential': Experiences of recovery in the individual placement and support intervention. *International Journal of Social Psychiatry* 2017; **63**: 400–6.

Associationer mellem individuel planlagt job med støtte (IPS), beskæftigelse og personlig og klinisk recovery

Formål: Formålet med dette systematiske review var at undersøge associationer mellem individuel planlagt job med støtte (IPS), beskæftigelse og personlig og klinisk bedring.

Metode: En systematisk littersøgning identificerede kontrollerede forsøg (RCT), der sammenligner IPS med standardindsatser. Effektmål var selvværd, empowerment, livskvalitet, symptomer på depression, negative eller psykotiske symptomer, angst og funktionsniveau. Seks RCT'er rapporterede data, der er egnede til metaanalyser, og derudover indgik der originale data fra fem studier.

Resultater: Resultaterne fra meta-analysen og analysen af poolede originale data viste ingen effekt af IPS, sammenlignet med kontrolgruppen, på depression, negative og psykotiske symptomer, selvværd, funktionsniveau, empowerment og livskvalitet. Der blev heller ikke fundet associationer mellem ovennævnte effektmål og kombination af IPS og arbejdsintensitet. Til gengæld var der associationer mellem bedring af negative symptomer og funktionsniveau hos deltagere der havde arbejdet, sammenlignet med deltagere der ikke havde arbejdet. Deltagere der arbejdede i opfølgningsperioden, blandt både IPS og kontrolgruppen, oplevede forbedrede negative symptomer sammenlignet med dem, der ikke arbejdede (standardiseret gennemsnitlig forskel [SMD] -,41, 95% CI -0,56, – 0,26). For deltagere der var i arbejde, blev der også fundet forbedring i funktionsniveau og livskvalitet (SMD 0,59, 95% CI 0,42 - 0.77 og SMD 0,34, 95% CI 50,14 - 0,54)[19].

Konklusioner: Beskæftigelse var associeret med forbedringer i negative symptomer, funktionsniveau og livskvalitet, men det er ikke muligt at konkludere på retningen i kausaliteten.

For yderligere information se den videnskabelige artikel under bilag

8: Wallstroem IG, Pedersen P, Christensen TN, *et al.* A Systematic Review of Individual Placement and Support, Employment, and Personal and Clinical Recovery. *Psychiatric Services* 2021; **72**: 1040–7.

Incidens rater og beskæftigelse trends i DK

Baggrund: Alvorlig psykisk sygdom, defineret som diagnoser i det skizofreniforme spektrum, bipolar affektiv sindslidelse og tilbagevendende depression, er alvorlige og ofte langvarige lidelser, der kan forårsage en høj grad af funktionsnedsættelse og tab af produktivitet. Udviklingen i forekomsten af alvorlig psykisk sygdom samt beskæftigelsesgraden før og efter diagnosen er midlertidig ukendt. Formålet var at undersøge udviklingen i forekomsten af alvorlig psykisk sygdom og at undersøge arbejdsmarkedstilknytningen før og efter diagnosen.

Metoder: Vi anvendte registerdata fra 2000 til 2013 på alle indlagte og ambulante psykiatriske patienter i Danmark. Incidens rater blev beregnet for diagnoser i det skizofreniforme spektrum (ICD-10: F20-F29), bipolar affektive lidelse (ICD-10: F30, F31) og tilbagevendende depression (ICD-10: F33). Beskæftigelse, uddannelse og førtidspensionen blev målt et år før og to år efter diagnosen.

Resultater: Vi observerede for perioden 2000-2013 en signifikant stigning i forekomsten af alvorlig psykisk sygdom og blandt de ny diagnosticerede var der et fald i beskæftigelsesgraden både før og efter diagnosen[20].

Konklusion: Den signifikante stigning i forekomsten af en alvorlig sindslidelse i Danmark, samt faldende beskæftigelsesfrekvenser både før og efter diagnosen understreger vigtigheden af målrettede beskæftigelsesindsatser.

For yderligere information se den videnskabelige artikel under bilag

9: Christensen TN, Wallstrøm IG, Eplov LF, Laursen TM, Nordentoft M. Incidence rates and employment trends in schizophrenia spectrum disorders, bipolar affective disorders and recurrent depression in the years 2000–2013: a Danish nationwide register-based study. *Nord J Psychiatry* 2022; **76**: 225–32.

Effekten af IPS i subgrupper af diagnose, misbrug og retspsykiatriske foranstaltninger (review)

Formål: Formålet med dette systematiske review, var at undersøge effekten af IPS i subgrupper af diagnoser af skizofreni, bipolar lidelse, svær depression, misbrug eller personer med retspsykiatriske foranstaltninger.

Metoder: Der blev gennemført en systematisk litteratursøgning i juni 2017, som blev opdateret i december 2020. Det systematiske review inkluderede 13 studier. Analyser af poolede originale data var baseret på de seks undersøgelser, der udleverede data (n=1594). Ingen studier med patienter med retspsykiatriske foranstaltninger opfyldte inklusionskriterierne. Antal timer og uger i arbejde blev analyseret ved hjælp af lineær regression. Beskæftigelse og tid til beskæftigelse blev analyseret ved hjælp af henholdsvis logistisk regression og cox-regression.

Resultater: Effekten på timer og uger i beskæftigelse efter 18 måneder var sammenlignelige for deltagere med skizofreni og bipolar lidelse, men kun statistisk signifikant for deltagere med skizofreni sammenlignet med sædvanlig indsats (SI) (EMD 109,1 timer (95 % CI 60,5-157,7), 6,1 uger (95 % CI 3,9-8,4)). Effekten var også signifikant for deltagere med alle typer af misbrug (121,2 timer (95 % CI 23,6-218,7), 6,8 uger (95 % CI 1,8-11,8). Deltagere med skizofreni, bipolar lidelse og alle typer af misbrug havde højere odds for at være ansat i ordinær beskæftigelse (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)) og vendte tilbage til arbejde hurtigere end SI (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)). Der blev ikke fundet statistisk signifikant effekt for gruppen med depression[21].

Konklusion: IPS var effektiv for grupperne med skizofreni, bipolar lidelse og misbrug; effekten på arbejdstimer og -uger var dog ikke statistisk signifikant for gruppen med bipolar lidelse. For personer med depression er virkningen af IPS stadig uklar. Ikke-signifikante resultater kan skyldes mangel på styrke.

For yderligere information se den videnskabelige artikel under bilag

10: Hellström L, Pedersen P, Christensen TN, *et al.* 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. *J Occup Rehabil* 2021; **31**: 699–710.

IPS MA – resultater fra et klinisk randomiseret forsøg

Baggrund: Som en del af Projekt Inklusion, blev effekten af en modificeret udgave af Individuelt Planlagt job med Støtte (IPS) målrettet mennesker med nyligt diagnosticeret angst, depression eller bipolar lidelse undersøgt - på engelsk "The Individual Placement and Support (IPS)-modified, early intervention for people with Mood and Anxiety disorder" (IPS-MA). IPS- MA blev udviklet da man over en årrække havde set en stigning i antallet af førtidspensioner tildelt på baggrund af mentale helbredsproblemer; særligt indenfor diagnoserne angst og depression[22]. IPS-MA var tænkt som et tillæg til de indsatser, der allerede fandtes i hhv. behandlings- og beskæftigelsessystemet, og opfyldte IPS-kriterierne, helt eller delvist, på nær princippet om at indsatsen skulle være en integreret del af den psykiatriske behandling. Mennesker med angst og affektive lidelser behandles oftest ved kortere, ambulante forløb, hvorfor det ikke var muligt at integrere indsatsen.

IPS-MA-indsatsen var en tosporet indsats, hvor deltagerne fik tildelt en mentor og en karriere-rådgiver, der sideløbende støttede deltageren i at vende tilbage i arbejde. Indsatsen bestod af følgende elementer:

• Individualiseret mentorstøtte, ydet af mentorer m. mange års erfaring fra arbejde i psykiatrien

• Koordinering ved mentor internt og eksternt overfor andre aktører (eks. kommune, sundhedssektor)

• Karriererådgivning målrettet mennesker med psykisk sygdom (af karriererådgivere m erfaring fra det private erhvervsliv)

• Uvildig hjælp til afklaring af privatøkonomien

• Virksomhedsrettet indsats for at understøtte den enkeltes mulighed for at komme i arbejde

Støtten var fleksibel og tidsubegrænset, og tilpasset den enkelte deltagers behov. Målet var ordinær beskæftigelse eller uddannelse, uden forudgående arbejdsafprøvning eller praktik. IPS-MA-indsatsen blev implementeret i, og udbudt af den private virksomhed SHERPA, der allerede udbød beskæftigelsesrettede indsatser til mennesker med psykiske lidelser.

For at sammenligne effekten af IPS-MA-indsatsen med den sædvanlige jobcenterindsats, blev et randomiseret forsøg initieret i 2011. Den overordnede hypotese var at IPS-MA-indsatsen efter to år

ville få 50 % flere tilbage i arbejde efter en sygemelding med angst, depression eller en bipolar lidelse, sammenlignet med den sædvanlige indsats.

Metode: Effekten af indsatsen blev undersøgt i et klinisk randomiseret forsøg fra 2011 og frem til 2016. I forsøget indgik 326 deltagere, der alle havde været indlagt eller i ambulant behandling med angst, depression eller bipolar lidelse i Region Hovedstaden. Deltagerne i projektet skulle være

relativt ny-diagnosticerede, de måtte kun have haft kontakt til det psykiatriske hospitalsvæsen inden for de seneste tre år, og skulle have været i arbejde eller uddannelse inde for samme treårige periode. De skulle være motiverede for at komme i arbejde eller uddannelse, men måtte ikke være arbejdsparate (matchgruppe 1). De måtte ikke have misbrug eller en somatisk sygdom som primær hindring for at være i arbejde/uddannelse. Deltagerne blev randomiseret til enten at modtage standard jobcenterindsats plus et IPS-MA-forløb (n=162) eller standard indsats (SI) alene (n=164). Deltagerne blev interviewet og svarede på online spørgeskemaer ved start, og efter hhv. et og to år. Det primære effektmål var arbejde eller uddannelse efter to år, mens sekundære effektmål var antal uger i arbejde eller uddannelse, grad af symptomer på angst eller depression, funktionsniveau og helbredsrelateret livskvalitet.[23]

Resultater: Efter to år var 44.4% i arbejde eller uddannelse i IPS-MA-gruppen, sammenlignet med 38.6% i kontrolgruppen, forskellen var dog ikke signifikant (p=0.20). Efter et år var 32.5% i arbejde eller uddannelse i IPS-MA-gruppen, sammenlignet med 28% i kontrolgruppen, heller ikke denne forskel var statistisk signifikant. Der var heller ikke statistisk signifikant forskel på nogle af de øvrige sekundære effektmål. De eneste signifikante fund var, at deltagerne i IPS-MA-gruppen var signifikant mere tilfredse, med den behandling de havde modtaget, både efter et og to år, og at IPS-MA-gruppen rapporterede at være mere klar til at lave den forandring der skulle til for at komme i arbejde eller uddannelse efter et år, men efter to år havde forskellen udlignet sig, og var ikke længere signifikant[24]

Konklusion: IPS-MA fik ikke flere i arbejde eller uddannelse end den sædvanlige jobcenterindsats. Den manglende effekt kan skyldes, at indsatsen ikke var integreret med behandlingsindsatsen, hvilket er en vigtig del af IPS-indsatsen.

For yderligere information, se videnskabelige artikler under bilag

11: Hellström L, Bech P, Nordentoft M, Lindschou J, Eplov LF. 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.

12: Hellstrom L, Bech P, Hjorthoj C, Nordentoft M, Lindschou J, Eplov LF. 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. Occup Environ Med 2017; 74: 717–25.

Resultater af sundhedsøkonomisk analyse

Baggrund: Effekten af en modificeret udgave af Individuelt Planlagt job med Støtte målrettet mennesker med nyligt diagnosticeret angst, depression eller bipolar lidelse (IPS-MA) blev undersøgt i et randomiseret forsøg, hvor 326 deltagere blev randomiseret til enten at modtage den modificerede indsats IPS-MA plus sædvanlig indsats (SI) eller SI alene. I effektstudiet blev der ikke fundet nogen statistisk signifikant forskel på de to grupper, ift. hvor mange der kom i arbejde efter 12 måneder. For at undersøge om indsatsen var omkostningseffektiv, blev en sundhedsøkonomisk analyse udført.

Metode: Omkostningerne i sundhedsvæsenet, beskæftigelses- og socialsektoren samt interventionsomkostningerne blev beregnet for opfølgningsperioden for hver af de to grupper (IPS-MA og kontrolgruppen), og forskellen testet med et t-test. Kvalitetsjusterede leveår (QALY) blev beregnet på baggrund af spørgeskemaet EQ-5D, og herefter blev incremental cost-effectiveness ratioer (ICER) beregnet for gevinst i QALY og antal timer i beskæftigelse. ICER blev fremstillet visuelt i scatterplot efter bootstrappping.

Resultater: Der blev fundet en samfundsøkonomisk besparelse ved IPS-MA-indsatsen sammenlignet med den sædvanlige indsats på 16.658 kr. i gennemsnit per person, akkumuleret i løbet af de 12 måneder. Forskellen var dog ikke statistisk signifikant. Der var en signifikant besparelse på beskæftigelsesindsatsen i jobcenteret på 31.965 kr. i IPS-MA-gruppen. Men produktionsgevinsten var signifikant højere i kontrolgruppen, der tjente 25.320 kr. mere per person i opfølgningsperioden sammenlignet med IPS-MA-gruppen. Forbedringen i kvalitetsjusterede leveår var størst i IPS-MA-gruppen, men forskellen var ikke statistisk signifikant. ICER'en tyder på at IPS-MA-indsatsen kunne være omkostningseffektiv, men resultatet er ikke robust. Fremstillingen af omkostningseffektiviteten i forhold til antal timer i arbejde viste, at indsatsen kunne være en anelse billigere, men deltagerne i IPS-MA-gruppen arbejdede signifikant færre timer end kontrolgruppen.[25]

Konklusion: IPS-MA-indsatsen var ikke dyrere end den sædvanlige indsats og kunne være omkostningseffektiv i forhold til QALY, men deltagerne arbejdede færre timer og tjente mindre i løbet af de 12 måneder. Dermed er indsatsen ikke omkostningseffektiv, målt på timer i arbejde.

For yderligere information, se videnskabelig artikel under bilag
13. Hellström et.al. Cost-effectiveness analysis of a supported employment intervention for people with mood and anxiety disorders in Denmark - the IPS-MA intervention. Nord J Psychiatry. 2021 Jul;75(5):389-396.

Prædiktorer for beskæftigelse

Baggrund: Psykiske lidelser, som angst og depression, har store konsekvenser både for samfundet og det enkelte individ; andelen af arbejdsløse og førtidspensioner er høj. For at kunne udvikle effektive beskæftigelsesrettede indsatser, er det vigtigt at vide hvilke faktorer, der har betydning for om folk kommer i arbejde.

Metode: Vi udførte sekundære analyser på data fra 289 deltagere i IPS-MA-studiet. Associationer mellem baselinekarakteristika og at være i beskæftigelse eller uddannelse efter 24 måneder blev først testet i univariate logistiske regressionsanalyser, hvorefter variable med en p-værdi under 0,1 blev inkluderet i multivariate analyser.

Resultater: I de univariate analyser var selvrapporteret funktionsniveau (p=0,032), højere alder (p=0,070) og højere motivation for forandring (p=0,001) associeret med at være i arbejde eller uddannelse, og blev dermed inkluderet i den multivariate analyse. Kun alder (p=0,030) og motivation for forandring (p=0,003) forblev signifikant associeret med tilbagevenden til arbejde eller uddannelse efter 24 måneder i den multivariate analyse.[26]

Konklusion: Højere alder og lavere motivation for forandring var associeret med en lavere chance for at vende tilbage til arbejde eller uddannelse. Faktorer, der kan modificere effekten af højere alder, bør identificeres, ligesom beskæftigelsesrettede indsatser bør fokusere på at forbedre faktorer relateret til borgernes motivation for forandring.

For yderligere information, se videnskabelig artikel under bilag

14. Hellström L, Christensen TN, Bojesen AB, Eplov LF. Predictors of Return to Work for People with Anxiety or Depression Participating in a Randomized Trial Investigating the Effect of a Supported Employment Intervention. J Occup Rehabil. 2023 Mar;33(1):61-70.

Trajectories og prædiktorer for beskæftigelse

Baggrund: Tilbagevenden til arbejde er en proces, der sker i forskellige tempi for mennesker med angst og affektive lidelser. Formålet med dette studie var at identificere mønstre (trajectories) i tilbagevenden til arbejde blandt deltagerne i IPS-MA-studiet og undersøge, om sociodemografiske eller kliniske faktorer, forudsagde medlemskab af en specifik trajectory-gruppe.

Metode: Vi anvendte data fra det randomiserede IPS-MA-studie (n=283). Beskæftigelse var defineret som 'uger i beskæftigelse i det seneste halve år' og blev målt efter ½, 1, 1½ og 2 år ved hjælp af data fra Dansk Register for Evaluering af Marginalisering (DREAM). Latent growth mixture modelling blev anvendt til at identificere trajectories for beskæftigelse, og logistisk regression blev brugt til at estimere prædiktorer for trajcetory medlemskab.

Resultater: Fire trajectories blev identificeret; 'Ikke i beskæftigelse' (70% (196/283)) (praktisk talt ingen tilbagevenden til arbejde); 'Forsinket tilbagevenden til beskæftigelse' (19 % (56/283)) (seks måneders forsinkelse før fuld tilbagevenden); 'Hurtig, ustabil tilbagevenden til beskæftigelse' (7% (19/283)) (medlemmerne vendte hurtigt tilbage til arbejde, men arbejdede kun halvdelen af tiden); og den mindste gruppe, 'Hurtig tilbagevenden til beskæftigelse' (4% (12/283)) (medlemmerne nåede hurtigt fuld beskæftigelse, men oplevede senere et fald i uger i beskæftigelse). Selvrapporteret funktionsniveau, ikke at bo sammen med en partner og motivation for forandring viste sig at være signifikant associeret med at være i beskæftigelse.[27]

Konklusion: De identificerede trajectories understøtter, at mange ikke har gavn af den beskæftigelsesrettede indsats eller har svært ved at fastholde beskæftigelse; der er derfor fortsat brug for øget fokus på og støtte til denne patientgruppe.

For yderligere information, se videnskabelige artikler bilag

15. Hellström L, Madsen T, Nordentoft M, Bech P, Eplov LF. Trajectories of Return to Work Among People on Sick Leave with Mood or Anxiety Disorders: Secondary Analysis from a Randomized Controlled Trial. J Occup Rehabil. 2018 Dec;28(4):666-677.

Trajectories for symptomer

Baggrund: Angst og depression er to heterogene lidelser, der ofte kombineres i videnskabelige undersøgelser. Få studier har sammenlignet udviklingen i depressions- og angstsymptomer blandt klinisk syge. Formålet med dette studie var at identificere specifikke trajectories for henholdsvis depressions- og angstsymptomer, samt undersøge prædiktorer for trajectory medlemskab.

Metode: Latent growth mixture modelling blev anvendt til at identificerer trajectories for angst og depressionssymptomer på data fra IPS-MA-studiet (n=261). Logistisk regression blev brugt til at estimere prædiktorer for trajectory medlemskab. Associationer mellem trajectories og remission af komorbid depression eller angst og tilbagevenden til arbejde blev også testet.

Resultater: Vi identificerede tre trajectories for hhv. depressions- og angstsymptomer; moderat faldende (60 %), moderat stabile (26 %) og lave stabile (14 %) depressionssymptomer, og mild faldende (59 %), moderat faldende (33 %) og moderat stabile (8 %) angstsymptomer. Modellen for depression viste lav præcision i forhold til at adskille de enkelte trajectories (entropi 0,66), og derfor blev prædiktorer for trajectory medlemskab ikke estimeret. For angst var lavere alder og højere grad af depressive symptomer associeret med at være i en mindre favorabel trajectory klasse. Remission af komorbide depressive symptomer efter to år var signifikant forskellig mellem trajectories (p<0,000). Færre var vendt tilbage til arbejde i de to moderate trajectory klasser sammenlignet med den mildt faldende angst trajectory.[28]

Konklusion: De identificerede angst trajectories bekræfter, at en ret stor andel i den moderat-stabile klasse havde symptomer på moderat angst, moderate komorbide depressive symptomer og mindre sandsynlighed for at være vendt tilbage til arbejdet, selv efter to år.

For yderligere information, se videnskabelige artikler bilag

16. Hellström L, Madsen T, Nordentoft M, Eplov LF. Trajectories of symptoms of anxiety and depression among people on sick leave with mood or anxiety disorders: Secondary analysis from a randomized controlled trial. J Psychiatr Res. 2021 May;137:250-257.

Samlet konklusion af projekt Inklusion.

I registerstudiet, påviste vi en signifikante stigning i forekomsten af en alvorlig sindslidelse i Danmark, samt faldende beskæftigelsesfrekvenser både før og efter diagnosen, hvilket understreger vigtigheden af målrettede beskæftigelsesindsatser for gruppen. I det randomiserede forsøg viste vi, at IPS er en effektiv indsats til at støtte personer med alvorlig sindslidelse til at opnå og fastholde ordinær beskæftigelse eller uddannelse, sammenlignet med den traditionelle jobcenterindsats. IPS-deltagerne var desuden mere tilfredse med den indsats de modtog og resultater fra det kvalitative studie viste at IPS-deltagerne oplevede forholdet til IPS-konsulenten som tillidsvækkende, seriøst og anerkendende. Derudover så vi en signifikant samfundsøkonomisk besparelse sammenlignet med standardindsatsen. Tidligere arbejdshistorik, motivation for forandring samt yngre alder viste ydermere at være signifikante prædiktorer for at få arbejde og effekterne af IPS er stærkest blandt personer med psykoselidelse og bipolar sindslidelse, hvor virkningen af IPS hos personer med depression fortsat er uklar. Med udgangspunkt i disse resultater og den eksisterende forskning er konklusionen, at IPS kan øge beskæftigelses- og uddannelsesgraden blandt personer med alvorlig psykisk sygdom, der har et ønske om at komme i arbejde eller uddannelse, og anbefalingen er at indsatsen udbredes til flest mulige.

Den randomiserede undersøgelse viste, at IPS-MA-indsatsen ikke fik flere i arbejde eller uddannelse end den sædvanlige jobcenterindsats. Deltagerne i IPS-MA-gruppen var dog mere tilfredse med den indsats de havde modtaget og rapporterede at være mere klar til at lave den forandring, der skulle til for at komme i arbejde eller uddannelse efter et år. Den sundhedsøkonomiske undersøgelse viste, at IPS-MA-indsatsen ikke var dyrere end standardindsatsen, og der var en tendens til at deltagerne i IPS-MA oplevede en større forbedring i kvalitetsjusterede leveår i løbet af det første år. Men deltagerne i IPS-MA arbejdede signifikant færre timer i løbet af de første 12 måneder af indsatsen.

Højere alder og mindre motivation for forandring prædikterede en lavere chance for at vende tilbage til arbejde eller uddannelse. Ligesom, selvrapporteret funktionsniveau og ikke at bo sammen med en partner også var associeret med at være i beskæftigelse. I studiet, der undersøgte mønstre i udviklingen af symptomer, fandt vi, for de der havde angst, at en stor andel fortsat havde symptomer på moderat angst, moderate komorbide depressive symptomer og mindre sandsynlighed for at være vendt tilbage til arbejdet, selv efter to år.

Baseret på de udførte studier, kan det ikke anbefales at implementere IPS-MA i sin nuværende form. Der bør dog fortsat arbejdes på, hvordan målgruppen bedst muligt støttes i at komme i arbejde eller uddannelse.

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Individual Placement and Support supplemented with cognitive remediation and work-related social skills training in Denmark: study protocol for a randomized controlled trial

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Abstract

Background: Individual Placement and Support (IPS) appears to be an effective vocational intervention for obtaining competitive employment for people with severe mental illness. However, no IPS studies or trials have been conducted in Denmark, a country characterized by a specialized labor market with a higher minimum wage and fewer entry-level jobs in comparison with other countries such as the US. Furthermore, long-term job retention and economic self-sufficiency have not been clearly demonstrated. Integrating methods such as cognitive remediation and work-related social skills training may be ways to address these issues.

Methods/Design: The trial design is an investigator-initiated, randomized, assessor-blinded, multi-center trial. A total of 750 patients with severe mental illness will be randomly assigned into three groups: (1) IPS, (2) IPS enhanced with cognitive remediation and work-related social skills training, and (3) service as usual. The primary outcome is number of hours in competitive employment or education at 18-month follow-up. Secondary and exploratory outcomes are money earned, days to first employment, symptoms, functional level, self-esteem, and self-efficacy at 18-month follow-up. Thirty- and 60-month follow-ups will be register-based.

Discussion: This will be one of the largest randomized trials investigating IPS to date. The trial will be conducted with high methodological quality in order to reduce the risk of bias. If the results of this trial show that IPS, or IPS enhanced with cognitive remediation and work-related social skills training, is superior to service as usual, this will support preliminary evidence. Furthermore, it will show that the method is generalizable to a variety of labor markets and welfare systems and provide important knowledge about the effect of adding cognitive remediation and social skills training to the IPS intervention.

Trial registration: ClinicalTrials registration number: NCT01722344 (registered 2 Nov. 2012).

Keywords: Individual placement and support, Supported employment, Cognitive remediation, Social skills training, Severe mental illness, Competitive employment, Competitive education

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Background

People with severe mental illnesses, defined as psychotic disorders, bipolar disorders, or major depression, identify employment or education as a key component to their recovery process, and approximately 65 % endorse employment as a goal [1–3]. However, employment seems to be a challenge in this population in which previous research has estimated a global unemployment rate of up to 90 %, which results in both personal and socioeconomic costs [4, 5].

Conventional vocational rehabilitation programs meet these challenges by employing a "train and place" approach, emphasizing prevocational training such as sheltered employment or trainee placements [1]. This approach remains the most widespread but has been shown to have very poor effects on competitive employment as well as low rates of client retention [6, 7].

In contrast, Individual Placement and Support (IPS) follows a "place and train" philosophy, which consists of an individualized and rapid search for competitive employment or education, avoiding prolonged prevocational training and preparation [8–10]. The intervention is integrated within the mental health services with emphasis on client preferences and choice regarding jobs and includes ongoing job support and benefit counseling [8–10].

The effects of the IPS intervention have been investigated in a number of randomized clinical trials, and reviews of these trials suggest that IPS is superior to other types of vocational rehabilitation programs in regard to obtaining competitive employment [6–9]. A review including 15 high-fidelity IPS trials shows an average employment rate among the IPS participants of 58.9 % compared with 23.2 % for control participants [7]. All of the control groups consisted of either treatment as usual, typically referral to the state vocational system, or well-established alternative vocational models [7]. Outcomes related to wages earned and hours worked were also found to be superior among those receiving the IPS intervention [7]. Previous research has not found that IPS leads to increased stress, exacerbation of symptoms, or other harmful clinical outcomes [8, 10]. The results of a recent Cochrane systematic review investigating IPS-supported employment for adults with severe mental illness additionally suggest that, compared with other vocational approaches, IPS is effective in improving a number of vocational outcomes relevant to people with severe mental illness [11]. However, the authors conclude that evidence from the included randomized trials was of "very low quality" mainly due to a high risk of bias (i.e., not describing allocation concealment). Furthermore, the meta-analysis excluded a majority of previous trials because of skewed data and populations of fewer than 200 people [11].

Moreover, it has been suggested that long-term job retention and economic self-sufficiency could be further improved by adding cognitive remediation and work-related social skills training to the intervention [10, 11]. Impairment in these functions is frequent among persons receiving IPS services and is known to be related to employment outcomes in persons with severe mental illness [12–14]. Two small-scale trials have found improved effects when the intervention was enhanced with either cognitive remediation or work-related social skills training [13, 15–17].

Randomized clinical trials of IPS have been conducted in different socioeconomic and cultural contexts with different results. A review found that four of five trials with the lowest employment rates were non-US trials [7]. Furthermore, a randomized trial from the UK investigating IPS compared with service as usual did not show significant vocational effects [18]. The authors suggest that implementation of IPS in labor markets and economies where economic disincentives may lead to lower levels of motivation can be challenging [18]. Until now, IPS trials have not been conducted in Denmark, where barriers to implementation and replication of previous international findings may exist. Firstly, Denmark is characterized by complex employment legislation and a highly specialized labor market with a high minimum wage and few entry-level jobs, which could impact both the implementation of IPS and potential effect sizes. Secondly, the social security system is generous compared with those of other countries, and this may be a perceived or real financial disincentive for returning to competitive employment and hence influence motivation levels [18, 19].

Thus, it is crucial to investigate whether IPS can be implemented in Denmark, and a large-scale trial with low risk of bias and a long follow-up period is needed. The present trial will be the largest randomized clinical trial to date to investigate the effects of IPS and IPS enhanced with cognitive remediation and work-related social skills training. The primary outcome is number of hours in competitive employment or education at 18-month follow-up.

Methods/Design

Trial design

The trial is designed as an investigator-initiated, randomized, three-arm, assessor-blinded, multi-center trial. A total of 750 patients with severe mental illness will be randomly assigned into (1) IPS, (2) IPS enhanced with cognitive remediation and work-related social skills training, and (3) service as usual.

The primary hypothesis is that participants allocated to the IPS intervention group (group 1) will have significantly higher work or study rates at 18-month follow-up

compared with participants allocated to service as usual (group 3). Furthermore, we assume that an enhancement of the IPS intervention with cognitive remediation and work-related social skills training (group 2) will increase the effects. To ensure high methodological quality, the trial is designed and reported according to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) Statement and the modified CONSORT (Consolidated Standards Of Reporting Trials) criteria for non-pharmacological trials [20, 21].

Recruitment and eligibility criteria

Eligible participants are adults (ages 18–67) diagnosed according to the International Classification of Diseases version 10 (ICD-10) with schizophrenia, schizotypal, or delusional disorders (F20–F29); or bipolar disorder (F31); or severe depression (F33). Participants must reside in one of two major Danish cities: Copenhagen (including the municipality of Frederiksberg) or Odense. They must be assigned to early intervention teams (OPUS teams) or community mental health services at Mental Health Center Copenhagen or the Department of Mental Health Odense-University Clinic. They must express a clear desire for competitive employment or education and provide verbal and written informed consent. Furthermore, participants must be able to speak and understand Danish well enough to participate without an interpreter, mainly in order to benefit from the group-based cognitive remediation therapy. A connection to vocational authorities with a formalized collaboration with the IPS teams is the foundation for the residence criterion. If this criterion leads to an insufficient number of patients, expansion of the geographic area of the trial will be considered. Participants who are interested in competitive employment or education are identified by case managers, who assess for eligibility and refer to the trial. To ensure that the participants meet the diagnostic criteria, they will be assessed by a trained and certified research assistant using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) diagnostic tool [22]. Informed consent will be obtained from each participant before assessment.

Randomization

After the assessment, a central web-based randomization will be performed by the Copenhagen Trial Unit [23] according to a computer-generated allocation sequence with permuted blocks of varying sizes. The allocation sequence and varying block sizes will be concealed from the investigators. A research secretary will perform the allocation by logging on to a website by using a personal password. Previous research has shown an effect of sex and of work history on vocational outcomes [24, 25]. Therefore, the allocation sequence will be stratified by sex and by work history (more or less than 2 months of competitive employment during the last 5 years). Furthermore, participants will be stratified by work readiness by using match categories, a tool used in Danish job centers [26]. We will assess the likelihood that the participant is ready to apply for competitive employment and will be self-sufficient within 3 months (match 2 or 3). Finally, the participants will be stratified by site.

The experimental interventions

Group 1 – IPS

The first experimental intervention group will receive IPS and service as usual (see Control group below). The details of the IPS intervention are described comprehensively in the IPS literature [1, 27] and are briefly outlined below with emphasis on the specific challenges and opportunities for implementation into a Danish context. The IPS intervention is based on eight key principles: (1) eligibility based on client choice, (2) focus on competitive employment or education, (3) integration of mental health and employment services, (4) attention to client preferences, (5) benefits counseling, (6) rapid job search, (7) systematic job development, and (8) individualized long-term job support [1, 7]. Competitive employment is defined as part-time or full-time jobs that exist in the open labor market and that pay at least a minimum wage and are open to everyone, regardless of their disability status [9]. Competitive education is defined as an education or training program that is related to an employment goal and not designed specifically for people with disabilities [27].

Danish employment legislation provides opportunities for financial support when obtaining competitive employment. This could be subsidized employment that in most cases will be consistent with the definition of competitive employment, as it consists of jobs that pay at least the minimum wage and are open to everyone. For more information, see Table 1.

Table 1 Danish employment legislation

In Denmark, subsided employment at a private workplace is offered to long-term unemployed individuals with or without a disability. Working conditions are agreed upon between authorities and employers and are formalized in a contract. The employee in a private workplace will receive at least minimum wage. Maximum duration of a subsidized job is 1 year, although many will continue in regular employment without subsidy if agreed upon with the employer. Participants will also receive help finding a fleksjob if this is already granted at intake to the study. Fleksjob is also subsidized employment, but the subsidy is conditional on the employee's ability to work. The employee will receive at least minimum wage for the actual hours of work. The job exists on the open labor market.

Employment specialists in Copenhagen are employed by the vocational authorities in the municipality (job centres) but will still be integrated within the mental health services.

It is expected that many of the participants in the trial will have an aim or motivation to start or resume education. This is expected, firstly, because many of the participants will be young adults recruited from early intervention teams (OPUS) and, secondly, because the education system in Denmark is financed by the state or the municipalities without tuition fees and with the opportunity to receive financial support from the State Educational Grant and Loan Scheme (SU). These options give employment specialists greater opportunities to focus on education compared with previous IPS reports. Employment specialists are encouraged to closely follow the methods described in the updated and expanded IPS manual "Applying the individual placement and support (IPS) model to help clients compete in the workforce" [27]. The manual, including worksheets, is translated into Danish, and the two IPS teams will be trained in the method by an IPS expert, who will also offer tele-supervision throughout the trial period. The IPS employment specialists will be evaluated by trained external reviewers who will use the IPS fidelity scale to ensure high fidelity and adherence to evidence-based practice [28]. The evaluation will take place 6 months after trial start and thereafter every sixth month until high fidelity is demonstrated. Subsequently, an annual evaluation will be performed.

Group 2 – IPS enhanced with cognitive remediation and work-related social skills training

The second experimental intervention group will receive IPS (see Group 1 – IPS) enhanced with cognitive remediation and work-related social skills training and service as usual (see Control group below). The cognitive remediation is, with a few adjustments, based on previous research by McGurk et al. [15] and uses an adapted version of the "Thinking skills for work" manual [13, 15]. This is designed as an adjunct to IPS and is aimed at integrating cognitive rehabilitation with the ongoing provision of IPS services. The enhancement program consists of 24 group-based sessions of computer training using newly developed software (CIRCuiTS) and incorporates evidence-based training principles such as errorless learning and massed practice [29]. The computer training provide practices across a broad range of cognitive functions hypothesized to be impaired in persons with severe mental illness, including attention, concentration, psychomotor speed, learning, memory, and executive functions. Each participant works through a so-called metacognitive journey consisting of 278 task instances divided into seven different stages. The participant receives ongoing feedback and is able to monitor their own scores, strategy use, progression in skills, and development or change in personal goals. In addition to receiving the computer training, participants are offered

12 sessions in coping strategies for dealing with cognitive challenges [13]. These sessions are aimed at helping participants develop effective strategies for improving their cognitive skills or reducing the effects of cognitive challenges in order to achieve vocational goals, maintain work, and increase performance [13]. Finally, the program consists of six work-related social skills training sessions with a focus on disclosure, communications skills, decoding norms for social interaction, and conflict management. A detailed manual based mainly on the "Thinking skills for work" manual was developed in Danish but was adapted to the present trial and extended with work-related social skills training. The manual has not been published but can be obtained by request from the authors. The Danish manual further deviates by providing less opportunity for individual training and by implementing CIRCuiTS instead of Cogpack computer software.

The intervention will be performed primarily in group format, and eight participants will be assigned to each group. Trained psychologists will be responsible for the group sessions, and employment specialists will be cotherapists. The program requires 30 weeks to complete, is complementary to IPS, and should not be considered prevocational training. While participating in groups, participants will seek regular employment or education. To ensure the quality of the intervention, employment specialists are trained by psychologists with experience in using the method. A fidelity scale of the intervention has been developed, and fidelity will be assessed at the same time as the IPS fidelity review.

Control group
Group 3 – service as usual

Participants allocated to the control group will receive "service as usual" only. This consists of participants continuing to receive OPUS or community mental health treatment. Also, it involves individual case management and medical review, referral to external vocational agencies, and involvement in group programs which may involve participation in vocationally oriented groups. The psychiatric treatment provided will be the same in all three groups throughout the trial period with the one exception that controls do not get the integrated IPS intervention. In general, the participants allocated to the control group are to have close mandatory contact with the local vocational authority (job centers), depending on what kind of benefits they receive. Hence, the participants in the control group will receive a variety of vocational rehabilitation support at the job centers in accordance with the train and place principle.

Blinding
Owing to the nature of the intervention, neither participants nor staff can be blinded to allocation but are

instructed not to reveal details that may cause the research assistant to deduce which intervention the participants are receiving. The research assistants who perform the assessments at baseline and follow-up will be blind to allocation. If the blinding cannot be maintained, a research assistant from the other site will perform the follow-up interviews. Blinding will be maintained until the end of the trial. Statistical analyses will be conducted with intervention groups coded as, for example, X, Y, and Z. Conclusions will be drawn with the blinding intact. First, we will assume that X is experimental group 1, Y is experimental group 2, and Z is control group 3. Then we will draw five additional conclusions, assuming the remaining five combinations. After this, the blind will be broken.

Outcome and assessments

The primary outcome is "hours in competitive employment or education" measured from baseline to 18-month follow-up. Employment and enrollment in education will be identified by using register data. Hours in competitive employment will be extracted from an extended version of the Danish Register for Evaluation of Marginalization (DREAM) database administered by the National Labor Market Authority [30]. The DREAM database contains information on employment, sickness leave, and education eligible for state education grants, disability pension, social security, and sickness benefits. The register covers the entire population, and data can be linked to a range of different registers, including the Danish income register, making it possible to obtain the exact number of employment hours. Data on education will be extracted from education statistics hosted by Statistics Denmark (http://www.statbank.dk) and supplemented by data from interviews for more detailed information on part-time studies.

The primary outcome will be supported by several other secondary and explorative outcome measures. Secondary outcomes are work or education at some point

during the follow-up period (yes/no), days to first employment or beginning of education, cognitive impairment, functional level, self-esteem, and self-efficacy assessed at baseline and 18-month follow-up. Data on employment and education will similarly be extracted from registers. Furthermore, semi-structured interviews using the Personal and Social Performance (PSP) scale [31] and the Brief Assessment of Cognition in Schizophrenia [32] will be used to assess cognitive impairment and functioning. Standardized validated survey instruments, including the Rosenberg self-esteem scale [33] and the General Self-Efficacy scale [34], will be used to assess self-esteem and self-efficacy. All secondary outcomes and the assessment instruments used are outlined in Table 2.

To avoid the risk of multiplicity and type I errors, we will limit our secondary outcomes to outcomes with at least 80 % power. Other outcomes are considered "exploratory" when drawing conclusions. This means that we will consider any statistically significant result in any of these outcomes as exploratory or hypothesis-generating. This is because we have no sample size estimation for these outcomes, and thus the risk of an early false positive is increased; it is further increased because of the risk of multiplicity as a result of too many outcomes.

Exploratory outcomes cover the 30 and 60 months of register follow-up along with additional vocational measures that will provide a more nuanced picture of vocational status, including average monthly earnings and hours of work per week among those who obtain competitive employment. Furthermore, a range of non-vocational outcomes such as client satisfaction, health-related quality of life, empowerment, recovery, and substance abuse will be used to address other important factors hypothesized to influence the participants. Psychopathology will be measured to ensure no adverse effects of the intervention.

All exploratory and safety measures and the assessment instruments used are outlined in Tables 3 and 4. Trained and certified research assistants will perform all assessments. Inter-rater reliability tests will be performed prior to the trial and at least quarterly

Table 2 Primary and secondary outcomes and data collection

Outcomes	Source of collection	Assessment	Baseline	18-month follow-up
Primary outcome	Register-based/Interview	Hours in competitive employment or education in follow-up period		X
Secondary outcomes	Register-based	Competitive employment or education at some point during follow-up period		X
	Register-based	Days to first employment or beginning of education		X
	Obtained through interview	Cognitive function measured with the Brief Assessment of Cognition in Schizophrenia [32] (BACS)	X	X
	Obtained through interview	Function measured with Personal and Social Performance (PSP) Scale [31]	X	X
	Self-reported questionnaire	Self-efficacy measured with General Self-Efficacy (GSE) scale [37]	X	X
	Self-reported questionnaire	Self-esteem measured with the Rosenberg Self-Esteem scale [38]	X	X

Table 3 Explorative measures and data collection

Outcomes	Source of collection	Assessment	Baseline	18-month follow-up	30 + 60-month register follow-up
Explorative outcomes	Register-based	Hours in competitive employment or education in follow-up period			X
	Register-based	Competitive employment or education at some point during follow-up period			X
	Register-based	Days to first employment or beginning of education			X
	Register-based	Days in employment or education		X	X
	Register-based	Average monthly earnings		X	X
	Register-based	Hours of work per week among those who obtain competitive employment		X	X
	Register-based	Long-term sick leave		X	X
	Register-based	Social benefits	X	X	X
	Obtained through interview	Function measured with Global Assessment of Functioning (GAF) [39]	X	X	
	Obtained through interview	Health-related quality of life measured with 12-Item Short Form Health Survey (SF-12) [40]	X	X	
	Self-reported questionnaire	Recovery measured with Mental Health and Recovery Measure (MHRM) [41]		X	
	Self-reported questionnaire	Empowerment measured with Empowerment Scale [42]	X	X	
	Self-reported questionnaires	Satisfaction with treatment. Measured with Client Satisfaction Questionnaire (CSQ) [43]		X	
	Register-based	Use of mental health services	X	X	X
	Obtained through interview	Substance abuse measured with Alcohol Use Disorders Identification Test (AUDIT) [44]	X	X	
	Self-reported questionnaire	Health-related quality-of-life measured with EQ 5D(EuroQOL five dimensions questionnaire) [45]	X	X	

throughout the assessment period on the following instruments: Scale for the Assessment of Negative Symptoms [35], Scale for the Assessment of Positive Symptoms [35], PSP scale [31], and Hamilton Depression Scale (HAM-D6) [36]. The aim is to achieve an interclass correlation coefficient of more than 0.7. Consensus ratings will be performed on the remaining instruments.

Adherence to the interventional program

The employment specialists and the IPS team leaders will assess the use of IPS services, including content and number of contacts between employment specialist and participants. The cognitive specialists will register adherence to the cognitive remediation and social skill groups, including group session attendance and whether home work is completed. In the control group, all contact

Table 4 Safety measures and data collection

Outcome measure	Source of collection	Assessment	Baseline	18-month follow-up	30 + 60-month register follow-up
Safety measures	Obtained through interview	Psychotic and negative symptoms measured with Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS)	X	X	
	Obtained through interview	Depressive symptoms measured with Hamilton Depression Scale [36] (HAM-D6)	X	X	
	Obtained through interview	Suicidal ideation and actions. Measured with European Parasuicide Study Interview Schedule (EPSIS)	X	X	
	Death cause register, Civil Registration System (CPR)	Deaths (all causes)	X	X	X
	Hospital records	Number and length of hospital admissions both somatic and psychiatric		X	X
	Hospital records	Use of outpatient services	X	X	X

between the participants and the social worker or vocational counselor will be assessed. It will also be possible to assess whether the controls are allocated to a vocational rehabilitation program of any kind and the duration and content of the rehabilitation. These data will be obtained from the DREAM register and from records in the job centers.

Sample size and power calculation

No previous IPS trials or similar studies have been conducted in Denmark that could contribute to an estimation of the expected average number of hours of work among participants in the IPS intervention. A European IPS multicenter trial found a difference between the IPS group and the control group (vocational services) of 150 h in competitive employment in an 18-month follow-up period, and standard deviation was 500 [19]. A difference of 150 h in competitive employment or education is considered clinically relevant. If the outcome within each intervention group is normally distributed with a standard deviation on 500 and with a true mean difference of 150 between the intervention and the control group, the present trial will need 250 participants in both intervention arms and additionally 250 control participants to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) of 80 %. The type I error probability associated with the null hypothesis is 1.25 %. A type I error of 1.25 % was chosen to give the possibility to make four comparisons: (1) IPS versus service as usual, (2) IPS versus IPS enhanced, (3) IPS enhanced versus service as usual, and (4) IPS + IPS enhanced versus service as usual. If we encounter difficulties in recruiting 250 participants

to each group, we will exclude comparison (4) as a primary comparison. With three primary comparisons, we use a type I error of 1.67 % in the sample size calculation, accumulating a sample size of 236 patients in each group. Power calculations on calculations of the secondary outcome measures were carried out (Table 5) and indicate that a sample size of 250 patients per group would be adequate to detect relevant significant differences.

Data analysis plan

The main null hypothesis to be tested is that there is no difference between the three groups in hours in competitive employment or education in the 18-month follow-up period. All randomized participants will be analyzed, including those who stop receiving treatment, according to the intention-to-treat principle. All continuous outcome measures, including the primary outcome "hours in competitive employment or education", will be analyzed by using generalized linear models. In situations in which the continuous measure is non-normally distributed, a non-parametric model will be used. Multiple imputations will be used to impute a distribution of missing values. Furthermore, linear mixed models with repeated measurements and unstructured covariance matrixes will be used to assess the potential interaction between time and intervention. The dichotomous secondary outcome "work or education at some point during the follow-up period" will be analyzed by using logistic regression. The secondary outcome "time-to-employment or education" will be analyzed by using the Cox proportional hazards model. All models will be adjusted for the stratification variables.

Table 5 Power calculation

Outcome measure	δ expected difference in mean	σ expected standard deviation	α	Power	Reference
Days to first employment or beginning of education	68	45	0.0125	1.000 (*t* test)	Bond et al. [8] (2008),
Cognitive function The Brief Assessment of Cognition in Schizophrenia [32]	0.3	0.7	0.0125	0.989 (*t* test)	McGurk et al. [13] (2005)
Function measured with Personal and Social Performance (PSP) scale [31]	7	14	0.0125	0.999 (*t* test)	Kawata et al. [31] (2008). Nasrallah et al. [46] (2008) (No IPS studies use PSP scale. δ is estimated)
Self-efficacy measured with General Self-Efficacy scale [37]	0.28	0.85	0.0125	0.880 (*t* test)	Tsang et al. [14] (2010)
Self-esteem measured with the Rosenberg Self-Esteem scale [38]	0.3	0.55	0.0125	0.992 (*t* test)	Mueser et al. [47] (2004), Howard et al. [18] (2010), Drake et al. [48] (1999). None of the studies shows difference in mean. σ is between 0.55 and 0.68.
Competitive employment or education during follow-up period Dichotomous yes/no	50 % vs. 34 %	-	0.0125	0.807 (chi-squared test)	Bond et al. [8] (2008)

Ethical considerations

Previous research does not indicate that IPS leads to an exacerbation of symptoms or has other negative clinical implications [10]. Entering competitive employment may, for some participants, be perceived as stressful. This will be addressed by close contact with participants, case managers, and employers to ensure adaptation of special requirements or sick leave if necessary. All adverse events (e.g., hospitalization, increase in symptoms, decrease in functioning, and incidents of suicide) will be registered and reported. All safety measures can be seen in Table 4.

Information about the trial is presented to all potential participants both verbally and in written form so they can make an informed decision about their participation before signing written consent. It will be clearly explained that participation is voluntary and that withdrawal can occur at any time without consequence for treatment possibilities. Decisions regarding participation will not influence clinical care in any way.

The trial protocol has been reviewed by the Ethics Committee in the Capital Region of Denmark (registration #H-3-2012FSP34), although they waived the need for ethical approval because it is not a biomedical trial. Furthermore, the trial has been reported to the Danish Data Protection Agency (registration #01768 RHP-2012-011) and is registered at http://www.clinicaltrials.gov (#NCT01722344).

Discussion

This is the first trial investigating the effects of IPS in Denmark and will be one of the largest randomized trials investigating IPS to date. As a comparison, 14 trials included in a Cochrane review showed a median sample size per arm of 70 participants and a range of between 20 and 156 [11]. Furthermore, this trial will be the first large-scale trial, with a long follow-up period, enhancing the IPS intervention with both cognitive remediation and social skills training. The design of the trial has several strengths. Firstly, a sample size calculation was made according to the primary outcome, hours in competitive employment or education. The power is estimated for all secondary outcome measures, showing that a sample size of 750 participants is sufficient to show a relevant effect size with a power above 80 %. Secondly, the risk of selection bias related to allocation sequence generation and concealment is limited, as the Copenhagen Trial Unit performs a central web-based randomization according to a computer-generated allocation sequence. Thirdly, assessors are blinded, and blinding will be used wherever possible to prevent bias. Data will be analyzed according to the intention-to-treat principle, which together with an intense follow-up of patients should limit the risk

of attrition bias. Finally, internal validity is addressed by implementing fidelity ratings. The fidelity ratings have high priority and will be conducted throughout the trial period to ensure that evidence-based practice is adhered to.

The trial also has some limitations. Firstly, there is a risk of performance bias because participants and practitioners are not blinded. It could be argued that both participants and practitioners conducting the experimental intervention would be more enthusiastic and keen to perform well because of the novelty of participating in a research project. To account for this, blinding is employed in all other aspects of the trial. Secondly, the control condition is heterogeneous. Participants will receive different vocational interventions, which will vary by individual and depend on factors such as type of social benefit the individual is receiving. Policy decisions could change the conditions in the job centers during the trial period and this could affect vocational rehabilitation, a fact that may limit the generalizability of the control condition. Thirdly, recruitment procedures may affect the external validity of the trial. The staff at the mental health centers is responsible for recruitment and may not successfully identify all eligible participants. Finally, there are initiatives in the Danish IPS model that exclude the possibility of highest IPS fidelity score. For example, the employment specialists will use a percentage of their time on the authority work in the job centers instead of manualized IPS.

If the results of this trial show IPS to be effective compared with the control group, these positive results will support the preliminary evidence that the method is generalizable to a variety of sociodemographic contexts. Furthermore, if IPS supplemented with cognitive remediation and work-related social skills training shows that the effects can be further improved, it will bring important knowledge for further research on and implementation of IPS.

Trial status

The trial was initiated in October 2012. As of January 2015, 480 patients had been randomly assigned.

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JAMA Psychiatry | **Original Investigation**

Effects of Individual Placement and Support Supplemented With Cognitive Remediation and Work-Focused Social Skills Training for People With Severe Mental Illness
A Randomized Clinical Trial

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+ Supplemental content

IMPORTANCE Individual placement and support (IPS) seems to be an effective vocational intervention for people with severe mental illness, but its effects have not yet been shown in the Danish welfare model. Also, effects may be enhanced by adding cognitive remediation and work-focused social skills training (IPS with enhancements [IPSE]).

OBJECTIVES To investigate the effects of IPS vs IPSE vs service as usual (SAU) on a population of individuals with severe mental illness in Denmark.

DESIGN, SETTING, AND PARTICIPANTS This was an investigator-initiated, 3-group, parallel, assessor-blinded randomized clinical trial that used early-intervention teams or community mental health services in 3 Danish cities to recruit participants with severe mental illness. Participants were randomly assigned to receive IPS, IPSE, or SAU from November 2012 to February 2016, and follow-up continued until August 2017.

INTERVENTIONS Participants allocated to the IPS intervention received vocational support per the principles of the IPS model. Participants in the IPSE arm received cognitive remediation and social skills training in addition to IPS. The group receiving SAU received vocational rehabilitation at the Danish job centers.

MAIN OUTCOMES AND MEASURES The primary outcome was the number of hours in competitive employment or education during the 18-month follow-up. Secondary outcomes included intergroup differences in employment or education at any point during follow-up; time to employment or education; and cognitive and social functioning, self-esteem, and self-efficacy.

RESULTS Of the 720 included participants (mean [SD] age, 32.8 [9.9] years; 276 [38.3%] women), 243 received IPS, 238 received IPSE, and 239 received SAU. Most participants (551 [76.5%]) were diagnosed with a schizophrenia spectrum disorder. During the 18-month follow-up, the IPSE group worked or studied a mean (SD) of 488.1 (735.6) hours, compared with 340.8 (573.8) hours in the group receiving SAU (success-rate difference [SRD], 0.151 [95% CI, 0.01-0.295]; P = .016). The mean (SD) in the IPS group was 411 (656.9) (SRD, 0.127 [95% CI, −0.017 to 0.276]; P = .004). There was no difference between IPS and IPSE in any vocational outcomes, and the 3 groups showed no differences in any nonvocational outcomes, except that the IPS and IPSE groups were more satisfied with the services received than the group receiving SAU (IPS vs SAU: SRD, 0.310 [95% CI, 0.167-0.445]); IPSE vs SAU: SRD, 0.341 [95% CI, 0.187-0.478]).

CONCLUSIONS AND RELEVANCE Compared with SAU, IPS and IPSE seem to be viable routes to increase employment and education rates in people with severe mental illness in Denmark, but no additional effects were observed by enhancing IPS.

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Employment and education are central to the recovery process for people with severe mental illness (SMI).[1] Apart from providing financial independence and security, employment contributes to a sense of belonging and identity and can benefit mental well-being.[2] Nevertheless, unemployment is high among people with SMI,[3,4] leading to substantial costs for both the individual and society.[5]

In response to these problems, a method of vocational rehabilitation called individual placement and support (IPS) has been developed.[6] In contrast with traditional approaches to vocational rehabilitation, IPS avoids prolonged prevocational training and provides a rapid, individualized search for competitive employment or education. Participants' preferences regarding jobs are emphasized, and the intervention is integrated within the mental health services. Additionally, job support is ongoing, and benefit counseling is provided.[6]

Although education is the primary goal for many people with SMI, especially young patients with a recent onset of the illness,[7] most previous IPS trials have mainly focused on supporting participants to obtain competitive employment. This is despite the fact that supported education is described in the updated and expanded IPS manual,[8] and it has been demonstrated that the IPS principles can be successfully extended to include support for education.[7,9]

Based on positive findings from numerous randomized clinical trials, IPS seems an effective intervention in obtaining competitive employment compared with other types of vocational rehabilitation programs.[10] However, about 40% of participants do not achieve their vocational goals, and many participants in IPS only work part time or lose their jobs because of poor work performance.[11] This may be attributable to cognitive impairments and low social functioning, which are defined as some of the strongest illness-related factors associated with unemployment among people with SMI.[12,13] In accordance, research suggest that IPS enhanced with either cognitive remediation or work-associated social skills training (IPSE) may improve the positive outcomes of IPS.[14,15]

The questions are whether the effects of enhancing the intervention can be replicated and whether the same effects of IPS can be achieved when education is included in the primary outcome and when conducted in a highly specialized labor market with a high minimum wage and a relatively generous social-security system. On this background, we conducted a 3-group randomized clinical trial in Denmark with the primary aim of investigating the difference in number of hours in competitive employment or education.

Methods

Trial Design

The trial was designed as an investigator-initiated, 3-group, parallel, multisite randomized clinical trial with blinded outcome assessment. The trial protocol was reviewed and approved by the ethics committee in the Capital Region of Denmark and the Danish Data Protection Agency. The only deviations from the trial protocol[16] were inclusion of an additional site (Silkeborg) and the division of the Copenhagen team

Key Points

Question What are the effects of individual placement and support vs individual placement and support enhanced with cognitive remediation and social skills training vs service as usual for people with severe mental illness in Denmark?

Findings In this randomized clinical trial of 720 adults with severe mental illness, the proportion achieving competitive employment or education was 59.9% in individual placement and support, 59.1% in those receiving individual placement and support with enhancements, and 46.5% in those receiving service as usual.

Meaning Individual placement and support and individual placement and support with enhancements are viable routes to increase employment and education among people with severe mental illness in a Danish context, but no additional effect was found by enhancing individual placement and support with cognitive remediation and work-focused social skills training.

into 2 independent teams. Informed consent was obtained from each participant before assessments began.

Eligibility Criteria

Participants were eligible if they had a diagnosis of schizophrenia, schizotypal disorder, delusional disorder (defined by *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* [*ICD-10*] codes F20-F29); bipolar disorder (*ICD-10* code F31); or recurrent depression (*ICD-10* code F33). All participants were adults (aged 18-64 years) living in 1 of 3 Danish cities: Copenhagen (including the municipality of Frederiksberg), Odense, or Silkeborg. All were assigned to early-intervention teams or community mental health services. All eligible participants expressed a clear desire in competitive employment or education and spoke and understood Danish sufficiently well to participate without an interpreter.

Recruitment

The participants were recruited by the case managers on the psychiatric outpatient teams or self-selected after encountering advertisements and information available at the psychiatric centers. To ensure participants met the diagnostic criteria, they were assessed by a trained and certified researcher (T.N.C., I.G.W., or a nonauthor) using the diagnostic interview Schedules for Clinical Assessment in Neuropsychiatry.

Randomization and Blinding

Recruited participants were randomized with a 1:1:1 ratio to IPS, IPSE, or service as usual (SAU). The sample was stratified by sex, work history (absence or presence of ≥2 months' competitive employment during the previous 5 years), work readiness,[17] and site (Copenhagen/Frederiksberg or Odense/Silkeborg). The Copenhagen Trial Unit conducted a central, computer-generated random allocation sequence with varying block sizes of 6 and 9.[18] The allocation sequence and block sizes were concealed from the investigators. Outcome assessors (T.N.C., I.G.W., or a nonauthor) and all investigators involved in the trial (T.N.C., I.G.W., E.S., A.B.B., C.G., M.N.,

and L.F.E.) were blinded to participants' allocation, but participants and employment specialists were not. The randomization code was not broken before all analyses had been performed and conclusions had been drawn.[19]

Interventions

All participants in the 3 groups continued to receive their usual psychiatric outpatient treatment, which consisted of at least individual case management based on cognitive therapeutic methods and medical review.[20] The content of the 3 vocational intervention groups is briefly outlined but more thoroughly described in the trial protocol (Supplement 1) and in eMethods 1 in Supplement 2.[16] Participants allocated to the IPS group received vocational support per the principles of the IPS model. In addition to IPS, the IPSE group received cognitive computer training using the software program Computerized Interactive Remediation of Cognition—a Training for Schizophrenia (CIRCUITS), Danish version (2012; Spika Ltd)[21] and training in cognitive coping and compensatory strategies using an adapted version of the *Thinking Skills for Work* manual.[14] The SAU group received the best available vocational rehabilitation provided by the national job centers.

Fidelity With IPS and IPSE

To ensure the quality and adherence to the IPS service, fidelity ratings were conducted by trained and external reviewers, who did not conduct baseline or follow-up interviews, using the Individual Placement and Support Fidelity Scale (IPS-25).[22] The evaluation took place 6 months after trial commencement, and subsequently an additional 6 ratings were performed. In addition, a fidelity scale was developed for the enhancement program, aimed at measuring the core elements of the intervention, as described in the manual. For quality improvement purposes, the assessors conducted a fidelity report after each review, summarizing ratings and providing recommendations for improvement.

Outcomes

Data were obtained through multiple sources at baseline and during the 18-month follow-up: researcher-administered semistructured interviews, self-reported questionnaires, and register-based data. The data were collected over 4.8 years (November 2012 to August 2017) by blinded researchers who were trained and certified in all instruments used. Interrater reliability is described in eMethods 3 in Supplement 2. All outcome measures reported were prespecified and reported in the study protocol.[16]

Primary Outcome

The primary outcome was number of hours in competitive employment or education during the 18 months' follow-up.[16] Employment outcomes were extracted from the Danish Register for Evaluation of Marginalization (DREAM) database extended with data from the Danish national income register with 100% response.[23-25] The registers cover the entire population and contain data on employment, including salaries. Educational outcomes were reported by the participants at the 18-month follow-up interview to elicit the most detailed

information on part-time studies and ascertain the exact number of study hours. The study time was measured only if the participant studied actively. All secondary and exploratory outcomes are described in the trial protocol (Supplement 1) and eMethods 2 and eMethods 4 of Supplement 2.

Statistical Analysis

Because we did not fully reach our planned sample size of 750, but rather only 720 participants (96.0%), we used as planned only 3 primary comparisons, with a type I error probability of 1.67%.[16] We hypothesized an effect size of 0.3 standardized mean differences for the primary outcome of hours in competitive employment or education, corresponding to an absolute difference between groups of 150 hours and an SD of 500 hours. This was informed by a previous European trial of IPS.[26] Three balanced groups with 236 patients in each group (N = 708) were required to achieve a statistical power of 80%. A priori power analysis was carried out on all secondary outcomes.[16]

The outcome analysis was based on the intention-to-treat principles, and to compensate for missing data, we used multiple imputations. Complete baseline data and register-based outcome data were used for the imputation model. Baseline characteristics are reported using means and SDs for numeric variables and numbers with percentages for categorical variables. The primary analyses for differences between groups at follow-up were carried out without adjusting for stratification variables. The reason for this was that the assumptions for including covariates in the analyses may have been violated, which would bias the estimation of the treatment effect sizes.[27] Supplementary analyses that reflect the original analysis plan are available in eTable 1 and eTable 2 in Supplement 2. The results are substantially the same regardless of the analytical strategy. Main estimates are presented in the form of success-rate differences (SRDs)[28] with bootstrapped inferential statistics. For binary outcomes, the SRD is simply the difference between the proportion of patients who received successful treatment in the 2 groups. For numerical outcomes, the SRD is derived from the Wilcoxon U statistic:

$$SRD = \frac{2U}{(N_0 \times N_1) - 1}$$

where U is the Wilcoxon U statistic and N_O and N_I are the sample sizes for the 2 groups. For numerical outcomes, this amounts to the difference in the probability of a random patient in the intervention group scoring higher (having a better outcome) than a random patient in the comparison group and the probability of a random patient in the comparison group scoring higher than a random patient in the intervention group. Therefore, scores greater than 0 imply a higher numerical value for the intervention group vs the comparison group, while scores less than 0 indicate a higher numerical value in the comparison group. The number of days to employment, education, or noncompetitive employment was analyzed using Cox proportional hazards regression and reported using hazard ratios. Parameter estimates and 95% CIs are based on observed data with no imputations. Data were analyzed from December 2017 to

Figure. Study Flowchart
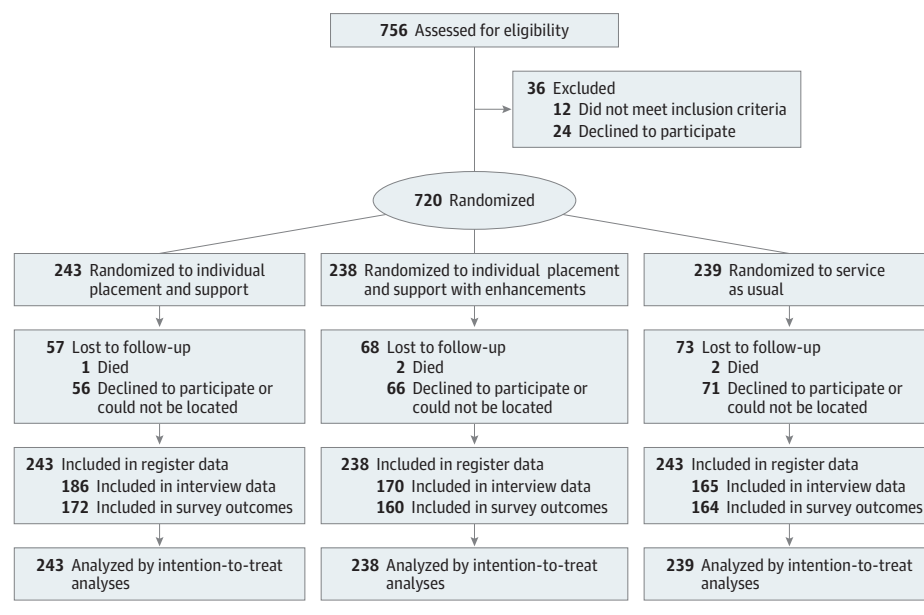
June 2019 with Stata version 14 (StataCorp) and R version 3.6.0 (R Foundation for Statistical Computing). All *P* values less than .017 (.05 divided by 3, to accommodate the study's 3 comparisons) were considered significant.

Results

The **Figure** illustrates the patient flow through the trial and the attrition from it. After exclusion of those not meeting inclusion criteria and those who declined to participate, 720 participants were randomly assigned into the 3 groups: IPS (n = 243), IPSE (n = 238), and SAU (n = 239).

Table 1 shows the baseline sociodemographic and clinical characteristics of the participants. The mean (SD) age was 33.0 (9.9) years, and we included more men (444 [61.6%]) than women. Most participants (551 [76.5%]) were diagnosed with a schizophrenia spectrum disorder, and 279 (38.8%) had a primary or lower secondary education. Further, the participants' global level of cognitive functioning, measured on the Brief Assessment of Cognition in Schizophrenia scale, was a mean (SD) *z* score of 2.70 (1.7) lower than the reference healthy population. The follow-up proportion was 72.5% for the sample as a whole (n = 522). However, there was 100% follow-up for all register-based measures, including all employment outcomes.

All IPS teams maintained good or fair levels of IPS fidelity throughout the trial. The scores ranged from 75 to 101 as measured on the IPS-25 scale. All sites demonstrated good fidelity to the IPSE manual, with scores between 21 to 29 points on the 30-point scale. However, 57 of 238 participants (23.9%) in the IPSE group did not attend the sessions with cognitive remediation, and the mean (SD) number of cognitive training sessions attended was 9.6 (9.7) of 30 sessions.

The comparison of IPSE vs SAU groups showed a mean difference of 147.3 (SE, 70.8) hours in competitive employment and education favoring IPSE. The corresponding SRD was 0.151 (95% CI, 0.01-0.295; *P* = .016). The mean difference between IPS vs SAU was 70.0 (SE, 66.4) hours, with an SRD of 0.127 (95% CI, −0.017 to 0.276; *P* = .004).

In an explorative analysis, we combined IPS and IPSE vs SAU. The SRD for working or studying more hours in the 2 IPS groups, compared with SAU, was 0.138 (95% CI, 0.009-0.263; *P* = .002). There was no significant difference between the outcomes of the IPS and IPSE groups in any of the vocational outcomes (**Tables 2**, **3**, and **4**).

All secondary and exploratory outcomes are shown in Tables 2, 3, and 4. Because of multiple testing and occasional lack of power, these analyses should be interpreted with caution. Over the 18-month follow-up period, participants in the IPS group were more likely than those in the SAU group to work competitively or be enrolled in education (112 [59.9%] vs 79 [46.5%]; SRD, 0.134 [95% CI, 0.009-0.257]; *P* = .002). The difference between IPSE and SAU was 101 (59.1%) vs 79 (46.5%) (SRD, 0.126 [95% CI, 0.003-0.256]; *P* = .03). When the IPS and IPSE groups were combined and compared with SAU, the SRD was 0.130 (95% CI, 0.025-0.239; *P* = .002).

The participants in the IPS and IPSE groups also obtained employment or education more rapidly than did the SAU group. It took the IPS group 286 (SE, 72.6) days and the IPSE group 346 (SE, 85.8) days vs the SAU group's 548 (SE, 61.7) days before 46.5% of each group's participants were employed or actively attending educational programs. Cox regression found a significant difference between IPS vs SAU (hazard ratio, 1.57 [95% CI, 1.14-2.18]; *P* = .006) and between IPSE vs SAU (hazard ratio, 1.54 [95% CI, 1.10-2.16]; *P* = .01) (Table 4). Kaplan-Meier curves are shown in eFigure in Supplement 2.

Table 1. Baseline Characteristics of 720 Participants in the Trial Randomized to Individual Placement and Support vs Individual Placement and Support Enhanced With Cognitive Remediation and Work-Focused Social Skills Training and Service as Usual

Characteristic	Participants, No. (%)		
	Individual Placement and Support (n = 243)	Individual Placement and Support With Enhancements[a] (n = 238)	Service as Usual (n = 239)
Sex			
Female	94 (38.7)	87 (36.6)	95 (39.8)
Male	149 (61.3)	151 (63.5)	144 (60.3)
Age, mean (SD), y	33.3 (10.3)	33.0 (9.5)	32.8 (9.9)
Previous work history[b]			
No	125 (51.4)	117 (49.2)	123 (51.5)
Yes	118 (48.6)	121 (50.8)	116 (48.5)
Education			
Master or equivalent	13 (5.4)	14 (5.9)	21 (8.8)
Bachelor or equivalent	28 (11.5)	22 (9.2)	28 (11.7)
Short-term tertiary education	43 (17.7)	53 (22.3)	44 (18.4)
Upper secondary education	61 (25.1)	57 (24.0)	57 (23.9)
Primary secondary education or lower (9 years of school or less)	98 (40.3)	92 (38.7)	89 (37.2)
Married or cohabiting			
No	197 (81.1)	194 (81.5)	187 (78.2)
Yes	46 (18.9)	44 (18.5)	52 (21.8)
Site			
Copenhagen, Frederiksberg	174 (71.6)	165 (69.3)	169 (70.7)
Odense, Silkeborg	69 (28.4)	73 (30.7)	70 (29.3)
Diagnoses			
Schizophrenia spectrum disorders[c]	184 (75.7)	181 (76.1)	186 (77.8)
Bipolar disorder[d]	32 (13.2)	30 (12.6)	25 (10.5)
Recurrent depression[e]	27 (11.1)	27 (11.3)	28 (11.7)
Match group[f]			
2	191 (78.6)	186 (78.2)	190 (79.5)
3	52 (21.4)	52 (21.9)	49 (20.5)
Psychiatric scale scores, mean (SD)			
Personal and Social Performance Scale score	47.3 (10.8)	47.2 (10.8)	47.0 (10.0)
Psychotic symptoms per SAPS	1.2 (1.3)	1.2 (1.3)	1.2 (1.3)
Negative symptoms per SANS	1.9 (0.8)	1.9 (0.8)	2.0 (0.8)
Disorganized symptoms per SAPS or SANS	0.3 (0.5)	0.3 (0.5)	0.3 (0.5)
Brief Assessment of Cognition in Schizophrenia Global	−2.6 (1.61)	−2.8 (1.9)	−2.7 (1.8)
Hamilton score	6.0 (4.2)	6.4 (4.2)	6.8 (4.1)
Self-efficacy	14.1 (6.3)	14.3 (6.1)	13.1 (6.4)
Rosenberg Self-esteem Scale score	15.6 (6.1)	15.6 (5.7)	16.0 (5.9)
SF-12 Total score	83.4 (7.9)	82.0 (7.9)	81.5 (7.8)

Abbreviations: SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms; SF-12, 12-Item Short-Form Health Survey.

[a] Individual placement and support enhanced with cognitive remediation and work-focused social skills training.

[b] Previous work history was defined as 2 or more months of paid work in the last 5 years.

[c] Defined by *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) codes F20 through F29.

[d] Defined by *ICD-10* codes F31.0 through F31.9.

[e] Defined by *ICD-10* codes F33.0 through F33.9.

[f] Danish legislation operates with 3 different match groups; match group 2 was assessed as being ready to participate in a vocational rehabilitation program but not able to be self-sufficient within 3 months and match group 3 was assessed as having severe, long-term problems and being unable to work or participate in prevocational training.

Consistent with most published trials, the association of IPS with outcomes on nonvocational measures appeared to be negligible (Tables 2 and 3), which also indicates that there were no adverse effects of the intervention. Nevertheless, we found significantly higher satisfaction with the vocational rehabilitation in the 2 experimental groups compared with SAU (IPS vs SAU: SRD, 0.310 [95% CI, 0.167-0.445]; *P* < .001 and IPSE vs SAU: SRD, 0.341 [95% CI, 0.187-0.478]; *P* < .001).

Discussion

Individuals with severe mental illness who participated in IPS or IPSE obtained higher employment and study rates or had more hours in employment and education than did participants in a conventional Danish vocational rehabilitation program (SAU). The participants in the IPS and IPSE groups also obtained employment or education faster and were more sat-

Table 2. Comparison of Effect on Primary and Secondary Outcomes After 18 Months' Follow-up for 720 Patients With Severe Mental Illness Randomized to the 3 Study Groups[a]

Primary and Secondary Outcomes	Mean (SD)			Success-Rate Difference (95% CI)		
	Individual Placement and Support	Individual Placement and Support With Enhancements[b]	Service as Usual	Individual Placement and Support vs Service as Usual	Individual Placement and Support With Enhancements vs Service as Usual	Individual Placement and Support vs Individual Placement and Support With Enhancements
Time spent in employment and education, h	411.0 (656.9)	488.1 (735.6)	340.8 (573.8)	0.127 (−0.017 to 0.276)	0.151 (0.01-0.295)	−0.034 (−0.178 to 0.109)
Number needed to treat, No.	NA	NA	NA	7.9	6.6	−29.4
P value, unadjusted/ adjusted with multiple imputations[c]	NA	NA	NA	.03/.004	.01/.016	.57/.35
Employment or education at some point, No. (%)	112 (59.9)	101 (59.1)	79 (46.5)	0.134 (0.009-0.257)	0.126 (0.003-0.256)	0.008 (−0.119 to 0.131)
Brief Assessment of Cognition in Schizophrenia score	−2.2 (1.8)	−2.2 (1.7)	−2.1 (1.9)	−0.044 (−0.195 to 0.102)	−0.028 (−0.175 to 0.124)	−0.015 (−0.165 to 0.127)
Personal and Social Performance Scale score	49.8 (14.1)	52.1 (14.5)	49.9 (12.9)	−0.005 (−0.152 to 0.141)	0.085 (−0.059 to 0.234)	−0.085 (−0.225 to 0.059)
General Self-efficacy Scale score	16.4 (6.1)	16.3 (6.3)	15.9 (6.7)	0.031 (−0.118 to 0.177)	0.009 (−0.144 to 0.161)	0.018 (−0.131 to 0.175)
Rosenberg Self-esteem Scale score	14.1 (5.8)	13.5 (5.8)	14.5 (6.0)	−0.022 (−0.163 to 0.131)	−0.082 (−0.233 to 0.063)	0.061 (−0.085 to 0.208)

Abbreviation: NA, not applicable.

[a] All analyses are unadjusted. Analyses adjusted for stratification variables are presented in eTable 1 in Supplement 2.

[b] Individual placement and support enhanced with cognitive remediation and work-focused social skills training.

[c] Multiple-imputations *P* values are derived from multiple imputation using 250 imputations and 5 iterations per imputation.

isfied with the support they received compared with those receiving SAU, but there was no significant difference between IPS and IPSE in any of the vocational outcomes.

With regard to the primary outcome (the number of hours in competitive employment or education), we hypothesized a clinically relevant mean difference of 150 hours between the groups when conducting the sample-size calculation. This was achieved in the comparison between IPSE and SAU, but this was not the case between IPS and SAU, between which a difference of 70 hours was detected. Nonetheless, when we also consider the 13% difference in study and employment rates, the difference in days to employment and education and the difference in satisfaction with the intervention between the IPS and IPSE groups and those receiving SAU, these effects are assessed as both substantial and clinically relevant. Since the SAU group also received a costly and substantial amount of vocational rehabilitation, we believe that these results are relevant to warrant its extra cost and time as well.

The control (SAU) group performed better than expected, including better than most previous IPS trials from countries with a comparable labor market and labor policy. In a Swedish randomized trial on IPS, 46% of participants in the IPS group obtained employment, compared with 11% in the SAU group.[29] In the present trial, 38% in the IPS group and 28% in the SAU group obtained competitive employment. When education was included, the figures were 60% vs 47%. Thus, the vocational outcomes in the SAU group in the present trial almost reached benchmarks established for high-fidelity IPS programs. However, it is worth noting that the control group was significantly less satisfied with the support they received than the 2 experimental groups. We believe that the strong focus on the individual's own preferences for work or education is an essential factor behind this difference, which has also been suggested by previous research.[1,30]

This trial differed from most previous IPS trials in focusing on both employment and education, making it difficult to make comparisons with previous international IPS trials. However, a recent meta-analysis demonstrated a pooled risk ratio of 2.40 (95% CI, 1.99-2.90) for competitive employment when IPS was compared with traditional vocational rehabilitation.[10] In the present trial, we also demonstrated a difference between IPS and SAU in the measure of employment or education at some point, but when we analyzed employment alone, the significant effect disappeared. The main reason for this could be a statistical power issue, because approximately half of the participants had education, rather than employment, as their goal at baseline.

Previous research has suggested that generous welfare systems, such as the Danish system, lead to lack of financial incentives, resulting in a low level of motivation for employment among the participants.[26] Nevertheless, even though many participants had a relatively small financial gain from working, we succeeded with the recruitment. In a qualitative study, the participants underlined that the key motivation for participating in the trial was to be able to contribute to and have a role in society.[1]

Consistent with earlier IPS research findings, we found no difference between the groups on nonvocational outcomes. However, a difference between groups in cognitive functioning was expected. A small improvement was found in all groups from baseline to the 18-month follow-up, but unexpectedly, no differences were found between the IPSE group and the IPS group or the SAU group at follow-up. Previous research[14] has found a higher overall composite cognitive score after inter-

Table 3. Comparison of Effect on Exploratory Outcomes After 18 Months' Follow-up for 720 Patients
With Severe Mental Illness Randomized to the 3 Study Groups

	Mean (SD)			Success-Rate Difference (95% CI)		
Exploratory Outcomes	Individual Placement and Support	Individual Placement and Support With Enhancements[a]	Service as Usual	Individual Placement and Support vs Service as Usual	Individual Placement and Support With Enhancements vs Service as Usual	Individual Placement and Support vs Individual Placement and Support With Enhancements
Labor-force engagement, mean (SD), h						
Employment	189.8 (450.9)	170.0 (400.6)	142.7 (360.6)	0.097 (−0.004 to 0.2)	0.06 (−0.035 to 0.159)	0.035 (−0.08 to 0.139)
Education	221.3 (481.3)	286.3 (538.4)	181.6 (476.2)	0.093 (−0.03 to 0.208)	0.132 (0.007-0.25)	−0.047 (−0.164 to 0.079)
Noncompetitive employment	134.0 (255.7)	97.8 (203.9)	178.2 (334.6)	−0.063 (−0.201 to 0.073)	−0.148 (−0.28 to −0.009)	0.083 (−0.053 to 0.219)
Total earnings, mean (SD), Danish kroner [$]	29 230 (71 075) [4388.13 (10 670.07)]	25 283 (61 809) [3795.59 (9279.02)]	24 694 (65 527) [3707.17 (9837.18)]	0.093 (−0.011 to 0.195)	0.057 (−0.048 to 0.16)	0.035 (−0.074 to 0.14)
Labor force engagement at any point, No. (%)						
Employment	92 (37.9)	80 (33.6)	66 (27.6)	0.102 (−0.003 to 0.205)	0.06 (−0.037 to 0.161)	0.042 (−0.066 to 0.147)
Education	58 (31.0)	58 (33.9)	40 (23.5)	0.075 (−0.036 to 0.186)	0.104 (−0.013 to 0.221)	−0.029 (−0.14 to 0.088)
Noncompetitive employment	72 (38.5)	54 (31.6)	72 (42.4)	−0.039 (−0.157 to 0.084)	−0.108 (−0.231 to 0.011)	0.069 (−0.046 to 0.187)
Survey and scale scores, mean (SD)						
Satisfaction with treatment	24.3 (5.0)	24.6 (5.1)	20.9 (6.2)	0.310 (0.167-0.445)	0.341 (0.187-0.478)	−0.038 (−0.187 to 0.108)
Brief Assessment of Cognition in Schizophrenia scores						
Memory domain	−1.3 (1.7)	−1.2 (1.4)	−1.3 (1.7)	−0.040 (−0.192 to 0.105)	0.025 (−0.126 to 0.175)	−0.073 (−0.223 to 0.079)
Speed domain	−2.2 (1.5)	−2.2 (1.6)	−2.1 (1.7)	−0.037 (−0.183 to 0.119)	−0.015 (−0.163 to 0.141)	−0.025 (−0.176 to 0.125)
Problem domain	−1.0 (2.3)	−1.1 (2.0)	−0.8 (1.9)	−0.044 (−0.199 to 0.104)	−0.117 (−0.277 to 0.046)	0.070 (−0.081 to 0.212)
Negative symptoms per SANS	1.6 (0.8)	1.5 (0.9)	1.5 (0.8)	0.049 (−0.101 to 0.189)	−0.016 (−0.163 to 0.137)	0.062 (−0.084 to 0.195)
Psychotic symptoms per SAPS	1.1 (1.3)	0.9 (1.2)	1.0 (1.3)	0.025 (−0.116 to 0.159)	−0.037 (−0.174 to 0.102)	0.058 (−0.07 to 0.193)
Disorganized symptoms per SANS or SAPS	0.3 (0.5)	0.3 (0.5)	0.3 (0.5)	−0.027 (−0.157 to 0.104)	−0.102 (−0.22 to 0.018)	0.074 (−0.049 to 0.197)
Medical care, mean (SD)						
Outpatient courses	1.6 (1.8)	1.5 (1.8)	1.7 (2.1)	0.006 (−0.12 to 0.13)	−0.014 (−0.135 to 0.104)	0.020 (−0.1 to 0.138)
Outpatient visits	29.2 (27.2)	28.9 (31.0)	33.8 (30.7)	−0.097 (−0.225 to 0.02)	−0.129 (−0.253 to −0.005)	0.035 (−0.094 to 0.159)
Hospitalizations	0.7 (1.6)	0.6 (1.6)	0.8 (1.8)	−0.040 (−0.135 to 0.056)	−0.040 (−0.131 to 0.06)	−0.002 (−0.099 to 0.093)

Abbreviations: SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms.

[a] Individual placement and support enhanced with cognitive remediation and work-focused social skills training.

ventions and follow-up assessment when IPS was enhanced with the *Thinking Skills for Work* program and compared with IPS alone. The reasons for not finding the same effect in the present trial could be because of participants' lack of motivation to participate in a highly complex and group-based cognitive program or because participants who started working prioritized this over the cognitive and social training. This was also reflected in the relative high dropout rate from the intervention compared with previous studies, which is likely to explain the missing effect. Since there was no significant difference between the IPS and IPSE groups in any of the

vocational outcomes and because cognitive remediation and work-focused social skills training increase both time to employment or education and costs of the intervention, it is not recommended to implement this supplement to IPS in the form used in this trial. If potential benefits of enhancing IPS with work-focused social skills training and cognitive remediation should be investigated in future research, specific factors associated with benefits to this enhancement should be identified, and it should be ensured that the intervention is appealing to the participants and they demonstrate need at baseline.

Table 4. Days to Employment, Education, or Noncompetitive Employment for 720 Patients With Severe Mental Illness Randomized to 3 Study Groups

Outcome	Time to Outcome, d, Mean (SD)			Hazard Ratio (95% CI)		
	Individual Placement and Support	Individual Placement and Support With Enhancements[a]	Service as Usual	Individual Placement and Support vs Service as Usual	Individual Placement and Support With Enhancements vs Service as Usual	Individual Placement and Support vs Individual Placement and Support With Enhancements
Employment or education	351.01 (197.18)	371.51 (194.92)	406.20 (188.17)	1.57 (1.14-2.18)	1.54 (1.10-2.16)	1.06 (0.78-1.43)
Employment	430.68 (180.32)	460.50 (165.32)	462.10 (169.00)	1.62 (1.11-2.35)	1.25 (0.84-1.85)	1.29 (0.91-1.83)
Education	456.76 (167.78)	455.13 (166.49)	486.48 (142.83)	1.39 (0.91-2.13)	1.74 (1.14-2.66)	0.85 (0.58-1.24)
Noncompetitive employment	415.52 (199.03)	478.47 (142.11)	415.26 (193.60)	0.83 (0.59-1.16)	0.60 (0.41-0.87)	1.39 (0.96-2.02)

[a] Individual placement and support enhanced with cognitive remediation and work-focused social skills training.

Strengths

We aimed at increasing the quality of the trial by avoiding a range of biases. First, sample-size and power calculations for the primary and all secondary outcomes were calculated prior the trial, to avoid substantial type I and II errors. Second, the trial had central randomization stratifications for important predictive factors; all outcome assessors and researchers, including statisticians, were blinded to allocation; and blinding was concealed until conclusions were drawn. Third, we used register data with 100% follow-up to measure employment outcomes and thereby avoided recall bias. Lastly, we performed fidelity ratings throughout the entire trial period to ensure adherence to the model.

Limitations

There are also limitations that should be mentioned. Owing to the nature of the intervention, it was not possible to blind the participants, employment specialists, psychiatric team members, and cognitive specialists to the allocations. Moreover, we cannot be sure that all eligible participants were recruited, because this depended on the mental health staff and participants' reactions to the advertisement, which could have led to selection bias.

Conclusions

We demonstrate that IPS and IPSE can be implemented effectively in a Scandinavian welfare model with relatively generous social benefits, a high minimum wage, and complex employment legislation. The participants were highly satisfied with the support, and based on these results and the consistent IPS literature, we suggest that these approaches are viable routes to increase employment and educational rates among people with severe mental illness in a Danish context. However, no additional significant effect was found by enhancing IPS with cognitive remediation and social skills training.

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Research Article

30-Month Follow-Up of Individual Placement and Support (IPS) and Cognitive Remediation for People with Severe Mental Illness: Results from a Randomized Clinical Trial

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Background. The individual placement and support (IPS) model for persons with severe mental illness has proven to be more effective than traditional vocational approaches in improving competitive work over 18 months. In this study, the longer-term effects of IPS over 30 months were investigated in a Danish setting. *Method.* In a randomized clinical trial, we compared the effects of IPS, IPS enhanced with cognitive remediation and work-related social skills training (IPSE), and service as usual (SAU). At three locations in Denmark, 720 patients with serious mental illnesses were randomly assigned to the three groups. Competitive employment, education, and hospital admissions were tracked for 30 months using Danish national registers. *Results.* The beneficial effects of IPS on competitive employment and education at the 18-month follow-up were sustained over the 30-month follow-up period. Participants receiving IPS or IPSE were more likely to obtain competitive employment or education than those who received service as usual (IPS 65%, IPSE 65%, SAU 53%, $p = 0.006$), and they worked on average more weeks competitively (IPS 25 weeks, IPSE 21 weeks, SAU 17 weeks; IPS vs. SAU $p = 0.004$ and IPSE vs. SAU $p = 0.007$). Moreover, participants in the two IPS groups had fewer outpatient visits during the 30-month follow-up. However, this was only statistically significant when comparing IPSE with SAU $p = 0.017$. *Conclusion.* In conclusion, IPS and IPS enhanced with cognitive remediation and work-related skills training demonstrated that the vocational effects of the interventions are retrained over 30 months in a Danish context.

1. Introduction

Compared to alternative vocational rehabilitation programs, the individual placement and support (IPS) model has consistently shown superiority in randomized controlled trials [1]. IPS is a standardized supported employment approach comprising eight critical principles recognized as essential for success when supporting people with severe mental illness to gain and retain employment [2]. In short, IPS participants receive ongoing and individualized support for

obtaining competitive employment or education where prolonged prevocational training is avoided. There is a strong focus on participants' job preferences, and the intervention is integrated into mental health services [2, 3].

In Denmark, the effects of IPS and IPS enhanced with cognitive remediation and work-related social skills training (IPSE) were tested in a randomized trial from 2012 to 2018. In this trial, the IPS and IPSE participants had higher employment and study rates and spent more time working than those enrolled in a standard vocational rehabilitation

program (SAU). Moreover, IPS was cost-effective, and the participants in the two IPS groups obtained employment or education faster and were more satisfied compared with those receiving SAU [4–6]. The Danish trial is comparable to most previous IPS trials with regard to the follow-up period. Most IPS trials have follow-up periods of 18 months or less, and the evidence of long-term effectiveness beyond 24 months is less established [7]. Nonetheless, there is some evidence of the long-term effect of IPS internationally. IPS trials from Hong Kong [8], Switzerland [9], and the US [10] with 3- and 5-year follow-up periods showed favorable effects of IPS compared with traditional vocational rehabilitation. Moreover, two small-uncontrolled studies from the US with 8 to 12-year follow-ups showed that 71% worked for more than half of the follow-up years [11] and that 75% of the participants worked beyond the initial study period, with 33% working at least five years during the ten years [12]. However, these studies are limited by relatively small sample sizes, lack of control conditions, and may have problems with recall bias because the outcomes were dependent on whether the participants can recall many years of work history.

Thus, there is strong evidence that IPS effectively improves the competitive work outcomes of people with severe mental illness, but its longer-term impact is less clear. The overall aim of the present study was to investigate if the effects of IPS and IPS enhanced with cognitive remediation and work-related social skills training (IPSE) found at 18-month follow-up are maintained over 30 months using data from Danish national registers.

2. Method

The effects of IPS, IPSE, and SAU were investigated in a randomized, three-arm parallel, multisite, superiority trial with blinded outcome assessment. Trial protocol [4] was conducted before the RCT and registered at ClinicalTrials.gov, NCT01722344. Moreover, the trial was approved by the Ethics Committee in the Capital Region of Denmark (registration #H-3-2012FSP34) and the Danish Data Protection Agency (registration #01768 RHP-2012-011).

The addition of a second site (Silkeborg) and the division of the Copenhagen team into two independent teams were the only modifications made to the original trial design, which enabled the recruitment of a sufficient number of participants in accordance with the sample size estimation.

2.1. Participants and Recruitment. The participants were either recruited by the psychiatric case managers or by themselves. Before randomization, a qualified and trained researcher assessed participants in a three-hour interview. The diagnostic interview tool schedules for clinical assessment in neuropsychiatry (SCAN) was used to evaluate if participants met the diagnostic criteria. Participants were eligible for the trial if they had a diagnosis of schizophrenia, schizotypal, or delusional disorders (F20–F29, ICD10), a diagnosis of bipolar disorder (F31, ICD10), or a diagnosis of recurrent depression (F33, ICD10). They should reside in one of three Danish cities: Copenhagen/Frederiksberg,

Odense, or Silkeborg, and be assigned to early intervention teams (OPUS teams) or community mental health services. All participants should be unemployed and not in education at baseline, but they should express a clear desire for competitive employment or education.

Moreover, they should be able to speak and understand Danish sufficiently well to participate without an interpreter and be between 18 and 64 years old. The only exclusion criteria were if the participant refused to give informed consent or received a retirement pension. According to the zero exclusion criteria in IPS, no patients were excluded due to poor work history, low function, severe symptoms, or substance abuse.

2.2. Randomization and Blinding. Eligible participants were randomly assigned to IPS, IPSE, or SAU after the baseline assessment. The randomization was computer-generated with a random allocation sequence and varying block sizes and stratified by site, sex, work history, and work readiness. The assessors and the research team were blinded to participants' allocation, and the randomization code was not revealed before all analyses at the 18-month follow-up were performed, and the conclusion was drawn. Hence, for this 30-month follow-up, the research team could not be blinded. It was accepted that participants, employment specialists, and the mental health team were unblinded to the allocation and, consequently, the risk of bias that may arise with this decision.

3. Interventions

Regardless of group allocation, all participants received the same level of psychiatric care from early intervention or community mental health teams [13]. The psychiatric treatment consisted of at least individual case management based on cognitive therapeutic methods and medical review.

3.1. Individual Placement and Support (IPS). Participants allocated to the IPS group received a service that complied with the eight key principles of IPS. The IPS manual [3], including worksheets, was translated into Danish before the trial. The employment specialists, who had a caseload of maximum of 25 participants, were recruited from the national Danish job centers, and they were part of a team consisting of at least one IPS team leader and three employment specialists. The IPS teams were integrated into the outpatient mental health teams, and the employment specialists had individual meetings with case managers and participated in medical conferences. Most of the working week was devoted to contacting potential employers and supporting participants in applying for and obtaining competitive employment or education based on the participants' preferences. Once the participants were employed or had started education, follow-along support was provided. The intervention was time-unlimited and continued as long as the participant wanted and needed support. The participants were enrolled for 12 months on average. Competitive employment was defined as part-time or full-time work open to all persons and remunerated by at least the

minimum wage for hours worked. Education was related to an employment goal and was not designed specifically for people with disabilities.

3.2. IPS Enhanced with Cognitive Remediation and Work-Related Social Skills Training (IPSE). The cognitive remediation consisted of cognitive computer training using the software CIRCuiTS [14] and group-based training in cognitive coping strategies following the thinking skills for work program and extended with work-related social skills training (WSST) [15, 16]. The computer training consisted of computer exercises that target strategy use and cognitive functions such as attention, memory, and executive functioning. Before the computer exercises, participants defined goals and identified strategies to improve their cognitive performance, which was regularly reviewed and modified [14]. The tasks gradually increased in difficulty depending on individual performance. In addition to the computer training, the program included teaching coping and compensatory strategies and providing support to generalize to everyday activities, such as using a calendar to improve planning abilities and developing routines to compensate for persisting difficulties and optimize work functioning.

Moreover, six sessions of work-related social skills training were offered. The aim was to develop, train, maintain, and generalize communication skills essential in achieving or retaining jobs or education and to train basic emotional and cognitive skills. Attention was paid to problem-solving skills and conflict management, as well as training in decoding norms for social interaction and how to be better at making informed and well-considered decisions. The intervention was performed in groups with a maximum of eight participants, and the sessions included an introduction of concepts, role-plays, homework exercises, and a review of real-world successes and failures. The group sessions were led by trained psychologists, and employment specialists participated as cotherapists. The sessions were offered twice a week in 90-minute sessions. In total, 24 sessions with computer training and the teaching of coping strategies and an additional six sessions with social skills training were offered.

3.3. Control Group (SAU). Control group participants continued to receive psychiatric outpatient treatment and counseling at the job centers. Based on the register data, the participants were referred to various vocational support options provided by the job centers and private companies from baseline to the 18-month follow-up. This consisted of meetings at the job center (mean = four meetings), mentor support (mean = 27 h), skills training courses, unpaid internships, and transitional employment (384 hours).

4. Outcome Measures

All included outcomes in the present study are considered exploratory outcomes because the primary and secondary outcomes of the trial were reported with 18-month follow-up data. The first outcome is the difference in weeks between groups in competitive employment or education measured from baseline until a 30-month follow-up using the Danish

Register for Evaluation of Marginalization (DREAM) database [17, 18]. The register covers the entire population and contains employment data, including salaries and education. The same outcome was divided into weeks of competitive employment or weeks of education. The second outcome was employment or education at one point during the follow-up period. The third outcome was the difference between groups in time to employment or education. The fourth outcome was differences between groups in psychiatric outpatient visits and hospitalization extracted from the Danish national patient registry [19]. In addition, three unpublished nonvocational survey outcomes from the 18-month follow-up are reported. This includes differences between groups in health-related quality of life measured with the 12-item short form health survey (SF-12) [20], social functioning measured with the global assessment of functioning (GAF-F) [21], and empowerment assessed by the empowerment scale (ES) [22].

5. Statistical Analysis

All analysis was based on the intention to treat principles, and because all the data included were register-based, we had a complete follow-up on all outcomes. We report baseline characteristics with mean and standard deviations (SD) for numeric variables and for categorical variables count (n) with percentages.

All estimates except the survival analysis are reported with a success rate difference (SRD) [23] with bootstrapped inferential statistics, which was the same method used when the 18-month results were reported. For dichotomous outcomes, the SRD is simply the difference between the proportion of vocational success in two groups. For numerical outcomes, the SRD is derived from Wilcoxon's U statistic: $SRD = 2U/(N_0 \bullet N_1) - 1$, where U is the Wilcoxon's U statistic and N_0 and N_1 are the sample sizes for the two groups. For numerical outcomes, this amounts to the difference in the probability of a random patient in the intervention group having a better outcome than a random patient in the comparison group. The probability of a random patient in the comparison group scoring higher than a random patient in the intervention group. Scores above 0, therefore, implicate a higher numerical value for the IPS group compared with the SAU group. Scores below 0 indicate a higher numerical value in the SAU group. Days to employment or education were analyzed using the Cox proportional hazard regression and reported using hazard ratios and Kaplan-Meier survival curves. All outcomes on outpatient visits and hospitalization are reported with mean and median with standard deviation (SD) and interquartile range (IqR), and p values are derived from the Wilcoxon statistical test. Because we compare all three groups, the p values for the outcomes should be interpreted according to an adjustment of the alpha level to a third (.05/3 = .0167), and 98.3% CI are reported for all effect estimates.

6. Results

Of the 756 participants assessed for eligibility, 36 were excluded: 10 did not meet the inclusion criteria, 24 declined
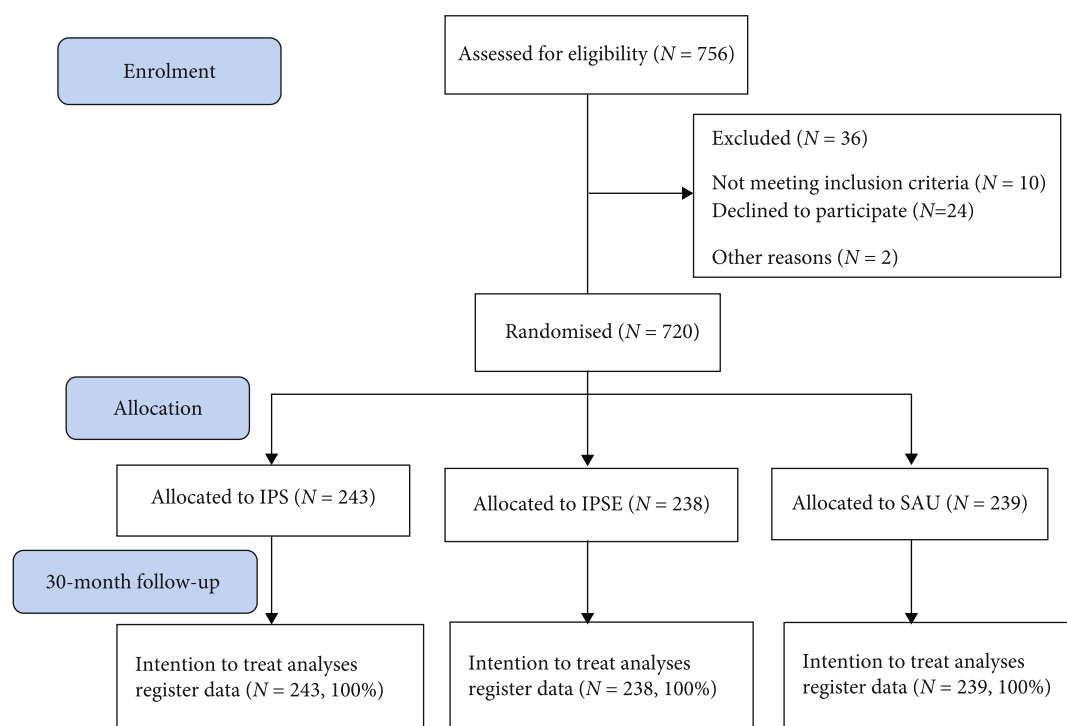
FIGURE 1: Study flow-chart.

to participate after they received more information about the trial, and two moved away before the baseline interview. A total of 720 participants were randomly assigned to the three groups: (1) IPS (N = 243), (2) IPSE (N = 238), and (3) SAU (N = 239). Because all measures in this study were register-based, there was a 100% follow-up (Figure 1).

At baseline, the participants' average age was 33 (SD 9.9) years, and 48% of them were women. The majority (77%) had a schizophrenia spectrum illness, whereas the remaining participants (12% and 11%, respectively) had a bipolar affective disorder or recurrent depression. The participants had a generally low level of education, with 39% having only completed elementary or lower secondary school. Moreover, the participants' global level of cognitive functioning was -2.70 standard deviations lower compared with the reference healthy population, measured on the Brief Assessment of Cognition in Schizophrenia (BACS) scale (Table 1). The mean IPS fidelity score of each site ranged from 75 to 101, measured on the IPS-25 scale, which indicates fair or good levels of IPS fidelity and adherence to the eight key principles of the IPS model.

In the 30-month follow-up period, IPS participants were more likely to work competitively or be enrolled in education at one point than those in the SAU group (65% vs. 52.7%; SRD, 0.123 [98% CI 0.012-0.231]; p = 0.006). Similar significant results were found when comparing IPSE with SAU (65.1% vs. 52.7%; SRD, 0.124 [98.3% CI 0.015-0.233]; p = 0.006). Additionally, there was a statistically significant difference between IPS and SAU when analyzing only competitive employment (46.5% vs. 35.1%; SRD, 0.114 [98.3% CI 0.006-0.226] p = 0.011), but no difference was found

between IPSE and SAU (41.6% vs. 35.1%; SRD, 0.065 [98% CI -0.036–0.174]; p = 0.148). Over the 30-month follow-up period, there was also a significant difference of 9.2 weeks in competitive employment or education between IPS and SAU giving an SRD of 0.146 (98% CI 0.02-0.268), p = 0,004. The difference between IPSE and SAU was 8.2 weeks, which gave an SRD of 0.139 (98% CI 0.022-0.265), p = 0.007. When analyzing only competitive employment, there was a difference between IPS and SAU of 7.6 weeks, giving an SRD of 0.126 (98.3% CI 0.012-0.243) p = 0.007, but no differences were found between IPSE and SAU in this outcome (SRD, 0.069 [98.3% CI -0.046–0.177]; p = 0.134). For a full overview, see Table 2.

Figures 2 and 3 illustrate the difference between the groups in employment or education at any given week in the 30-month follow-up period. We found that the participants in the two IPS groups from week 12 after baseline to the 30-month follow-up were holding more competitive jobs and education on average when compared to SAU. In the last week of the 30 months, 38% of the IPS group were in education or competitively employed. This was the case for 35% of the IPSE group and 27% of the SAU group. When analyzing competitive employment separately, there was an increase in the employment rates in all three groups during the 30 months, but in the last weeks of the period, the IPSE and SAU groups were less employed, with 21% and 22%, respectively, compared with 28% in the IPS group.

When analyzing time to employment and education using Cox regression, a significant difference between IPS vs. SAU was found (hazard ratio, 1.52 [98.3% CI, 1.09-2.10]; p = 0.002). When only competitive employment was

TABLE 1: Baseline characteristics of 720 participants in the trial randomized to IPS, IPSE, or SAU.

	IPS ($N = 243$)	IPSE ($N = 238$)	SAU ($N = 239$)
Sex, N (%)			
Female	94 (38.7)	87 (36.6)	95 (39.8)
Male	149 (61.3)	151 (63.5)	144 (60.3)
Age, mean (SD)	33.3 (10.3)	33.0 (9.5)	32.8 (9.9)
Previous work history N (%)*			
No	125 (51.4)	117 (49.2)	123 (51.5)
Yes	118 (48.6)	121 (50.8)	116 (48.5)
Education, N (%)			
Master or equivalent	13 (5.4)	14 (5.9)	21 (8.8)
Bachelor or equivalent	28 (11.5)	22 (9.2)	28 (11.7)
Short-term tertiary education	43 (17.7)	53 (22.3)	44 (18.4)
Upper secondary education	61 (25.1)	57 (24.0)	57 (23.9)
Primary/lower secondary education	98 (40.3)	92 (38.7)	89 (37.2)
Married or cohabiting, N (%)			
No	197 (81.1)	194 (81.5)	187 (78.2)
Yes	46 (18.9)	44 (18.5)	52 (21.8)
Site, N (%)			
Copenhagen, Frederiksberg	174 (71.6)	165 (69.3)	169 (70.7)
Odense, Silkeborg	69 (28.4)	73 (30.7)	70 (29.3)
Diagnoses, N (%)			
Schizophrenia spectrum disorders (ICD10 codes: F20-F29), N (%)	184 (75.7)	181 (76.1)	186 (77.8)
Bipolar disorder (ICD10 codes: F31.0-F31.9), N (%)	32 (13.2)	30 (12.6)	25 (10.5)
Recurrent depression (ICD10 codes: F33.0-F33.9), N (%)	27 (11.1)	27 (11.3)	28 (11.7)
PSP score, mean (SD)	47.3 (10.8)	47.2 (10.8)	47.0 (10.0)
Psychotic symptoms (SAPS), mean (SD)	1.2 (1.3)	1.2 (1.3)	1.2 (1.3)
Negative symptoms (SANS), mean (SD)	1.9 (0.8)	1.9 (0.8)	2.0 (0.8)
Disorganized symptoms (SAPS/SANS), mean (SD)	0.3 (0.5)	0.3 (0.5)	0.3 (0.5)
BACS global, mean (SD)	-2.6 (1.61)	-2.8 (1.9)	-2.7 (1.8)
Hamilton score, mean (SD)	6.0 (4.2)	6.4 (4.2)	6.8 (4.1)
Self-efficacy, mean (SD)	14.1 (6.3)	14.3 (6.1)	13.1 (6.4)
Rosenberg's self-esteem (SD)	15.6 (6.1)	15.6 (5.7)	16.0 (5.9)
SF-12 total (SD)	83.4 (7.9)	82.0 (7.9)	81.5 (7.8)

*Previous work history: ≥2 months paid job last five years.

analyzed, there was a statistically significant difference between IPS and SAU (Table 3). The online supplementary provides the Kaplan-Meier curves. As shown in Table 4, we found a difference between the groups in the use of psychiatric care, where the participants in the two IPS groups had fewer psychiatric outpatient contacts. IPS participants had, on average, 49, IPSE 48, and SAU 55 contacts. However, when we tested for this difference, the results were only statistically significant when comparing IPSE with SAU. Overall, the two IPS groups had fewer days hospitalized when compared with SAU, but this difference was not statistically significant (Table 4). Figure 4 shows the average outpatient contacts per month over the 30-month follow-up period. No differences were found between the three groups in health-related quality of life (SF-12), social functioning (GAF-F), or empowerment (ES) at the 18-month follow-up (online Supplementary (available here)).

7. Discussion

This study's key finding was that participants in the IPS or IPSE interventions for people with serious mental illnesses had more weeks in competitive employment or education than those who participated in traditional vocational rehabilitation. IPS participants worked more weeks in competitive employment compared with SAU, but this was not the case for IPSE participants. Moreover, the IPS groups had fewer psychiatric outpatient visits when compared with SAU.

The findings suggest that the beneficial vocational effects of IPS are sustained over the 30-month follow-up but also that the supplement to IPS with cognitive remediation and work-related social skills training does not add any additional effects. There was no difference between the IPSE and SAU when not including education in the outcome

Table 2: Comparison of effect on exploratory vocational outcomes after 30 months of follow-up for 720 patients with severe mental illness randomized to IPS, IPSE, and SAU.

| Outcomes	IPS Mean (SD)	IPSE Mean (SD)	SAU Mean (SD)	IPS vs. SAU Success rate difference (98.3% CI)	p value (Boot. p value)	IPSE vs. SAU Success rate difference (98.3% CI)	p value (Boot. p value)	IPS vs. IPSE Success rate difference (98.3% CI)	p value (Boot. p value)
Weeks in employment and education	37.8 (41.3)	36.8 (40.1)	28.6 (39.4)	0.1460.02-0.268	0.004 (0.005)	0.139 (0.022-0.256)	0.007 (0.008)	0.009 (-0.116-0.130)	0.863 (0.864)
Weeks in employment	24.9 (37.1)	20.6 (33.5)	17.3 (32.9)	0.126 (0.012-0.243)	0.007 (0.006)	0.069 (-0.046-0.177)	0.134 (0.135)	0.059 (-0.061-0.170)	0.217 (0.214)
Weeks in education	14.0 (27.5)	17.2 (30.8)	12.0 (27.1)	0.042 (-0.067-0.142)	0.332 (0.329)	0.08 (-0.025-0.181)	0.07 (0.071)	-0.039 (-0.146-0.060)	0.385 (0.386)
Labor force engagement at any point	%	%	%	Success rate difference (98.3% CI)	p value (imp. based)	Success rate difference (98.3% CI)	p value (imp. based)	Success rate difference (98.3% CI)	p value (imp. based)
Employment or education at any point	65.0%	65.1%	52.7%	0.123 (0.012-0.231)	0.006 (0.008)	0.124 (0.015-0.233)	0.006 (0.007)	-0.001 (-0.101-0.104)	0.981 (0.988)
Employment at any point	46.5%	41.6%	35.1%	0.114 (0.006-0.226)	0.011 (0.016)	0.065 (-0.036-0.174)	0.148 (0.148)	0.049 (-0.058-0.157)	0.279 (0.279)
Education at any point	32.5%	35.3%	28.9%	0.036 (-0.068-0.132)	0.387 (0.391)	0.064 (-0.036-0.169)	0.133 (0.129)	-0.028 (-0.132-0.073)	0.520 (0.513)

Employment or education
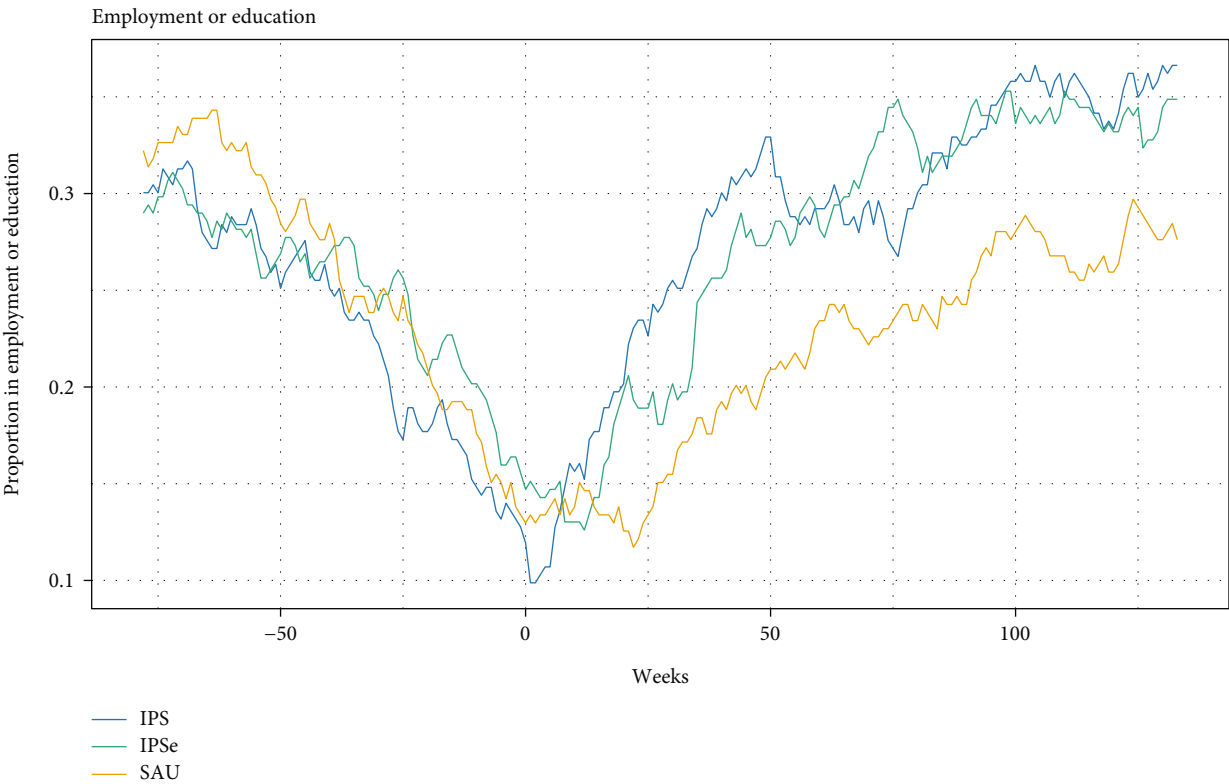
FIGURE 2: Employment and education rates at any given week from 75 weeks before baseline to 141 weeks after baseline.
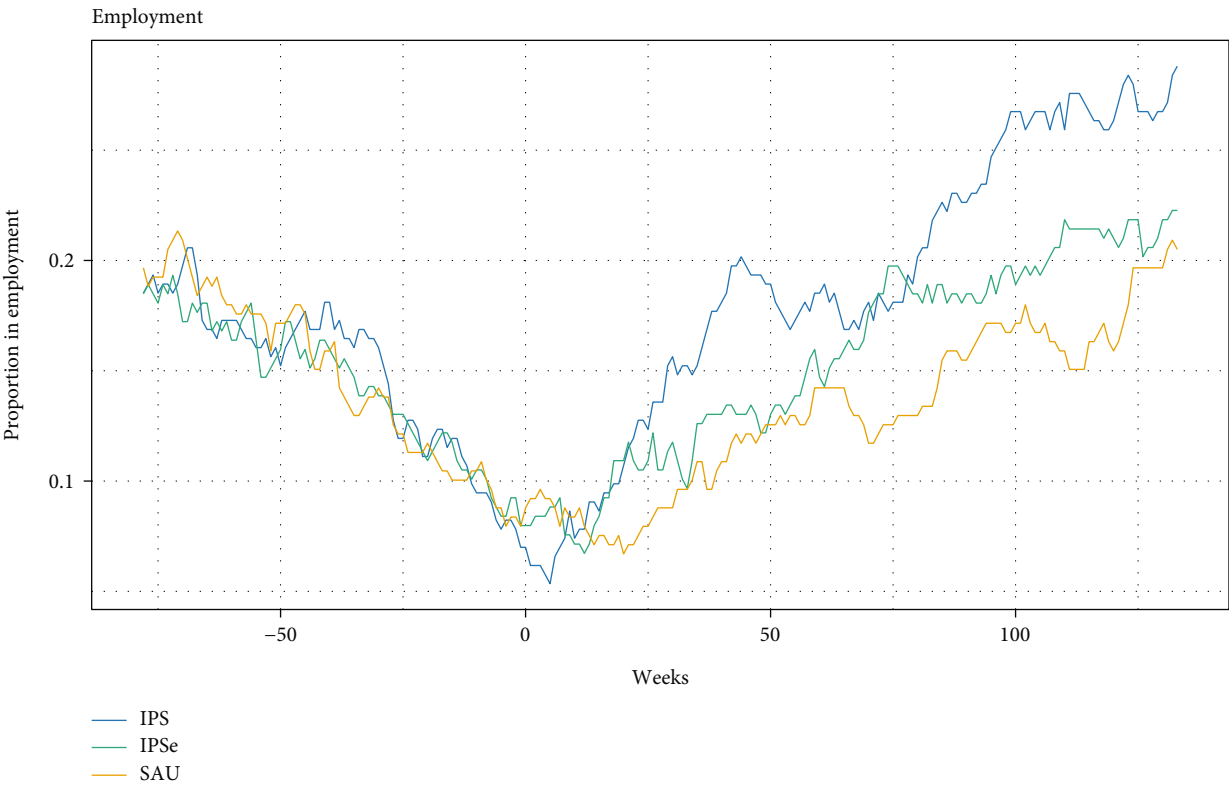
Employment

FIGURE 3: Employment rates at any given week from 75 weeks before baseline to 141 weeks after baseline.

TABLE 3: Days to employment and education for 720 patients with severe mental illness randomized to IPS, IPSE, and SAU.

	IPS vs. SAU		IPSE vs. SAU		IPS vs. IPSE	
	HR (98.3% CI)	p value	HR (98.3% CI)	p value	HR (98.3% CI)	p value
Employment or education	1.515 (1.09-2.10)	0.002	1.364 (0.98-1.90)	0.026	1.114 (0.82-1.51)	0.398
Employment	1.564 (1.06-2.30)	0.005	1.254 (0.84-1.87)	0.176	1.251 (0.87-1.80)	0.142
Education	1.202 (0.78-1.87)	0.314	1.242 (0.80-1.92)	0.236	0.972 (0.64-1.48)	0.870

TABLE 4: Comparison of the use of psychiatry in the 30 months of follow-up for 720 patients with severe mental illness randomized to IPS, IPSE, and SAU.

Outcomes	IPS		IPSE		SAU		IPS vs. SAU	IPSE vs. SAU	IPSE vs. IPS
	Mean (SD)	Median (IqR)	Mean (SD)	Median (IqR)	Mean (SD)	Median (IqR)	p values	p values	p values
Outpatient visits	48.8 (40.1)	43.0 (16.5-68.5)	47.8 (48.3)	33.5 (15.0-62.5)	55.4 (49.5)	41.0 (22.0-74.0)	0.240	0.017	0.268
Outpatient course	2.8 (3.3)	2.0 (1.0-3.0)	2.5 (2.7)	2.0 (1.0-3.0)	2.9 (3.3)	2.0 (1.0-4.0)	0.809	0.258	0.388
Emergency visits	0.15 (0.91)	0.00 (0.00-0.00)	0.21 (0.83)	0.00 (0.00-0.00)	0.10 (0.36)	0.00 (0.00-0.00)	0.297	0.363	0.057
Hospitalisations	1.3 (2.9)	0.0 (0.0-1.0)	1.0 (2.3)	0.0 (0.0-1.0)	1.3 (2.8)	0.0 (0.0-1.0)	0.242	0.269	0.886
Days hospitalized	21.9 (62.2)	0.0 (0.0-10.0)	18.9 (50.4)	0.0 (0.0-5.0)	30.9 (85.6)	0.0 (0.0-12.5)	0.313	0.336	0.895
	N (%)		N (%)		N (%)		p values	p values	p values
Outpatient visits	242 (99.6)		233 (97.9)		234 (97.9)		0.097	0.996	0.096
Emergency visits	13 (5.3)		24 (10.1)		19 (7.9)		0.252	0.417	0.052
Hospitalisations	76 (31.3)		80 (33.6)		89 (37.2)		0.168	0.409	0.585

measure. This finding was similar to the results from the 18-month follow-up, and as previously reported, the lack of additional effect may be explained by a relatively high drop-out rate. 24% of the IPSE participants did not attend any sessions with cognitive remediation or work-related social skills training due to a lack of motivation or fear of participating in a group setting. Moreover, only 52% of the participants attended more than 6 out of the 30 sessions.

The present trial was different from most prior IPS trials in that we also included participants who, at baseline, intended to pursue education rather than employment. As a result, it is challenging to draw comparisons with prior international IPS trials that only included participants who intended to pursue employment. However, Hoffmann et al. found in a 5-year follow-up of an IPS trial from Switzerland that 65% in the IPS group obtained employment, and they worked on average 107 weeks compared with 37 weeks in the SAU group [9]. In comparison, there were 46.5% in the Danish IPS group who obtained competitive employment, and when education was added to the measure, 65% obtained employment or education over a 2.5-year follow-up. When looking at weeks of employment in the present trial, the IPS group, on average, worked 25 weeks compared with 17 weeks in the SAU group. One explanation for why we are not finding the same rates of competitive employment as reported in previous IPS trials may be that about

half of the participants had education as their primary goal rather than employment, and the follow-up period was insufficient to confirm that the education later transferred into competitive employment.

Interestingly, receiving IPS service in the present study was also associated with lower levels of outpatient psychiatric treatment over the 30 months. Most randomized trials of IPS have not reported such differences in psychiatric care besides a European multisite study [24] and a trial from Switzerland [9]. The substantial integration of IPS within local mental health care may help to explain the difference in outpatient contacts reported in the present trial. The psychiatric case managers revealed that they spent less time on social work and used less time on meetings with the personnel at the job centers after IPS started. Because the patients' social benefits counseling and support for obtaining and maintaining a job or education were provided by the IPS employment specialists, it is possible that they had less need to engage with the psychiatric case managers.

7.1. Strengths and limitations. The use of representative longitudinal register data for the complete population with 100% follow-up, providing accurate information on vocational results, and use of psychiatric care was the study's main strength.
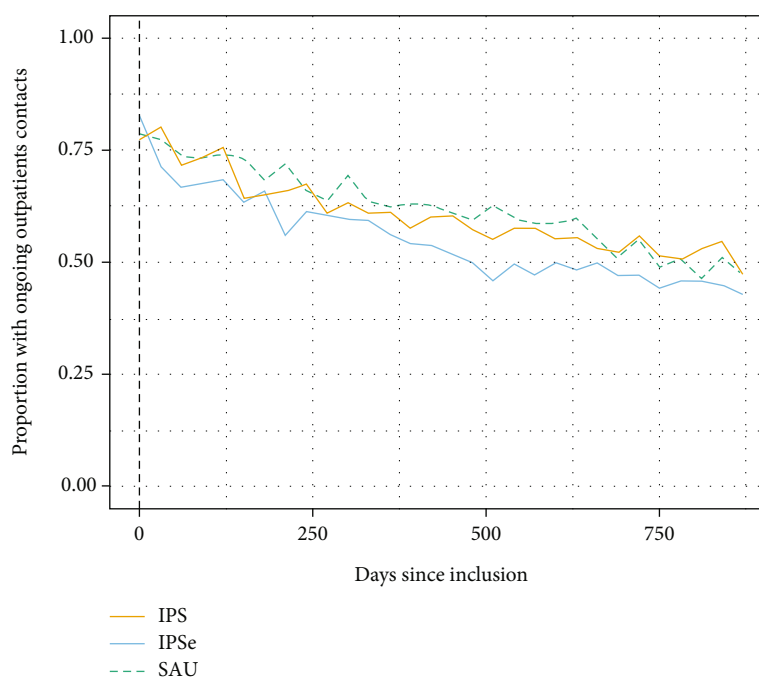
FIGURE 4: The average outpatient contacts per month over the 30-month follow-up.

Also, randomization stratifying for important predictive factors and a large sample of 720 participants increased the quality of the trial. Moreover, fidelity ratings were performed throughout the entire trial period to ensure adherence to the IPS method.

A limitation in the trial was that the participants, employment specialists, and mental health care staff were unblinded to the participants' allocation, and in this 30-month follow-up, the researchers were also unblinded. Moreover, as reported earlier, the length and number of cognitive and social skills training sessions may not have been sufficient to archive strong effect sizes for the IPSE group due to a high dropout rate.

8. Implication

Based on the findings of this trial, we propose that all municipalities in Denmark apply the IPS strategy to increase the employment rates of people with severe mental illness. Since the results from the 18-month follow-up, an increasing number of municipalities in Denmark have decided to implement the IPS model in the job centers. The results from this 30-month follow-up study add another good argument for making a national strategy in Denmark where all citizens with serious mental illnesses are offered evidence-based IPS service. However, there is still a need for further research with longer follow-up periods to determine if the obtained education is completed and further transferred into competitive employment. As we did not find any significant difference between IPS and IPS enhanced with cognitive remediation and social skills training, it is still unclear if this enhancement adds additional effects to the IPS intervention.

Data Availability

Due to the general data protection regulation, the register-based data used in this study cannot be publicly available. The data used is provided and hosted by Statistics Denmark, and only the authors of this study are allowed access.

Disclosure

The funders of the study had no role in study design, data collection, data analysis, or data interpretation.

Conflicts of Interest

The authors declare to have no conflicts of interest.

Supplementary Materials

Figure E1: the Kaplan-Meier curves of time to employment or education. Table 1: comparison of the nonvocational effect after 18 months of follow-up for 720 patients with severe mental illness randomized to the 3 study groups. (Supplementary Materials)

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Research Article

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Cost-utility and cost-effectiveness of individual placement support and cognitive remediation in people with severe mental illness: Results from a randomized clinical trial

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Abstract

Background: Administrators and policymakers are increasingly interested in individual placement and support (IPS) as a way of helping people with severe mental illness (SMI) obtain employment or education. It is thus important to investigate the cost-effectiveness to secure that resources are being used properly.
Methods: In a randomized clinical trial, 720 people diagnosed with SMI were allocated into three groups; (a) IPS, (b) IPS supplemented with cognitive remediation a social skills training (IPSE), and (c) Service as usual (SAU). Health care costs, municipal social care costs, and labor market service costs were extracted from nationwide registers and combined with data on use of IPS services. Cost-utility and cost-effectiveness analyses were conducted with two primary outcomes: quality-adjusted life years (QALY) and hours in employment. Incremental cost-effectiveness ratios (ICER) were computed for both QALY, using participant's responses to the EQ-5D questionnaire, and for hours in employment.
Results: Both IPS and IPSE were less costly, and more effective than SAU. Overall, there was a statistically significant cost difference of €9,543 when comparing IPS with SAU and €7,288 when comparing IPSE with SAU. ICER's did generally not render statistically significant results. However, there was a tendency toward the IPS and IPSE interventions being dominant, that is, cheaper with greater effect in health-related quality of life and hours in employment or education compared to usual care.
Conclusion: Individual placement support with and without a supplement of cognitive remediation tends to be cost saving and more effective compared to SAU.

Introduction

Although gainful employment repeatedly has been associated with better mental health and well-being, most people with severe mental illness (SMI) are unemployed [1–4]. This is an unfortunate situation, not only because employment has shown to contribute to recovery for the individual, but also because lost productivity generates significant costs to society besides the direct expenses of care and treatment [5].

International research has shown that the vocational rehabilitation intervention individual placement and support (IPS) is effective in helping people with SMI to obtain employment or education, and that training in cognitive and social functioning may increase the effects [6–8]. On this background, the effects of IPS, and IPS supplemented with cognitive remediation and work-related social skills training (IPSE) were investigated in a randomized, clinical trial (RCT) in Denmark during 2012–2018. The content of the interventions is thoroughly described in the trial protocol [9]. In short, the IPS intervention consisted of an individualized and rapid search for competitive employment based on the participants' preferences. The intervention was integrated within the mental health services and the participants received time-unlimited support. The IPSE intervention consisted of IPS supplemented with 24 sessions of cognitive computer training aiming at improving basic cognitive functions such as attention, memory, and executive functioning. In addition, participants were taught cognitive coping and compensatory strategies. Moreover, the participants obtained training on work-related social skills focusing on how to disclose mental illness at the workplace, communication skills, decoding norms for social interaction, and conflict management.

The results of the trial showed that participants in the IPS group were more likely than those in the service as usual (SAU) group, to work competitively, or be enrolled in education, during the 18-month follow-up (59.9 vs 46.5%; SRD 0.134 [95% 0.009–0.257]). The difference between IPSE and SAU was 59.0 vs 46.5% (SRD 0.126; 95% CI 0.003–0.256). The IPS and IPSE participants also

worked or studied more hours, and they were significantly more satisfied with the treatment received compared with the participants who received treatment as usual [10].

Despite IPS being established as an international evidence-based practice, only few cost-effectiveness studies of the intervention have been conducted [11–14]. The cost-effectiveness of IPS was investigated in six European cities, and IPS was found to produce better outcomes than alternative vocational services at lower cost overall to the health and social care systems [14]. However, the results varied along the labor market structure of the countries and did not attach monetary values to any observed improvements in health or quality of life. The Danish health care service is characterized by relatively easy access to psychiatric care and the labor market is characterized by good unemployment support, compared with many other countries [15]. These aspects may affect the cost-effectiveness of the IPS intervention compared with previous studies.

Aims of the study

The overall aim of this study was to investigate the cost-utility in terms of quality-adjusted life years (QALY) and cost-effectiveness of IPS, in terms of hours in employment. The intention was that the results may inform policymakers, administrators in the job centers and health care planners in deciding future investments and implementation of vocational rehabilitation.

Methods

Participants were recruited from community mental health services or early intervention teams (OPUS teams) in one of the three Danish cities; Copenhagen (including the municipality of Frederiksberg), Odense, or Silkeborg. Participants were eligible if they had a diagnosis of schizophrenia, schizotypal, or delusional disorders (F20–F29) or bipolar disorder (F31), or recurrent depression (F33) according to the International Classification of Diseases and Related Health Problems—10th Revision (ICD 10). Participants had to be between 18 and 64 years old and they should express a clear aim of employment or education. Moreover, all participants should be assigned to early-intervention teams or community mental health services at one of the three included sites. To confirm that participants met the diagnostic criteria they were assessed by a trained and certified researcher using the diagnostic interview instrument The Schedules for Clinical Assessment in Neuropsychiatry version 2.184.

In total 720 individuals were randomly assigned into three arms; (a) IPS, $n = 243$, (b) IPSE, $n = 238$, and (c) SAU, $n = 239$. Participants allocated to SAU continued to receive counseling at the job centers and received treatment in early intervention teams (OPUS-teams) or community mental health treatment teams, in line with the two experimental groups.

All participants were assessed at baseline and 18-month follow-up in the period from 2012 to 2018 using researcher-administered semi-structured interviews, and self-reported questionnaires on outcome measures as social functioning, symptoms, self-esteem, and self-efficacy [10]. Health-related quality of life (HRQoL) was assessed using participants' responses to the EuroQol five-dimensional questionnaire (EQ-5D) [16]. The self-administered instrument comprises five dimensions which are mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The participants self-rated their level of severity for each dimension using a three-level scale. (a) having no problems, (b) having some or moderate problems, and (c) being unable to do/having extreme problems. The validity and reliability of EQ-5D have been established across many conditions and populations and demonstrates good psychometric properties comparable to other generic measures, and it is one of the most frequently used measures in health-utility evaluations [17].

For each individual, the in- and out-patient costs in hospital care (both somatic and psychiatric care), primary health care costs, costs of pharmaceuticals, services provided by municipalities (labor market interventions and social service), and the IPS interventions costs were calculated accumulated within the follow-up period. The costs were assessed from a societal perspective meaning that costs outside the health care sector were included. Health care costs were obtained using the National Patient Register which is a key health register that covers somatic as well as psychiatric admissions, outpatient contacts, and emergency room contacts in all Danish hospitals [18]. Hospital costs were computed using nationally developed diagnosis-related groups tariffs [19]. Other health care costs, including costs in the primary sector and prescription medicine, were retrieved from the National Health Service Register [20] and the Pharmaceutical Database [21]. Costs of labor market interventions provided by the Danish job centers were obtained from register data in the Danish Agency for Labour Market and Recruitment. These interventions were primarily used by the SAU group and consisted of counseling at the job center, mentor support, or vocational rehabilitation interventions provided either by the job centers or private companies. Social services costs consisted of counseling, psychosocial initiatives, and personal assistance provided by the municipal social services. The costs of the IPS and IPSE interventions were calculated by using patient registration recorded by the IPS employment specialists or the psychologist who was responsible for the cognitive remediation groups. Only face-to-face contacts were included in the analyses, as was the case for the costs registered for the SAU group. Productivity gain was estimated by calculating hours in competitive employment multiplied by the average wage. If the productivity gain was positive, it counted as a negative cost and was therefore subtracted from total costs. All costs included in the analyses are described in more detail in Table 1. The average costs per participant were calculated in Euro (2016 price level), and the differences in costs between the intervention groups from baseline to follow-up were analyzed with *t*-tests. For the cost-effectiveness analyses a difference-in-difference approach was used by calculating the costs from baseline to 18 months follow-up deducted the costs from 18 months prior randomization.

QALY [23], and hours in employment were the effect measures in the present study. Traditionally, QALY are calculated by estimating the remaining life expectancy for a patient following a treatment or intervention multiplied with an HRQoL score (on a 0–1 scale). In the present study, however, we did not expect the IPS or IPSE interventions to have an impact on life expectancy beyond the intervention of 1.5 years. Thus, the difference between baseline and follow-up QALY measures only reflects HRQoL. EQ-5D scores were transformed into a single measure between 0 and 1 using the Danish preference weighting [16, 24]. The preference weights were calculated using a time trade-off survey among the general Danish population [24]. Discounting was deemed infeasible because of the uneven distribution of costs over the 18 months period (with most costs incurred at the beginning), and limited information about the distribution of health gain over the period.

Table 1. Cost components included in the cost-effectiveness analysis.

Costs	Definition	Source
Hospital costs	Inpatient, outpatient, and emergency room contacts in somatic and psychiatric hospitals, valued with DRG-tariffs.	The National Patient Register with DRG and outpatient tariffs [19,22].
Primary health care costs	Contacts to general practitioners, practicing specialists, and other health care professionals reimbursed (or partly reimbursed) by the Danish National Health Service, for example, dental care or psychological treatment. Costs are valued with national service tariffs.	The National Health Service Register [20].
Prescription pharmaceuticals	The full price (regardless of subsidies, etc.) of prescription drugs purchased in Danish pharmacies.	The Pharmaceutical Database [21].
Costs of labor market interventions	All interventions initiated by the municipal job centers: counseling, mentor support, or vocational rehabilitation interventions, primarily offered to the control group as part of SAU were valued at €20 per hour, mentor support in all groups was valued at €33 per hour and personal counseling in all groups was valued at €51 per hour. Education and on-the-job training were considered not to have additional costs.	Data obtained from the Danish Agency for Labour Market and Recruitment.
Costs of municipal social interventions	Social interventions, comprising counseling, psycho-social initiatives, and personal assistance and other means of non-monetary support.	Data obtained from Copenhagen municipality for those participants that lived in Copenhagen (70% of participants). Means per group were calculated and used throughout.
Intervention costs	Costs of the IPS intervention, valued at €1.33 per minute. The IPSE had an additional cost of €600 per patient.	Data obtained from the intervention, for participants from one site. The means for this site was used throughout.
Productivity	Productivity gain was estimated by calculating hours in competitive employment multiplied by the average wage. If the productivity gain was positive, it counted as a negative cost and was therefore subtracted from total costs.	Days in competitive employment are measured in the electronic income register from the Danish Agency for labor market and recruitment.

Abbreviations: DRG, Danish national diagnosis-related groups; IPS, individual placement and supports; SAU, service as usual.

Cost-utility and cost-effectiveness

Cost utility was measured as the additional cost of gaining one additional QALY, or, in the present context, the additional cost of gaining one utility measure.

Incremental cost-effectiveness ratios (ICER) were computed as the difference between intervention groups and control group in costs, divided by the difference between groups in QALY gain from baseline to follow-up [25]:

$$ICER = \frac{\Delta C_{CONTROL} - \Delta C_{INTERVENTION}}{\Delta E_{CONTROL} - \Delta E_{INTERVENTION}}$$

ΔC denotes the difference in costs from 18 months before baseline, to 18 months after baseline. ΔE denotes the difference in QALY from baseline to follow-up. If the ICER was negative, it was interpreted as the treatment being dominant to the comparator, dominance meaning that the dominant treatment is more effective and costs less. The ICER's were bootstrapped with 10,000 replications, and the 2.5 and 97.5 quantiles were interpreted as confidence limits. The bootstrapped analyses were visualized in a cost-effectiveness scatter plot [25, 26]. The plot presents the likelihood of getting a similar result if the experiment was repeated 10,000 times. The observations in the south-eastern quadrant of the plot represent cases where the intervention was both cheaper and better (dominant) in relation to QALY and thus worth implementing directly whereas the north-western quadrant represents cases where the intervention was more expensive and less effective (dominated) in which the intervention could simply be rejected. The north-eastern quadrant represents cases where the intervention was more expensive and better, and the south-western quadrant represents cases where the intervention was less expensive and less effective (Assess CE). In these cases, a more thorough health economic evaluation

should be conducted before deciding if the intervention should be implemented. The primary analysis consists of complete cases, meaning that only participants who responded to EQ-5D at baseline and follow-up were included. However, as a sensitivity analysis, those missing at follow-up were included using multiple imputations (mi) with truncated regression in STATA. The regression analysis included EQ-5D at baseline, age, gender, and diagnosis as explanatory variables. Moreover, we conducted subgroups analyses on age (above or below median age), sex, diagnosis (mood disorders [F31/F33], and schizophrenia spectrum disorders [F2]), and education (primary/lower secondary education or higher educational degree).

The 10,000 bootstrap samples were used to generate a cost-effectiveness acceptability curve (CEAC) [25, 27]. The CEACs relate the ICER estimate to different monetary values of a QALY that decision-makers could be willing to pay. The CEAC was computed in a probabilistic sensitivity analysis where the probability of the treatment being cost-effective was evaluated at a societal threshold of €0 for willingness-to-pay for a QALY, up to a societal willingness to pay of €35,000. The latter limit is based on considerations from the Danish Health Technology Assessment guideline, according to which there is no official Danish threshold for willingness-to-pay for a QALY in Denmark but the €35,000 is often considered the upper limit [28].

Finally, cost-effectiveness was investigated in relation to hours in work and/or education in the follow-up period. The difference between groups in hours in work or education is presented with success rate difference derived from Wilcoxon's U statistic, as in the original effectiveness study [10]. The ICER was calculated with the same methods as in the cost-utility analyses, and bootstrapped data were used to generate a cost-effectiveness plane where the two IPS groups combined are compared with SAU.

This study was conducted according to the Consolidated Health Economic Evaluation Reporting Standards statement. All analyses were conducted at the Statistics Denmark research server, where personal information about individuals is encrypted, thus ensuring compliance with data security regulations. SAS® v 9.4 was used for data management and STATA® MP v 15 was used for analysis. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Results

Table 2 shows the baseline characteristics of the participants. The average age was 33 (SD 9.9) years, and 62% of the included participants were men. Most participants (77%) were diagnosed with a schizophrenia spectrum disorder, and the rest were diagnosed with bipolar affective disorder (12%) or recurrent depression (11%). Overall, the participants were relatively low educated with 39% having a primary or lower secondary education as the highest educational degree.

There was no clinically relevant difference between the three groups in any baseline measures. 64% ($N = 462$) of the participants answered the EQ-5D questionnaire at baseline and follow-up and could be included in the complete case analyses. There was no significant difference in the dropout rates between the three groups and no significant difference in baseline EQ-5D score between those who answered EQ-5D at follow-up and those who did not.

Table 3 shows the total costs during the 18-month follow-up period. For participants in IPS, the costs of psychiatric hospital care

Table 2. Baseline characteristics of 720 participants in the trial.

	IPS ($N = 243$)	IPSE ($N = 238$)	SAU ($N = 239$)
Sex, *N* (%)			
Female	94 (38.7)	87 (36.6)	95 (39.8)
Male	149 (61.3)	151 (63.5)	144 (60.3)
Age, mean (SD)	33.3 (10.3)	33.0 (9.5)	32.8 (9.9)
Education, *N* (%)			
Master or equivalent	13 (5.4)	14 (5.9)	21 (8.8)
Bachelor or equivalent	28 (11.5)	22 (9.2)	28 (11.7)
Short-term tertiary education	43 (17.7)	53 (22.3)	44 (18.4)
Upper secondary education	61 (25.1)	57 (24.0)	57 (23.9)
Primary/lower secondary education	98 (40.3)	92 (38.7)	89 (37.2)
Diagnoses, *N* (%)			
Schizophrenia spectrum disorders (ICD10 Codes: F20-F29), *N* (%)	184 (75.7)	181 (76.1)	186 (77.8)
Bipolar disorder (ICD10 Codes: F31.0-F31.9), *N* (%)	32 (13.2)	30 (12.6)	25 (10.5)
Recurrent depression (Icd-10 F33.0-F33.9), *N* (%)	27 (11.1)	27 (11.3)	28 (11.7)
EQ-5D (SD)	0.71 (0.18)	0.69 (0.20)	0.70 (0.20)

Abbreviations: IPS, individual placement and support, IPSE, IPS + cognitive remediation and social skills training; SAU, service as usual.

Table 3. Costs and QALY's during the 18 months after randomization, EURO.

Costs	IPS costs	SAU costs	Probability of equality of means IPS vs SAU	IPSE costs	Probability of equality of means IPSE vs SAU
Somatic hospital	1,447	1,573	0.7293	1,260	0.3209
Prescription pharmaceuticals	1,438	1,377	0.7877	943	0.0237
Primary health care	286	286	0.9972	271	0.6120
Mental health hospital care	14,549	18,279	0.0961	13,743	0.0426
Labor market interventions	403	3,395	<0.0001	415	<0.0001
Municipal social interventions	1,759	3,636	N/A	3,121	N/A
intervention costs	914	0	N/A	2,543	N/A
Productivity gain (subtracted from total costs)	−7,214	−5,422	0.2052	−6,458	0.4351
Total costs	13,582	23,125	0.0010	15,837	0.0106
QALY gain	0.0329	0.0074	0.2960	0.0702	0.0146

Abbreviations: IPS, individual placement and support; IPSE, IPS + cognitive remediation and social skills training; QALY, quality adjusted life years, SAU, service as usual.

Table 4. Cost-effectiveness results, complete case analysis, costs in EURO's.

	Cost development, € (95% CI)	QALY gained (95% CI)	ICER, € per QALY gained (95% CI obtained by bootstrapping)
		IPSE vs SAU *N* = 295	
IPSE (*N* = 145)	**−8,951** (−14,107; −3,794)	**0.070** (0.033; 0.107)	
SAU (*N* = 150)	−4,687 (−9,813; 440)	0.007 (−0.027; 0.042)	Dominant (−393,892; 57,516)
Difference	−4,264 (−11,506; 2,978)	**0.063** (0.012; 0.113)	
		IPS vs SAU *n* = 317	
IPS (*N* = 167)	**−10,219** (−15,241; −5,198)	0.033 (−0.000; 0.066)	
SAU (*N* = 150)	−4,687 (−9,813; 440)	0.007 (−0.027; 0.042)	Dominant (−2.08e+7; 229,165)
Difference	−5,533 (−12,694; 1,628)	0.025 (−0.022; 0.073)	
		IPSE vs IPS *n* = 312	
IPSE (*N* = 145)	**−8,951** (−14,107; −3,794)	**0.070** (0.033; 0.107)	
IPS (*N* = 167)	**−10,219** (−15,241; −5,198)	0.033 (−0.000; 0.066)	33.953 (−518,284; 85,311)
Difference	1,269 (−5,923; 8,461)	0.037 (−0.012; 0.087)	

Note: Figures in bold are statistically significant at 5% level.

Abbreviations: CI, confidence interval; ICER, incremental cost effectiveness; IPS, individual placement and support; IPSE, IPS + cognitive remediation and social skills training; QALY, quality adjusted life years; SAU, service as usual.

were €3,730 lower per person, compared to the SAU-group, and the IPSE group had €4,545 lower costs in psychiatric hospital care compared to the participants who received SAU. The IPS and IPSE participants also had statistically lower costs of labor market interventions provided by the job centers, compared with SAU. In addition, IPS participants earned an average of €1,792 and IPSE €756 more than the control group, meaning that the production gains were higher in the two IPS groups. Overall, there was a statistically significant cost difference of €9,543 when comparing IPS with SAU and €7,288 when comparing IPSE with SAU (Table 3).

In Table 4, QALY gains and the resulting ICER are shown, based on the complete case analysis, that is, where patients with missing QALY information were excluded from the analysis. For all groups, there were improvements in QALY. The gains in the experimental groups were greater than in the control group. The largest gain was seen for IPSE, which was significantly greater than the gain seen in the control group (the difference was 0.063 [95% CI 0.012–0.113]). In both IPS groups, the ICER was dominant, that is, cheaper with greater effect, but these results were not statistically significant. When comparing the two intervention groups the IPSE group had a higher gain in HRQoL, but at an extra cost, when compared with IPS.

The IPS and IPSE groups remained dominant compared to SAU when using imputed data. However, the difference in HRQoL between the groups was reduced while the cost difference increased (online supplementary table 1). In subgroup analyses on age, sex, diagnosis, and education, IPS and IPSE also remained dominant to SAU. However, it seems that the cost difference was driven by those with a primary/lower secondary education, while the difference in HRQoL was driven by those with a higher educational degree. For a full overview, all subgroup analyses are available in the online supplementary material (Tables 1–8).

Figures 1–3 reflect the cost-effectiveness (ICER) results presented in Table 4. IPS and IPSE appear to be dominant compared with SAU. When comparing IPSE with SAU 88% of the scattered dots of ICERs were located in the SE quadrant, that is, better and cheaper, while this was the case for 80% of the dots when IPS was

compared with SAU. Overall, IPS and IPSE were superior to SAU in terms of higher HRQoL and lower costs, albeit not statistically significant.

A probabilistic sensitivity analysis was conducted where the probability of IPS or IPSE being cost-effective was evaluated at different societal thresholds for willingness to pay for a QALY. Based on the lack of variation in this analysis, the uncertainty of the estimates was considered minor important. With a societal threshold of €0 for willingness-to-pay for a QALY, corresponding to the case where society is unwilling to pay for a QALY gain, there is a probability of 88.3% of IPSE being cost-effective because IPSE in most cases is dominant, cheaper, and better. At a societal willingness to pay of €35,000, the probability is more than 95%. For IPS vs SAU, the probability of cost-effectiveness at €35,000 is 95.6%. When comparing IPSE and IPS, the probability of cost-effectiveness only exceeds 50% at a societal threshold of €35,000 (Figure 4).

Table 5 and Figure 5 reflect the cost-effectiveness in terms of the number of hours in work or education during the 18-month follow-up period. The two IPS groups worked and studied significantly more hours when compared to SAU. (448 vs 341 h, *p* = 0.002) and at an overall lower cost (€−6,214). The ICER shows that IPS and IPSE are dominant to SAU where 95.5% of the scattered dots of ICERs were located in the SE quadrant, that is, better and cheaper.

Discussion

IPS and IPS supplemented with cognitive remediation were less costly than SAU, with €9,543 lower costs (IPS vs SAU) and €7,288 lower costs (IPSE vs SAU). Additionally, there was a slight improvement in QALY after 18 months in the two IPS groups. However, this gain was only statistically significant among the IPSE participants when compared with SAU. The incremental cost-effectiveness ratio indicated that IPS and IPSE were dominant, for example, both better (measured in QALY) and cheaper compared to SAU, but these results were not statistically significant. However, the results appear robust when data were bootstrapped and visually presented in a scatter plot. In addition, the two IPS groups were cost-effective compared to hours in work or education. Participants in both IPS
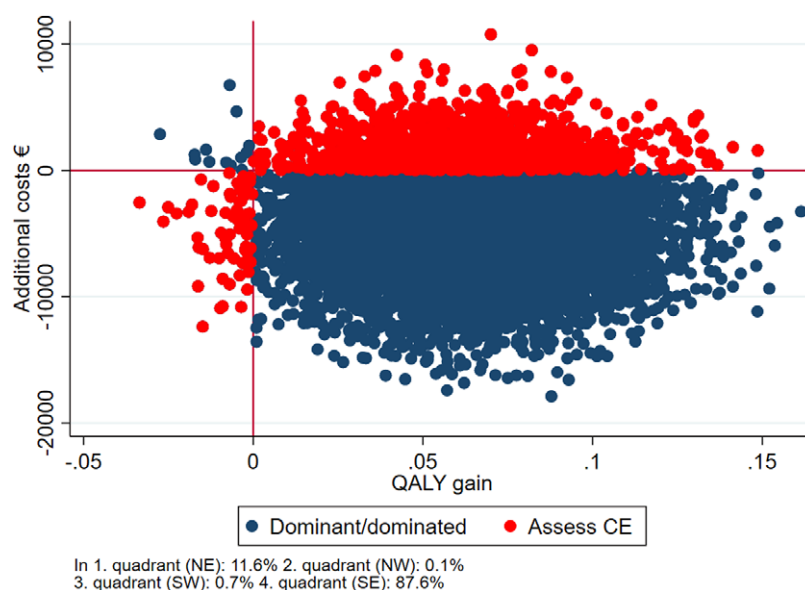
Figure 1. Cost-effectiveness plane IPSE vs SAU, complete case analysis.
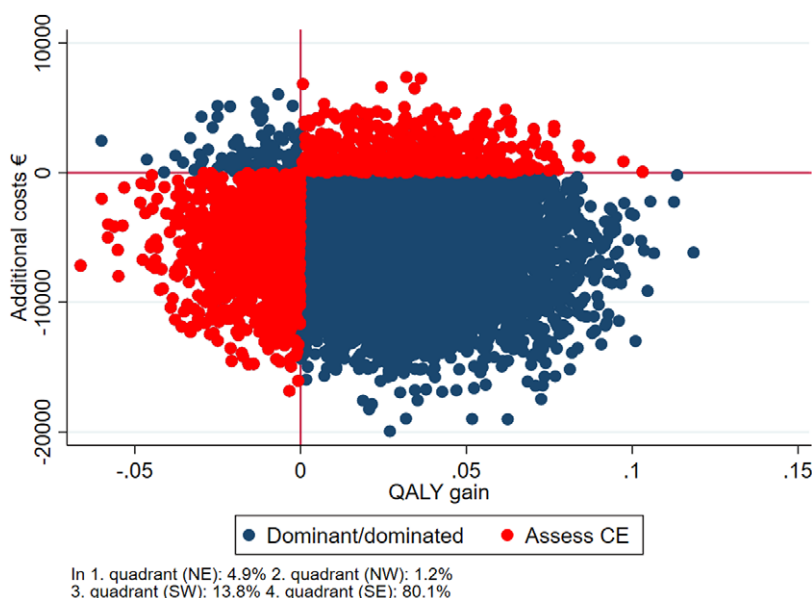
Figure 2. Cost-effectiveness plane, IPS vs SAU, complete case analysis.

groups worked or studied more hours and had lower costs compared with SAU.

The lower costs in the IPS and IPSE groups reflected in part the positive effects of IPS on labor market affiliation but most of the difference was related to consistently lower health care costs and municipal costs in both experimental groups. The reasons for the reduced health care costs in IPS and IPSE are likely multifaceted. One explanation, and a commonly used argument, is that participation in IPS improves participants' social functioning which results in less need for services and lower costs for mental health care [12]. Another explanation may be that work in itself mediates symptom reduction and enhance self-esteem, which reduces the need for psychiatric treatment [11, 29]. As reported earlier in the effectiveness study there were no statistically significant differences in social functioning or any psychiatric symptoms between groups which makes the second explanation more reasonable [10]. This is

also supported by results from a correlation study on the RCT, where those who obtained employment or education had higher self-esteem and functioning and less psychiatric symptoms compared to those who did not. Furthermore, the difference in lower costs between the IPS groups and SAU was mainly driven by outpatient contacts and not hospitalization [10]. This could be explained by the high integration of IPS within local mental health services in the present study. During the trial, the psychiatric case managers informed that after IPS was implemented they used less time on social work and collaboration with the staff at the job centers. Hence, the patients may have had less need for contacts with the psychiatric case managers because counseling in social benefits and support for finding and retaining employment or education were delegated to the IPS employment specialists.

Previous IPS cost-effectiveness studies have also demonstrated lower health care costs among IPS participants compared with
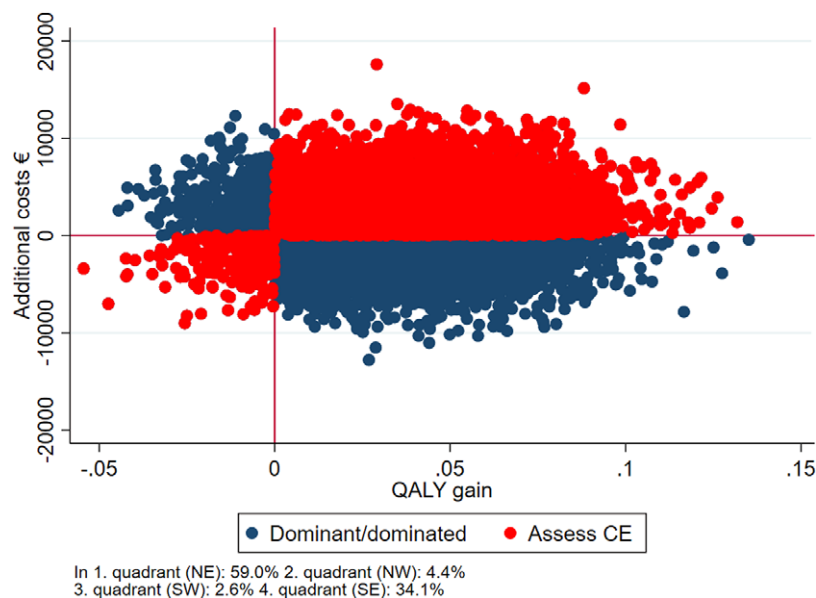
Figure 3. Cost-effectiveness plane, IPSE vs IPS, complete case analysis.
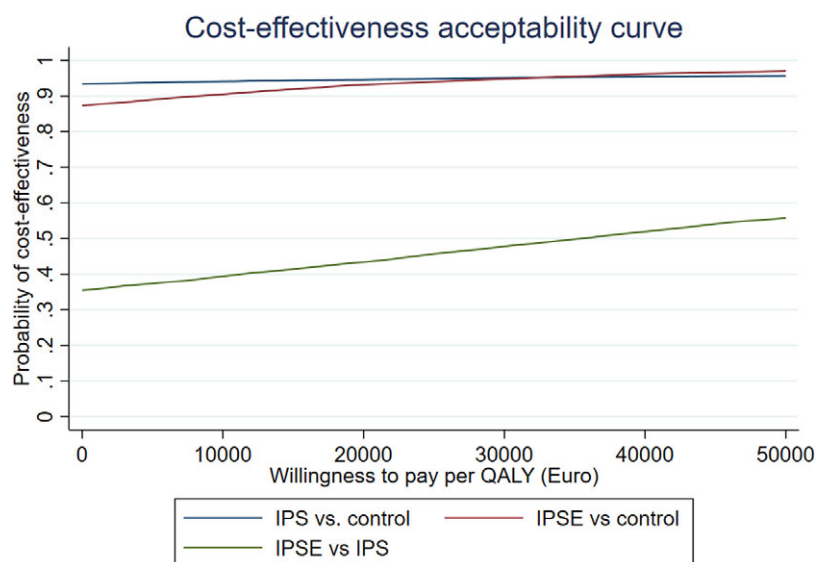
Figure 4. Cost-effectiveness acceptability curve.

Table 5. Cost-effectiveness results, complete case analysis, costs in EURO's, and hours obtained in employment and education.

	Cost development, € (95% CI)	Hours in employment or education (95% CI)	ICER, € per hour gained (95% CI)
	IPS + IPSE vs SAU (N = 521)		
IPS + IPSE (N = 356)	**−10,284** (−13,772; −6.812)	448 (375; 520)	
SAU (n = 165)	−4,079 (−8,702; 545)	341 (254; 427)	Dominant (−486–5)
Difference	**−6,214** (−12,176; −251)	**107** SRD = 0.138 (0.009; 0.263; p = 0.002)[a]	

Note: Figures in bold are statistically significant at 5% level.
Abbreviations: CI, confidence interval; IPS, individual placement and support; IPSE, IPS + cognitive remediation and social skills training; QALY, quality adjusted life years; SAU, service as usual; SDR, success rate difference.
[a]Success rate difference derived from Wilcoxon's U statistic.
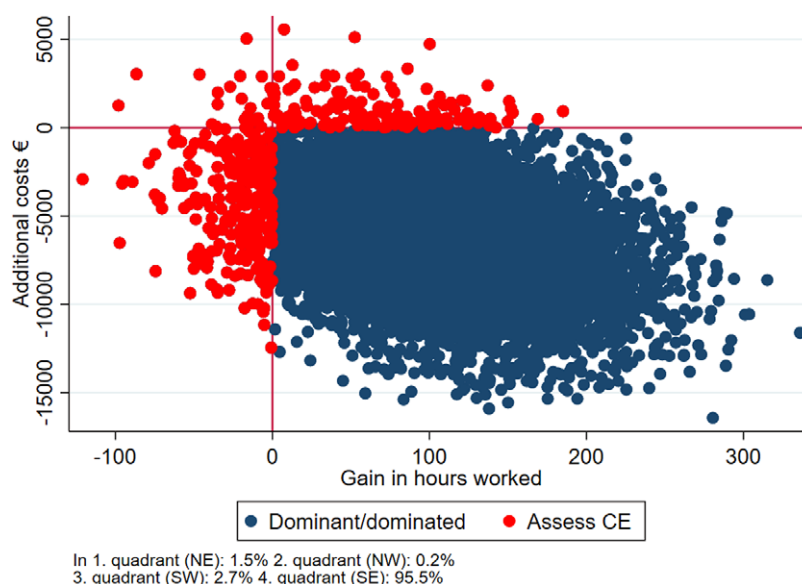
Figure 5. Cost-effectiveness plane of hours in work or education vs costs, between IPS + IPSE vs SAU.

control groups, but the differences have been less pronounced than the findings in the present study. In the Supported Work and Needs trial by Heslin et al. [30] it was found that IPS participants had fewer days in hospital and outpatient care compared with SAU participants giving a cost difference of £2,361 in favor of the IPS intervention, but this was not statistically significant. In a cost-effectiveness study of IPS in six European cities by Knapp et al., the IPS group had significantly lower cost in inpatient services than participants receiving SAU in the first 12 months of the study [14]. However, the difference diminished over the subsequent 12 months, and there were no differences between groups related to outpatient care. In a study by Dixon et al., no statistically significant differences in mental health costs were found between IPS and control group participants [12]. Compared to previous trials the cost difference in mental health care estimated in the present study of €3,730 and €4,545 between IPS and IPSE vs SAU is considerable.

To the best of our knowledge, no other IPS studies for people with SMI include QALY as an effect measure, and therefore no results can frame the findings of the present study. However, a Swedish RCT investigating the effects of supported employment adapted for people with affective disorders found an insignificant QALY gain of 0.046 (95% CI −0.05 to 0.13) in the supported employment group, and 0.056 (95% CI −0.06 to 0.17) in the group who received traditional vocational rehabilitation [31]. In the present study, a small gain in QALY was seen in all three groups, but mostly in the IPSE group with a statistically significant gain of 0.07, and a significant difference of 0.063 when compared with SAU. These points toward improved mental health among the IPSE participants, which most likely have been generated by the additional provision of cognitive remediation and social skills training in this group. However, there were no differences between IPSE and SAU in any other non-vocational outcomes, such as cognitive function, level of depression, or social functioning in the original effectiveness study. The increased HRQoL in the IPSE group may then be explained by the higher rates of employment and education, rather than the cognitive remediation, which again could contribute to explaining the lower mental health care costs. However, it could also be that the additional training in

this group was too time-consuming and therefore resulted in fewer outpatient psychiatric contacts.

A major strength of the present health economic analysis was the access to population-based register-based data on both health care costs and costs in the municipalities and national Danish employment agencies. There are also a few limitations. Most importantly, we had limited knowledge about treatment received outside of the public sector. Services such as psychotherapy and job coaching may have been purchased in the private sector. Another limitation is the scarce information about municipal services. We only had access to information from Copenhagen municipality and therefore had to apply group averages computed on Copenhagen data on the entire population, hence not capturing the variance of these costs.

In conclusion, this study presents a strong case for implementation of IPS and IPSE in a population of individuals with schizophrenia, bipolar, and other affective disorders in Denmark. Apart from supporting more participants to education and competitive employment, the costs of the two IPS groups were lower, and the HRQoL was higher when comparing with SAU. However, these positive effects are not guaranteed in future implementation. Variations in financing and contracting and change in the labor market policies, as well as the ability of providers to implement the service with high fidelity, are all likely to shape the cost and effectiveness of IPS.

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ORIGINAL PAPER

Predictors of work and education among people with severe mental illness who participated in the Danish individual placement and support study: findings from a randomized clinical trial

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Abstract

Purpose People with severe mental illness experience disproportionately high rates of unemployment. Nonetheless, a substantial amount of research has demonstrated vocational benefits of the Individual Placement and Support (IPS) model and IPS supplemented with cognitive remediation (IPSE). The present study sought to examine demographic and clinical predictors of employment or education among people with severe mental illness and to investigate if IPS or IPSE can compensate for risk factors for unemployment.

Methods Seven hundred twenty participants were randomly assigned to IPS, IPSE or Service as Usual. During the 18-month follow-up period participants in the two experimental groups obtained significantly more work or education. A series of univariate and multiple logistic regression analyses were conducted to assess the predictive power of demographic and clinical factors for the total population and for the three groups individually.

Results The strongest predictor for vocational recovery, besides treatment allocation, was previous work history (OR = 1.78; 95% CI = 1.28–2.47). Men had a lower probability for vocational recovery compared to women (OR = 0.71; 95% CI = 0.50–0.99) and higher age was also negatively associated with work or education (OR = 0.79; 95% CI = 0.67–0.93). Moreover, vocational recovery was predicted by higher readiness for change, measured on the readiness for change scale (OR = 1.42; 95% CI = 1.19–1.70). Participation in IPS or IPSE could not compensate for negative risk factors such as low cognitive function or negative symptoms.

Conclusions In a multiple logistic regression analysis age, previous work history and motivation for change were statistically significant predictors of obtaining work or education among people with severe mental illness who participated in the Danish IPS trial.

Keywords Individual Placement and Support (IPS) · Supported employment · Cognitive remediation · Vocational rehabilitation · Severe mental illness

Introduction

Despite the majority of unemployed people who experience severe mental illness (SMI) have a strong desire to work [1], it is well documented that the employment rate for this group is remarkably low compared with the background population [2, 3]. Nonetheless, a substantial amount of research has demonstrated vocational benefits of the Individual Placement and Support (IPS) model. IPS is a well-defined form of supported employment that consists of an individualized and rapid search for competitive employment or education, with emphasis on client preferences, and with integration in mental health treatment teams [1]. IPS is widely recognized as an evidence-based intervention based on results of 30 randomised clinical trials showing that IPS is more effective than traditional vocational rehabilitation in obtaining competitive employment (RR = 1.63, 95% CI = [1.46, 1.82]) [4]. In a recent Danish trial that included 720 participants

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randomized to IPS or IPS supplemented with cognitive remediation and social skills training or services as usual, it was found that 60% in the two IPS groups obtained competitive employment or education during the 18 months follow-up compared with 46% in the group receiving service as usual [5]. However, likewise the majority of other trials investigating the effects of IPS, 40% of the participants did not archive their vocational goals despite their motivation to work or study [6, 7].

Previous research has attempted to identify demographic and clinical factors that predict who is more likely to achieve vocational recovery, but the results have often been inconsistent or even contradictory [8–10]. However, relative consistent are the findings that prior work history, negative symptoms and cognitive functioning predict the success of vocational programmes [8, 10, 11]. Moreover, clinical characteristics such as substance abuse and severe psychotic symptoms have often been used to exclude people with severe mental illness from vocational services. Nonetheless, it has been indicated that IPS may compensate for the negative impact of these risk factors [12, 13]. Identifying participants who have difficulty achieving their vocational goals and addressing the potential barriers to employment or education may be a way to improve the efficiency of the IPS intervention.

The aim of this study was to identify individual and sociodemographic factors that predict vocational recovery among people with severe mental illness in the Danish IPS trial and to investigate the potential advantages of participating in individual placement and support to overcome specific risk factors for unemployment. We hypothesized that the predictive strength of demographic and client factors, including poor work history negative symptoms and cognitive functioning, would be weaker for IPS participants.

Methods

Trial design and participants

Data for the present study was a secondary analysis from the Danish IPS trial, which is described in detail in the study protocol and effect article [5, 14]. In short, it was a randomised three-group parallel, assessor-blinded trial.

Between 2012 and 2018 participants were recruited from community mental health centres or early intervention teams (OPUS teams) in three Danish cities: Copenhagen (including the municipality of Frederiksberg), Odense, or Silkeborg. Inclusion criteria were as follows: (1) diagnosis of schizophrenia spectrum disorder (F20–F29); bipolar disorder (F31); or recurrent depression (F33) according to the International Classification of Diseases version 10 (ICD-10); (2) aged 18–64 years; (3) able to speak and understand Danish

sufficiently well to participate without an interpreter; (4) a desire to work competitively or completing education. The participants were recruited by the case managers on the psychiatric out-patient teams or self-selected after encountering advertisements and information available at the psychiatric centres. 756 participants were assessed for eligibility, and 36 were excluded because they did not meet inclusion criteria or declined to participate after receiving further information about the intervention. After the baseline interview 720 participants were randomly assigned to receive IPS ($N=243$), IPS supplemented with cognitive remediation and social skills training (IPSE) ($N=238$), or service as usual (SAU) ($N=239$). Outcome assessors and all investigators involved in the trial were blinded, but participants and employment specialists were not. None of the participants was working or studying at baseline but had all expressed a clear interest in working competitively or starting education.

Over the 18-months follow-up period participants in the IPS group reached a significantly higher cumulative rate of competitive employment or education compared with participants who received service as usual. (59.9% vs. 46.5%; SRD 0.13 (95% CI 0.009–0.257). The difference between IPSE and SAU was (59.0% vs 46.5%; SRD 0.126 (95% CI 0.003–0.256). When the two IPS groups were combined and compared with SAU, the difference was (SRD 0.130 (95% CI 0.025–0.239). Participants in the two IPS groups also obtained employment or education faster, and they were significantly more satisfied with the treatment received [5].

Measures

Data were obtained through researcher-administered semi-structured interviews by blinded researchers who were trained and certified in all instruments used, and by self-reported questionnaires, and register-based data. The primary outcome measure in this predictor study was whether participants obtained vocational recovery, defined as obtaining competitive employment or starting education, during the 18-months follow-up period. Employment outcomes were extracted from the Danish Register for Evaluation of Marginalization (DREAM) database extended with data from the Danish national income register with a 100% response rate [15, 16]. The registers cover the entire population and contain data on employment including salaries, sickness and cash benefits and disability pension. Educational outcomes were reported by the participants at the 18-month follow-up interview and were measured only if the participant studied actively in education aiming for competitive employment.

Sociodemographic predictor variables included sex, age and marital status (married or cohabitation). Baseline education was also collected and dichotomized as 9 years of school or higher. The cut-off at 9 years was chosen because

this is the duration of the primary/lower secondary school in Denmark. A total of 38.8% had a primary or lower secondary education as the highest educational degree at baseline which also means that the cut-off resulted in a relatively equal distribution in the two groups. Previous work history was assessed as 2 months of work the last five years before baseline. The cut-off of 5 years was to ensure that the most marginalized citizens were captured in this measure. Those people that the job-centre employees often do not dare to hope for can obtain ordinary employment. Five years has also been the cut-off in previous IPS studies [17–19] Clinical predictor variables included diagnoses which were divided into schizophrenia spectrum disorder (F20–F29 ICD-10), bipolar disorder (F31–F31.9 ICD-10) and recurrent depression (F33–F33.9 ICD-10). The diagnoses were validated by a trained and certified researcher using the diagnostic interview Schedules for Clinical Assessment in Neuropsychiatry (SCAN) [20]. Psychotic and negative symptoms were measured with scale for the assessment of positive symptoms (SAPS) and scale for the assessment of negative symptoms (SANS) [21]. The outcome was divided into three domains; (a) Positive dimension symptoms including global rating of hallucinations and global rating of delusions; (b) Disorganized dimension including global rating of positive formal thought disorder, global rating of bizarre behaviour and inappropriate affect; (c) Negative dimension including global rating affective flattening or blunting, global rating of alogia, global rating of avolition and apathy and global rating of anhedonia and asociality [22]. Social functioning was measured with the Personal and Social Performance (PSP) scale, using a total score on the 100-point scale created out of the ratings on the four subdimensions; (1) socially useful activities; (2) personal and social relationships; (3) self-care and (4) disturbing and aggressive behaviour [23]. Symptoms of depression were measured by the Hamilton depression rating scale (HAM-D6) [24]. The six items were summed up to a score between 0 and 22 point. Cognitive function was measured with the Brief Assessment of Cognition in Schizophrenia (BACS) scale [25]. The BACS composite score was performed by transforming each baseline raw score, of the six subtests, to z-scores based on the mean and standard deviation from a healthy Danish control group [26]. A composite global BACS score was calculated as the mean of the standardized six z-scores and then rescaled based on the population reference values. Participants' self-esteem was assessed with the self-reported questionnaire the Rosenberg self-esteem scale. After the positively worded items were reversed the items were summed up to a score ranging from 10 to 40, with higher scores indicating higher self-esteem. Participants, self-efficacy was assessed with the general self-efficacy scale. All responses were added up to a sum score with a range from 10 to 40 points. The readiness to seek employment or education was measured by the Change

Questionnaire (CQ) consisting of 12 items covering six constructs: desire, ability, reasons, need, commitment and taking steps towards making the change, each with a score from 0 (definitely not) to 10 (definitely) [27]. The scores were summed to a total score from 0 to 120, and a higher score equals higher readiness to change. Substance abuse one month prior baseline was measured with Alcohol Use Disorders Identification Test (AUDIT) [28] and divided in the following measures; (1) at least 10 heavy drink days the last month; (2) cannabis at least three times the last month or (3) drugs other than cannabis the last month.

Statistical analyses

Baseline characteristics are reported using mean and standard deviations for numeric variables and count (*n*) with percentages for categorical variables. The original outcome analysis was based on the intention to treat principles and to compensate for missing data on the education outcome, we used multiple imputation. This process is described thoroughly in the main trial reporting [5]. Missing values on the outcome variable are here substituted with the rounded average of all imputed sets. First, correlation analyses were conducted to examine the bivariate relationships among independent, covariate, and outcome variables. Secondly, a series of univariate logistic regression analyses were conducted to assess the unadjusted association between baseline predictor variables and competitive employment or education at 18 months follow-up. To be able to compare the relative effects of predictors measured on different scales all continuous variables were standardized. Thus, the odds ratios express the relative increase in odds of employment or education as the predictor variable moves up one standard deviation. thirdly, all predictor variables associated with the outcome vocational recovery at a p value below 0.1 were retained for subsequent multivariate logistic regression analyses. Finally, the sample was divided into the original intervention groups and interactions of significant predictors with intervention groups were analysed, to demonstrate if IPS or IPS supplemented with cognitive remediation and work-related social skills training overcomes some of the client barriers.

Results

In Table 1 the baseline characteristics are described for the total population (*n* = 720) and separately for those reaching competitive employment or education (*n* = 390, 54%) and those who did not reach the endpoint within the 18-months follow-up period (*n* = 330, 46%). Of the total population, 77% were diagnosed with a schizophrenia spectrum disorder, 12% with bipolar disorder and 11% with recurrent

Table 1 Baseline characteristics divided in participants who obtained competitive employment or education and those who did not

	Employment or education during follow-up, $N = 390$		No employment or education during follow-up, $N = 330$		Total sample, $N = 720$	
	N	(%)	N	(%)	N	(%)
Study conditions						
IPS	140	(35.9)	103	(31.2)	243	(33.8)
IPSE	152	(39)	86	(26.1)	238	(33.1)
Service as usual	98	(25.1)	141	(42.7)	239	(33.2)
Sex						
Women	162	(41.5)	114	(34.5)	276	(38.33)
Men	228	(58.5)	216	(65.5)	444	(61.67)
Married or cohabiting						
Yes	81	(20.8)	61	(18.5)	142	(19.72)
Primary/secondary education or lower[a]	148	(37.9)	131	(39.7)	279	(38.75)
Previous work history[b]	221	(56.7)	134	(40.6)	355	(49.31)
Diagnoses						
Schizophrenia spectrum disorders (ICD-10: F20–F29)	296	(75.9)	255	(77.3)	551	(76.53)
Bipolar disorder (ICD10: F31.0–F31.9)	52	(13.3)	35	(10.6)	87	(12.08)
Recurrent depression (ICD-10: F33.0–F33.9)	42	(10.8)	40	(12.1)	82	(11.39)
Alcohol and substance use						
At least 10 heavy drink days per month	15	(3.8)	11	(3.3)	26	(3.6)
Cannabis at least three times 1 month prior	38	(9.7)	37	(11.2)	75	(10.4)
Drugs other than cannabis 1 month prior	11	(2.8)	11	(3.3)	22	(3.1)
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Age	32.17	(9.65)	34.06	(10.11)	33.04	(9.9)
Psychiatric scale scores						
Personal and Social Performance Scale score	47.9	(10.49)	46.26	(10.45)	47.15	(10.5)
Psychotic symptoms (SAPS)	1.18	(1.32)	1.21	(1.32)	1.19	(1.32)
Negative symptoms (SANS)	1.82	(0.76)	2.05	(0.8)	1.92	(0.78)
Disorganized symptoms (SAPS-SANS)	0.26	(0.47)	0.29	(0.46)	0.27	(0.46)
Cognitive functioning (BACS)	-2.53	(1.72)	-2.91	(1.7)	-2.70	(1.72)
Depressive symptoms- (Hamilton)	6.05	(4.08)	6.73	(4.24)	6.41	(4.16)
Self-efficacy (General self-efficacy Scale)	14.7	(6.11)	12.82	(6.36)	13.8	(6.3)
Self Esteem (Rosenberg Self Esteem Scale)	14.81	(6.06)	13.65	(5.63)	14.27	(5.89)
Readiness for change (Change questionnaire)	101.61	(14.79)	94.19	(19.28)	81.87	(14.47)

p values based on Chi-squared test for categorical variables and rank-sum tests for numerical variables

IPS Individual Placement and Support, *IPSE* IPS enhanced with cognitive remediation and work-related social skills training, *SANS* Scale for the Assessment of Negative Symptoms, *SAPS* Scale for the Assessment of Positive Symptoms, *BACS* Brief Assessment of Cognition in Schizophrenia

[a] 9 years of school or less

[b] At least 2 months paid job within last 5 years

depression [5]. Sixty-two percent were male, and the average age was 33 years at the time of inclusion. Fifty-one percent had a poor working history with less than 2 months of work within the last 5 years prior to baseline. Further, the participants' global level of cognitive functioning, was -2.70 standard deviations lower compared with the reference healthy population.

Participants in the two IPS groups combined had 2.2 times higher odds of having worked or studied during the 18-month follow-period compared to participants in the treatment as usual group (OR = 2.22 95% CI 1.62 − 3.05). All other bivariate associations between baseline predictors and vocational recovery during the follow-up period are presented in Table 2. Predictors associated with employment

Table 2 Predictors of vocational recovery at 18-month follow-up found by univariate and multiple logistic regression

	Simple			Multiple		
	OR	CI	*p* value	OR	CI	*p* value
Men	0.74	0.55–1.01	0.055	0.71	0.50–0.99	0.046
Age (10-year increments)	0.83	0.71–0.96	0.011	0.79	0.67–0.93	0.005
Married or cohabiting	1.16	0.80–1.67	0.443			
Primary/secondary education or lower[a]	0.93	0.69–1.26	0.631			
Previous work history[b]	1.91	1.42–2.58	0.000	1.78	1.28–2.47	0.001
Bipolar disorder (ICD10: F31.0–F31.9)	1.30	0.82–2.05	0.264			
Recurrent depression (ICD-10: F33.0–F33.9)	0.87	0.55–1.39	0.570			
Personal and Social Performance Scale score	1.17	1.01–1.36	0.039	0.91	0.75–1.10	0.315
Psychotic symptoms (SAPS) (1.32 points increments)	0.98	0.85–1.13	0.778			
Negative symptoms (SANS) (0.78 points increments)	0.74	0.64–0.86	0.000	0.87	0.71–1.07	0.188
Disorganized symptoms (SAPS-SANS) (0.46 points increments)	0.93	0.81–1.08	0.359			
Cognitive functioning (BACS) (1.72 points increments)	1.25	1.08–1.46	0.003	1.16	0.97–1.37	0.099
Depressive symptoms (Hamilton) (1.72 points increments)	0.85	0.73–0.98	0.030	0.93	0.77–1.13	0.476
Self-efficacy (general self-efficacy Scale) (6.3 points increments)	1.36	1.16–1.59	0.000	1.13	0.91–1.40	0.287
Rosenberg Self Esteem Scale	1.22	1.05–1.42	0.012	1.09	0.87–1.37	0.472
Readiness for change (change questionnaire) (14.47 points increments)	1.56	1.33–1.84	0.000	1.42	1.19–1.70	0.000
At least 10 heavy drink days per month	1.16	0.53–2.63	0.714			
Cannabis at least three times 1 month prior	0.85	0.53–1.38	0.521			
Drugs other than cannabis 1 month prior	0.84	0.36–1.99	0.691			

IPS Individual Placement and Support, *IPSE* IPS enhanced with cognitive remediation and work-related social skills training, *SANS* Scale for the Assessment of Negative Symptoms, *SAPS* Scale for the Assessment of Positive Symptoms, *BACS* Brief Assessment of Cognition in Schizophrenia

[a]9 years of school or les

[b]At least 2 months paid job within last 5 years

or education with a p value below 0.05 were younger age, previous work history, higher social functioning (PSP Scale) fewer negative symptoms (SANS), higher cognitive function (BACS), fewer symptoms of depression (HAM-D6), higher self-efficacy (general self-efficacy scale), higher self-esteem (Rosenberg Self Esteem Scale) and higher readiness to change (change questionnaire). The strongest predictor for vocational recovery, besides treatment allocation, was previous work history. Participants who had been in work within the last five years prior to baseline were 1.9 times more likely to obtain employment or education in the 18 months follow-up period (OR = 1.91; 95% CI 1.42–2.58). Other variables that were evaluated but were not significantly associated with vocational recovery included being married or cohabiting, educational level, diagnosis, psychotic symptoms and alcohol/substance use.

In the subsequent multivariate logistic regression analyses sex, age, previous work history and readiness for changes were retrained as significant predictors for work or education. Again, the strongest predictor was previous work history. Participants who had been working at least two months prior to baseline were 1.9 times more likely to obtain employment or education (OR 1.91; 95% CI 1.42 − 2.57).

Cognitive functioning, negative symptoms, depression, self-efficacy, and self-esteem were not retrained as a significant predictor in the multivariate analysis. There were only a few statistically significant correlations among the baseline predictors, but none were large enough to indicate severe multicollinearity. The strongest correlations were between negative symptoms and functioning, self-esteem and depressive symptoms/self-efficacy with correlation coefficients of 0.51–0.63. All other relevant correlations were below 0.3. The full correlation matrix is available in the online supplementary materials. The associations reported above (except for treatment allocation) are not causal relationships that suggest the endpoint status to be some function of the predictor. Instead, the predictors likely often reflect the same underlying features that either facilitate or inhibit transfer to employment or education.

To qualify these correlational associations, we also estimate to what extent the significant predictors might moderate the treatment effects. This is done by testing differences in regression coefficients of predictors across treatment conditions.

The associations of the significant predictors when stratified by treatment allocation are shown in Table 3. Previous

Table 3 Significant predictors of vocational recovery stratified by study condition (a) and tests of the corresponding interaction terms (b)

	SAU			IPS			IPSE		
	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
(a) Predictors stratified by study condition									
Sex (men)	0.80	0.47–1.36	0.413	0.94	0.56–1.59	0.822	0.46	0.25–0.81	0.009
Age	1.01	0.77–1.30	0.967	0.74	0.58–0.95	0.020	0.72	0.54–0.95	0.022
Previous work history[a]	2.58	1.52–4.41	0.000	1.72	1.03–2.90	0.038	1.64	0.96–2.80	0.070
Personal and Social Performance Scale score	1.23	0.94–1.64	0.137	1.34	1.04–1.75	0.024	0.96	0.74–1.26	0.784
Negative symptoms (SANS)	0.87	0.67–1.13	0.291	0.72	0.55–0.94	0.016	0.67	0.51–0.88	0.005
Cognitive functioning (BACS)	1.19	0.91–1.57	0.202	1.67	1.26–2.26	0.001	1.10	0.86–1.41	0.431
Readiness to change	1.61	1.19–2.22	0.003	1.57	1.22–2.05	0.001	1.59	1.16–2.20	0.004
Depressive symptoms-(Hamilton)	0.96	0.73–1.25	0.735	0.80	0.61–1.03	0.085	0.85	0.66–1.10	0.227
Self-efficacy (General self-efficacy Scale)	1.16	0.89–1.53	0.265	1.47	1.12–1.94	0.006	1.38	1.04–1.85	0.029
Rosenberg Self Esteem Scale	1.17	0.89–1.53	0.256	1.45	1.12–1.92	0.006	1.01	0.76–1.35	0.923
Readiness for change (Change questionnaire)	1.61	1.19–2.22	0.003	1.57	1.22–2.05	0.001	1.59	1.16–2.20	0.004
	IPS vs SAU			**IPSE vs SAU**			**IPSE vs IPS**		
	OR	CI	*p* value	OR	CI	*p* value	OR	CI	*p* value
(b) Formal tests of interactions between each predictor and study condition									
Sex (men)	1.17	0.56–2.46	0.674	0.57	0.26–1.25	0.164	0.49	0.22–1.06	0.073
Age	0.74	0.52–1.06	0.100	0.72	0.49–1.05	0.089	0.97	0.67–1.41	0.875
Previous work history[a]	0.67	0.32–1.40	0.287	0.63	0.30–1.35	0.236	0.95	0.45–1.99	0.889
Personal and Social Performance Scale score	1.09	0.75–1.59	0.660	0.78	0.53–1.14	0.206	0.72	0.49–1.03	0.077
Negative symptoms (SANS)	0.83	0.57–1.21	0.335	0.78	0.53–1.13	0.191	0.93	0.64–1.36	0.716
Cognitive functioning (BACS)	1.40	0.94–2.09	0.096	0.92	0.64–1.33	0.673	0.66	0.45–0.96	0.032
Readiness to change	0.98	0.65–1.46	0.907	0.99	0.63–1.54	0.958	1.01	0.67–1.53	0.953
Depressive symptoms-(Hamilton)	0.83	0.58–1.21	0.338	0.89	0.62–1.29	0.547	1.07	0.74–1.54	0.720
Self-Efficacy (General self-efficacy Scale)	1.26	0.86–1.85	0.235	1.19	0.80–1.76	0.396	0.94	0.63–1.40	0.764
Rosenberg Self Esteem Scale	1.24	0.85–1.83	0.260	0.87	0.59–1.28	0.478	0.70	0.47–1.03	0.072
Readiness for change (change questionnaire)	0.98	0.65–1.46	0.907	0.99	0.63–1.54	0.958	1.01	0.67–1.53	0.953

IPS Individual Placement and Support, *IPSE* IPS enhanced with cognitive remediation and work-related social skills training, *SANS* Scale for the Assessment of Negative Symptoms, *SAPS* Scale for the Assessment of Positive Symptoms, *BACS* Brief Assessment of Cognition in Schizophrenia

[a] At least 2 months paid job within last 5 years

Work history was a significant predictor in the SAU group who were 2.58 times more likely to have worked or studied in the 18-month follow-up period. The predictive power of work history was less in the IPS and IPSE groups where participants were 1.72 and 1.64 times more likely to obtain work or education respectively. However, when we test for the differences in association strengths between IPS and IPSE vs. SAU in any of the predictors the differences were statistically insignificant.

Discussion

In a sample of 720 unemployed people with severe mental illness, a recent history of working was the strongest predictor of vocational recovery. Other client factors that added predictive power in the univariate logistic regression analysis were lower age, higher social functioning, fewer negative symptoms, higher cognitive function, fewer symptoms of depression, higher self-efficacy, higher self-esteem and higher readiness to change. When added together in one predictive model, only female gender, lower age, previous work history and readiness for change remained significant predictors of obtaining competitive employment or education within the 18-months of follow-up. This also suggests that cognitive functioning, symptom severity, self-esteem and self-efficacy are less important individual determinants for obtaining competitive employment or education for the population in question.

The finding that previous work history was the strongest predictor for vocational recovery in both the univariate and multiple regression analysis are consistent with findings

from most previous studies [8, 13, 19, 29, 30]. There was also a tendency toward that IPS mitigate the negative effects of poor work history. However, this result was not statistically significant and could not confirm the findings in the Mental Health Treatment Study (MHTS) which was a multisite randomized controlled trial comparing the effectiveness IPS and service as usual among 2055 participants with severe mental illness [12]. In this study IPS participants were 2.2 times more likely to obtain employment if they had been working within the last two years prior baseline and SAU participants were 5.6 times more likely to obtain employment.

The association between higher cognitive functioning and vocational recovery in the univariate regression analysis also supports the findings from many previous studies [8, 10, 11]. In the present trial we sought to address this issue by supplementing IPS with cognitive computer training and training in cognitive coping strategies. However, this supplement did not affect the cognitive functioning or the number of participants who entered employment or education [5]. A small improvement was found in global cognitive functioning in all groups from baseline to the 18-month follow-up, but no difference was found between IPSE, IPS or SAU. This also explains that the predictive power of cognitive functioning was the same in IPSE and SAU. Moreover, cognitive functioning lost its predictive power in the multivariate logistic regression analyses which suggests that cognitive functioning is less important than for example self-assessed readiness to work. To date augmentations of IPS have mainly focussed on cognitive remediation and social skills training [31], but there are a host of other barriers such as lack of self-esteem and self-efficacy, negative symptoms, and lack of self-assessed readiness to change warranting targeted interventions. In this study self-assessed readiness to change seems as a stronger explanatory factor than psychiatric symptoms and cognitive functioning, and readiness to changes was also retrained as a significant predictor in the multivariate regression analysis. On this background future research, may profit from investigating the effects of individualized clinical interventions, provided by the out-patient psychiatry, such as motivational interviewing, tailored to this specific barrier to employment.

Notably, several client factors did not predict employment, including measures often identified as risk factors for social exclusion such as alcohol and substance use, psychotic symptoms and educational level. The findings, that substance abuse, was not associated with vocational recovery challenges the common practice in mental health care end vocational rehabilitation of labelling clients with certain clinical and background attributes as low chance of succeeding in work or education. This again stresses the importance of the zero-exclusion strategy in IPS as it can be extremely difficult for mental health professional

to assess the probability of success in an IPS programme. The fact that negative symptoms, depressive symptoms, self-efficacy, and self-esteem lose their predictive power in the multivariate analysis may in part be because these measures are closely related constructs. Self-esteem is an underlying measure in Ham-D6, and the general self-efficacy scale, and negative symptoms can be difficult to separate from depressive symptoms. These measures were also those how had the highest correlation coefficient, but the analysis did not indicate multicollinearity in terms of inflated or unstable coefficients.

Despite we included a variance of client and demographic factors that have been hypnotised to be important predictors for vocational recovery in the literature, there are other important factors which it was not possible to investigate in the present study. For example, a growing body of research has demonstrated that stigma is a major obstacle to find and keep work among people with SMI [2]. Employers and co-workers often have limited knowledge of SMI, resulting in mistrust and discrimination. In a cross-sectional survey in 27 countries, including 729 participants with schizophrenia, negative discrimination in finding a job was experienced by 29% of the participants [32]. Also, low expectations to people with SMI held by employers and mental health professionals is another prominent barrier to employment [33, 34]. Vocational rehabilitation is often not included in the treatment care plans of people with SMI, which may reflect low expectations among professionals [2]. The low expectations are caused by a dominance of treatment that emphasis symptoms and cure instead of a model of recovery, resulting in mental health professionals may underestimate the skills and resources of their patients and overestimate the risk to employers. It was not possible to include such factors as a baseline predictor in the present study, but it is important to remember that the barriers that many people with severe mental illness encounter in their attempt to obtain employment or education is not only related to their illness and past experience, but to a large extent also more structural challenges which are fundamentally beyond the person's ability to act.

Conclusion

In a randomised clinical trial investigating the effects of individual placement and support (IPS) and IPS supplemented with cognitive remediation; age, previous work history and motivation for change were statistically significant predictors of obtaining work or education. Moreover, in contrast to previous findings, participation in IPS or IPSE could not significantly compensate for negative risk factors such as low cognitive function or lack of previous work history.

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Trajectories of Vocational Recovery Among Persons with Severe Mental Illness Participating in a Randomized Three-Group Superiority Trial of Individual Placement and Support (IPS) in Denmark

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Abstract

Purpose To investigate longitudinal trajectories of vocational recovery (VR) among individuals with severe mental illness (SMI) who participated in the Danish Individual Placement and Support (IPS) trial, and whether the IPS intervention, socio-demographic and disease-specific characteristics predicted trajectory membership.

Methods In an observational study design, we used previously collected data from the Danish IPS trial (N = 720). VR was defined as 'weeks in competitive employment or education in the past 6 months and was measured after 0.5, 1, 1.5, 2 and 2.5 years, using data from the Danish Register for Evaluation of Marginalization (DREAM) database. Latent growth mixture modelling in Mplus statistical software (version 7) was applied to identify trajectories of VR. Multinomial logistic regression analyses were used to estimate predictors for trajectory membership.

Results Four trajectories were identified: 'Low VR' (61.3%), 'Low Increasing VR (8.2%), 'Increasing Decreasing VR' (7.2%) and 'High VR' (23.4%). Receiving the IPS intervention increased odds of membership in 'High VR' compared to 'Low VR' (OR = 2.18; 95% CI 1.37–3.48) and so did higher education (OR = 2.25; 95% CI 1.39–3.64), higher cognitive function (OR = 1.17; 95% CI 1.02–1.35), higher motivation to change (OR = 1.04; 95% CI 1.02–1.05) and previous work history (OR = 1.64; 95% CI 1.09–2.46). Higher age decreased odds of membership in the 'High VR' (OR = 0.95; 95% CI 0.93–0.98) compared to 'Low VR'.

Conclusion There was high heterogeneity in the identified VR trajectories, despite that all participants expressed a desire for work and education at baseline. Improvements of the IPS intervention are needed to support specific groups in achieving and retaining employment.

Keywords Severe mental illness · Vocational rehabilitation · Vocational recovery · Longitudinal · Trajectories

Introduction

Severe mental illness (SMI) are often associated with functional disabilities leading to reduced educational training, working capacity and early retirements [1, 2]. Work and education can besides providing financial independence

and security contribute to a sense of meaning, belonging and identity, which can improve mental wellbeing [3]. Thus, employment is considered to be essential in the individual recovery process of SMI [4]. Consequently, vocational rehabilitation interventions such as 'Individual Placement and Support' (IPS) aiming to improve the success of returning to work or education has been developed for individuals with SMI. IPS aids in rapidly finding and securing competitive job positions or attending education courses, which are consistent with individual skills, experiences, and preferences. IPS provide healthcare- and social benefit counselling and individual support is ongoing [5]. IPS has shown to be effective among persons with SMI in a Danish mental health care outpatient setting [6] and in a meta-analysis of randomized trials across countries in obtaining competitive employment

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compared with traditional stepwise vocational approaches [6, 7]. Randomized trials provide valuable knowledge of the effect of interventions, i.e. how many in each intervention arm returned to employment at specific follow-up time points. However, to get a more detailed picture of the heterogeneity of the vocational recovery (VR) process—defined as securing a position in competitive employment or attending a course of education at any time point during the follow-up period—identification of longitudinal VR trajectories among persons with SMI are needed. Knowledge of VR trajectories could contribute with valuable knowledge in the development of future vocational interventions with a more individualized approach to support and treatment.

To our knowledge, no studies of VR trajectories have been conducted in the context of IPS programs targeting individuals with SMI. Some observational longitudinal studies have investigated employment or return to work (RTW) trajectories among individuals on sick leave due to mental or other health-related problems [8–12]. E.g. an observational study has been conducted on data from the Danish IPS-MA trial (n = 283) that was modified for individuals on sick-leave due to mood and anxiety disorders [13]. During the 2 year follow-up period, four different RTW trajectories were identified: 'rapid-RTW'; 'delayed-RTW'; 'rapid-unstable-RTW'; and 'non-RTW' and different personal and clinical characteristics were found to predict trajectory membership e.g. a higher motivation to change predicted membership in the 'rapid-RTW' trajectory compared to the 'non-RTW' trajectory [12]. However, further replication of these findings in a larger sample was indicated. A longitudinal Dutch study of 9517 employees with sickness absence due to mental health problems, showed five different trajectories with profound variability in RTW and chance of relapse. Differences between employees in the slower and faster trajectories were observed regarding gender, age, type of mental health problem and work organisation etc. [10]. However, relevant information on psychological variables e.g. self-efficacy or whether the employees participated in interventions was lacking. Thus, observational studies in this field indicate large individual RTW variability and differences in personal and work-related characteristics related to the trajectories. Studies involving persons with psychotic disorders have demonstrated that poor VR is associated with work factors, such as limited work history [14], and illness-related factors, such as higher levels of psychiatric symptomatology [15, 16] and greater cognitive impairments [15, 17]. However, limited work has sought to investigate factors that may be associated with VR in the context of IPS programs. Therefore, an observational study of VR trajectories among individuals with SMI participating in IPS is warranted. Moreover, predictors of trajectory membership i.e. the IPS intervention, socio-demographic and disease specific characteristics could provide valuable knowledge

of individuals with SMI struggling to maintain or achieve employment and contribute to the development of more personalised vocational rehabilitation interventions.

In this observational study, we utilized the nationwide DREAM register with information on competitive employment and education and aimed to: (1) Identify trajectories of VR over a 2.5-year period among individuals with SMI who participated in the Danish IPS trial, and (2) Investigate whether baseline measured factors e.g. the IPS intervention, sociodemographic or clinical factors predicted VR trajectory membership.

Methods

Study Design and Participants

The study was designed as an observational study investigating longitudinal trajectories of VR among individuals with SMI. Additionally, the characteristics (e.g. the IPS intervention, sociodemographic or clinical factors) of participants related to each trajectory is examined by comparing predictors of membership between the different trajectory classes. We used previously collected data from the Danish IPS trial, which included 720 adults with SMI and previously has been described in detail [18]. In brief, the trial was designed as an investigator-initiated randomised, three-group parallel, multisite trial with blinded outcome assessment. The participants were assigned to early intervention teams (OPUS teams) or community mental health services. Individuals who expressed a clear desire for competitive employment or education were identified by case managers in the psychiatric outpatient teams, who assessed for eligibility and referred participants to the trial. Additionally, participants were recruited through self-selection, advertisements and information available at the psychiatric centres. To ensure participants met the diagnostic criteria, they were assessed by a trained and certified researcher using the diagnostic interview Schedules for Clinical Assessment in Neuropsychiatry (SCAN). The content of the three vocational intervention groups has previously been described in detail [18]. In brief, all participants in the three groups continued to receive their usual psychiatric outpatient treatment which consisted of individual case management based on cognitive therapeutic methods and medical review [19]. The participants allocated to the IPS group (N = 243) received vocational support following the principles of the IPS model. The other intervention group (N = 238) received in addition to IPS, cognitive computer training using the software CIR-CuiTS [20], and teaching in cognitive coping and compensatory strategies using an adapted version of the "Thinking skills for work" manual [21]. The control group (N = 239)

received the best available vocational rehabilitation provided by the national jobcentres.

Eligibility Criteria

The participants in the IPS trial were aged between 18 and 64 years, and had a diagnosis of schizophrenia, schizotypal disorder, delusional disorder (F20–F29), bipolar disorder (F31) or recurrent depression (F33) according to the International Classification of Diseases version 10 (ICD-10). The participants lived in one of three Danish cities: Copenhagen (including the municipality of Frederiksberg), Odense or Silkeborg and were assigned to early intervention teams (OPUS teams) or community mental health services. The participants in the IPS trial expressed a clear desire for competitive employment or education. All participants provided verbal and written informed consent and spoke and understood Danish sufficiently well to participate without an interpreter.

Measures

To identify trajectories of VR we used data extracted from the DREAM database which obtain continuous information regarding use of social benefits [22]. From the DREAM data, we had information on employment and education status on all participants included throughout the trial period regardless of loss to follow-up. The number of weeks of employment or education was collected successively every half year after baseline until the final follow-up after 2.5 years—resulting in five measures of weeks in competitive employment or education within the last six months: weeks: 1–26; weeks 27–52; weeks 53–78; weeks 79–104; and weeks 105–130.

Variables examined as predictors of possible trajectory membership were chosen based on previous similar studies of predictors that influence RTW among persons on sick-leave due to mental illness, [10–12, 23], as well as available predictors measured at trial inclusion in the data-material i.e. IPS intervention group (controls versus the two intervention arms combined), age, gender, level of education, civil status, parenthood, location (Copenhagen versus Odense or Silkeborg), previous work history (yes or no to ≥ 2 months in total of paid work in the last 5 years), psychiatric diagnosis (F2, F31 and F33) defined by the ICD-10. Psychotic and negative symptoms were measured with the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS) [24] and depression symptoms were measured with the Hamilton Depression Scale (HAM-D6) [25]. We applied the Global Assessment

of Functioning (GAF-F) [26] and the Personal and Social Performance (PSP) scale [27] to assess level of functioning. Cognition was measured with the Brief Assessment of Cognition in Schizophrenia (BACS) [28]. Health-related quality of life was measured with 12-item Short Form Health Survey (SF-12) divided into two weighted mental (MCS) and physical component summary (PCS) scores [29]. Substance abuse i.e. number of days with heavy alcohol drinking, psychoactive drugs other than cannabis (Yes/No) and/ or cannabis days within the last month prior baseline was examined with Alcohol Use Disorders Identification Test (AUDIT) [30]. All these outcomes were obtained through the baseline interviews. Self-reported information from patients were answered online at baseline and included measures based on the Rosenberg Self-esteem scale [31], the Empowerment scale [32] and the General Self-efficacy scale [33]. The readiness to seek employment or education was measured by the Change Questionnaire (CQ) [34]. In the predictor analyses of IPS intervention group, we pooled the two intervention groups (N = 481).

Statistical Analysis

We applied latent growth mixture modelling (LGMM) in Mplus statistical software (version 7) to identify unique classes (trajectories) of returning to work [35]. All 720 participants were included in the LGMM and we handled missing data by application of Full Information Maximum Likelihood (FIML) [36]. Initially, a series of linear and quadratic and cubic LGMM-models were estimated ranging from one to five classes. The evaluation of models was based on Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC), and the Sample-Size adjusted BIC (adj. BIC) as well as entropy of the model. Model fit improvement with addition of an extra class was tested by Lo–Mendell–Rubin, Vuong–Lo–Mendell–Rubin and the Bootstrap likelihood ratio tests, respectively, which were also part of the evaluation of models. Lastly, model selection was also based on proper class sizes (at least 5% of the sample included in a class) and subjective evaluation of the models' parsimony and theoretical meaningfulness.

We used a three-step approach to test whether baseline predictors were associated with class membership [37]. In this approach, covariates (i.e. possible predictors) were treated as auxiliary variables and did not affect the formation of classes, but their association with the latent classes was tested on their probabilistic nature of belongingness to each class. First, univariable multinomial logistic regression analyses were carried out to estimate associations between each predictor variable and latent class membership. Secondly,

multivariable regression analyses including all the significant (p < 0.05) covariates from the univariable analyses were carried out to identify predictors of class membership. We report results from the multinomial logistic regression analyses as odds ratios (OR) including 95% confidence intervals (95% CI).

Results

Previously published data on baseline characteristics of 720 participants in the IPS trial [6, 38] is shown in Table 1. Almost evenly distributed in the three intervention arms, around ~76% had a diagnosis of schizophrenia spectrum

Table 1 Baseline characteristics of 720 participants in the trial randomised to individual placement and support (IPS), vs. IPS enhanced with cognitive remediation and work-related social skills training (IPSE), vs. service as usual (SAU) (Previously published in Christensen et al. [6])

	IPS (N = 243)	IPSE (N = 238)	SAU (N = 239)
Sex, N (%)			
Female	94 (38.7)	87 (36.6)	95 (39.8)
Male	149 (61.3)	151 (63.5)	144 (60.3)
Age, mean (SD)	33.3 (10.3)	33.0 (9.5)	32.8 (9.9)
Previous work history N (%)[a]			
No	125 (51.4)	117 (49.2)	123 (51.5)
Yes	118 (48.6)	121 (50.8)	116 (48.5)
Education, N (%)			
Master or equivalent	13 (5.4)	14 (5.9)	21 (8.8)
Bachelor or equivalent	28 (11.5)	22 (9.2)	28 (11.7)
Short-term tertiary education	43 (17.7)	53 (22.3)	44 (18.4)
Upper secondary education	61 (25.1)	57 (24.0)	57 (23.9)
Primary/lower secondary education	98 (40.3)	92 (38.7)	89 (37.2)
Married or cohabiting, N (%)			
No	197 (81.1)	194 (81.5)	187 (78.2)
Yes	46 (18.9)	44 (18.5)	52 (21.8)
Site, N (%)			
Copenhagen, Frederiksberg	174 (71.6)	165 (69.3)	169 (70.7)
Odense, Silkeborg	69 (28.4)	73 (30.7)	70 (29.3)
Diagnoses, N (%)			
Schizophrenia spectrum disorders (ICD10 codes: F20-F29), N (%)	184 (75.7)	181 (76.1)	186 (77.8)
Bipolar disorder (ICD10 codes: F31.0–F31.9), N (%)	32 (13.2)	30 (12.6)	25 (10.5)
Recurrent depression (ICD-10 F33.0–F33.9), N (%)	27 (11.1)	27 (11.3)	28 (11.7)
Match group N (%)[b]			
Match group 2	191 (78.6)	186 (78.2)	190 (79.5)
Match group 3	52 (21.4)	52 (21.9)	49 (20.5)
PSP Score mean (SD)	47.3 (10.8)	47.2 (10.8)	47.0 (10.0)
Psychotic symptoms (SAPS), mean (SD)	1.2 (1.3)	1.2 (1.3)	1.2 (1.3)
Negative symptoms (SANS), mean (SD)	1.9 (0.8)	1.9 (0.8)	2.0 (0.8)
Disorganized symptoms (SAPS/SANS) mean (SD)	0.3 (0.5)	0.3 (0.5)	0.3 (0.5)
BACS Global, mean (SD)	− 2.6 (1.61)	− 2.8 (1.9)	− 2.7 (1.8)
Hamilton score mean (SD)	6.0 (4.2)	6.4 (4.2)	6.8 (4.1)
Self-efficacy mean (SD)	14.1 (6.3)	14.3 (6.1)	13.1 (6.4)
Rosenberg self-esteem (SD)	15.6 (6.1)	15.6 (5.7)	16.0 (5.9)
SF-12 total (SD)	83.4 (7.9)	82.0 (7.9)	81.5 (7.8)
Motivation for change, total (SD)	98.7 (18.1)	98.77 (15.3)	97.8 (17.7)

[a]Previous work history: ≥ 2 months paid job last 5 years

[b]Danish legislation operates with three different match groups: Match group 2: Assessed ready to participate in a vocational rehabilitation programme but not able be to be self-sufficient within 3 months. Match group 3: Assessed to have severe long-term problems and unable to work or participate in prevocational training

disorders, ~ 61% were male, mean age was 33 years and around half had a previous work history ie. ≥ 2 months in total of paid work in the last 5 years (Table 1). We estimated linear, quadratic and cubic term LGMM models from one to five classes and tested models both with free and fixed variance around the intercept, slope, quadratic and cubic term (Table 2). AIC, BIC and adjusted BIC fit estimates were consistently lower in the cubic LGMM model compared with the linear and quadratic LGMM models indicating better model estimates for the cubic model. Correspondingly, the lowest fit estimates within all the cubic models were in the models with fixed variance around the cubic term. In Table 2, Goodness-of-fit statistics for this cubic LGMM analyses are shown. Entropy is high (> 0.99) in all 1–5 class models also indicating good model fit. Through all the models AIC, BIC and adjusted BIC fit estimates fell when adding extra classes, however, the fall in estimates became lower and lower. While fit estimates generally did improve (estimates decreased) with addition of classes, both the Vuong–Lo–Mendell–Rubin likelihood ratio test and the Lo–Mendell–Rubin adjusted likelihood ratio test showed non-significant tests (p > 0.05) for adding classes above the 4-class model, though the bootstrap likelihood ratio test showed significant figures in adding classes in all models. Class sizes were acceptable in the 4-class model (61.3% vs 23.4% vs 8.2% vs 7.2%) as well as class accuracy based on posterior probabilities were all above 0.98. As the 5-class model identified the same trajectories as the 4-class model except for more or less splitting the 8.2%-class (from the 4-class model) into two parallel trajectories, thus resulting in two very small classes, and as the Vuong–Lo–Mendell–Rubin likelihood ratio test and the Lo–Mendell–Rubin adjusted likelihood ratio test indicated that a 5-class model would not significantly improve the model estimation we chose the 4-class cubic model to best represent our data (Table 2).

Trajectories

Figure 1 presents the 4-class model. The dotted black curve represents the average VR for the whole sample, whereas the coloured lines represent the variation in latent trajectories identified through LGMM estimation. One class, named 'Low VR' (61.3%), have estimated low averages for number of VR weeks at all follow-up times, and especially at the last follow-up (2.5 years after baseline) the average weeks of being back in work in this trajectory is only 0.44 weeks within the last 6 months (Fig. 1). Another class 'High VR', consisting of 23.4% of the sample, had an increasing number of weeks in work and at the last follow-up the average is 24.95 weeks in work within the last 6 months, i.e. close
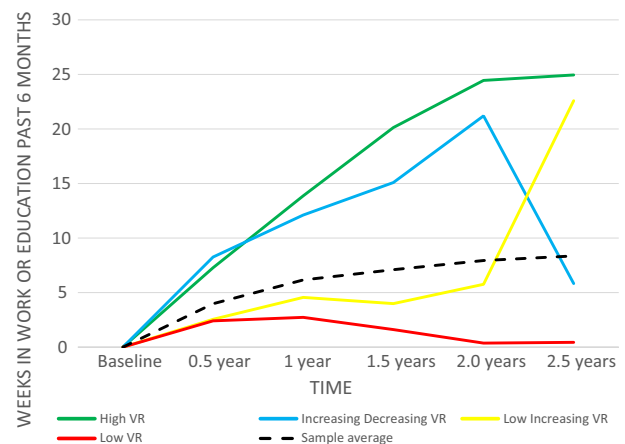
Fig. 1 Depicting the 4 identified trajectories of vocational recovery (VR) and the sample average VR

Table 2 Fit estimates for the trajectory classes

	Fit estimates			P-values			Classification measures		
	Akaike Information Criteria (AIC)	Bayesian Information Criteria (BIC)	Sample-size adjusted BIC (adj. BIC)	Vuong–Lo–Men-dell–Rubin likelihood ratio test	Lo–Men-dell–Rubin adjusted likelihood ratio test	Bootstrap likelihood ratio test	Entropy	Class accuracy	Class size (%)
1 class	24,582	24,651	24,604						
2 class	23,673	23,760	23,699	< 0.000	< 0.000	< 0.000	0.989	0.999; 0.993	69; 31
3 class	23,170	23,280	23,204	0.006	0.007	< 0.000	0.991	0.97; 0.999; 0.999	8; 66; 26
4 class	22,680	22,817	22,722	0.005	0.006	< 0.000	0.994	0.998; 0.994; 0.984; 0.998	23; 7; 8; 61
5 class	22,467	22,627	22,516	0.158	0.163	< 0.000	0.992	0.993; 0.973; 0.972; 0.991; 0.999	22; 6; 4; 7; 61

to full-time work which is equivalent to 26.5–27 weeks per half-year (Fig. 1). A third class, representing 8.2% and named 'Low Increasing VR' identified a trajectory with low VR until the final follow-up at 2.5 years where the average weeks of VR in the last 6 months was 22.59. Finally, a fourth class consisted of 7.2%, named 'Increasing Decreasing VR', represented a group of individuals who averagely increased their weeks in VR until a decrease in weeks occurred between the 2 and 2.5 years follow-up (at last follow-up they averagely worked 5.83 weeks in the last 6 months) (Fig. 1).

Predictors of Trajectory Membership

Univariable and multivariable predictors determining membership of classes are shown in Tables 3, 4 and 5. Multivariable analyses indicated that six variables significantly predicted membership in 'High VR' compared with the 'Low VR' as the reference (Table 3), thus having received the IPS intervention increased odds of membership in 'High VR' (OR = 2.18; 95% CI 1.37–3.48) and so did higher educational level (OR = 2.25; 95% CI 1.39–3.64), higher cognitive function on the BACS score (OR = 1.17; 95% CI 1.02–1.35), higher motivation for change (OR = 1.04; 95% CI 1.02–1.05) and previous work history (OR = 1.64; 95% CI 1.09–2.46). However, higher age at baseline decreased odds of membership in the 'High VR' (OR = 0.95; 95% CI 0.93–0.98) compared with the 'Low VR' (Table 3). When comparing predictors of membership between 'Low VR' and the class 'Increasing Decreasing VR', both the variable high educational level and high motivation to change increased membership in the 'Increasing Decreasing VR' by 2.03 (95% CI 1.05–3.92) and 1.03 (95% CI 1.00–1.05), respectively (Table 3). When using the 'High VR' as reference we found no significant predictors in multivariable analyses between 'High VR' and 'Increasing–Decreasing VR', however, higher age predicted membership in 'Low Increasing VR' when compared with 'High VR' (OR = 1.04; 95% CI 1.01–1.08) (Table 4). Lastly, when comparing the two small classes with 'Low Increasing VR' as the reference only the variable having a higher self-esteem score at baseline significantly predicted membership in the 'Increasing Decreasing VR' (OR = 1.08; 95% CI 1.02–1.15) (Table 5).

Discussion

In this study, we examined heterogeneity of the VR process among 720 persons with SMI participating in the Danish IPS trial and identified four trajectories: 'Low VR' (61.3%), 'Low Increasing VR' (8.2%), 'Increasing Decreasing VR' (7.2%) and 'High VR' (23.4%). Individual factors that predicted membership in 'High VR' compared to membership in the 'Low VR' in the multivariable regression model were

receiving the IPS intervention, lower age, higher education, previous history of paid work, higher cognitive functioning and motivation for change.

To our knowledge, no other studies have been published on trajectories among persons with SMI receiving the IPS-intervention. However, trajectory studies including broader target groups have been published [10, 11], and one study has been published on trajectories of RTW among persons recently diagnosed with mood and anxiety disorders participating in the Danish modified version of IPS-MA trial (n = 283) using LGMM trajectory analysis [12, 13]. During the 2 year follow-up period, four trajectories were identified: 'Non-RTW' (70%), 'Rapid-unstable-RTW' (7%), 'Delayed-RTW' (19%) and 'Rapid-RTW' (4%) [12], which was partly comparable to the trajectories identified in this present study. E.g. both studies found a large proportion of the participants in a 'Low VR' (61.3%) and a 'Non-RTW' (70%) trajectory, respectively. However, in the IPS-MA trial, no participants had RTW in this trajectory, whereas in the present study a relatively high proportion had returned to either job or education but at a low average number of weeks. Additionally, we found 23.4% with membership in the 'High VR' represented by persons with SMI who within the first 1.5 years almost reached full employment, whereas those who did reach full RTW (the rapid- and delayed-RTW classes) in the IPS-MA study experienced a decrease in work participation in the last year indicating that the individuals in these trajectories may have needed ongoing treatment and support in order to maintain employment. In addition, it is important to mention that the examined IPS trial has proven to be effective on returning to employment [6], whereas the modified version of IPS has not [13]. Thus, target group, fidelity to the full IPS program protocol, effectiveness of the intervention, average number of weeks in employment, degree and duration of vocational support etc. might influence the VR process and the possibility to compare results directly across different trajectory studies.

The finding that previous history of paid work predicted membership in 'High VR' in both the univariate and multiple regression analysis are consistent with findings from most previous studies [14, 39–42], as well as a recent predictor study of the Danish IPS trial on the same data-material utilizing logistic regression analysis [38]. Interestingly, in this present study utilizing LGMM trajectory analysis, we found an association between higher cognitive functioning and 'High VR' in both the univariate and multiple regression analysis. Also, higher education predicted membership in 'High VR' vs. 'Low VR'. The findings supports the findings from previous studies [42–45] and expanded on the results from the recent predictor study—indicating that this study is contributing with a nuance of the results of the VR process among participants in the IPS trial, which might be more applicable for practice. Notably, we confirmed

Table 3 Predictors of trajectory membership using 'Low VR' as the reference group

| Variable | High VR 168/720 (23.4%)[a] | | | | Increasing Decreasing VR 52/720 (7.2%)[a] | | | | Low Increasing VR 59/720 (8.2%)[a] | | | |
| | Univariable | | Multivariable | | Univariable | | Multivariable | | Univariable | | Multivariable | |
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age	**0.97 (0.95–0.99)**	**0.004**	**0.95 (0.93–0.98)**	**0.001**	0.98 (0.95–1.01)	0.185			1.01 (0.99–1.04)	0.376		
Male	0.79 (0.55–1.14)	0.21			0.93 (0.51–1.69)	0.808			0.91 (0.52–1.60)	0.74		
Female	1				1				1			
Higher education	**1.93 (1.32–2.82)**	**0.001**	**2.25 (1.39–3.64)**	**0.001**	**2.22 (1.16–4.24)**	**0.015**	**2.03 (1.05–3.92)**	**0.035**	**2.03 (1.11–3.73)**	**0.022**	**1.87 (1.01–3.44)**	**0.045**
Lower education	1				1		1		1		1	
Married/cohabiting YES	**1.58 (1.03–2.41)**	**0.035**	1.54 (0.93–2.55)	0.091	0.83 (0.37–1.85)	0.65			1.17 (0.59–2.33)	0.656		
Married/cohabiting NO	1				1				1			
Parent YES	1.44 (0.95–2.19)	0.088			0.88 (0.41–1.88)	0.732			1.57 (0.84–2.94)	0.163		
Parent NO	1				1				1			
Odense/Silkeborg-location	0.92 (0.62–1.37)	0.689			1.53 (0.84–2.79)	0.162			1.08 (0.59–1.96)	0.812		
Copenhagen-location	1				1				1			
≥2 months of paid work in the last 5 years YES	**2.04 (1.42–2.94)**	**<0.0001**	**1.64 (1.09–2.46)**	**0.018**	1.54 (0.86–2.76)	0.142			**1.94 (1.11–3.41)**	**0.021**	**1.78 (1.01–3.15)**	**0.046**
≥2 months of paid work in the last 5 years NO	**1**		**1**		1				**1**			
IPS intervention group	**1.66 (1.11–2.47)**	**0.013**	**2.18 (1.37–3.48)**	**0.001**	1.28 (0.69–2.39)	0.435			1.11 (0.62–1.99)	0.726		
Control group	1		1		1				1			
Schizophrenia diagnosis YES	0.98 (0.65–1.50)	0.936			0.99 (0.50–1.97)	0.977			0.73 (0.39–1.35)	0.316		
Schizophrenia diagnosis NO	1				1				1			
Bipolar diagnosis YES	1.54 (0.92–2.58)	0.104			1.09 (0.44–2.71)	0.848			1.32 (0.58–2.98)	0.508		
Bipolar diagnosis NO	1				1				1			
Recurrent depression YES	0.60 (0.32–1.13)	0.115			0.94 (0.38–2.30)	0.885			1.30 (0.60–2.82)	0.51		
Recurrent depression NO	1				1				1			
Hamilton (HAM-D6)	**0.96 (0.92–1.00)**	**0.042**	0.96 (0.91–1.02)	0.233	0.99 (0.93–1.06)	0.738			1.02 (0.96–1.09)	0.507		
Functioning Global (GAF-F)	**1.03 (1.01–1.05)**	**0.002**	1.00 (0.95–1.05)	0.895	1.02 (0.99–1.05)	0.189			0.99 (0.97–1.02)	0.467		
Cognition (BACS)	**1.22 (1.08–1.38)**	**0.001**	**1.17 (1.02–1.35)**	**0.025**	1.08 (0.93–1.26)	0.339			1.16 (1.00–1.35)	0.056		
Level of functioning (PSP)	**1.03 (1.01–1.05)**	**0.001**	1.02 (0.97–1.07)	0.485	1.02 (0.99–1.04)	0.305			1.00 (0.97–1.02)	0.81		
Psychotic symptoms (SAPS)	0.93 (0.81–1.07)	0.328			1.05 (0.84–1.32)	0.658			0.98 (0.79–1.22)	0.854		
Negative symptoms (SANS)	0.71 (0.57–0.89)	0.003			0.86 (0.59–1.25)	0.427			1.01 (0.67–1.52)	0.972		
Disorganized symptoms	0.87 (0.57–1.33)	0.526			1.32 (0.78–2.22)	0.304			0.97 (0.53–1.75)	0.911		
Physical health (PCS, SF-12)	0.97 (0.94–1.00)	0.076			1.02 (0.97–1.08)	0.393			0.99 (0.94–1.04)	0.612		
Mental health (MCS, SF-12)	**1.02 (1.00–1.04)**	**0.043**	1.11 (0.81–1.52)	0.525	1.00 (0.97–1.04)	0.859			1.00 (0.97–1.03)	0.918		
Rosenberg Self-esteem scale	1.02 (0.99–1.06)	0.155			1.04 (0.99–1.09)	0.159			0.96 (0.91–1.00)	0.051		

Table 3 (continued)

Variable	High VR 168/720 (23.4%)[a]				Increasing Decreasing VR 52/720 (7.2%)[a]				Low Increasing VR 59/720 (8.2%)[a]			
	Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Rogers Empowerment scale	**1.03 (0.99–1.06)**	**0.012**	1.00 (0.96–1.03)	0.974	1.01 (0.97–1.04)	0.648			0.99 (0.96–1.03)	0.623		
General Self-Efficacy scale	**1.03 (1.01–1.06)**	**0.021**	0.99 (0.95–1.04)	0.803	1.02 (0.97–1.07)	0.395			0.97 (0.93–1.02)	0.273		
Motivation for Change (CQ)	**1.04 (1.02–1.05)**	**<0.0001**	**1.04 (1.02–1.05)**	**<0.0001**	**1.03 (1.00–1.05)**	**0.016**	**1.03 (1.00–1.05)**	**0.014**	1.01 (1.00–1.03)	0.081		
Heavy-drink days (≥ 6 drinks)	1.02 (0.98–1.06)	0.402			1.00 (0.91–1.09)	0.905			1.02 (0.96–1.08)	0.572		
Cannabis days	0.97 (0.94–1.01)	0.138			0.96 (0.89–1.02)	0.185			0.98 (0.92–1.03)	0.361		
Using drugs YES	0.55 (0.16–1.96)	0.359			1.22 (0.27–5.57)	0.795			1.65 (0.45–6.00)	0.448		
Using drugs NO	1				1				1			

Bold values indicate $p < 0.05$

[a] n/n (%) is based on most likely latent class membership

previous findings that self-assessed motivation to change measured by the CQ predicted membership in 'High VR' compared with 'Low VR' [12, 38]. Previously, it was found that higher motivation to change predicted membership in the rapid-RTW class compared with the non-RTW class [12]. The CQ consists of 12 items covering six constructs: desire, ability, reasons, need, commitment and taking steps towards a specified change goal—in this case employment or education [34]—suggesting that future research may profit from investigating the effects of individualized interventions focusing on motivational interviewing, tailored to this specific behavioural barrier to employment.

High education and motivation for change predicted membership in the 'Increase–decrease VR' compared with 'Low VR'. One may hypothesise, that high education and motivation provides relatively easy access to the labour market, but often in high-demanding and sometimes stressful jobs, which might be challenging for the target group. The decrease in VR after 2 years of employment in this trajectory may indicate that sustaining employment was difficult and that participants may have needed further treatment and ongoing support. The IPS intervention is characterized by ongoing job support [5]. However, a further focus on workplace adjustments could support participants in sustaining employment during relapse of symptoms and recovery of work functioning, and thereby prevent sickness absence. Higher age predicted membership in 'Low Increasing VR' compared with 'High VR'—indicating that older persons with SMI might need more time and patience in their process towards VR. This finding is consistent with previous research [42, 46]—and in line with a register-based study from the Netherlands (2020) finding that employees on sickness absence due to mental health problems were older in the slow RTW trajectories compared with employees in the fast RTW trajectories [10]. Lastly, a higher self-esteem score at baseline significantly predicted membership in the 'Increasing Decreasing VR' compared to 'Low Increasing VR'—indicating that high self-esteem might influence the individual belief of VR. Nevertheless, further research into vocational interventions aimed at persons with SMI should focus on maintaining self-esteem and confidence on the workplace and on adjustments that could support participants in maintaining employment and motivation, even in case of relapse. Moreover, further studies including other possible explanatory factors e.g. stigma, RTW self-efficacy etc. and with a longer follow-up period would enhance the knowledge of VR trajectories in the long-term.

Strengths and Limitations

Strengths of the study include that we had complete data information on weeks in employment or education at five timepoints from the DREAM database throughout the

Table 4 Predictors of trajectory membership using 'High VR' as the reference group

| Variable | Increasing Decreasing VR 52/720 (7.2%)[a] | | | | Low Increasing VR 59/720 (8.2%)[a] | | | |
| | Univariable | | Multivariable | | Univariable | | Multivariable | |
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age	1.01 (0.97–1.04)	0.691			**1.04 (1.01–1.07)**	**0.006**	**1.04 (1.01–1.08)**	**0.01**
Male	1.17 (0.62–2.22)	0.628			1.15 (0.62–2.12)	0.665		
Female	1				1			
Higher education	1.15 (0.57–2.33)	0.688			1.06 (0.54–2.05)	0.872		
Lower education	1				1			
Married/cohabiting YES	0.53 (0.23–1.21)	0.133			0.74 (0.36–1.54)	0.425		
Married/cohabiting NO	1				1			
Parent YES	0.61 (0.27–1.36)	0.224			1.09 (0.55–2.14)	0.81		
Parent NO	1				1			
Odense/Silkeborg-location	1.66 (0.86–3.20)	0.129			1.17 (0.60–2.25)	0.647		
Copenhagen-location	1				1			
≥ 2 months of paid work in the last 5 years YES	0.76 (0.50–1.15)	0.383			0.95 (0.51–1.76)	0.871		
≥ 2 months of paid work in the last 5 years NO	1				1			
IPS intervention group	0.67 (0.35–1.28)	0.464			0.67 (0.35–1.28)	0.227		
Control group	1				1			
Schizophrenia diagnosis YES	1.01 (0.48–2.12)	0.985			0.74 (0.38–1.46)	0.39		
Schizophrenia diagnosis NO	1				1			
Bipolar diagnosis YES	0.71 (0.27–1.85)	0.485			0.86 (0.36–2.04)	0.729		
Bipolar diagnosis NO	1				1			
Recurrent depression YES	1.56 (0.56–4.35)	0.397			2.16 (0.86–5.42)	0.1		
Recurrent depression NO	1				1			
Hamilton (HAM-D6)	1.03 (0.96–1.11)	0.367			1.07 (1.00–1.15)	0.067		
Functioning Global (GAF-F)	0.99 (0.96–1.02)	0.62			**0.96 (0.94–0.99)**	**0.01**	0.96 (0.90–1.02)	0.199
Cognition (BACS)	0.88 (0.74–1.05)	0.164			0.95 (0.79–1.13)	0.564		
Level of functioning (PSP)	0.98 (0.95–1.02)	0.312			**0.97 (0.94–0.99)**	**0.02**	1.01 (0.95–1.08)	0.686
Psychotic symptoms (SAPS)	1.13 (0.88–1.45)	0.343			1.05 (0.82–1.34)	0.698		
Negative symptoms (SANS)	1.21 (0.81–1.79)	0.357			1.41 (0.91–2.18)	0.123		
Disorganized symptoms	1.51 (0.82–2.78)	0.191			1.11 (0.57–2.17)	0.766		
Physical health (PCS, SF-12)	1.05 (1.00–1.11)	0.074			1.02 (0.97–1.07)	0.51		
Mental health (MCS, SF-12)	0.98 (0.95–1.02)	0.312			0.98 (0.94–1.01)	0.191		
Rosenberg Self-esteem scale	1.01 (0.96–1.07)	0.619			**0.94 (0.89–0.98)**	**0.007**	0.94 (0.88–1.00)	0.063
Rogers Empowerment scale	0.98 (0.95–1.02)	0.27			0.96 (0.93–1.00)	0.06		
General Self-Efficacy scale	0.99 (0.94–1.04)	0.648			**0.94 (0.90–0.99)**	**0.019**	1.01 (0.94–1.07)	0.85
Motivation for Change (CQ)	0.99 (0.97–1.01)	0.412			**0.98 (0.96–0.99)**	**0.014**	0.98 (0.96–1.00)	0.083
Heavy-drink days (≥ 6 drinks)	0.98 (0.89–1.07)	0.63			1.00 (0.94–1.06)	1.000		
Cannabis days	0.98 (0.91–1.05)	0.61			1.00 (0.94–1.06)	0.98		
Using drugs YES	2.21 (0.36–13.75)	0.394			2.98 (0.57–15.46)	0.193		
Using drugs NO	1				1			

Bold values indicate p < 0.05

[a]n/n (%) is based on most likely latent class membership

2.5 year study period, thus the LGMM analysis was not affected by missing data on the outcomes measure—resulting in enough power to investigate our primary aim; trajectories of the VR process. The results of the LGMM cubic model indicated a good model fit. Moreover, individual interviews were obtained with all 720 participants and approximately 93% of the participants answered the self-reported online questionnaires—resulting in enough power

Table 5 Predictors of trajectory membership using 'Low Increasing VR' as the reference group

Variable	Increasing Decreasing VR 52/720 (7.2%)[a]			
	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age	0.97 (0.93–1.01)	0.091		
Male	1.02 (0.47–2.22)	0.955		
Female	1			
Higher education	1.09 (0.47–2.54)	0.837		
Lower education	1			
Married/cohabiting YES	0.71 (0.26–1.92)	0.501		
Married/cohabiting NO	1			
Parent YES	0.56 (0.22–1.41)	0.219		
Parent NO	1			
Odense-location	1.42 (0.64–3.16)	0.383		
Copenhagen-location	1			
≥ 2 months of paid work in the last 5 years YES	0.80 (0.37–1.70)	0.555		
≥ 2 months of paid work in the last 5 years NO	1			
IPS intervention group	1.15 (0.52–2.59)	0.726		
Control group	1			
Schizophrenia diagnosis YES	1.36 (0.57–3.22)	0.491		
Schizophrenia diagnosis NO	1			
Bipolar diagnosis YES	0.83 (0.26–2.60)	0.748		
Bipolar diagnosis NO	1			
Recurrent depression YES	0.72 (0.24–2.20)	0.566		
Recurrent depression NO	1			
Hamilton Depression (HAM-D6)	0.97 (0.89–1.05)	0.451		
Functioning Global (GAF-F)	1.03 (0.99–1.07)	0.117		
Cognition (BACS)	0.93 (0.76–1.14)	0.473		
Level of functioning (PSP)	1.02 (0.98–1.05)	0.326		
Psychotic symptoms (SAPS)	1.08 (0.80–1.45)	0.638		
Negative symptoms (SANS)	0.85 (0.50–1.45)	0.557		
Disorganized symptoms	1.36 (0.65–2.85)	0.414		
Physical health (PCS, SF-12)	1.04 (0.97–1.11)	0.299		
Mental health (MCS, SF-12)	1.01 (0.96–1.05)	0.831		
Rosenberg Self-esteem scale	**1.08 (1.02–1.15)**	**0.012**	**1.08 (1.02–1.15)**	**0.012**
Rogers Empowerment scale	1.02 (0.97–1.06)	0.475		
General Self-Efficacy scale	1.05 (0.98–1.12)	0.143		
Motivation for Change (CQ)	1.01 (0.99–1.04)	0.296		
Heavy-drink days (≥ 6 drinks)	0.98 (0.89–1.07)	0.63		
Cannabis days	0.98 (0.90–1.07)	0.646		
Using drugs YES	0.74 (0.12–4.68)	0.751		
Using drugs NO	1			

Bold values indicate $p < 0.05$

[a]n/n (%) is based on most likely latent class membership

to investigate our secondary aim; associations of baseline variables with trajectory classes. The data material included rich information that was valuable from a research perspective investigating the individual VR process e.g. diagnoses of mental illnesses, prior work history, self-efficacy, motivation to change, allocation to the IPS intervention etc.

Nevertheless, it was a limitation that several of the trajectories were small with respect to 'n', why some of the predictor analyses might not have reached statistical significance because of low statistical power. Moreover, the DREAM database has some limitations. E.g. it is possible to receive state education grant without being actively studying. If a

student does not actively deactivate the grant, it will be registered as studying in DREAM. However, DREAM data is considered very suitable for longitudinal studies [22]. The participants in the current study received outpatient treatment for SMI in a variety of sociodemographic contexts and had all expressed that they would like to be in education or employment. Thus, the findings may only be generalizable for people with SMI, who have expressed a desire for education or competitive employment and who are enrolled in outpatient psychiatry.

Conclusion

This observational study supports that there is a high heterogeneity in the identified VR trajectories, despite that all participants expressed a desire for work and education at baseline. In conclusion, we identified four trajectory classes of VR among participants with SMI in the IPS trial i.e. above half had low VR, a quarter had high VR and the remaining had difficulties sustaining employment. Receiving the IPS intervention increased odds of membership in 'High VR' compared to 'Low VR' and so did lower age, higher education, previous history of paid work, higher cognitive functioning and motivation for change. The results indicate that the IPS intervention was sufficient in supporting the individual VR process. Nevertheless, improvements of the IPS intervention are still needed to even out inequality between groups and support specific groups in achieving and retaining employment. Further research into vocational rehabilitation interventions focusing on person-centered workplace adjustments aimed at the individual with SMI is needed.

Declarations

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Original Article

'I have potential': Experiences of recovery in the individual placement and support intervention

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Abstract

Background: The individual placement and support (IPS) intervention supports persons with severe mental illness in achieving competitive employment. Although the IPS intervention is labelled a recovery-oriented intervention, little is known about how participants experience IPS to influence recovery. The aim was to investigate how IPS and employment influence recovery in persons with severe mental illness.
Material: A qualitative phenomenological hermeneutic study of experiences of 12 participants in IPS.
Discussion and conclusion: IPS and competitive work have an impact on personal recovery, may influence work functioning and decrease depressive symptoms, but do not seem to have an impact on psychotic symptoms.

Keywords

Individual placement and support, clinical and personal recovery, severe mental illness, employment, self-esteem, experiences

Introduction

Employment is a frequently stated life goal among persons with severe mental illness (SMI) (Bengtsson-Tops & Hansson, 1999; Ramsay et al., 2011). In spite of the desire to work, employment rates among persons with SMI are low (Greve & Nielsen, 2013; Lerner & Henke, 2008; Marwaha, Durrani, & Singh, 2013; Marwaha & Johnson, 2004). One way to address this problem is through the evidence-based, recovery-oriented individual placement and support (IPS) intervention which helps persons with SMI achieve competitive employment (Bond, Drake, & Becker, 2008; Kinoshita et al., 2013). IPS is labelled recovery-oriented intervention and the guidelines of IPS (e.g. zero exclusion, attention to participant preferences and time-unlimited individualized support) foster hope, self-determination and social integration (Bond, Salyers, Rollins, Rapp, & Zipple, 2004; Schneider et al., 2009). However, in general, knowledge of the influence of IPS is sparse when measured by recovery outcomes including mental health symptoms, level of function and self-esteem (van Rijn, Carlier, Schuring, & Burdorf, 2016). On the other hand, the main target of IPS, namely, competitive employment, has significantly been associated with an increase in level of function and self-esteem (Charzynska, Kucharska, & Mortimer, 2015; Michon et al., 2014). The important question is whether it is the IPS intervention

itself or its main target, competitive employment, which promotes recovery?

One branch of the recovery literature distinguishes between clinical and personal recovery (Davidson, Lawless, & Leary, 2005; Roe, Mashiach-Eizenberg, & Lysaker, 2011; Slade, 2010). C*linical recovery* is understood as an outcome, measured by symptom reduction and increased level of function. *Personal recovery* is seen as a process defined by the individual, not necessarily in terms of symptom reduction, but rather by what helps the individual move beyond the role of being a patient with

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mental illness. The CHIME framework describes the personal recovery as a process including five elements: Connectedness, Hope and optimism, Identity, Meaning and purpose in life and Empowerment (Leamy, Bird, Le Boutillier, Williams, & Slade, 2011). In this study, recovery is seen as the product of both clinical and personal recovery. In other words, the authors had a predefined concept of recovery, which may differ from how participants perceive recovery. In addition, the multidisciplinary team of authors – psychiatrists, sociologists and nurses – including the perception of the IPS model constitute our pre-understanding. To gain new insights from participants' experiences, our pre-understanding was attempted to be bracketed (Dahlberg, Dahlberg, & Nyström, 2001). Former qualitative studies have investigated how IPS and employment influence participants but do not use a pre-understanding of recovery (Areberg, Bjorkman, & Bejerholm, 2013; Boyce et al., 2008; Boycott, Akhtar, & Schneider, 2015; Johnson et al., 2009; Koletsi et al., 2009; Lexen, Hofgren, & Bejerholm, 2013).

The aim of the study was to describe how IPS and employment may influence recovery as experienced by persons with SMI.

Method

Design

A qualitative phenomenological hermeneutic research design was employed including a reflective lifeworld approach focusing on how the world is experienced by humans (Dahlberg et al., 2001; Malterud, 2011). Through interviews, IPS participants unfolded their experiences of how IPS and employment influenced their recovery.

Study setting

The qualitative study was conducted from December 2015 to March 2016, simultaneously with a randomized controlled trial (RCT), with the purpose of investigating efficacy of the IPS method in Denmark (Christensen et al., 2015). The qualitative study rose during data collection in the RCT. Since supplement of a qualitative study would not in any way interfere with the original RCT design, there were no methodological contradictions in including the qualitative part in this post-protocol way. The IPS intervention was provided by the employment specialist (ES) and followed 'place and train' philosophy. Main focus was individualized search for competitive employment based on participant's preferences, avoiding prevocational training. The intervention was integrated within the mental health services and included ongoing job support and benefit counselling (Drake, Bond, & Becker, 2012). In general, before entering IPS, participants had regular mandatory contact with local vocational authority (job centres), depending on what kind of benefits they received. Often, participants had undergone vocational rehabilitation at job centres in accordance with 'train and place' philosophy, with a focus on prevocational training, for example, sheltered employment or internships.

Participants

Participants of the IPS intervention were residents of Copenhagen, assigned to community mental health services and diagnosed with SMI, defined as: schizophrenia, schizotypal or delusional disorders (F20–F29); bipolar disorder (F31); or severe depression (F33), according to WHO International Classification of Diseases version 10 (World Health Organization, 1993). Furthermore, all IPS participants expressed a clear desire for competitive work.

In order to recruit interviewees for the study, a poster was placed in the IPS office waiting area to encourage IPS participants to sign up as interviewees. This way, recruitment of participants was unaffected by IPS staff and mental health personnel. In the data collection period, 175 participants were assigned to the IPS RCT in Copenhagen. A total of 12 signed up for the qualitative study. The diagnoses within the group fell into the categories F2, F31 and F33. Male/female ratio was 9/3, and age range was 28–59 years. Three participants were employed, seven were under education and two were neither working nor taking education during their participation in IPS. Sample size for the study was found sufficient to allow for identification of general themes and followed the concept of information power, as described by Malterud, Siersma, and Guassora (2015). Accordingly, the chosen sample size depended on degree of study aim specificity, sample specificity, use of established theory, quality of dialogue and analysis strategy. The study aim was neither categorized as narrow nor broad rather somewhere in between. In addition, the sample specificity of the study was neither characterized dense nor sparse, rather intermediary. The study used well-established theory from recovery literature; the quality of dialogue was strengthened by three pilot interviews, and the interviewer was an experienced psychiatrist used to perform interviews with the target group.

Data collection

The qualitative interview was found to be a viable mean of acquiring knowledge embedded in participants' lifeworld (Kvale, 2007). Individual semi-structured interviews were deemed suitable for acquiring an understanding of how IPS and employment influenced recovery. The semi-structured interview guide contained themes related to participants' reflections regarding (1) Entering IPS; (2) Which elements of IPS were found to be important? (3) Did IPS contribute to personal changes? (4) How and to what extent IPS and work were found to be important to recovery? Prior to data collection, three pilot interviews were performed. Questions were asked in a way that invited

Table 1. Coding process.

Quotations	Subtheme(s)		Main theme
'He understands where I am right now; if he has to do more or less, do I need more contact or less? Is it because I'm doing well or is it because I'm not doing well at all'	Understands where I am and adjusts the support to my situation		*The work of the ES is based on the individuals' specific needs*
'He helped me with this issue … I was afraid something was wrong in my head. He arranged for … well who it was who paid, I do not know … but he saw to it that I was examined in the Dementia Clinic. And it was … it was great for me … 'cause, I was desperate'	More than just work	A friend by my side; one I can call on	
'I came to think: what if I am doing really well, will I be left on my own then … and what do I do if I get ill again … all those panic thoughts. And I chose to share them with the ES, and she said: well, we won't let you go until you can manage on your own'	Someone I can relate to	A close relationship to the ES provides security	
'Before IPS, I didn't expect that I would even attempt a job or school or anything. But that changed: I dared to start both a job and an education, and things changed even more, because now I believe I can do it, there are things I am good at. I'm not apologizing for myself anymore, I have something to offer'	Belief in one-self		

participants to describe their experiences. All interviews were performed, audio-recorded and transcribed verbatim by first author. Interviews lasted from 45 to 90 minutes.

Data analysis

Interviews were analysed using Armedio Giorgi's (1997) phenomenological analysis method, adopted by Kirsti Malterud (2011), consisting of four steps: (1) preliminary themes were identified; (2) preliminary themes formed the foundation for identifying meaning units into different codes; (3) each code contained a number of sub-codes, illuminating different aspects of the code; and (4) essences of codes were summarized generating general categories (see Table 1) and hermeneutic interpretive review of participants' lived experiences formed part of the discussion.

Throughout the research process, authors critically discussed emerging codes and categories. These reflective discussions continued until consensus was reached. Analysis was supported by NVivo 11.0 software.

Ethics

The project is registered with the Danish Data Protection Agency (j.no. 2008-58-0035) and with the Danish Ethical Committee (j.no. S-20152000-163). All participants were thoroughly informed about the study and gave written consent. All direct references to individuals and all quotations have been anonymized.

Results

The study aimed to describe how IPS and employment might influence participants' recovery. Overall, for the participants, the ES personified the IPS intervention. The ES was viewed as a supportive, understanding and reassuring person who

was able to initiate stalled employment processes and provided an assertive service with close and frequent contact with the IPS participants. According to some participants, recovery was influenced by the IPS intervention through interactions with the ES leading to an increase in self-esteem and skills to change life patterns. Others credited employment with being most influential to their recovery and recognized IPS as an important component in its achievement.

Four main themes of the participants' experiences emerged: (1) participants hoped IPS improved their job-seeking situation; (2) the work of the ES is based on the individuals' specific needs; (3) employment considerably impacts everyday life and future plans; and (4) self-esteem, new skills and employment contribute to recovery.

Participants hoped IPS improved their job-seeking situation

When participants described IPS they contrasted it with meetings they had had at job centres, where they were allocated to different case workers. This procedure led to impersonal and unproductive relationships with case workers. Participants described situations where meetings with case workers about their job situation led nowhere:

> Well, nothing really happened. When they don't know, what was decided on at the last meeting and the meeting before that, then obviously, the meeting with them is a waste of time.

> With IPS we meet more often … they are friendly compared to the job centre […] they do these follow-up meetings all the time, so there is progress.

In other situations, case workers communicated in a condescending way and did not listen to the participants or made no effort to try to understand them:

… he began to provoke me, saying he knew my type and I was just lazy and I was just … and when I picked him up on these statements, I was accused of being psychotic.

Meetings at job centres were described as stressful and contributing to either persistence or aggravation of mental illness. Participants' expectations of the IPS intervention were dominated by hope of improving their job-seeking situation which they felt was stuck. As well, the opportunity of being assigned to one single ES instead of a variety of case workers was found important.

The work of the ES is based on the individuals' specific needs

The ES was by participants experienced as a person providing an assertive service, ensuring a close and frequent contact. Participants described a variance of situations where they experienced the ES met their individual needs:

> He understands where I am right now; if he has to do more or less, do I need more contact or less?

Participants described the ES as a person who was able to initiate processes in the field of employment but also in other areas where issues seemed to hamper getting into employment. For example, participants experienced psychological support from the ES in situations involving loss of close relatives or crisis with spouse or children. As well, the ES took charge in cases where participants felt shelved by the system:

> He helped me with this issue … I was afraid something was wrong in my head. He arranged for … well who it was who paid, I do not know … but he saw to it that I was examined in the Dementia Clinic. And it was … it was great for me … 'cause, I was desperate.

These examples illustrate how the ES temporarily set aside the job-seeking process in order to concentrate about solving aggravating issues important to participants.

The ES encouraged participants to take initiatives and supported them in the job-seeking process, for example, in writing job applications or visiting potential future employers. In those situations, participants felt responsible and in charge as the ES stayed in the background. This was described as crucial to the participants as it contributed to the feeling of being able to handle and control such situations. Participants described the ES as committed and serious about helping them back on track. The ES made them feel trust and security. Other qualities highlighted by the participants when they described how the ES met their needs were openness and honesty:

> I came to think: what if I am doing really well, will I be left on my own then … and what do I do if I get ill again … all those panic thoughts. And I chose to share them with the ES, and

she said: well, we won't let you go until you can manage on your own.

Participants described how collaboration with the ES made them feel that they were no longer 'just a number in the system'. They felt they had someone who listened to them, took them seriously and treated them properly. Being approached in this manner made participants feel that the ES met their needs of being treated respectfully.

The ES influenced participants' ways of thinking. They felt affirmed by the ES, who made them feel valuable and important. This affirmation was experienced as necessary to participants in order for them to continue to make progress in their job-seeking process:

> Before IPS, I didn't expect that I would even attempt a job or school or anything. But that changed: I dared to start both a job and an education, and things changed even more, because now I believe I can do it, there are things I am good at. I'm not apologizing for myself anymore, I have something to offer.

Being met as a person with individual needs; supported, both in the job-seeking process and in other situations; encouraged and treated respectfully made participants feel acknowledged by the ES. According to participants, this acknowledgement promoted changes in their self-perception and self-esteem. Mental barriers to employment were broken and they developed positive attitudes towards themselves, their decisions and their actions. Participants' self-perceptions of being capable of succeeding with employment grew during IPS.

Employment considerably impacts everyday life and future plans

To work, to contribute and to have a role in society were important to participants. The fact that other people appreciated the work they did, and depended on it, mattered a great deal. Employment added stability and normality to participants' everyday lives:

> I'm not good at doing nothing. Then I fade away; smoke too much marihuana and stuff. Whereas when I'm out there doing my job, my life gets normal.

The IPS intervention and the employment opportunities generated by it made it easier for participants to fulfil goals and dreams. They realized that life consisted of more than being mentally ill. Employment was connected with being able to buy things without having to turn every penny, travelling abroad or starting a family. Some participants doubted whether they should pursue their dreams:

> When it comes to my illness and my diagnoses I'm very much in doubt; should I have children? If they grew up to be exactly like me, it would be unbearable … then it would be my fault.

But to have children and to have my own family – that's the goal of my life.

Employment influenced participants' ways of thinking and behaving. They found that employment influenced the structure of their day. Getting up in the morning, having to shop and prepare dinner had for some participants not been part of their everyday lives before employment. Participants also talked about the importance of having colleagues to chat to and build relationships with. Social aspects such as colleagues saying 'Good morning', showing concern for them and asking them 'how their weekend had been' contributed to a feeling of inclusion. One participant described how he managed to turn the strict hierarchy at work, the 'you won't be spared' mentality, into something useful:

It runs from the top and down, and the person lower down is the one who takes all the crap … You won't be spared […] But I choose to look at it positively … it teaches me to be able to handle things … to face the world the way it is.

The psychological working environment influenced participants' feelings of fellowship and helped them adapt to workplace mentality.

Self-esteem, new skills and employment contribute to recovery

There were nuances in the ways in which participants attributed to IPS influence on recovery. Some participants considered increased self-esteem and skills to change life patterns as components involved in recovery. They perceived those components as having been positively influenced by IPS:

IPS changes the way I look at myself … when other people look at me in a positive way … I don't feel I'm a burden or inadequate … it makes me feel human.

[…] actually, it's atypical for me to handle conflicts at work like this […] I simply chose not to respond to anything they were accusing me of … just letting people calm down.

Others specified employment as most influential to their recovery and recognized IPS as an important component in gaining it. Employment contributed to daily structure, financial flexibility, shared fellowship with colleagues, feelings of being part of society and getting closer to realizing dreams and goals.

Others, who understood recovery as correlated to reduction in mental health symptoms, did not attribute to IPS or employment any influence over their recovery:

IPS doesn't eliminate the symptoms plaguing me all of the time … I can't walk down the street without getting the feeling that the cars are about to hit me or that the sound of people's talk is getting too loud for my ears.

Recovery was variously understood by participants, which explains the discrepancy of views on how IPS and employment influenced recovery. To some, IPS contributed to recovery by promoting self-esteem and skills to change life patterns. To others, IPS contributed indirectly to recovery through generated employment opportunities. And to others again, neither IPS nor employment contributed to recovery since the intervention failed to reduce mental health symptoms. Those who shared the last opinion were plagued by psychotic symptoms, whereas those who took the previous two viewpoints experienced negative and depressive symptoms, and none or milder intermittent psychotic symptoms.

Discussion

The study results emphasize the acknowledging approach used by the ES, which encouraged participants' initiatives, increased self-esteem and influenced the skills to change life patterns. The ES was confidence-inspiring, serious in helping participants back on track and respectful in the support. Employment influenced structure of the day, expanded participants' network and brought them closer to realizing goals and dreams. The study presents reasonable explanation of how IPS and employment may influence participants' personal and clinical recovery.

Personal recovery

The five elements of achieving personal recovery described by CHIME: Connectedness, Hope, Identity, Meaning and purpose in life and Empowerment (Leamy et al., 2011) are reproduced in the study. Participants spoke of being part of society and having supportive, collaborative relationships with professionals as important to recovery. These elements are captured by CHIME's connectedness category. The hope category entails dreams and aspirations. Both IPS and employment contributed to realization that life amounted to more than being mentally ill. Dreams of being able to travel outside the country or start a family were no longer thought of as unrealistic. The acknowledging approach adopted by the ES which promoted participants' self-esteem is in line with CHIME's identity category where a re-definition of a positive sense of identity is key to recovery. This category also embraces professionals' treatment of consumers as individuals, which participants valued in as much as they felt that the ES listened, treated them properly and seriously. CHIME's meaning and purpose in life category includes having meaningful social roles. While the IPS intervention in itself does not support this category, the employment opportunities generated by it does. Employment contributed to habits of getting up in the morning, sharing fellowship with colleagues and feelings of being part of society. The empowerment category entails personal responsibility. IPS participants felt responsible and in charge when writing job applications and visiting potential future employers. In those situations the ES stayed

in the background, still supportive but without taking the lead. Judging from participants' experiences, IPS and employment contain elements which can be identified by the five personal recovery processes described by CHIME.

Clinical recovery

The study found nuances in how IPS and employment were perceived to have influenced clinical recovery. Participants suffering from psychotic symptoms were clearly of the opinion that neither IPS nor employment influenced symptom severity. Even though they were capable of finding and keeping a job, they did not consider themselves as being in recovery or having recovered. They identified recovery solely in terms of reduction of mental health symptoms which neither IPS nor employment improved. In contrast to this, participants suffering from negative symptoms or depressive symptoms described how employment helped them get up in the morning and structure the day. Furthermore, fellowship with colleagues was found to be important. Without these elements, the participants explained, they could easily decline into social withdrawal and isolation.

Participants were capable of seeking and maintaining jobs with help and support from the ES. Hereby their level of function increased. However, the study does not give us insight into whether participants reached a level of work function where they could dispense with continuous support or whether the higher level of work function remain dependent on constant job support.

Both Koletsi et al. (2009) and Lexen et al. (2013) report participants experiencing employment distracted them from mental health symptoms. This partly contradicts this study where some participants credited neither work nor IPS with any influence on psychotic symptoms. Participants suffering from psychotic symptoms did neither seem to pay attention to elements of personal recovery as they solely equated recovery with the reduction of mental health symptoms which belong within the category of clinical recovery. These results may suggest that psychotic symptoms could inhibit the personal recovery process. If this is the case, it would imply an existence of an interaction between clinical and personal recovery. In contrast, participants suffering from negative or depressive symptoms felt to a marked degree that being employed influenced their recovery. They credited employment with remedying symptoms of social withdrawal and isolation. CHIME's Meaning and purpose in life category includes fellowship with colleagues and being able to get up in the morning. These elements of personal recovery influenced the severity of negative and depressive symptoms and hence clinical recovery. This might be a further instance of interaction between personal and clinical recovery and correlates with results from another study investigating the influence of IPS on empowerment (Bejerholm & Bjorkman, 2011). This study found negative correlations between depressive symptoms and empowerment. Davidson et al. (2005) suggested using clinical and personal recovery as complementary concepts for different purposes. Our results may show that IPS and work impact both personal and clinical recovery. Additionally, important interactions between personal and clinical recovery may exist. In order to understand recovery and further develop recovery-oriented interventions, we suggest that future studies focus on the interactions between personal and clinical recovery.

Limitations

Participants of the study were residents of Copenhagen. The study would benefit from the inclusion of IPS participants from other cities or rural districts since culture and mentalities differ in small localities compared to metropolitan centres. Therefore, IPS participants from other locations might have different experiences of job centre case workers and IPS consultants than the participants in Copenhagen. The recruitment strategy, where a poster encouraged IPS participants to sign up as interviewees for a qualitative study, was to avoid selection of a certain participant subgroup. Nevertheless, the interviewees ended up being participants who favoured IPS which should be taken into account when discussing the transferability of findings. To provide a more differentiated picture of participants' experiences, the ES were asked to encourage critical IPS participants to sign up as interviewees. A longer inclusion period and inclusions of participants from other locations might have led to a more comprehensive account of experiences.

Conclusion

This study indicates that IPS and competitive work might have an impact on personal recovery, may influence work functioning and decrease negative and depressive symptoms, but does not seem to have an impact on psychotic symptoms. The study shows important interactions between personal and clinical recovery.

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A Systematic Review of Individual Placement and Support, Employment, and Personal and Clinical Recovery

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Objective: The objective of this review was to assess associations between Individual Placement and Support (IPS), employment, and personal and clinical recovery among persons with severe mental illness at 18-month follow-up.

Methods: A systematic literature search identified randomized controlled trials (RCTs) comparing IPS with services as usual. Outcomes were self-esteem, empowerment, quality of life, symptoms of depression, negative or psychotic symptoms, anxiety, and level of functioning. A total of six RCTs reported data suitable for meta-analyses, and pooled original data from five studies were also analyzed.

Results: Meta-analyses and analyses of pooled original data indicated that receipt of the IPS intervention alone did not improve any of the recovery outcomes. Participants who worked during the study period, whether or not they were IPS participants, experienced improved negative symptoms, compared with those who did not work (standardized mean difference [SMD]=-0.41, 95% confidence interval [CI]=-0.56, -0.26). For participants who worked, whether or not they were IPS participants, improvements were also found in level of functioning and quality of life (SMD=0.59, 95% CI=0.42, 0.77 and SMD=0.34, 95% CI=0.14, 0.54, respectively).

Conclusions: Employment was associated with improvements in negative symptoms, level of functioning, and quality of life.

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Severe mental illness, such as schizophrenia, bipolar disorder, and major depression, often leads to large and long-lasting human costs. These include a lower level of functioning, low self-esteem, loss of earnings, and financial deprivation (1–6). The evidence-based program Individual Placement and Support (IPS) aims to help persons with severe mental illness obtain and keep work and is in this regard superior to other vocational rehabilitation programs (7–9). The IPS program is based on eight empirically supported principles: competitive employment as a goal; rapid job search; program eligibility based on the participant's choice; attention to the participant's preferences regarding type of job and disclosure of psychiatric illness to potential employers; integration of IPS with mental health services; time-unlimited, individualized support after a job is obtained; social insurance and benefits counseling; and systematic job development and engagement with employers.

IPS is frequently described as a recovery-oriented intervention (10, 11), not only because it endeavors to help people get jobs, but more fundamentally, because it is aimed at supporting people in living an independent functionally engaged life. Moreover, principles of IPS (such as attention to participants' preferences; time-unlimited, individualized support; and rapid job search) might be expected to foster

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HIGHLIGHTS

- Competitive employment was associated with improvements in negative symptoms, level of functioning, and quality of life, whether individuals received Individual Placement and Support (IPS) or services as usual.

- At 18-month follow-up, associations between IPS and clinical and personal recovery were no stronger than they were for services as usual.

- The combination of IPS and competitive employment did not further enhance recovery, compared with competitive employment alone.

hope, self-determination, and inclusion (11). Nevertheless, empirical support for IPS as a recovery-promoting practice is unclear, and there is a need to address this question.

The concept of recovery is often divided into personal and clinical recovery. Personal recovery focuses on living a satisfying, hopeful, and contributing life, even with limitations caused by the illness, whereas clinical recovery focuses on improvements in mental health symptoms and level of functioning (12–14). When investigating whether IPS is associated with improvements in recovery, other than improved work functioning, it should be borne in mind that obtaining employment has been connected with modest improvements in self-esteem, quality of life, and other areas of functioning (15, 16). Therefore, it is worthwhile exploring whether IPS is associated with additional benefits to recovery beyond those of employment. The aim of this systematic literature review was to assess the associations between IPS, employment, and personal and clinical recovery among persons with severe mental illness at 18-month follow-up. It was assumed that 18 months was a sufficient time span to measure these associations.

The following hypotheses were tested. IPS is more strongly associated with personal recovery (self-esteem, self-efficacy, hope, empowerment, and quality of life) and clinical recovery (symptoms of depression, negative and psychotic symptoms, anxiety, and level of functioning), compared with services as usual (interventions not using IPS or modified or adapted versions of IPS). IPS is more strongly associated with personal and clinical recovery, compared with services as usual, when outcomes are stratified by number of weeks worked. Number of weeks worked, independent of IPS, is associated with increases in personal and clinical recovery.

METHODS

This review followed an a priori–defined protocol published on PROSPERO, (https://www.crd.york.ac.uk/prospero; protocol CRD42017055587). The protocol was developed following the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) (17). Guided by this protocol, a literature search was conducted, and meta-analyses of data from eligible studies were utilized to answer the hypotheses. If the hypotheses could not be answered by using meta-analyses, study authors were contacted and asked to provide data for the analyses of pooled original data.

Literature Search

Comprehensive literature searches were conducted on June 21, 2017, and updated on January 11, 2019, by two librarians at the University of Southern Denmark. The following databases were searched: MEDLINE, Embase, PsycINFO, Scopus, Web of Science, Cochrane, CINAHL, Sociological Abstracts, and OTseeker. Additionally, ClinicalTrials.gov and the World Health Organization International Trials Registry Platform (WHO ICTRP search portal) were searched for unpublished material. No limitations regarding year of publication or language were imposed. Bibliographies from primary studies and review articles were hand searched. (A figure presenting the updated search strategy is included in an online supplement to this article.)

Inclusion criteria. Scales used for outcome measures in the studies included in this review were psychometrically described in peer-reviewed journals and used without modifications. Study participants were unemployed adults of either sex and ages 18–65, with severe mental illness (defined as schizophrenia; schizoaffective, schizotypal, or delusional disorders; bipolar disorder; or severe depression) according to *ICD-10* or *DSM-5* (18, 19).

Studies included in this review compared IPS with services as usual or other interventions that did not use IPS or approaches derived from it. IPS was evaluated with regular fidelity reviews and achieved good or fair fidelity (20, 21). The included studies measured outcomes at 18-month follow -up. The studies included outcome measures related to self-esteem, empowerment, quality of life, hope, self-efficacy, depression, psychotic and negative symptoms, anxiety, and level of functioning.

Search process. The electronic literature search resulted in identification of 2,167 unique citations (see online supplement). A total of 2,099 citations were excluded on the basis of title and abstract screening, leaving 68 articles for full-text review. The primary reasons for exclusion after full-text review were that the intervention failed to fulfill the IPS fidelity criteria or that results were not measured at 18-month follow-up. In the systematic review, eight RCTs were included (16, 22–31). Of those, six trials were found eligible for meta-analysis (16, 22–26, 29–31), and five trials were found eligible for pooled original data (16, 22–25, 30, 31). Two of the eight trials could not be analyzed by using meta-analyses, and the study authors of those trials were unable to provide data for the analyses of pooled original data (27, 28). (Details on the selection process, data extraction, and study characteristics are provided in the online supplement.)

Exposure Variables
IPS and services as usual were exposure variables. Moreover, number of weeks in employment was used as an exposure variable. This variable was chosen because the IPS intervention encourages participants to find the right work-life balance, instead of aiming at the more work, the better (32). The variable number of weeks in employment was defined by three categories: no employment, fewer than the median weeks in employment, and more than the median weeks in employment. Median weeks in employment was defined according to each trial on the basis of the median number of weeks worked for all participants who worked at least 1 week.

Overall, services as usual was defined in the same way in the included studies—namely, as traditional vocational

services. These services were facilitated by mental health professionals or by public services on the basis of an assessment of patients' rehabilitation needs. Services as usual included prevocational activities, such as voluntary jobs before placement in regular jobs, and thus these services were based on the more traditional principles of "train and place."

Outcome Measures

A table in the online supplement provides details on the scales used by the six trials. Hope and self-efficacy outcomes were excluded, because these were measured in only a single trial (22, 31).

Statistical Methods

The meta-analyses were conducted on standardized mean differences (SMDs) calculated from the means and standard deviations in the raw data for self-esteem, empowerment, quality of life, depressive symptoms, negative and psychotic symptoms, anxiety, and level of functioning. Kukla and Bond (29) did not provide raw data but reported means and SDs suitable for meta-analyses. The effect sizes used in the meta-analyses were calculated as the raw difference in the mean scores between IPS and services as usual at 18-month follow-up divided by the pooled SD.

Descriptive baseline data for pooled original data are presented by using means and SDs for numerical variables and Ns and percentages for categorical variables. For analyses of pooled original data, the numerical outcomes (self-esteem, empowerment, quality of life, psychotic and negative symptoms, anxiety, and level of functioning) were all standardized within each study to have one common scale (mean=0, SD=1) when treatment effects for the forest plots were estimated. These standardized effect estimates are the same as those used in the meta-analysis. These variables were analyzed by using linear regression with robust standard errors. For depressive symptoms, a standardization of the numerical baseline score was used to adjust for baseline severity. Depressive symptoms were categorized into three levels (mild, moderate, and severe); the proportional-odds model was used, and log scale estimates are reported. All estimates derived from pooled original data were adjusted for age, gender, site, and trial, as well as the baseline score of the variable in question.

Analyses were carried out on numerous secondary and exploratory outcomes. Therefore, the alpha level of significance was Bonferroni-corrected by number of outcomes, which led to a level of significance of p<0.007. For all analyses, 95% confidence intervals (CIs) were used. Heterogeneity in effect estimates was assessed using the I^2 statistic (33).

RESULTS

Meta-Analysis

As noted above, six trials (N=1,243 participants) reported data suitable for meta-analyses: Bejerholm et al. (22, 25), Burns et al. (23, 24), Bond et al. (26), Kukla and Bond (29), Christensen et al. (31), Michon et al. (16), and Mueser et al. (30). Meta-analyses indicated that the associations between IPS and clinical and personal recovery were no stronger than the associations between services as usual and clinical and personal recovery (Figure 1). Overall effect sizes were small, ranging from –0.04 to 0.16, 95% CI=–0.2, 0.35. No heterogeneity above 0.0% was observed, except for quality of life (I^2=45.9%, p=0.116).

Pooled Original Data

Authors from five of eight trials provided raw data for pooled analyses: Bejerholm et al. (22, 25), Burns et al. (23, 24), Christensen et al. (31), Michon et al. (16), and Mueser et al. (30).

Characteristics of Study Population From Pooled Original Data

A total of 1,488 participants were included from the five studies. Participants with diagnoses other than psychotic or affective illness were excluded (N=52). The same applied to participants with all missing data on the outcomes considered (N=337). Moreover, 43 participants were excluded because of missing data on number of weeks worked. Thus the population for the studies providing raw data consisted of 1,056 participants.

Of this study population, most were male, and the mean age was 35 (Table 1). Diagnoses spanned schizophrenia or psychotic illnesses, bipolar disorder, and depression. The number of participants receiving IPS was 595 (56%) (data not shown in table). Of the 1,056 participants, the numbers employed were as follows: zero weeks, N=682 (65%); fewer than the median weeks, N=190 (18%); and more than or equal to the median weeks, N=184 (17%).

Associations Between IPS Combined With Weeks in Employment and Recovery

No associations were observed between IPS combined with weeks in employment and clinical and personal recovery (Table 2). Among participants working zero weeks, a tendency was noted for negative symptoms to improve more for the group receiving services as usual group than for the IPS group (SMD=−0.20, p=0.017). After Bonferroni correction, this tendency was not significant.

Associations Between Weeks of Employment and Changes in Recovery Independent of IPS

Improvements were found for negative symptoms among employed participants, compared with participants who were not employed (employed fewer than the median weeks, SMD=−0.25, 95% CI=−0.40, 0.09; employed more than or equal to the median weeks, SMD=−0.41, 95% CI=−0.56, −0.26) (Figure 2; see table in online supplement). Additionally, level of functioning improved for employed participants, compared with those not employed (employed fewer than the

median weeks, SMD=0.23, 95% CI=0.07, 0.39; employed more than or equal to the median weeks, SMD=0.59, 95% CI=0.42, 0.77). Quality of life improved for participants employed for more than the median weeks (SMD=0.34, 95% CI=0.14, 0.54), compared with participants employed fewer than the median weeks (SMD = 0.03, 95% CI= −0.16, 0.22).
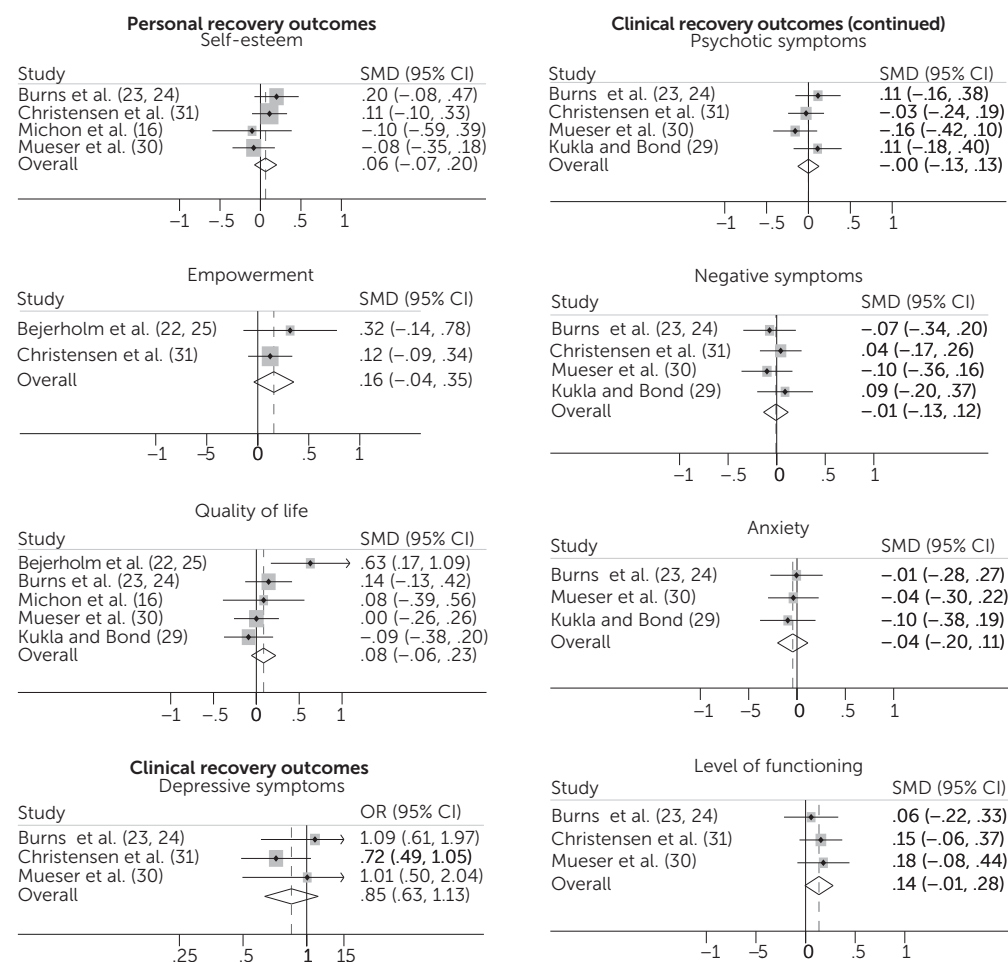
DISCUSSION

The aim of this systematic review was to assess the associations between IPS, employment, and personal and clinical recovery among persons with severe mental illness at 18-month follow-up. The aim was considered to be best answered by means of meta-analyses and analyses of pooled original data. Six trials provided data for the meta-analyses, and five trials provided data for the pooled data analyses, respectively.

FIGURE 1. Forest plots comparing effects of Individual Placement and Support (IPS) and services as usual on personal and clinical recovery outcomes[a]

[a] SMD, standardized mean difference; 95% CI, 95% confidence interval.

Associations Between IPS and Recovery

The analysis suggests that IPS has no stronger association, compared with services as usual, in improving personal and clinical recovery. Meta-analyses showed small effect sizes in all measured outcomes, indicating that any effects of IPS on personal and clinical recovery were restricted to a narrow region of small effects. Results from pooled original data regarding whether the combination of IPS and competitive employment was connected to a further increment in recovery, compared with employment alone, showed no further enhancement.

A number of causes should be considered in explaining this relation. First, IPS does not explicitly focus on the items measured in the recovery scales. Employment is the core aim of IPS and thus the proximal outcome, whereas clinical and personal recovery are distal outcomes and less directly affected by IPS. Thus it is likely that IPS is limited to affecting its core aim only. Furthermore, a relatively large group

of IPS participants did not succeed in finding employment, and a substantial portion of the employed participants attained short-term jobs at a low wage, which might also contribute to null findings in the recovery outcomes. Second, methodological challenges may have affected the outcomes. It is worth considering whether self-reported rating scales, which are used in data collection to measure outcomes such as self-esteem and empowerment, actually capture the intended phenomena. Perhaps self-reported rating scales are too crude and large-meshed to capture important details. Third, recovery outcomes might be affected by numerous factors in a person's life other than IPS—e.g., interpersonal relationships, side effects of medication, or other options made available from community mental health centers or volunteer organizations. Consequently, changes derived from IPS alone might be difficult to demonstrate.

One way to handle these challenges might be to introduce other methodologies. Research traditions within phenomenological psychopathology draw on other methods. In such approaches, phenomena are studied by using

TABLE 1. Characteristics of studies included in analyses of pooled original data

Characteristic	Bejerholm et al. (22, 25)		Burns et al. (23, 24)		Christensen et al. (31)		Michon et al. (16)		Mueser et al. (30)		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
Sample size	66		227		533		61		169		1,056	
Male	34	52	142	63	323	61	47	77	105	62	651	62
Female	32	49	85	37	210	39	14	23	64	38	405	38
Diagnosis												
Schizophrenia	55	83	184	81	410	77	50	82	130	77	829	79
Bipolar disorder	6	9	43	19	64	12	5	8	10	6	128	12
Depression	5	8	0	—	59	11	4	7	29	17	97	9
Unknown	0	—	0	—	0	—	2	3	0	—	2	<1
Any employment												
Receiving services as usual	4	11	28	27	50	29	6	18	26	23	114	25
Receiving IPS[a]	12	43	73	60	131	36	8	30	45	79	269	45

	Med	IQR	Med	IQR	Med	IQR	Med	IQR	Med	IQR	Med	IQR
Weeks in employment (among employed)[b]												
Receiving services as usual	25	8–44	13	3–29	29	17–56	32	14–62	13	6–36	23	8–44
Receiving IPS[a]	29	10–44	37	9–53	26	13–46	20	7–28	22	10–47	29	10–47

	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Age	39.5	7.5	37.5	9.8	33.3	9.9	36.1	10.0	37.7	9.2	35.4	9.9
Baseline scores on measures of personal and clinical recovery[c]												
Self-esteem			22.7	5.1	14.3	5.7	18.7	3.6	18.4	4.8	18.0	6.0
Empowerment	80.0	7.1			47.2	8.5					51.0	13.4
Quality of life	52.6	18.1	54.9	20.0			51.1	16.9	56.6	19.2	54.7	19.2
Depressive symptoms			6.3	4.1	6.3	4.1					6.3	4.1
Negative symptoms			15.1	6.1	14.6	3.2			17.7	6.1	15.3	4.8
Psychotic symptoms			13.0	4.8	12.6	3.4			13.5	4.6	12.9	4.0
Anxiety			2.8	1.4					2.3	1.3	2.6	1.3
Level of functioning			54.3	13.1	45.2	10.0			51.1	8.5	48.6	11.3

[a] IPS, Individual Placement and Support.
[b] Median (Med) and interquartile range (IQR) were calculated only for individuals with >0 weeks of employment.
[c] Scores on outcome measures of self-esteem, empowerment, quality of life, psychotic and negative symptoms, anxiety, and level of functioning were all standardized within each study to have a common scale (mean=0, SD=1). However, baseline scores shown here are observed scores (not standardized). Possible scores for self-esteem range from 0 to 30, with higher scores indicating better self-esteem. Possible scores on empowerment range from 0 to 84, with higher scores indicating a greater sense of empowerment. Possible scores on quality of life range from 0 to 100, with higher scores indicating better quality of life. Possible scores on depressive symptoms range from 0 to 22, with higher scores indicating increased symptom load. Possible scores for negative symptoms range from 7 to 35, with higher scores indicating more negative symptoms. Possible scores for psychotic symptoms range from 7 to 30, with higher scores indicating more psychotic symptoms. Possible scores for anxiety range from 1 to 7, with higher scores indicating increased severity of anxiety symptoms. Possible scores on level of functioning range from 3 to 90, with higher scores indicating increased level of functioning.

video-recorded, semistructured interviews, and the sample size varies from 50 to 100 participants, allowing for use of both qualitative and statistical analysis (34). Considering new methods for investigating associations between IPS and personal and clinical recovery might lead the IPS literature into new pathways. Finally, it is worth mentioning that in the trials selected for this study measurement of the effect of IPS and employment on recovery was not their primary objective. We believe that trials that aim to investigate the impact of IPS on personal and clinical recovery are warranted to clarify and address causality in this regard.

Associations Between Employment and Recovery

The study found reductions in negative symptoms among employed participants, compared with participants not working. The results were within the same range as those in a study by Petersen et al. (35) on integrated psychiatric treatment for patients with a first episode of psychotic illness. Those authors concluded that the effect size was small but of clinical relevance. Even though the reduction in negative symptoms found in the study reported here was small, it could still be important for participants and clinicians, considering that most antipsychotic medication is not superior to placebo in treating negative symptoms (36). Moreover, because of the great variety of adverse side effects of antipsychotic medication, it is important to have nonpharmaceutical alternatives available to help improve negative symptoms.

As in other studies, employed participants improved in level of functioning, compared with participants who were not employed (37). This finding should be interpreted cautiously, because occupational functioning, in particular, forms part of the evaluation when level of functioning is assessed (38). Changing employment status from unemployment to employment causes noticeable increases in GAF

TABLE 2. Standard mean differences (SMDs) in 18-month follow-up scores between participants receiving Individual Placement and Support (IPS) and those receiving services as usual (N=1,056 total participants), by number of weeks worked during study period[a]

| | Weeks of employment | | | | | |
| | Zero (N=683, 65%) | | Fewer than median (N=190, 18%) | | More than or equal to median (N=184, 17%) | |
Outcome	SMD	95% CI	SMD	95% CI	SMD	95% CI
Self-esteem	.04	−.10, .18	.04	−.25, .33	.03	−.36, .41
Empowerment	.11	−.06, .28	.16	−.29, .60	−.02	−.42, .37
Quality of life	.16	−.07, .38	−.07	−.39, .26	−.19	−.55, .16
Negative symptoms	.20	.04, .36	−.01	−.30, .28	.03	−.29, .35
Psychotic symptoms	.00	−.15, .15	.13	−.12, .39	−.04	−.33, .25
Anxiety	−.13	−.40, .13	.24	−.22, .70	−.07	−.64, .50
Level of functioning	−.04	−.20, .11	.09	−.20, .38	−.02	−.40, .36
	Coeff[b]	95% CI	Coeff[b]	95% CI	Coeff[b]	95% CI
Depressive symptoms	−.04	−16, .08	−.06	−.26, .15	−.15	−.40, .09

[a] SMD estimates are standardized measures of the difference between two groups—IPS versus services as usual (reference group). An SMD of .5 indicates that the IPS groups average score is half a standard deviation above the mean score of the group receiving services as usual.
[b] Logistic regression coefficient.

scores of between 5 and 10 points—an increase considered to be of clinical importance (39).

Participants employed for more than the median weeks improved in quality of life. This corresponds to the moderate effect size reported by van Rijn et al. (40).

It is beyond the scope of this study to draw conclusions about causality. Whether employment induced improvements in the above-mentioned outcomes or whether improvements in outcomes led to increases in employment capacity cannot be decided. However, on the basis of these findings and those

of previous studies, it is worth discussing whether IPS should be recommended to community mental health services in general. The results of this study showed that the IPS intervention by itself did not support clinical and personal recovery outcomes. This finding is in accordance with those from previous meta-analyses on supported employment (9, 40). On the other hand, the results showed no negative clinical implications connected to participation in IPS. Just as important, results pointed out important associations between employment and recovery outcomes, such as negative symptoms and quality of

FIGURE 2. Associations between personal and clinical recovery outcomes and employment, independent of receipt of Individual Placement and Support
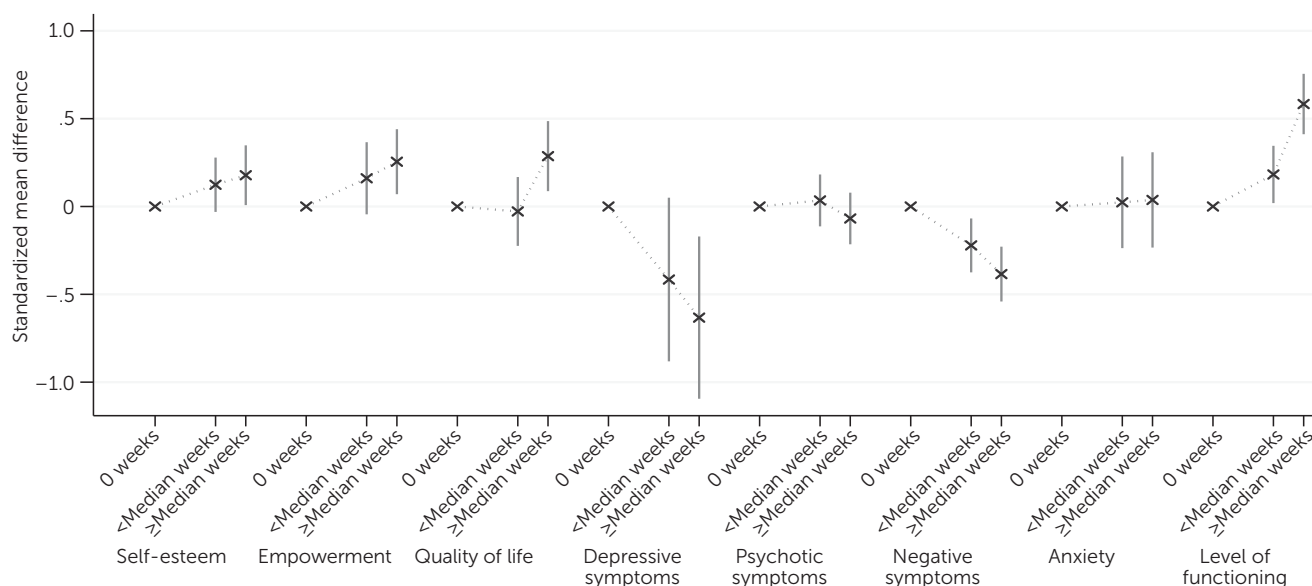
life. These results, together with evidence from other studies, reviews, and meta-analyses convincingly showing that IPS is the most effective rehabilitation service to help persons with severe mental illness achieve competitive employment, point toward a recommendation that mental health services implement IPS. Future research is needed regarding causal relationships between employment and recovery outcomes.

Strength and Limitations

The study was based on a comprehensive systematic review of randomized controlled trials (RCTs) aimed at finding all possible studies performed in the area. Even though the number of studies in the meta-analysis was small, some studies were new and not included in older meta-analyses. Moreover, this meta-analysis analyzed only studies in which the intervention was IPS. Most other reviews and meta-analyses included a variety of supported employment services. The findings of associations between IPS, employment, and personal and clinical recovery were obtained through pooling original data, which permitted adjustments for potential confounders and which would not have been possible in a meta-analysis. The five studies that provided raw data all achieved good and fair fidelity, and study quality was generally good, although three of five studies did not use blinded assessors, which may have compromised outcome reporting and produced overestimated effect sizes.

The studies included four European (16, 22–25, 31) and one American (30) RCT. Because one European trial investigated effectiveness of IPS in six European countries (23, 24), data were from a total of ten countries, contributing to high generalizability. Authors of three studies did not provide raw data (27–29). In addition, these studies reported no effects on recovery when IPS was compared with services as usual. Thus inclusion of the three studies would probably not have changed the effect; however, it could have improved power in the analyses. Even though the generalizability was high, the trials represent western countries only (United States and European countries). Associations between IPS, recovery, and employment in nonwestern cultures remain to be determined.

The studies did not use identical scales for outcome measures, i.e., different scales were used in measuring psychotic and negative symptoms. Thus a standard conversion was applied. The numerical outcomes were all standardized to limit the introduction of bias from varying scales and variances; for example, a higher variance in one study would lead to a disproportionate weight given to that study in the overall estimates.

This review examined various recovery outcomes in order to broadly span the topic. However, the multiple outcomes limited the strength of the analyses by increasing risk of type 1 error. This was addressed by a Bonferroni correction ($p \leq 0.007$). The review did not succeed in addressing all outcome measures, because hope and self-efficacy were measured in only a few studies.

The studies included were those in which outcomes were evaluated only after 18 months, which was a pragmatic choice for this review. In addition, it would have been preferable to examine associations between IPS, employment, and recovery according to shorter follow-up periods—e.g., 6 or 12 months. This would have expanded the already large number of outcomes and further increased the risk of type 1 error.

Information on race and ethnicity was not reported, making it difficult to determine whether differences in outcomes might have existed across racial or ethnic minority groups.

CONCLUSIONS

The study found that at 18-month follow-up, associations between IPS and clinical and personal recovery were no stronger than they were for services as usual. The study found associations between weeks in employment, independent of IPS, and improvements in negative symptoms, level of functioning, and quality of life, but causality could not be addressed. The combination of IPS and competitive employment did not further enhance recovery outcomes, compared with employment alone. Future studies should focus on causality between negative symptoms, quality of life, and employment among persons receiving IPS.

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Incidence rates and employment trends in schizophrenia spectrum disorders, bipolar affective disorders and recurrent depression in the years 2000–2013: a Danish nationwide register-based study

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ARTICLE

Incidence rates and employment trends in schizophrenia spectrum disorders, bipolar affective disorders and recurrent depression in the years 2000–2013: a Danish nationwide register-based study

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ABSTRACT

Aims: The study aimed to investigate time trends in incidence rates in schizophrenic spectrum disorders (ICD-10: F20–F29), bipolar affective disorder (ICD-10: F30, F31), and recurrent depression (ICD-10: F33) and to investigate the rates of employment for all incident cases.

Method: We used nationwide longitudinal data from 2000 to 2013 on all psychiatric inpatients and outpatients contacts in Denmark. Age-adjusted incidence rate ratios were calculated for the three diagnostic groups, and rates of employment, education, and disability pension were measured 1 year before and 2 years after the diagnosis for all the incident cases.

Results: The incidence rates increased significantly in all diagnostic groups and both sexes. Comparing the incidence rates in 2013 with 2000 yielded an incidence rate ratio of 1.67 (95% CI 1.51–1.84) for schizophrenic spectrum disorders, 3.82 (95% CI 3.23–4.52) for bipolar affective disorder, and 2.80 (95% CI 2.58–3.04) for recurrent depression. During the same observation period, the employment rates decreased, both 1 year before and 2 years after diagnosis in all three subgroups. In the year 2002, employment rates, 2 years after diagnosis, were 24.6% for schizophrenia spectrum disorder, 35.0% for bipolar affective disorder and 47.1% for recurrent depression. These rates had declined to 15.8%, 26.8%, and 34.7%, respectively, in 2013.

Conclusion: This study of three severe mental illness subgroups shows significant increasing incidence rates and decreasing employment rates both before and after the diagnosis between 2000 and 2013, highlighting the importance of timely and correct volume of the psychiatric treatment and vocational rehabilitation programs.

Introduction

Severe mental illness (SMI) defined as schizophrenia spectrum disorders, bipolar affective disorders, or recurrent depression are serious and often long-lasting disorders causing a high degree of disability. Recent research has reported that the incidence rates of schizophrenia, schizotypal and delusional disorders [1] as well as mood disorders [2] have increased. However, it is unclear if the incidence rates continue to increase and whether similar patterns occur in a narrower definition of mood disorders consisting of bipolar affective disorders (ICD:10; F30 and F31) and recurrent depression (ICD:10; F33), which often are more severe and persistent than the broad definition of mood disorders. Moreover, it is unknown to what extent the newly diagnosed individuals are employed before and after their diagnosis and how time trends in employment have developed while the incidence rates have increased.

It is well documented that SMI is associated with lower levels of employment and imposes substantial costs to society besides the direct expenses of care and treatment [3–8]. At the individual level, implications for being employed can be pervasive as employment provides financial security, gives daily structure, increases the quality of life, and may prevent social exclusion and hospital admissions [9–11]. Employment rates in the prevalent population with schizophrenia vary between 10–20% in the most recent European studies, with a higher level of employment among first-episode patients [4]. Further, the employment rate appears to have declined over the last 50 years [4]. Among people with bipolar disorders, the employment rates vary between 40–60% [8], and slightly higher rates have been observed among people with major depression [7]. Similar to schizophrenia, higher employment rates have been reported in early bipolar disorder than in the later stages of the illness [8]. Although

research has linked SMI to unemployment and loss of productivity, the results differ by type of measurement and estimation methods. These studies typically used a cross-sectional design and faced difficulties trying to obtain reliable diagnoses and representative information on labour market outcomes [4,8].

A longitudinal perspective on incidence and employment rates of SMI is important to assess the expected costs to society and may also provide valuable information for policy-makers and health plan administrators to ensure a timely and correct volume of psychiatric treatment and vocational rehabilitation programs. In addition, during the last decades, there has been a strong focus on education and active labour market policies in Denmark with the implementation of stronger economic incentives to motivate people into employment or start education. Information on the time trends in work may indicate whether this focus has supported specific subgroups to increase the employment and study rates. The time trends in employment and education among the incident cases will moreover indicate the severity of the illness as employment and education can be considered as a proxy for the severity of the illness among the newly diagnosed individuals.

The aim was to investigate time trends in incidence rates in schizophrenic spectrum disorders (ICD-10: F20–F29), bipolar affective disorder (ICD-10: F30, F31), and recurrent depression (ICD-10: F33) and to investigate the rates of employment for all the incident cases. To our knowledge, no previous studies have examined both developments in incidence rates and the labour market attachment of the SMI subgroups using longitudinal register data for an entire country's population.

Methods

Data sources

We used nationwide longitudinal data from 2000 to 2013 on all psychiatric in- and outpatient contacts registered in the Danish Psychiatric Central Register [12] and linked with data from the Integrated Database for Labour Market Research [13,14] using the personal identification number uniquely assigned to all Danish citizens [15].

The Danish Psychiatric Central Register contains diagnostic information on all psychiatric hospital admissions since 1969 and contacts to emergency departments and outpatient clinics from 1995. The Integrated Database for Labour Market Research contains abundant information on individual socio-economic factors including education, work, any kind of work subsidy, cash benefits or early retirement pension, sex, and age. Data are available from 1980 and cover the entire Danish population including the total workforce, and all companies in both the public and private sector [13,14].

Study population and observation period

The entire Danish population born in 1955 and onwards was included and the incidence of SMI was observed during 2000–2013. The year 2000 was chosen as the start year for the observation period to avoid the first 6 years after the diagnostic criteria were changed from ICD-8 to ICD-10 in 1994. The included diagnoses for SMI are presented in Table 1.

The following exclusions were made:

- Individuals diagnosed before the year 2000 (based on either ICD-10 or equivalent ICD-8 diagnoses)
- Individuals diagnosed before the age of five (considered the earliest possible age for obtaining an SMI diagnosis)
- Individuals diagnosed before the age of 18 were excluded from all analyses on labour market attachment to ensure they had completed mandatory primary school and were entitled to cash benefits or at least minimum wage in their line of work.

Measures and statistical analyses

Incidence rates were calculated as the number of new incident cases divided by the total number of person-years for each year during the observation period and presented per 100,000 person-years for the three diagnostic groups stratified by age (5–19, 19–25, 25–34, 34+) and sex. Log-linear Poisson regression was used to analyse age-adjusted incidence rate ratio for the three diagnostic groups, with the logarithm to the person-years as an offset variable stratified by sex. Wald's estimates were used to calculate all 95% confidence intervals. Among incident cases, the annual prevalence of labour market attachment was calculated 1 year before the date of diagnosis and 2 years after diagnosis (i.e. if a person is employed, unemployed, studying, outside the labour market [pension and early retirement pension] and disability pension). Finally, the employment rates (defined as competitive employment during most of the follow-up month) were estimated for the entire Danish working-age (18–65 years) population from 2000 to 2013.

Results

During 2000–2013, a total of 25,671 individuals were diagnosed with a schizophrenia spectrum disorder, 10,013 with bipolar disorders, and 34,299 with recurrent depression. In each of the three diagnostic groups, the total annual incident cases increased over the observation period (Figure 1).

Table 1. Severe Mental Illness (SMI) diagnoses according to International Classification of Diseases (ICD) version 8 and 10.

Included diagnoses	ICD-10	ICD-8
Schizophrenia spectrum disorders	F20–F29	295.x9, 297.x9, 298.29-298.99, 299.04, 299.05, 299.09.
Bipolar affective disorder	F30, F31	296.x9, 298.19
Recurrent depression	F33	296.09, 296.29, 298.09, 300.49

Incidence rates per 100,000 person years for schizophrenia spectrum disorder among women

Incidence rates per 100,000 person years for schizophrenia spectrum disorder among men

Incidence rate per 100,000 persons years for bipolar affective disorder among women

Incidence rates per 100,000 person years for bipolar affective disorder among men

Incidence rates per 100,000 person years for recurrent depression among women

Incidence rates per 100,000 person years for recurrent depression among men

Figure 1. The incidence rate per 100,000 person-years stratified by gender and age.

Schizophrenia spectrum disorders

In the year 2000, a total of 1388 individuals were diagnosed with a schizophrenia spectrum disorder which increased to 2447 individuals in the year 2013. Incidence Rates (IR) increased in both genders and all age groups except in the group above 34 years (Figure 1). The highest IR was observed in the age group 19–25 years; IR increased from 128 to 235 per 100,000 PY in males and 87 to 171 per 100,000 PY in females. A small decrease in IR was found in the age group above 34 years; from 53 to 48 per 100,000 PY in males and 49 to 33 per 100,000 PY in females. When combining all age groups, a significant increase in the IRR was found in both sexes. Comparing the incidence rate in 2013 with the incidence rate in 2000 yielded an IRR of 1.67 (95% CI 1.51–1.84) for females and 1.55 (95% CI 1.42–1.70) for males.

There was a decline in the employment rate from 1 year before the diagnose of a schizophrenia spectrum disorder compared with 2 years after. In 2010 the proportion employed 1 year before the diagnosis was 27.4%. 3 years after in 2013 the rate was 15.8% (Figure 2). In the same period, we found an increase of 9.8% in the number receiving a disability pension. Moreover, there was a decrease in the proportion employed from 2000 to 2013, both 1 year before and 2 years after the diagnosis. In the year 1999, 1 year before diagnosis, 44.8% were employed. This had decreased to 27.4% in 2010 (Figure 3). The same tendency was seen 2 years after the diagnosis where a decrease from 24.6% to 15.8% was found, corresponding to a difference of 8.8% in the employment rate. In the Danish background population, the employment rates declined from 76% to 72% during the same period.
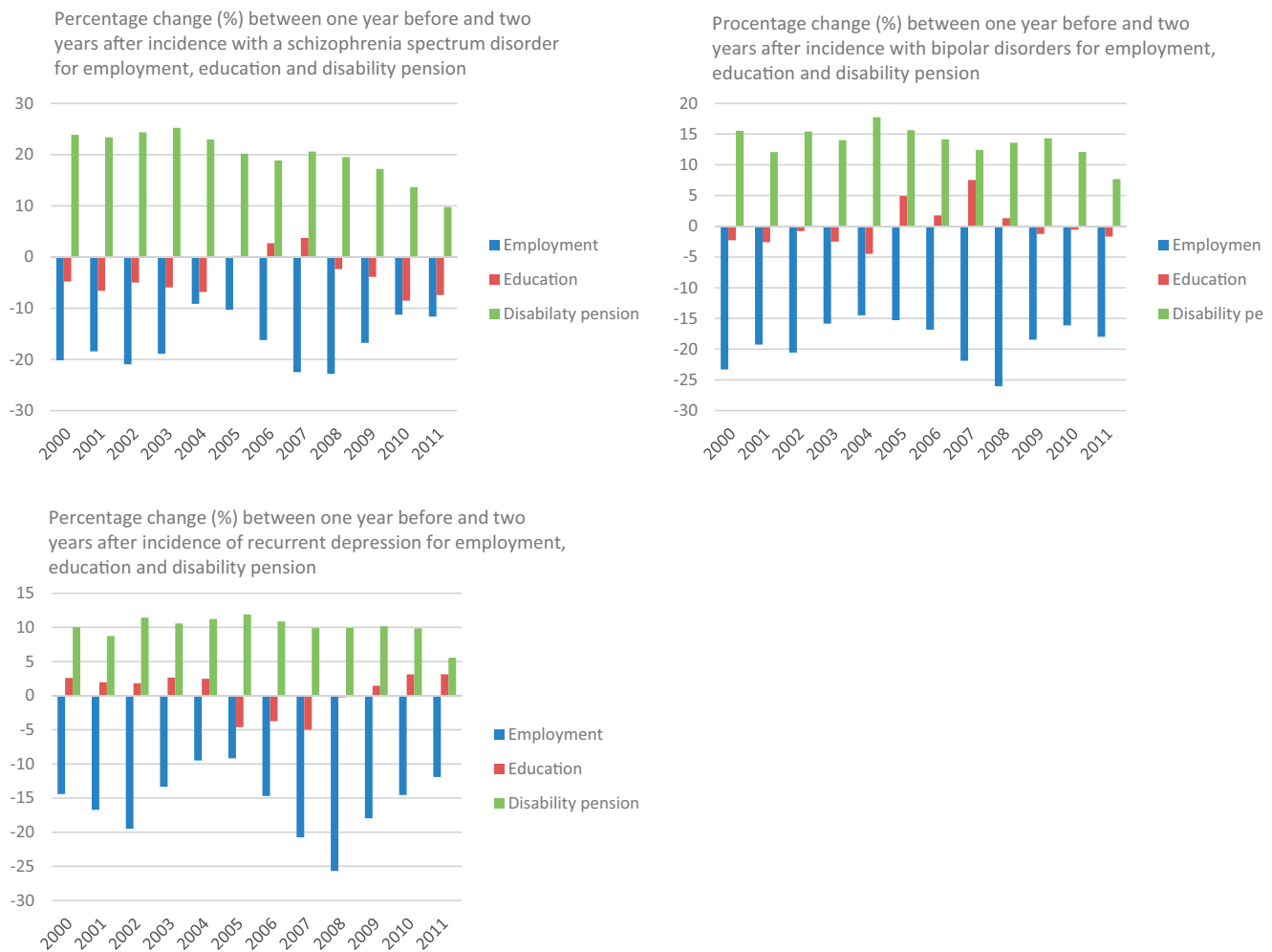
Figure 2. Percentage change between 1 year before and 2 years after incidence with a severe mental illness.

Bipolar disorder

The annual number of new cases of bipolar disorder increased from 315 to 1366 incident cases during the observation period. The IR per 100,000 PY increased in both genders and all age groups (Figure 1). When combining all age groups and comparing the incidence rate in 2013 with the incidence rate in 2000 we found an IRR of 3.82 (95% CI 3.23–4.52) for females and 2.93 (95% CI 2.45–3.51) for males.

Individuals diagnosed with bipolar disorder were overall more likely to be employed both before and after the diagnosis compared with individuals diagnosed with a schizophrenia spectrum disorder. However, the differences between 1 year before and 2 years after the diagnosis were greater. In the year 2010, 44.8% were competitively employed. 3 years after this number decreased to 26.8%, giving a difference of 18.0% (Figure 2). In the same period, the number receiving disability pension had increased from 13.0% to 19.8%. There was also a decrease in the proportion employed from 2000 to 2013. 1 year before and 2 years after the incidence the employment rates dropped from 58.3% to 44.8% (13.5%) and from 35.0% to 26.8% (8.2%) respectively (Figure 3). In the same period, the rates of education increased by 6.6% and 8%.

Recurrent depression

The highest number of annual new cases was found for recurrent depression with an increase from 1133 to 3895 during the observation period. The IR per 100,000 PY increased in both sexes and all age groups (Figure 1). We found the highest IR in 2013 among females in the age group 19–25 and 25–34 with an IR of 258 and 281 per 100,000 PY, respectively. When combining all age groups and comparing the incidence rate in 2013 with the incidence rate in 2000 we found an IRR of 2.80 (95% CI 2.58 to 3.04) for females and 2.95 (95% CI 2.63 to 3.30) for males.

People with recurrent depression were overall more likely to be employed both 1 year before and 2 years after the diagnosis, compared with the two other diagnostic groups (Figure 3). However, there was also a decrease in the proportion employed from 2000 to 2013. 1 year before the incidence of recurrent depression, the employment rates dropped from 61.5% to 46.6% corresponding to a difference of 14.9%. 2 years after the rates dropped from 47.1% to 34.7% corresponding to a difference of 12.4% (Figure 3). In the same period, the proportion of people enrolled in education increased. However, the increase in education was lower than the decline found in employment rates.
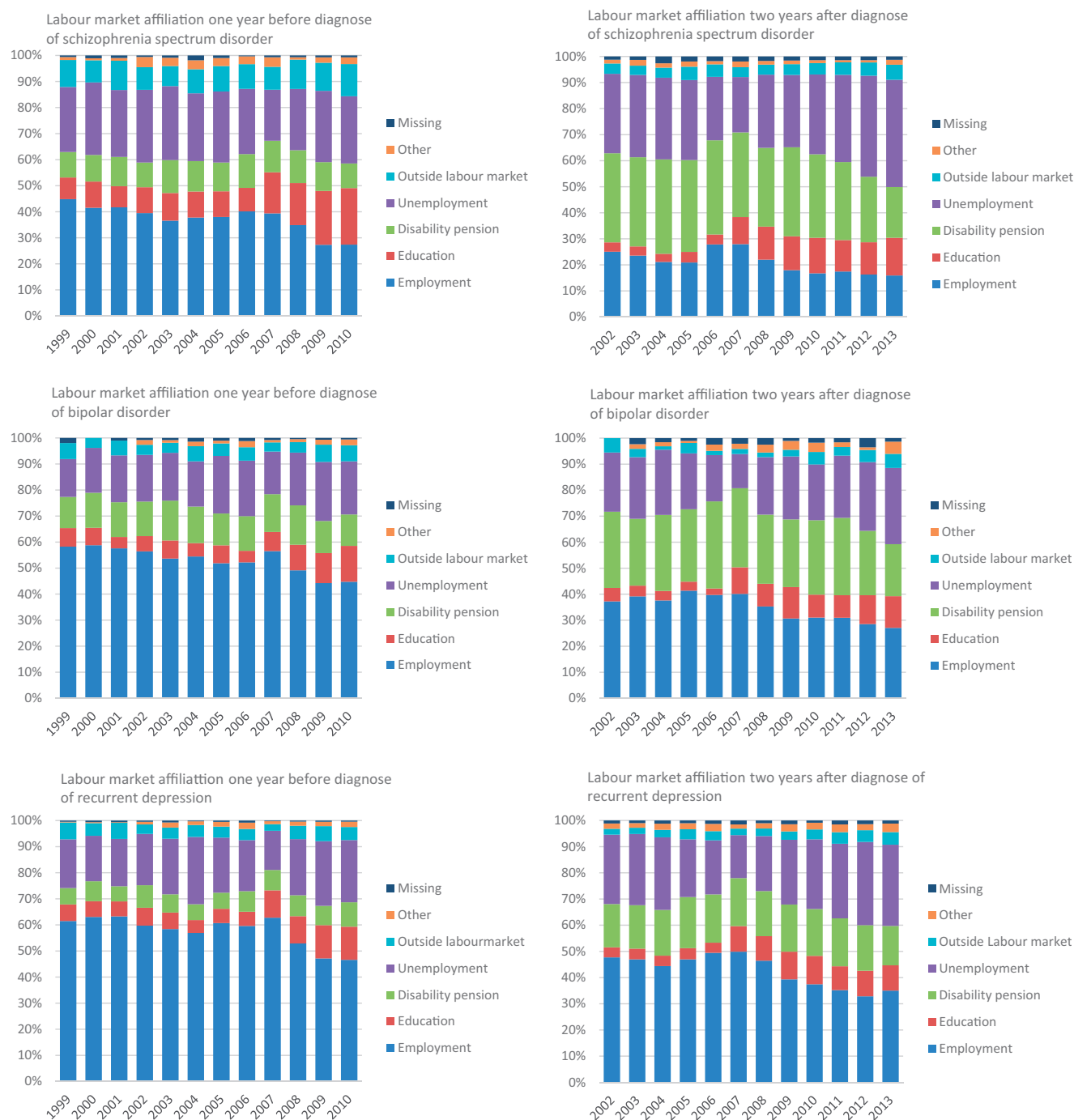
Figure 3. Labour market affiliations 1 year before and 2 years after diagnosis.

Discussion

In this register-based study, we found a significant increase in the incidence rates in three SMI subgroups in a representative Danish sample, and among the incident cases, we found a decline in the employment rates both before and after the diagnosis from the year 2000 to 2013. This decline was more than twice as high as in the background population. Moreover, a marked decline in the employment rates, from 1 year before to 2 years after the diagnosis, was found in all diagnostic groups.

This study supported the emerging evidence that the incidence of mental illness is increasing, despite the inclusion of

more recent data and the definition of severe mental illness being more narrowly defined [1,2]. The increasing incidence of bipolar disorder and recurrent depression in both sexes was driven by the increase in the age groups 19–25, 25–34 and 34+. Whereas the increased incidence of schizophrenia spectrum disorders was mainly driven by the increase observed in the age group 19–25 years. In line with previous research, we found that the majority of people diagnosed with recurrent depression or bipolar affective disorder were females, while the majority of people diagnosed with schizophrenia spectrum disorders were males [16–18]. The possible explanations for the gender gap in depression have in

previous research been identified as manifold and include both biological, sociological, and psychological explanations [19]. Moreover, there is a substantial body of research showing that there is a gender difference in help-seeking behaviours [20]. Females are more likely to report depressive symptoms and to seek medical help. Empirical evidence shows that low treatment rates for men cannot be explained by better health, but must be attributed to a discrepancy between the perception of need and help-seeking behaviour [21].

Given the nature of this study, we cannot determine if the changes we found in the incidence rates were true changes or due to changes in the diagnostic criteria used. We chose the starting point of the study to be the year 2000 to avoid the first years after the diagnostic criteria were changed from ICD-8 to ICD-10 in Denmark. Thus, it would be reasonable to assume that at this point the ICD10 was well implemented and we do not have indications that the criteria for diagnosing have changed over the study years. However, the increased incidence may be caused by a stronger focus on early detection and prevention of mental illness as well as an expansion of the treatment capacity. In 2001, the Danish health authority initiated an extension of child and youth psychiatry, with recommendations that the national hospital system should provide diagnostics and treatment for all patient categories within the age groups 0–18 years old. As a result, the number of patients in child and adolescent psychiatry increased by 165% from 2001 to 2011, and the number of outpatient visits doubled [22]. In the same period, the number of patients raised by 25% in adult psychiatry and the capacity to offer treatment for newly diagnosed patients with first-episode psychosis in the schizophrenia spectrum increased tenfold [23]. A similar development occurred in the social sector in the municipalities where there has been a reorganization of the capacity to a stronger focus on preventive and early interventions [24]. This focus on early detection, prevention and increased treatment capacity may have resulted in more people being diagnosed. However, increased awareness may also have prevented children and adolescents from developing psychological problems that required further treatment and prevented the incidence of a severe psychiatric diagnosis. Besides the expansion of treatment capacity, increased substance abuse could be another explanation of the increased incidence rates, as cannabis use has increased among people aged 16–24 years in the study period. In the year 2000, 13.5% had a recent use, and this increased to 17.6% in 2013 [25]. The number of people in substance abuse treatment almost doubled in the same period [25]. There is evidence of an increased risk of psychosis of 41% in people who have ever used cannabis compared with non-users but the evidence for affective outcomes is less strong [26]. However, the relatively small increase in young people using cannabis and the expected effects on mental health can not explain the magnitude of increases in incidence rates observed in this study.

The results of this study do not indicate that the increasing incidence was caused by less severe disorders being wrongly over-diagnosed. If this was the case, it seems reasonable to assume that the newly diagnosed would have a higher functional level, which then would have been reflected in higher employment rates. This was not the case. While there was an increase in the incidence rates in SMI from 2000 to 2013, there was also a decrease in the employment rates, both before and after the diagnosis, ranging from 8% to 21% in the three diagnostic groups. In the Danish working-age background population, there was a decrease of 4% in the same period. This decrease can mainly be explained by the recession starting in 2008, but it seems that the impact of the recession was higher among people with SMI compared with the background population. Moreover, the strong focus and investments in education in the Danish labour market policy seems to have worked as intended for the SMI group, as more people entered education in the observation period. However, the active labour market policy with stronger financial incentives to employment seems not to have been equally successful.

Strengths and limitations

The major strength of the present study was that we used representative longitudinal register data for an entire country's population giving valid information on time trends in both incidences- and employment rates. We excluded all individuals who previously have had psychiatric contact and were diagnosed with one of the included diagnoses, which ensured that the cases included represented first-time diagnosed cases. Moreover, in contrast to previous research, we measured the employment rates among the incidence cases to obtain an indication of whether the increases in IR were due to less severe cases being diagnosed.

Limitations of this study should also be mentioned. Firstly, contacts to primary care, that is, general practitioners, private psychiatrists and psychologists or support from the municipality were not included. However, Danish health authorities consider people with SMI as primary targets in the secondary health sector. Hence, only a small group of patients will obtain an SMI diagnosis in primary health care. Secondly, the Danish Psychiatric Central Register does not contain diagnostic information on hospital admissions before 1969. This means that the oldest cases were 14 years when the registration started and could have had the diagnosis before they entered the study. In addition, the register does not contain information on outpatient contact before the year 1995. However, before the year 1995 the outpatient services were limited in Denmark. Thirdly, we did not adjust for well-known risk factors as ethnicity, substance use, migration, or the general increase in any psychiatric disorder. This may have indicated some of the reasons why the incidence rates increased. Lastly, we did not have a matched control group which could have provided more valid information on the differences in labour market attachment between the SMI subgroups and the background population.

Conclusion and future perspectives

To conclude, we found a significant increase in the incidence rates in three severe mental illness subgroups, and among the incident cases, we found a decline in the employment rates both before and after the diagnosis and from the years 2000 to 2013. Although the present study answered many questions, an important question to be answered is how the Danish mental health services and national job centres can support that more people are employed after the incidence of severe mental illness. The results of this study highlight the importance of timely and correct volume of the psychiatric treatment and vocational rehabilitation programs and that the period around the diagnosis is crucial to prevent exclusion from the labour market. Previous reports have concluded that the disintegration of psychiatric treatment and employment services is one of the main barriers to labour market inclusion in Denmark [27]. Hence, an early integrated vocational intervention for all three subgroups of SMI is needed. The integrated vocational rehabilitation program, Individual Placement and Support (IPS) might be the solution as research has demonstrated a significant vocational effect of this intervention when provided to unemployed people with a severe mental illness [28,29].

Ethical approval

The study was conducted with permission from the Danish Data Protection Agency. Since data were exclusively obtained from registers approval from the national committee on health research ethics was not necessary.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

Data will not be shared due to restrictions from the Danish protection agency.

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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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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 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 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].

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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 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 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.

2. 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 ≥ 73 on the IPS-25 scale, and ≥ 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

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

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 con-sensus. 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 raw-data 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 inde-pendently assessed the included studies, and consensus was reached through discussion. It was not possible to blind par-ticipants 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

Fig. 1 PRISMA 2009 Flow Diagram
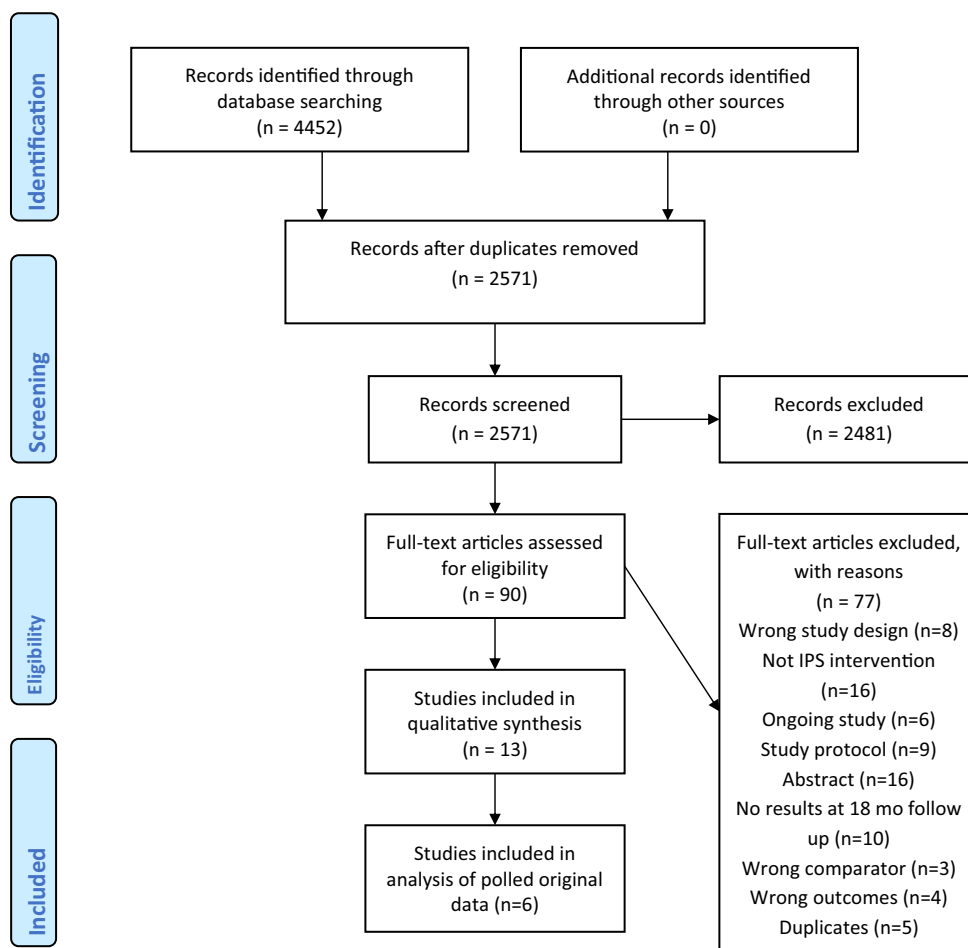
to the intervention not being IPS, or the record being a conference abstract. This left us with 13 studies based on 13 trials including 3406 participants (see Appendix Table B for characteristic of studies).

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].

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

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

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 OR/EMD (95% CI)	p-value	Adjusted OR/EMD (95% CI)	p-value
All (n = 1594)						
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

[a]OR

[b]EMD, adjusted for: age, gender, study and site

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.

Fig. 2 Time until employment
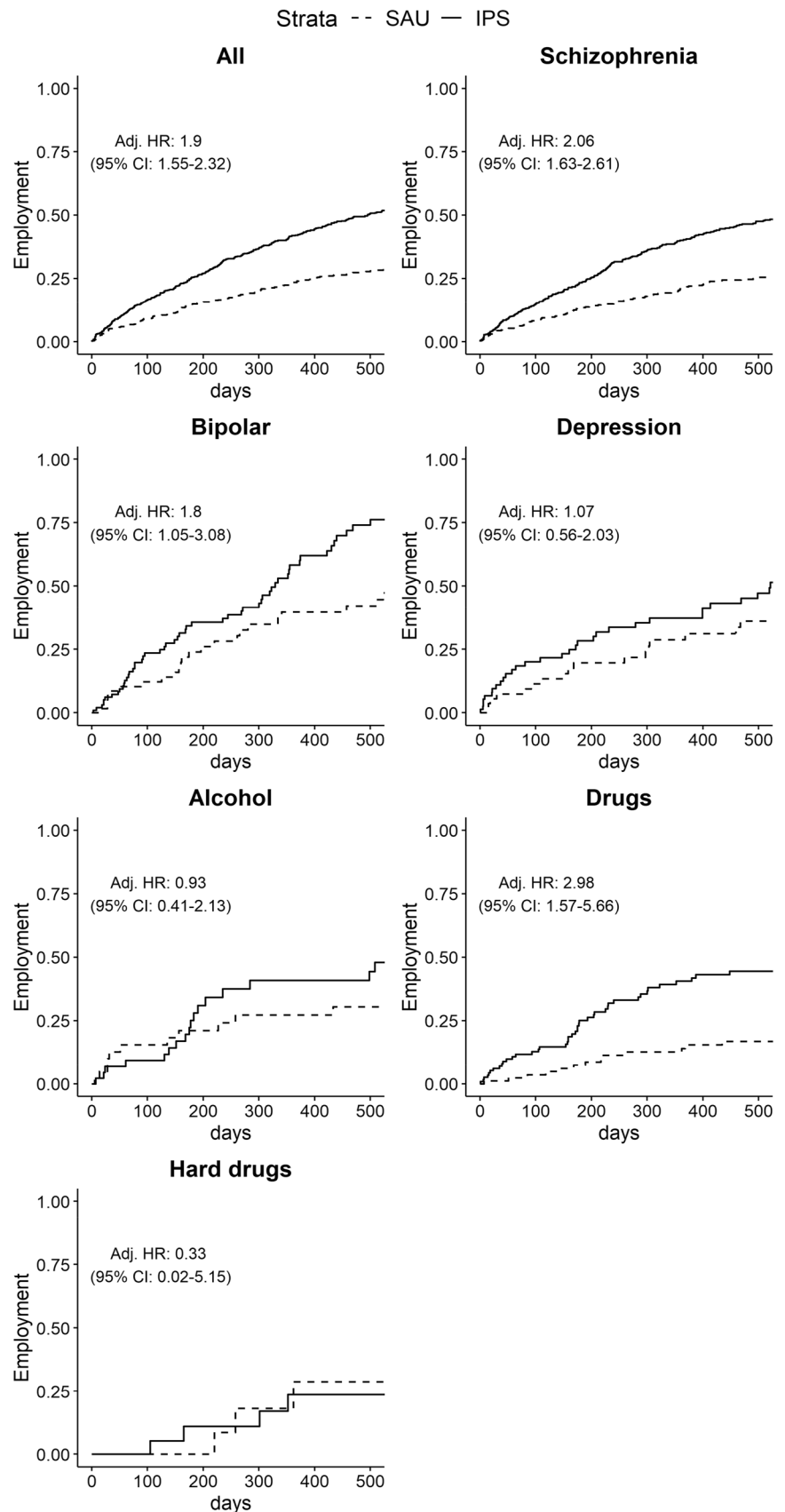
Overall, IPS was more effective in helping participants obtain competitive employment, work more hours and weeks, and get work faster than SAU. The magnitude of these effects was similar in participants with schizophrenia and bipolar disorder but only statistically significant for those with schizophrenia. 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 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 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.

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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TRIALS

The effect of IPS-modified, an early intervention for people with mood and anxiety disorders: study protocol for a randomised clinical superiority trial

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Abstract

Background: Anxiety and affective disorders can be disabling and have a major impact on the ability to work. In Denmark, people with a mental disorder, and mainly non-psychotic disorders, represent a substantial and increasing part of those receiving disability pensions. Previous studies have indicated that Individual Placement and Support (IPS) has a positive effect on employment when provided to people with severe mental illness. This modified IPS intervention is aimed at supporting people with recently diagnosed anxiety or affective disorders in regaining their ability to work and facilitate their return to work or education.

Aim: To investigate whether an early modified IPS intervention has an effect on employment and education when provided to people with recently diagnosed anxiety or affective disorders in a Danish context.

Methods/Design: The trial is a randomised, assessor-blinded, clinical superiority trial of an early modified IPS intervention in addition to treatment-as-usual compared to treatment-as-usual alone for 324 participants diagnosed with an affective disorder or anxiety disorder living in the Capital Region of Denmark. The primary outcome is competitive employment or education at 24 months. Secondary outcomes are days of competitive employment or education, illness symptoms and level of functioning including quality of life at follow-up 12 and 24 months after baseline.

Discussion: If the modified IPS intervention is shown to be superior to treatment-as-usual, a larger number of disability pensions can probably be avoided and long-term sickness absences reduced, with major benefits to society and patients. This trial will add to the evidence of how best to support people's return to employment or education after a psychiatric disorder.

Trial registration: NCT01721824

Keywords: Supported employment, Affective disorder, Anxiety, Competitive employment, Mentor support

Background

Anxiety and affective disorders are often associated with functional disability and can have a major impact on the ability to work [1-4]. Through the 1990s, depression alone was responsible for an annual loss of US$ 17 billion due to work absenteeism and a total cost of US$ 43.7 billion (34.8 billion Euro) each year in direct and indirect societal costs in the USA [4]. In Denmark, mental health problems account for a total of 7.3 billion Euro each year in direct and indirect societal costs [5]. Disability pension and long-term sickness absence account for the majority [5,6]. A significant amount of the total sickness absence in Denmark is due to mental illness, and disability pensions are increasingly awarded due to non-psychotic mental illness [6,7]. Hence it is crucial to start initiatives to support patients with mental health problems in retaining or regaining their employment or education.

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The Individual Placement and Support (IPS)-modified, early intervention for people with mood and anxiety disorder (IPS-MA) is an individualised supported employment intervention, aiming at supporting people with recently diagnosed anxiety or affective disorders to obtain and sustain competitive employment through mentor support. It was created in 2011, based on the experience of a 1-year pilot study, aspects from the supported employment intervention IPS and findings from the literature. The method has never been investigated in a clinical trial.

A recent systematic review of randomised trials as well as controlled non-randomised cohort studies [8] found an overall lack of evidence concerning vocational rehabilitation for patients with recently diagnosed bipolar disorders, depression or anxiety disorders, but points to three important initiatives to consider: preventive interventions, return-to-work interventions and interventions concerning short- or long-term loss of employment. Preventive interventions have only been investigated for patients with depression or depressive symptoms, and show evidence in favour of individualised interventions [9-11]. Considering return to work interventions, studies suggest that an individual intervention should be combined with work-place interventions in close collaboration with mental health services [4,12,13]. Returning to work when diagnosed with depression, anxiety or bipolar disorders is also affected by personal and social factors; hence, it is important to incorporate interventions supporting these matters.

Today, vocational rehabilitation mainly consists of two different approaches: pre-vocational training, often referred to as the train-and-place model, and supported employment, referred to as place-and-train [14]. With pre-vocational training, people are trained in company internship programmes, sheltered workshops or wage-subsidised jobs before obtaining competitive employment. Supported employment aims at a rapid search for competitive employment, with on-going support after employment. In Denmark pre-vocational training is still standard.

The most intensively studied supported employment intervention is IPS [15,16], where job consultants are integrated in and act in close collaboration with the mental health services. Several randomised trials [14,17-27] have indicated that IPS is more effective in helping patients with severe mental illness obtain and sustain competitive employment compared to traditional pre-vocational training. A meta-analysis [28] of four randomised trials [29-32] found that, after 18 months, 70.4% had obtained competitive employment in the IPS group compared to 24.3% in the control group. In a review including 11 randomised trials comparing IPS to traditional pre-vocational training, 61% of the patients obtained competitive employment in the IPS group versus 23% in the control group [15]. No studies were found investigating the effect of IPS when provided to people with recently diagnosed affective or anxiety disorder. It is recommended that the intervention be modified and accommodated to psychosocial and medical aspects, and thoroughly investigated in order to show an effect when offered to, for instance, patients with recently diagnosed anxiety or affective disorders [16]. Further studies are needed in order to investigate the effect of such interventions, in addition to mental health treatment, on people's return to work.

Sherpa ran the pilot study, from October 2010 to September 2011 (unpublished data), during which 46 patients with depression, anxiety or a bipolar disorder were referred to Sherpa from two mental health centres in Copenhagen. Two mentors and a career counsellor were employed at the time. Twenty of the participating patients had obtained either employment or education after a median of 4.2 months (range 1 to 8 months).

The above-mentioned findings from the literature, aspects from the IPS, and the experiences from the 1-year pilot study led to the creation of IPS-MA in 2011.

The IPS-MA is an individualised supported employment intervention, considering personal and social factors, as well as career counselling and financial guidance. Focus is on a rapid search for competitive employment or education, and not sheltered workshops or long internship programmes. Since people with affective disorders or anxiety are treated by either their general practitioner, psychiatric private practitioner or in mental health centres in Denmark, it is difficult to integrate IPS-MA with treatment to the same extend as in IPS. According to IPS-MA, mentors must have an assertive approach to mental health carers and social workers, and collaborate with mental health services as well as job centres and municipalities, and thereby help coordinate services provided by these.

This is the first trial comparing the effect of IPS-MA to treatment-as-usual when provided to people with recently diagnosed anxiety or affective disorders. The hypothesis is that more people receiving IPS-MA will return to work or education compared to the control group.

Methods
Design
The Sherpa trial is a randomised, assessor-blinded, clinical superiority trial comparing IPS-MA in addition to treatment-as-usual with treatment-as-usual alone in 324 patients recently diagnosed with an affective disorder or an anxiety disorder (Figure 1).

Participants
Participants will be recruited from Mental Health Centres and private practising psychiatrists within the Capital Region of Denmark from 1 October 2011 until 31 January 2014. Inpatients as well as outpatients are eligible.

Figure 1 Flow chart for participants in the trial.
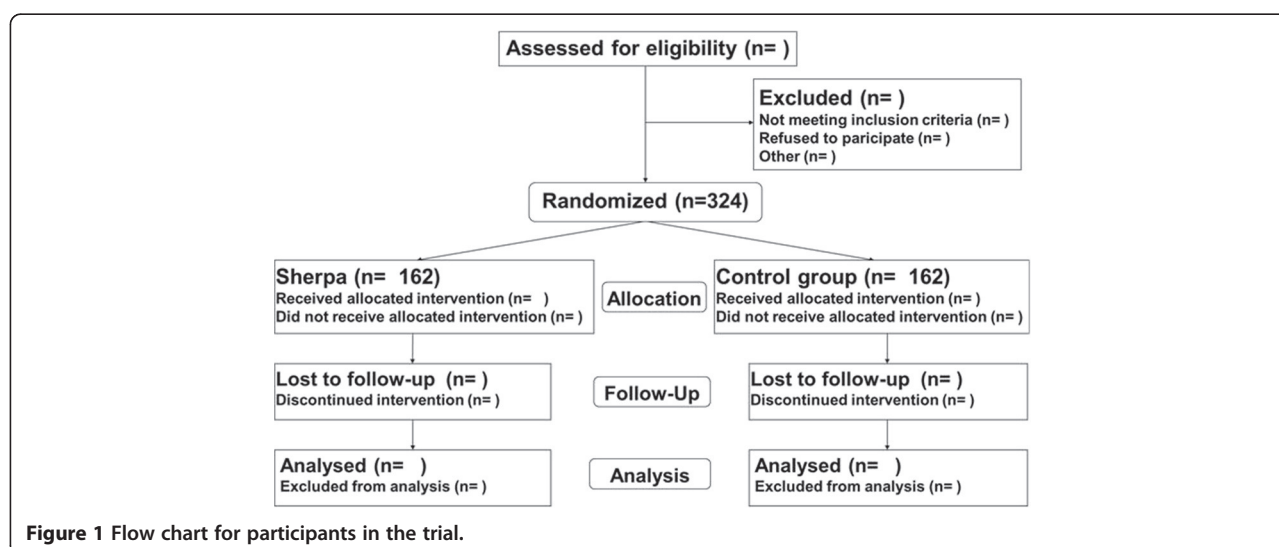
Inclusion criteria

Participants must be aged 18 to 60 years, diagnosed by the referring psychiatrists according to the International Classification of Diseases 10th edition criteria of affective disorders (F30-39) or anxiety disorders (F40-41), and not have had contact with mental health services for more than 3 years. They must have been employed or enrolled in education at some time during the past 2 years. They must have a pronounced wish to return to either employment or education, but not being ready to do so within the following 3 months, and equal to 'match group' 2 or 3. ('Match groups' are categories used by the job centres in Denmark [33] to estimate how far people are from the labour market. Match group 2 refers to people who can participate in pre-vocational training or courses, but who would not be able to take an ordinary job and be off social benefits within 3 months. Match group 3 refers to people with problems so severe that they cannot work or participate in pre-vocational training). Participants must have the ability to read and understand Danish, and give informed consent verbally and in writing.

Exclusion criteria

Participants will be excluded if they have somatic co-morbidity causing reduced ability to work, primary large-scale alcohol or substance abuse, a legal guardian, forensic psychiatric arrangements, or if they do not give informed consent.

Recruitment and randomisation

Eligible patients are informed about Sherpa, given the written information, and subsequently referred to Sherpa by their psychiatrists, nurse or social worker. A Sherpa employee calls the patient to make an appointment for inclusion and baseline interview. The assessor will interview the participants, but a Sherpa mentor will always attend the interview in order to manage the randomisation after the assessor has left and inform the participant about allocation. When a participant is included in the trial, central randomisation is performed when the Sherpa mentor calls the Copenhagen Trial Unit and gives the relevant participant information.

Randomisation is performed according to a computer-generated allocation sequence with a varying block size concealed from the investigators. The randomisation is stratified by a) four diagnoses (F31: Bipolar affective disorder; F30, F32-39: Affective disorders; F40: Phobic anxiety disorders; or F41: Other anxiety disorders), and b) two match groups (match group 2 or 3).

Blinding

It is not possible to blind the participants, the Sherpa mentors, or career counsellors, practitioners and carers who deliver the intervention. However, they are strongly urged not to reveal the allocation to the rest of the research team. The assessor and research team will be blinded to the allocated intervention group throughout the entire trial period. Should blinding be violated, a second assessor will complete the follow-up interview. Furthermore, during statistical analyses, the two intervention groups will be coded as, for example, X and Y, and the code will not be broken until the research team has drawn two conclusions; one assuming X is the intervention group and Y is the control group, and one conclusion assuming the opposite.

Interventions
The experimental intervention

Participants randomised to the Sherpa group will be offered IPS-MA in addition to treatment-as-usual (see description for the control group). A Danish protocol describing the

IPS-MA method can be acquired by contacting the corresponding author. An English version is under construction. The IPS-MA method is based on eight principles: 1) Sherpa is the patient's advocate, not an authority or a healthcare provider; 2) the process is led by the individual's goals and focus is on patient resources; 3) assistance is flexible, without time limits, and responsive to the needs of the patient; 4) the goal is competitive employment or education, without pre-vocational training; 5) the belief is that returning to work is possible despite a mental illness, but therapeutic recommendations in terms of postponement are acknowledged; 6) liaison with healthcare and social workers ensures a coordinated service; 7) a meaningful and realistic career plan will be developed and evaluated continuously after job start; and 8) Sherpa is an interdisciplinary team, which will be reflected in the assistance of each individual.

Five basic services comprise IPS-MA:

1) *Individualised mentor support based on psychiatric knowledge.* Sherpa mentors all have a background as professionals in mental health services. In cooperation with the participant, the Sherpa mentor helps develop a plan of action in which resources and problems in social life as well as working life are clarified. The Sherpa mentor supports the participant in how to structure and manage everyday life, renew contact with friends and/or family, prepare important meetings and live a healthy everyday life with the disorder. The Sherpa mentors very often act as lay representatives for the participants at meetings at the local job centres or municipalities.

2) *Coordination of services provided by Sherpa or external providers.* Through their professional skills, Sherpa mentors help avoid lack of coordination and unnecessary waiting time and make sure that all available services are provided. Sherpa mentors have an assertive approach to mental health carers and social workers and thereby ensure that relevant information is distributed between services.

3) *Career counselling.* Professional career counsellors support participants in creating a realistic match between their competences and the demands of the job market. Participants will be given advice on how to write a curriculum vitae and job applications, on job seeking strategies, and help in practicing job interviews and negotiating employment contracts.

4) *Impartial help to clarify private economy* is offered by a consultancy firm, the Settlement [34], run by volunteers. The firm consists of two employees and a group of volunteers with professional backgrounds in economics, law and social counselling.

5) *Contact with employers* to help participants obtain jobs, and keep them.

Participants are provided with a Sherpa mentor who will be their mentor throughout the entire intervention period. The search for job or education will commence as soon as possible. Mentor support will continue for as long as needed after employment or education is started. During the first 6 months, the participant and mentor most often meet once a week for 1 to 1.5 hours on average. After 6 months the number of contacts varies and can be by telephone or email. The number and duration of contacts depend on the needs of the participant. Each mentor has a maximum caseload of 20 participants, half of which have been in Sherpa for more than 6 months.

Sherpa team

The Sherpa team is an interdisciplinary team, consisting of six mentors and two career counsellors. Sherpa mentors all have solid experience as health professionals in mental health services and include one nurse, two social workers and three occupational therapists. Career counsellors have worked as career counsellors, or with recruitment or human resources in the private business sector. Sherpa mentors and career counsellors work closely together and share offices.

Training and supervision

Newly appointed Sherpa mentors will have a 1-week introduction to working routines, and will attend a 2-day workshop introducing the IPS-MA method. Mentors with experience in the method will conduct the introduction. Team members are furthermore obliged to participate in annual refresher courses.

Team members will have monthly supervision provided by a trained psychologist.

The control group

Participants randomised to the control group will receive 'treatment-as-usual' as offered by the job centres in Denmark [35]. Services vary according to match group and the participant's possibilities for social support. Participants receiving sickness benefits must attend their first meeting in the job centre within 8 weeks of sickness leave. Match group 2 participants attend follow-up interviews every 4 weeks, whereas match group 3 participants attend follow-up interviews every 3 months. Participants on social security will attend job-seeking interviews every 3 months.

Participants under the age of 30 have the right and obligation to participate in pre-vocational training after no more than 13 weeks of unemployment. Pre-vocational training has to last for at least 6 months. Young participants must not be without some sort of pre-vocational training for more than 4 weeks. Participants over the age of 30 have the right and obligation to participate in pre-vocational training after no more than 9 months of unemployment.

After an individual evaluation, job centres can offer certain pre-vocational training services: company internship programmes in public or private companies as well as in sheltered workshops, wage subsidy jobs, skill development and guidance, and mentor support (often offered by a colleague who helps the participant adapt to the new workplace regarding norms and social competences). Participants receiving sickness benefits can be provided with gradual return to employment, assistive tools, a personal assistant or reimbursement of sickness benefits to the employer from the first day of sickness leave [35].

Participant withdrawal

Participants can choose to withdraw from the trial at any time during the intervention period, without it having any consequences for the treatment they will receive, but they will politely be reminded of the importance of their participation. Participants who choose to withdraw from the trial are asked to specify which aspects of the trial they withdraw from: participation in the experimental intervention, participation in the follow-up interviews, use of data collected at central registers, or complete withdrawal including use of already collected data.

Fidelity

To ensure that the services provided by Sherpa are in concordance with the IPS-MA method, an independent investigator will monitor fidelity to the IPS-MA method twice during the first year of the intervention, and subsequently once every year. Fidelity will be monitored using the IPS-MA Fidelity Scale (unpublished, available through corresponding author) by interviewing participants, mentors, and career counsellors, observing team-meetings and meetings between mentor and participant, as well as examining the individual plans of action and the data management systems used. The IPS-MA Fidelity Scale was developed based on the IPS Fidelity Scale [36]. Core elements important to the IPS-MA method investigated are: caseload, mentors' and career counsellors' roles, interdisciplinary team with group supervision, individualised mentor support, development and evaluation of individual plans of action, coordination of services, providing career and economic counselling, focus on rapid search for ordinary employment or education, no time limitations, and individualised support for the participants and their employers, community-based services, assertive engagement and outreach.

Assessments

Participants will be interviewed and asked to fill in questionnaires at baseline and at follow-up after 12 and 24 months. At baseline, socio-demographic information on education, income base, marital status, number of children and somatic disease will be collected.

To confirm the diagnosis, the Mini International Neuropsychiatric Interview (MINI) [37] is used at baseline. Baseline interviews will always be face-to-face, most often in the participants' home. Participants will fill in questionnaires at home.

Outcomes

The primary outcome is competitive employment (including being on rehabilitation benefits, flexible jobs, and wage-subsidised jobs) or education at 24 months. Information about employment and education will be extracted from the DREAM database [38]. The database is administered by The National Labour Market Authority and contains information on employment, sickness leave, and education eligible to state education grant, pre-vocational training, disability pension, social security, and sickness benefits.

Secondary outcomes are: 1) number of days of competitive employment or education; 2) level of symptoms assessed by the Hamilton Depression Scale (HAM-D6) [39,40]; 3) level of symptoms assessed by the Hamilton Anxiety Scale (HAM-A6) [39,41]; 4) level of functioning assessed by The Global Assessment of Functioning (GAF) [39,42,43]; and 5) level of health-related quality of life by The WHO-Five Well-being Index(WHO-5) [39]. Secondary outcomes are assessed after 12 and 24 months.

Exploratory outcomes are: competitive employment (including being on rehabilitation benefits, flexible jobs and wage subsidy jobs) or education at 12 months, reassignment from Match group 2 or 3 to Match group 1, attending company internship programs in public or private companies as well as in sheltered workshops, and information extracted from the DREAM database. Manic symptoms are assessed by the Bech-Rafaelsen Mania Scale (MAS) [39,44]. Social performance regarding four domains (socially useful activities, personal and social relationships, self-care and disturbing and aggressive behaviour) is assessed by The Personal and Social Performance (PSP) [45,46]. The Sheehan Disability Scale [47] measures functional level regarding social relationships, work, spare time and family. Health-related quality of life in terms of psychological well-being is assessed by the WHO-5 [39,48] and empowerment by the Empowerment Scale [49]. The Changes Questionnaire [50] will be used to assess how motivated participants are as to seeking employment or education. The Client Satisfaction Questionnaire [51] assesses satisfaction with treatment and the EQ-5D (EuroQol) [52] assesses health-related quality of life. The latter of the two will be used in a future health-related cost-benefit analysis. All

scales and questionnaires used for measuring outcomes are validated scales [37,39-47,49-52].

Register-based information

Information on vital status, use of mental health services, both as in- and outpatient, number of days of admission, sickness absence and use of social benefits will be gathered from the DREAM database or the Danish Psychiatric Case Register (DPCR) [53]. DPCR is the patient-registry system used by the mental health services in Denmark; it contains information on all hospital admissions, number and duration, outpatient contacts and deaths.

An overview of all data collected and the source of collection is shown in Table 1.

All data will be handled in accordance with the Danish Data Protection Agency.

Training and inter-rater reliability

Three assessors conduct the interviews: Britt Reuter Morthorst (BM), Marie Lønberg Hansen (MLH) and LH. BM and LH have a masters in health science, and MLH in public health science. BM has 15 years experience as a nurse in mental health, and is an experienced assessor. Assessors have all received the necessary training in the relevant instruments. All assessors have participated in joint ratings for HAM-D and HAM-A with PB. Regarding the MINI, MAS, PSP and GAF, at least seven joint ratings have been conducted in order to ensure inter-rater reliability.

Table 1 Data collection at baseline and follow-up

Source of collection	Assessment	Baseline	12 months follow-up	24 months follow-up
Interview	Hamilton Depression Scale (HAM-D6)	x	x	x
	Hamilton Anxiety Scale (HAM-A6)	x	x	x
	Bech-Rafaelsen Mania Scale (MAS)	x	x	x
	Personal and Social Perfomance scale (PSP)	x	x	x
	Global Assessment of Functioning (GAF)	x	x	x
	Suicidal ideation	x	x	x
Self report	Sheehan Disability Scale (SDS)	x	x	x
	Quality of life (WHO-5)	x	x	x
	Empowerment Scale	x	x	x
	Changes Questionnaire	x	x	x
	Client Satisfaction Questionnaire (CSQ)	x	x	x
	Health-related quality of life EQ-5D (EuroQol)	x	x	x
Hospital records	Number of hospital admissions		x	x
	Length of hospital admissions		x	x
	Use of outpatient services		x	x
	Death (all causes)		x	x
	Suicide		x	x
Dream/interview	Sociodemographic information	x	x	x
Dream	Labour market affiliation	x	x	x
Dream/interview	Civil status	x	x	x
DPCR	First contact with mental health care	x		
Dream/interview	Children	x	x	x
Dream/interview	Education	x	x	x
Dream/interview	Cohabitation status	x	x	x
DPCR	Use of mental health service		x	x
Dream	Number of sick days		x	x
Dream	Use of social benefits		x	x
Self report	Treatment and use of other service from the social and healthcare sector		x	
Self report	Service provided by Sherpa		x	

DPCR, The Danish Psychiatric Case Register.

For the evaluation of inter-rater reliability the intra-class coefficient was used [54]. The level of significance was a coefficient of 0.70 or higher.

LH has participated in joint HAM-D6 and HAM-A6 rating sessions with PB. In total, 28 joint sessions between PB and LH were evaluated and for HAM-D6 the intra-class coefficient was 0.81 ($P < 0.001$). Together LH and BM have seen seven patients in joint training sessions; intra-class correlations were: PSP = 0.92, GAF-Functioning = 0.84, GAF-Symptoms = 0.75.

Power and sample size

We have been unable to find data on how many people actually return to employment or education with traditional pre-vocational training after anxiety or an affective disorder in either the Danish or the national literature. Therefore, we have leaned towards the findings in OPUS, a programme in which young people with schizophrenia receive early intensive treatment for 24 months. In OPUS it was found that 40% returned to employment or education versus 32% in the control group (Merete Nordentoft, personal communication). Based on this knowledge, we conservatively estimate that 30% will regain employment or education following traditional pre-vocational training.

Across a broad range of studies of severe mental illness and IPS versus traditional pre-vocational training, studies show that approximately 50% more of the participants in the IPS groups regain employment compared to the control groups [15]. We therefore expect to find that 50% more of the participants in the Sherpa group compared to the control group will regain employment or education, and have estimated the true difference in the experimental and control group to be 15%-points; hence, 45% of the participants in the Sherpa group will regain employment. To be able to reject the null hypothesis that the proportion of participants who regain employment or education in the experimental and control group is equal with a probability (power) of 80%, 162 participants will be required in each group (total 324). The Type I error probability associated with the test of

this null hypothesis is 5%. We also estimated the sample size using a power of 90%. This resulted in a total of 434 participants (2×217). We therefore plan to recruit a minimum of 324 participants and, in order to reduce the risk of type II error, we will aim to recruit up to 434 participants, if possible, in the 2-year recruitment period. Power and sample size calculations have been made using the PS Power and Sample Size Calculations program version 3.0.14 [55,56].

The power for the secondary outcomes has been estimated based on a number of 162 participants in each group (Table 2). Since it has not been possible to find studies or trials similar to our trial regarding patient group or method, expected effect size concerning number of days in employment or education has been conservatively estimated. The studies found [1,9,19,21,22,57-59] did not find any difference between groups after 12 months considering GAF-F, WHO-5, HAM-D6 or HAM-A6. If we find a difference between groups, we want it to be clinically relevant; therefore, the effect sizes equals the clinically relevant difference.

Statistical analyses

Data analyses will be based on the intention-to-treat principle, which means that data will be included in the group to which the participant was randomised, regardless of intervention received. Data will be analysed using the IBM SPSS Statistics version 20 for Windows.

To assess homogeneity of the two groups at baseline, demographic data such as age, gender, marital status, education level, support (social benefits, social security and so forth), diagnosis and Match group at baseline will be presented.

Dichotomous outcomes will be analysed using logistic regression. For primary and secondary outcomes, an unadjusted analysis of the effect of the Sherpa method as an add-on to treatment-as-usual versus exclusively treatment-as-usual will be carried out, as well as an analysis adjusted for stratification variables (diagnosis and Match group). Multiple multivariate imputations will be used to impute a distribution of missing values.

Table 2 Power calculations for secondary outcomes, calculated from a sample size of 324 participants

Measure	Mean difference	Standard deviation of the pooled mean	Type I error	Reference	Power
No of days of competitive employment of education at 12 months	60 days	150 days	5%	Kin W 2008 [21], Burns 2007 [14]	95%
GAF-F	5	15	5%	Hoffmann 2011 [19], Howard 2010 [58]	85%
WHO-5	10	19	5%	Latimer 2006 [22], Burns 2009 [14]	99%
HAM-D6	2	4	5%	Wang 2007 [10], Lexis 2011 [9], Brouwers 2006 [1], Van Oostrom 2010 [59]	99%
HAM-A6	2	4	5%	Wang 2007 [10], Lexis 2011 [9], Brouwers 2006 [1], Van Oostrom 2010 [59]	99%

GAF, Global Assessment of Functioning; HAM-A6, Hamilton Anxiety Scale; HAM-D6, Hamilton Depression Scale; WHO-5, WHO-Five Well-being Index.

Continuous outcomes will be analysed in a mixed model with repeated measurements. This model is based on the assumption that data are missing at random or missing completely at random [60].

Feasibility

In 2010, 11,712 inpatient visits were registered in the Mental Health Care Centres of the Capital Region of Denmark, not including emergency wards [61]. During the same period of time there were 4,538 first-time psychiatric emergency ward visits in the Capital Region of Denmark [61]. Based on these figures we find it realistic to include a minimum of 324 participants from 1 October 2011 until 31 December 2013.

Each mentor has a maximum caseload of 20 participants per year; six mentors are currently engaged in Sherpa. Thus it is also realistic regarding the capacity of Sherpa mentors to include and complete the intervention for 162 participants in 3 years.

Ethical considerations

All participants in this trial, randomised to experimental as well as control group, are offered treatment according to best practice. The trial will follow international ethical guidelines of informed consent in clinical trials. Participants will receive written and verbal information about the trial so as to be able to give an informed consent. Consent has to be given verbally and in writing. Participation is voluntary, and participants can withdraw their consent at any time during the trial without it having any consequences for their treatment. Previous trials have not found any risks or adverse reactions to the supported employment intervention [19,31,62,63]. If any of the participants present suicidal ideations, the mentor and assessor will make sure that they can be distracted from these thoughts, have a crisis plan, are not alone after the interview and, if in doubt of any of the above, they will offer to follow the participant to the psychiatric emergency ward.

The trial protocol was submitted to the Regional Ethics Committees of the Capital Region for review (journal no: H-2-2011-FSP20). The committee assessed the protocol to be exempt from formal approval, since it is not a biomedical trial. The trial has been reported to the Danish Data Protection Agency (RHP journal no: 2007-58-0015, local journal no: RHP-2011-20) and has been registered at http://www.clinicaltrials.gov identifier: NCT01721824.

Trial status

The trial is on-going; 290 participants have been randomised, and recruitment continues until 31 January 2014.

Discussion

The IPS-MA method is based on a 1-year pilot study and the evidence supporting IPS in other countries. To our knowledge this is the first trial investigating the effect of a supported employment intervention when provided to people with a recently diagnosed affective disorder or anxiety disorder, an area with only sparse knowledge about effective interventions. A strength of the study is the centralised computer-based randomisation which ensures an adequate generation of the allocation sequence and adequate allocation concealment. The use of blinded outcome assessors for the primary outcome and the fact that it is a register-based outcome as well as the use of intention-to-treat analysis decreases the risk of biased effect estimates. The trial is registered at http://www.clinicaltrials. gov, which helps preventing selective and incomplete outcome reporting. The primary outcome is register-based, which ensures almost complete follow-up due to the comprehensiveness of Danish registers.

The fact that we monitor fidelity to the IPS-MA method on a yearly basis is another strength of this trial. We do so to ensure that mentors and career counsellors are true to the method.

A limitation to this trial is that we are not able to blind participants, mentors or carers. Some might argue that it is difficult to sustain the blinding of the assessor during follow-up, and this is certainly a risk of bias. Should blinding be violated, a second assessor will complete the follow-up interview.

Even though participants are recruited from mental health centres throughout the Capital Region of Denmark, and should be fairly representative of the population in the region, we may have a reduced external validity. As it is the staff at the mental health centres that identify eligible participants, not everybody with an affective disorder or anxiety disorder eligible might have been asked to participate; patients are not systematically screened for eligibility.

Due to differences in labour markets and well-fare systems, results may not be directly generalisable to other countries.

Impact of the results

The results of this trial will add to the limited knowledge regarding vocational rehabilitation for people with recently diagnosed anxiety or affective disorders. If potential positive results can be confirmed in other trials, the IPS-MA method can be implemented at the job centres nationwide, and would probably prevent a large number of disability pensions and long-term sickness absences with major benefits to society and patients.

IPS-MACompeting interests

LH's PhD is exclusively founded by the Obel Family Foundation. Due to administrative convenience, PhD

student LH was formally employed by Sherpa from 1 June 2011 until 31 August 2013. LH has throughout the entire period been working at the Research Unit at Mental Health Centre Copenhagen, where she is now employed. Managerial responsibility and supervision lie with LFE and PB. Sherpa has had no role in the trial design, and will have no role in collection of data, analysis of data, data interpretation, or in publication of data from the trial. None of the other authors have any competing interest.

Abbreviations
DPCR: Danish psychiatric case register; GAF: Global assessment of functioning; HAM-A6: Hamilton anxiety scale; HAM-D6: Hamilton depression scale; IPS: Individual placement and support; IPS-MA: IPS-modified, early intervention for people with mood and anxiety disorder; MAS: The Bech-Rafaelsen mania scale; MINI: Mini international neuropsychiatric interview; PSP: Personal and social performance; WHO-5: WHO-Five well-being index.

Competing interests
The authors declared that they have no competing interests.

Authors' contributions
LFE conceived the trial, participated in the planning and design, and read and critically revised the manuscript for important intellectual content. LH participated in the planning and design of the trial, conducted the research interviews, drafted the manuscript and, along with LFE, critically revised it for important intellectual content. MN participated in the planning and design of the trial, and has read and critically revised the manuscript. JL participated in the planning and design of the trial, and has read and critically revised the manuscript. PB participated in the planning and design of the trial, was responsible of the training of the assessors, and has read and critically revised the manuscript. All authors read and approved the final version of the manuscript.

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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

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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]

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
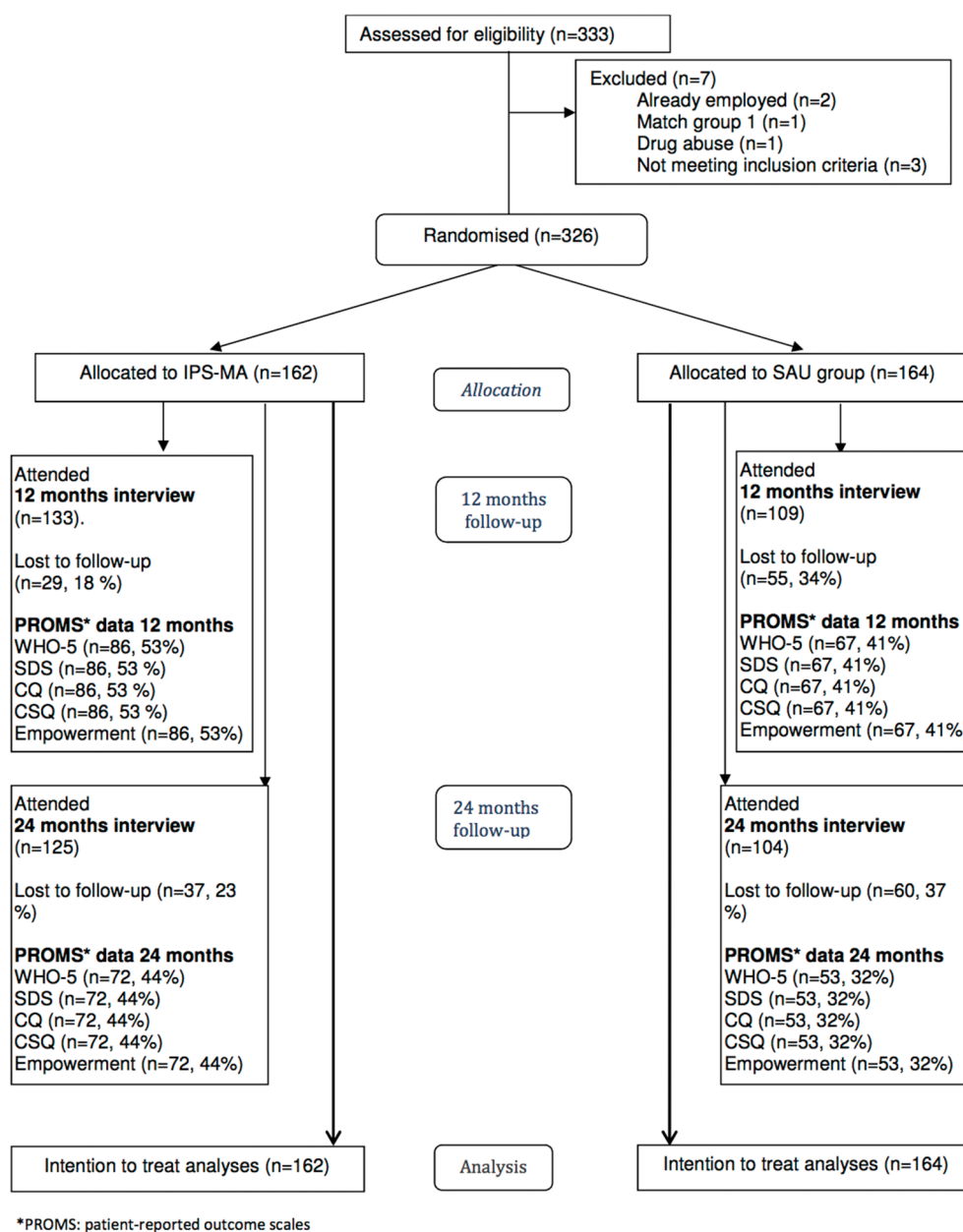
Figure 1 Flow chart of participants in the IPS-MA trial. CSQ, Client Satisfaction Questionnaire; CQ, Changes Questionnaire; IPS-MA, Individual Placement and Support modified for people with mood and anxiety disorders; MAS, Bech-Rafaelsen Mania Scale; PSP, Personal and Social Performance; ; SAU, services 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

Workplace

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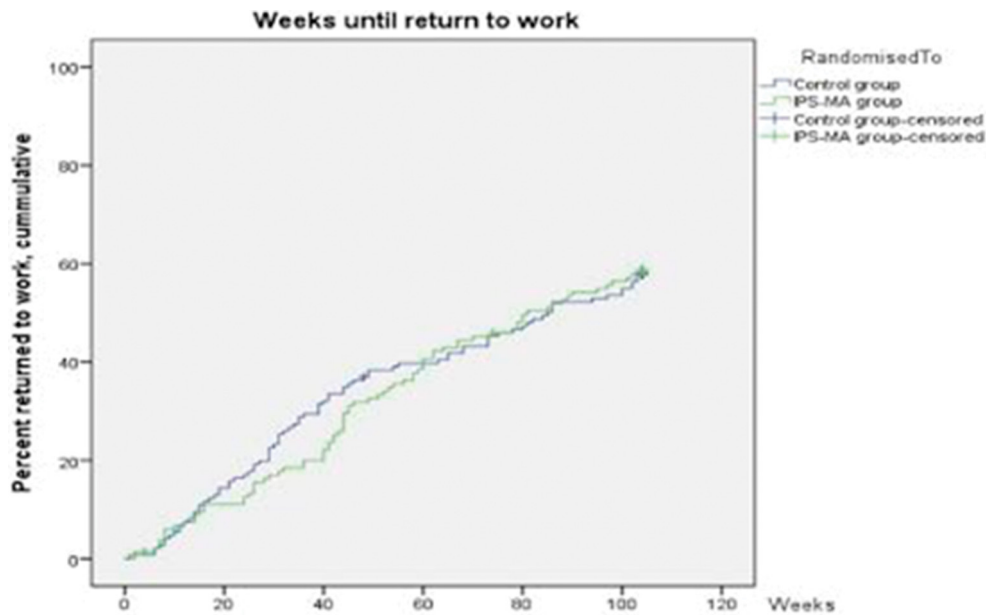
Figure 2 Time until return to work or education for 283 participants included in the analysis, randomised to IPS-MA (n=136) or SAU (n =147). IPS-MA, Individual Placement and Support modified for people with mood and anxiety disorders; SAU, services as usual.

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.

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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

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Notes

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ARTICLE

Cost-effectiveness analysis of a supported employment intervention for people with mood and anxiety disorders in Denmark – the IPS-MA intervention

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ABSTRACT

Objectives: We aimed to investigate the cost-utility and cost-effectiveness of a modified Individual Placement and Support intervention for people with mood and anxiety disorders (IPS-MA).
Methods: Costs were assessed from a societal perspective. Health care costs were derived from registers and combined with data on use of IPS-MA services, municipal social care, and labour market services. EQ-5D was used to compute QALY. Missing data were imputed in a sensitivity analysis. We also computed the cost per gain in hours worked. Incremental cost-effectiveness ratios (ICER) were computed and bootstrapped to obtain confidence intervals for QALY and gain in hours worked.
Results: We found no difference in overall costs between groups. A significant saving was found in use of labour market services in the IPS-MA group. But the IPS-MA group had significantly lower wage earnings compared to the control group. The intervention group had a higher, though statistically insignificant, increase in QALYs than the control group. The ICER did not show statistically significant results, but there was a tendency, that IPS-MA could have a positive effect on health-related quality of life without any additional costs. However, participants in the IPS-MA group had a significantly lower gain in hours worked compared to the control group.
Conclusions: Despite a significant saving in use of labour market services, IPS-MA was not cost-effective. Participants in the IPS-MA group worked significantly fewer hours and earned significantly less than participants in the control group at 1-year follow-up.

Introduction

The effectiveness of the vocational rehabilitation programme Individual Placement and Support (IPS) is well established as an evidence-based method to support people with severe mental illness in gaining competitive employment [1,2]. However, the effectiveness of IPS has primarily been investigated for people with severe mental illness, and evidence is sparse regarding people with mood and anxiety disorders. Given the different courses different mental disorders, one could speculate that the effect of IPS might differ according to diagnosis, accordingly IPS modified for specific groups of patients have been investigated in recent years [3,4]. In Sweden the Individual Enabling and Support (IES) model, an IPS intervention adapted for people with affective disorders, was found to be superior to traditional vocational rehabilitation [3]. Another randomized trial investigated the effectiveness of an IPS intervention modified for people with mood and anxiety disorders (IPS-MA) compared to services as usual (SAU) in a Danish context [4]. The IPS-MA intervention has previously been described in detail [4,5], but briefly, the intervention consisted of mentor support and career counselling, including five basic services: individualized 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, which meant, that even though participants were discharged from treatment and terminated at the jobcentres, support from the mentors and career counsellors continued until participants had sustainably returned to work or education. Most studies of IPS have employment as their primary outcome, however many patients are rather young when they are diagnosed, and have not yet finished an education, accordingly education is their goal [6,7]. On this background, education on ordinary terms was included as an outcome in the IPS-MA trial. No difference was found between the IPS-MA group and the control group on number of participants who had returned to work or education after 1 or 2 years, number of weeks they had worked, or how fast they returned to work. Nevertheless, participants in the IPS-MA group were significantly more satisfied with the treatment they received compared to the SAU group after both 1 and 2 years [4].

Surprisingly, only few studies have investigated the cost-effectiveness of IPS [8,9]. An European study [8] investigated

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the cost-effectiveness of IPS compared to SAU in six European countries. In five of the six countries the IPS intervention was found to dominate SAU, being both less costly and more effective in getting people into competitive employment. In the sixth country the intervention was also found to be more effective but at a higher cost. The different labour market structures in the six countries is thought to have caused the varying effect across countries. Saha et al. [10] recently investigated the cost-effectiveness of the IES model, and found IES to be cost-effective, however, they did not find any difference in quality-adjusted life years (QALYs). The authors argue, that this might be due to a small sample size and a limited timeframe of 1 year [10].

Since the organisation of IPS-MA is different than IPS's, and the context and welfare systems varies between countries, it is relevant to investigate the cost-effectiveness of the IPS-MA intervention in association to health-related quality of life and employment in a Danish setting, using trial data merged with register-based data.

Data and methods

In total 326 participants were recruited from mental health centres and private practicing psychiatrists within the Capital Region of Denmark from 2011 to 2014. Participants had to be between 18 and 60 years old, and diagnosed according to the International Classification of Diseases – 10th edition [11] (ICD-10) with an affective disorder (ICD-10: F30-39) or anxiety (ICD-10: F40-41). In order to include participants who had only recently been diagnosed and who were not too far from the labour market, participants could not have had contact with mental health services for more than the past 3 years, and they had to have been employed or enrolled in education at some time during the past 3 years. Participants had to be motivated to return to work or education; however, they should be estimated not to be ready to return to work within three months. This was estimated by the researcher at the inclusion interview, using a screening tool used by the jobcenters [12]. Finally, participants should be able to read and understand Danish; and give informed consent. Participants were excluded if they had somatic comorbidity causing reduced ability to work; large-scale alcohol or substance abuse as their primary challenge (assessed by means of the MINI International Neuropsychiatric Interview [13]); or a legal guardian or forensic psychiatric arrangements. Participants were randomized to either IPS-MA plus SAU ($n = 162$) or SAU alone ($n = 164$), hence the IPS-MA intervention was an add-on to the services people would usually receive from mental health services, social services and the municipalities.

The intervention was developed, implemented and tested in cooperation with a private company, Sherpa, that already provided supported employment interventions for people with a wide range of mental disorders [14]. Sherpa consisted of two career counsellors with a background in human resources and six mentors with many years of experience as mental health professionals [4].

Participants in the IPS-MA trial were interviewed at baseline and at 12- and 24-months follow-up with clinician-administered scales covering employment/education status, level of functioning, and symptoms. Furthermore, patient-reported outcomes were answered online at all three time-points. These measures comprised several instruments, including EQ-5D [15]. EQ-5D is a generic preference-based measure of health-related quality of life comprising five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Level of perceived problems within each dimension is scored according to three levels (1) indicating no problems, (2) indicating some problems, and (3) indicating extreme problems [16]. EQ-5D has been validated in many populations and countries and is one of the most frequently used measures in health economic evaluations [17], hence, it was chosen to be able to compare our findings to other cost-effectiveness analysis in the field of supported employment.

Costs were assessed from a societal perspective. Health care-, social care-, and intervention costs were calculated for each individual in the 24-month follow-up period. Costs are in euro (2016 price level) and derived from registers as described in Table 1. Hospital care is registered in the National Patient Register [18], and costs were computed using nationally developed diagnosis-related groups (DRG) tariffs [19]. Psychiatric hospital care is registered in a separate register [22] and no DRG-tariffs have been implemented. Psychiatric care is therefore valued by a unit cost of bed days, emergency room (ER) visits, and outpatient visits.

Intervention costs were analysed in a bottom-up approach using registration of services from the Sherpa organisation (Table 1). Mentors and career counsellors registered their contacts in a time-management system, from which they could extract data on specific services provided, and average time consumption per service could be estimated. The length of patient trajectory varied considerably, with a mean of 636 days (range: 32–1433). More than 25% of participants received the IPS-MA intervention for more than 2 years. Costs were calculated for the first year and the first 2 years for all participants, regardless of the length of their participation. Due to a large loss to follow up after 2 years (61.7%) only estimates for the first year are used in the cost-utility and cost-effectiveness analyses. Usual services could be provided by either municipal social services (e.g. group therapy or psycho-social support interventions) or labour market services. Data on social services used in the two groups was only available for the group of patients living in Copenhagen municipality (about 46% of the study population), therefore this information was only used to investigate if major differences between the two groups existed. Costs of labour market interventions were obtained from the Danish Agency for Labour Market and Recruitment [23]. Under the municipal jobcentres, citizens can receive mentor support, counselling, or courses and on-the-job internships. The latter is considered to have no additional costs. Only job-seeking courses for the control group were included, because all other course activity was considered formal education. Job-seeking courses was part of the IPS-MA intervention. Productivity

Table 1. Cost components included in cost-effectiveness analyses.

Cost*	Definition	Source
Hospital costs	Inpatient, outpatient and emergency room contacts in somatic and psychiatric hospitals, valued with Danish national diagnosis-related groups (DRG)-tariffs.	The National Patient Register with DRG and outpatient tariffs [18,19].
Primary health care costs	Contacts to general practitioners, practicing specialists and other health care professionals reimbursed (or partly reimbursed) by the Danish National Health Service, e.g. dental care or psychological treatment. Costs are valued with national service tariffs.	The National Health Service Register [20]
Consumption of prescription pharmaceuticals.	The full price (regardless of subsidies etc) of prescription drugs purchased in Danish pharmacies.	The Pharmaceutical Database [21]
Costs of labour market interventions.	All interventions initiated by the municipal job centres: job seeking courses, offered to the control group as part of service as usual were valued at €20 per hour, mentor support in all groups was valued at €33 per hour and personal counselling in all groups was valued at €51 per hour. Education and on-the-job training were considered to not have additional costs	Data obtained from the Danish Agency for Labour Market and Recruitment
Costs of municipal social interventions	Social interventions, comprising counselling, course activities and other means of non-monetary support.	Data obtained from Copenhagen municipality for those participants that lived in Copenhagen (46 % of participants). Means per group were calculated.
Intervention costs.	Costs of the IPS-MA intervention is calculated as the number of Sherpa services used, an estimate of the mean time used per service multiplied by the hourly wage of a social worker (40€).	Data was registered by the employees in Sherpa
Productivity costs	Labour market affiliation, costs are measured as lost gains, or absence from gainful (competitive or supported) employment multiplied by an average wage. Protected employment included.	Days in gainful employment are measured in the electronic income register from the Danish Agency for Labour Market and Recruitment

*Costs are in euro and 2016 price level.

costs were estimated using tax information on wage and number of hours worked during the first year after the intervention. The costs included in the analyses are presented in Table 1.

Differences in costs within the first year are investigated using intervention costs, health care costs, productivity costs and labour market services as costs measures. Attributable costs, meaning costs in the intervention group minus costs in the control group, were computed both by crude estimation and in a regression analysis where age, gender, diagnosis and costs in the period prior to randomisation were included. The total costs were accumulated within the follow-up period, and the differences between the IPS-MA group and SAU were calculated by means of t-tests.

The effect of the IPS-MA intervention is measured in QALY, which is a measure used in cost-utility analysis [24]. QALY's consist of remaining life expectancy multiplied with a factor denoting health-related quality of life (HRQoL). In this study, we did not consider life expectancy beyond the intervention, and the QALY measure therefore reflects HRQoL only. EQ-5D-scores were transformed into single measures using the Danish preference weighting [25,26]. As a sensitivity analysis, the EQ-5D score at 12 months was imputed using multiple imputation (mi) with truncated regression in STATA. QALY-gains were analysed both on raw and imputed data, using the difference in HRQoL from baseline to 1 year as expression of the development in QALYs, thus assuming a time horizon of 1 year for the QALY-gain.

Cost-utility was measured as the additional cost of gaining one additional QALY. Additional costs were computed as the difference-in-difference of costs, that is: The cost development was calculated as the costs in the year following randomisation, minus the costs in the year before randomisation for both groups. And the difference between the two differences are considered the additional costs.

Costs were measured as described above. Because QALYs were only measured for the first year after randomisation, so was cost-utility. For QALYs, the development was calculated as the mean difference in HRQoL from randomisation to 1-year follow-up.

The incremental cost-effectiveness ratio (ICER) was computed as:

$$ICER = \frac{C_{Intervention} - C_{Control}}{Q_{Intervention} - Q_{Control}}$$

where C denotes the development of costs from baseline (the year before randomisation) to follow-up (1 year after randomisation) and Q denotes the development in QALYs from baseline to follow-up. The ICER expresses the additional cost of gaining one QALY [24]. The magnitude of the ICER will, in this case, suggest whether the intervention is cost-effective, meaning that the cost of gaining an additional QALY is reasonable. To assess the uncertainty around the ICER estimates, we used 10,000 bootstrap samples, the 2.5 and 97.5 quantiles of the bootstrapped data were interpreted as confidence limits [24]. Each dot in the scatter plots represent one

of the bootstrapped samples. Observations in the bottom-right quadrant reflects scenarios where the intervention is cheaper and better (Dominant) in relation to QALY and thus worth implementing directly. The upper-left quadrant reflects scenarios where the intervention is more expensive and less effective (Dominated) in which case the intervention could simply be rejected. In the upper-right quadrant the intervention is better but more expensive, and in the lower-left quadrant the intervention is cheaper but less effective (Assess CE), in these cases a more thorough health economic review should be conducted before deciding whether the intervention should be implemented. Cost-effectiveness was also investigated in relation to numbers of hours worked. In the randomised trial we only had access to data on weeks worked, but post hoc, we have gained access to data on numbers of hours worked from the electronic income register from the Danish Agency for Labour Market and Recruitment [23]. These data give us a more precise picture, and we therefore decided to include the data in the present analysis. Number of hours worked within the first year of the intervention was calculated for each of the two groups, based on degree of employment ranging from 0 to 37 h per week. In a linear regression the difference between groups was tested. The ICER was also calculated for cost-effectiveness with the development in hours worked as effectiveness measure. This computation included all patients, because it utilises register data only and there was thus no loss to follow-up. We calculated the development in hours worked as the difference between the year before and the year after randomisation.

We utilised the 10,000 bootstrap samples to calculate cost-effectiveness acceptability curves (CEACs) [24]. The CEACs relate the ICER estimates to different monetary values of a QALY that decision makers could be willing to pay. The CEAC show the proportion of ICER estimates that are lower than the willingness-to-pay (WTP) meaning that the IPS-MA intervention is cost-effective at this specific WTP [27].

All analyses were conducted at the Statistics Denmark server [28], where personal information about individuals are encrypted, thus ensuring compliance with the data security regulations. A significance level < 0.05 was considered statistically significant. SAS® v 9.4 [29] was used for data management and STATA® MP v 15 [30] was used for analysis.

Results

Table 2 shows the total costs accumulated within the first 12 months of the follow-up period distributed between IPS-MA and the control group. Costs of the IPS-MA intervention amounts to an average of €1183 per person in the first year. Overall, there is a small, but insignificant saving of €2221 in total costs at 1 year in the intervention group (p = 0.423). The difference is primarily due to the IPS-MA group using labour market services less than the control group (€4262, p = 0.009), as there are no statistically significant differences between groups in the use of somatic, mental and primary health care and prescription pharmaceuticals. On average, participants in the IPS-MA group earned €3376 less than the

control group, i.e. the productivity gain is significantly higher in the control group (p = 0.017).

In Table 3 the development in costs and QALYs gained in the two groups, as well as the incremental cost-effectiveness ratios are shown.

In complete case as well as in imputed analyses, both groups have statistically significant lower costs in the follow-up period than in the year prior to randomisation (IPS-MA: −9281(−12,518; −6046) and CT: −7730(−10,906; −4554)) (Table 3). None of the cost differences are statistically significant though (complete case diff: 1551(−3,004; 6107). Both groups experience a statistically significant increase in QALYs from randomisation to 1-year follow-up (IPS-MA: .144 (.097; .190) vs CT: .121(.081; .161)). However, only when missing QALY values are imputed, the IPS-MA group has a significantly higher increase in QALYs than the control group (difference IPS-MA vs CT: −.072 (−.133; −.012)). This indicates that the intervention is not cost saving, however, it might be associated with a higher gain in QALY compared to SAU.

None of the ICER estimates are statistically significant. The scatter plot resulting from the complete case calculation is shown in Figure 1. The dots to the right indicate that the intervention is better compared to SAU regarding gains in QALYs and the dots below 0 in additional costs that the intervention is cost saving. There might be a tendency that IPS-MA was slightly cost-saving and associated with a small gain in QALY. However, the results are not very robust.

The CEAC (Supplementary Figure 1) shows that with a societal willingness-to-pay of €30,000 per QALY gained there is an 95% probability of IPS-MA being cost-effective compared to SAU, meaning that with 95% probability society would be willing to pay €30.000 to gain an extra QALY. However, from the imputed data (Supplementary Figure 2) it appears that the probability has dropped to around 83%.

Regarding the cost-effectiveness in relation to numbers of hours worked, participants in the control group had worked significantly more hours during the 12-month follow-up than participants in IPS-MA (mean 297 h, SE: 30.73 vs 177 h, SE: 39.91, p = 0.018) (Supplementary Table 1). In Figure 2 cost-effectiveness is calculated according to numbers of hours worked during the 12-month follow-up. There is a tendency that IPS-MA might be somewhat less expensive than SAU, but participants in IPS-MA worked significantly fewer hours.

Discussion

In a cost-utility and cost-effectiveness analyses, we have investigated whether IPS-MA was cost-effective compared to SAU. We found a tendency that IPS-MA was related to a small insignificant saving in costs, and a small gain in health-related quality of life. However, results were not very robust. Furthermore, participants in the control group worked significantly more hours during the 12 months follow up compared to the IPS-MA group.

Only few studies have investigated the cost-effectiveness of IPS and only one study investigated the cost-effectiveness of a modified IPS intervention aimed at people with affective disorders. Most of the studies of IPS found this intervention

Table 2. Total costs, 1 year after randomization, by group, €.

	Intervention group	Control group	Attributable costs	Test for equality of means
Somatic health care	1248	1030	218	$p = .488$
Mental health care	5489	8161	−2672	$p = .078$
Prescription pharmaceuticals	560	610	−50	$p = .63$
Primary health care	593	639	−46	$p = .52$
Labour market services	1329	5591	−4262	$p = .009$
Intervention costs	1183	–	1183	n/a
Municipal social services	302	283	19	n/a
Average wage earnings*	5034	8410	−3.376	$p = .017$
Total costs at 1 year	5485	7706	−2221	$p = .423$

Note. Computations on full study population: $N = 326$. *Subtracted from total costs.

Table 3. Incremental cost-effectiveness in Euro, €.

	Mean cost development, IPS-MA (95 % confidence intervals), €	Mean cost development, control (95%confidence intervals), €	QALY gained, IPS-MA (95 % confidence intervals), mean	QALY gained, control (95 % confidence intervals), mean	ICER, IPS-MA vs control (95 % confidence intervals)
Complete case	**−9281**	**−7730**	**.144**	**.121**	Dominant
($N = 143$)	(−12,518; −6046)	(−10,906; −4554)	(.097; .190)	(.081; .161)	(−2.05e + 09;
Difference IPS-MA-control	1551 (−3,004; 6,107)		−.023 (−.085;.040)		2.05e + 09)
Imputed QALYs* ($N = 255$)	**−8085**	**−9144**	**.056**	−.017	14,610
	(−10,859; −5311)	(−12,397; −5,891)	(.010; .101)	(−.057; .023)	(−646,591; 675–811)
Difference IPS-MA-control	−1059 (−5311; 3194)		**−.072** (−.133; −.012)		

Note. Figures in bold typeface are statistically significant at 5 % level. *: QALY refers to gain in HRQoL.
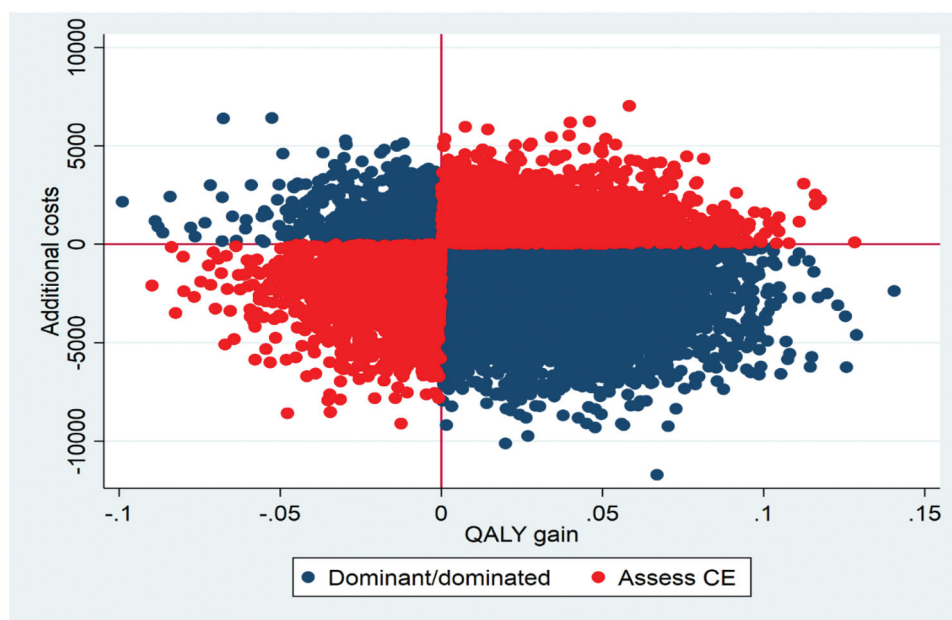

Figure 1. Cost-effectiveness of IPS-MA relative to SAU, complete case.

to be cost-effective and Saha et al. also found the modified IPS intervention – the IES intervention – to be related to a saving of €7247 and cost-effective compared to services as usual [10]. This is in contrast with our study. A simple explanation could be that IPS-MA had a different organisational set up than the above-mentioned studies. Rather than being integrated with mental health services, Sherpa, the company delivering the IPS-MA intervention acted as a link between mental health services and jobcentres, without any authority. This may have prevented the IPS-MA support from being provided as intended.

The organisation of the IPS-MA intervention is clearly a limitation compared to IPS, and would have affected fidelity following the original IPS fidelity scale [31]. However, because people with mood and anxiety disorders are treated in many different settings in Denmark, it was not possible to integrate job support with treatment to the same extent as in IPS. We anticipated that the mentors having an assertive outreach to job centers and mental health centers in order to coordinate services would be sufficient, however, this was probably not the case.
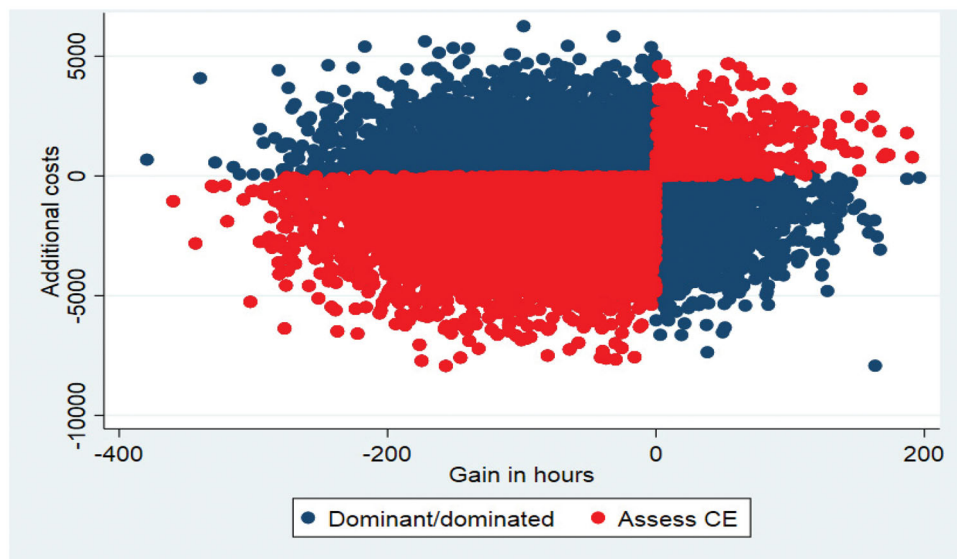
Figure 2. Cost-effectiveness related to gain in numbers of hours worked during 12 month follow up.

Fidelity measures are important in order to secure correct and sustained implementation and effectiveness of a new intervention. During the IPS-MA trial fidelity was measured four times. Each time, comments were made on the implementation of the workplace intervention which was part of the IPS-MA intervention; that is the support in contacting potential employers and negotiating workplace accommodations like shorter hours or lighter duties. Despite several attempts to highlight the importance of the workplace intervention, it was stated in the last fidelity review that the support seemed to be deliberately deselected; Sherpa stated that they wanted to focus on the participants' 'healthy self' and did not wish to introduce the participant to a potential new employer as an employee with impairments. In line with this, Sherpa did not have regular discussions with the participants regarding disclose of their mental illness. However, in IPS the workplace intervention as well as disclosure, or a regular discussion of disclosure is a very important part of the support and two of the eight items most strongly associated with return to work [31]. It is not unlikely, that the lack of implementation of the workplace intervention and regular discussion of disclosure could in part explain the lack of effect of the IPS-MA intervention.

There is an ongoing discussion that EQ-5D may not be sensitive enough to capture changes in HRQoL in patients with mental disorders [32,33], this may have underestimated the changes in HRQoL and affected the QALY, making it difficult to recognise a difference between groups. However, EQ-5D was chosen since it is the most frequently used measure in the calculation of QALYs. Future cost-effectiveness studies, including people with mental disorders might consider using a different measure more sensitive to changes in areas of HRQoL relevant for people with mental disorders [33].

It is well known that health professionals tend to underestimate work capacity [34], and fear work to be too stressful for individuals with mental disorders [35]. In IPS-MA the mentors, who all had a background as health professionals was taught the principles and values of IPS, for instance that

the goal was a rapid return to work, that most are able to work, and will benefit from working regardless of persistent symptoms. Furthermore, the career counsellors were recruited from the private business sector and were encouraged to focus on the competences and goals of the participants, and not diagnosis or symptoms. It cannot be ruled out that return to work has been postponed, or that participants have worked fewer hours due to the mentors and career counsellors trying to protect the participants from perceived stress related to returning to work. However, one could also speculate, that the control group has experienced pressure from the jobcentres or an economic incentive to return to work full time, whereas the IPS-MA group may have had support in negotiating part time return to work or longer sick leave, which could explain why the IPS-MA group worked fewer hours.

Since the IPS-MA intervention was very intensive, thus quite expensive, and furthermore an add-on to SAU, we had expected the intervention to be more expensive than SAU, however, this was not the case, as the total cost of IPS-MA was the same as SAU. Looking at the cost in more detail, we found that the IPS-MA group used labour market services significantly less than the control group. This could indicate that the support offered by IPS-MA was adequate and superseded services provided by the usual labour market services. However, it may also be, that participants randomized to the control group have sought support elsewhere, inspired by the information they received about IPS-MA.

We found that participants in IPS-MA had significantly lower average wage earnings compared to the control group during the 1-year follow-up. This is surprising, since the aim of the intervention was to support participants in a fast return to competitive employment, which we would have expected to generate higher earnings. The result is also in contrast with the findings of other studies [10,36]. Saha et al. found participants in the IES group to have a productivity gain €5.948 higher than the control group. The lower productivity gain is in line with the finding, that participants in

the IPS-MA group worked significantly fewer hours during the 12 months follow-up and could be explained by participants in the IPS-MA group working part-time to a higher extent. It would have been interesting to investigate whether participants received adequate workplace accommodations, and if participants got sick listed again to a higher extent in one of the two groups. This was outside the scope of the present study.

Strengths and limitations

A major strength of this study is that we had access to complete data from highly reliable registers on both health care costs, employment, wage earnings and services provided by the labour market services.

It is a limitation, however, that we did not have information about services used outside the public health care sector. If participants had sought treatment in the private sector, which does not render reimbursement it is not registered, and therefore not part of our estimate. If the control group had sought treatment in the private sector to a higher extent, the cost estimates in the control group could be underestimated and the difference in costs could be higher. Furthermore, we only had access to information on use of municipal services from the municipality of Copenhagen, therefore this information was only used to investigate if there were major differences between the two groups and any variance in these costs was not reflected in the results.

Another limitation is the high number of missing data on EQ-5D at one-, and especially 2-year follow-up. The high loss to follow-up was primarily on the patient reported outcomes which participants should answer online. Despite numerous reminders this was not done. The questionnaire was quit, comprehensive, which may have discouraged participants. Even though we used multiple imputations to account for the missing data, the rather large amount of missing data may have affected the results. It is likely that the study was under-powered for the purpose of an economic evaluation. It is possible that results after 2 years could have rendered more statistically significant results, however this was not deemed feasible because of the many missing observations. Therefore, as in Saha *et al*, the time horizon of 1 year, is a limitation. Many participants returned to work after 1-year follow-up, and had we been able to use data from 2-year follow-up, the result of the cost-effectiveness analysis might have been different.

In this study, the ICERs indicate that IPS-MA was slightly cost-saving and associated with a small gain in QALY, however, people worked significantly fewer hours. Since the ICERs are not robust, one should be careful to make any conclusions based on the ICERs. The lack of robustness of the ICER may be caused by a small sample size, aggravated by missing QALY data, large variations in costs and small variations in QALYs. It may also be, that the EQ-5D instrument is not sufficiently sensitive to changes in mental health-related quality of life.

In conclusion, IPS-MA was comparable to SAU in terms of QALYs, and costs, but participants in IPS-MA worked significantly fewer hours during the first 12 months, hence based on results from the present cost-effectiveness analysis the IPS-MA intervention was not cost-effective, and could not be recommended for implementation in its present form.

Ethical approval

Disclosure statement

Informed consent

All participants provided oral and written informed consent prior to inclusion in the study.

Authors contributions

All authors participated in the planning and design of the study, interpretation of the results, and have read and critically revised the manuscript. MK conducted the analysis and drafting of figures, and tables. LH wrote the manuscript. RTW made a systematic search for studies of cost-effectiveness in the area and wrote part of the introduction. MK wrote the materials and methods section regarding the cost-effectiveness analysis.

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Predictors of Return to Work for People with Anxiety or Depression Participating in a Randomized Trial Investigating the Effect of a Supported Employment Intervention

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Abstract

Purpose Common mental disorders have a severe impact on society and individuals; rates of unemployment and disability pensions are high. Knowing which factors facilitate or hinder people's return to work is important when designing effective vocational rehabilitation interventions. *Methods* We conducted secondary analyses on data from 289 participants with depression or anxiety included in the Individual Placement and Support modified for people with mood and anxiety disorders (IPS-MA) trial. Associations of baseline characteristics and employment or education after 24 months were tested in univariate logistic regression analyses, variables with a p-value below 0.1 were included in multivariate analyses. *Results* In the univariate analyses, self-reported level of functioning ($p = 0.032$), higher age ($p = 0.070$), and higher level of readiness to change ($p = 0.001$) were associated with the outcome and included in the multivariate analysis. Only age ($p = 0.030$) and readiness to change ($p = 0.003$) remained significantly associated with return to work or education after 24 months in the multivariate analysis. *Conclusion* Higher age and lower readiness to change were associated with a lower chance of having returned to work or education. Factors modifying the effect of higher age should be identified, just as vocational rehabilitation should focus on improving factors related to people's readiness to change.

Keywords Predictors · Return to work · Depression · Anxiety

Background

Globally, people with common mental disorders like depression and anxiety are estimated to cost 1 trillion US Dollars per year in lost productivity alone [1]. In Denmark, the unemployment rate among people with mental disorders is more than 60%, and of those receiving long-term sickness benefits, 70% have a mental illness [2]. Moreover, anxiety is the number one reason for being granted a disability pension [3]. Besides the impact on society, unemployment may also have serious consequences for the individual with regards to economic insecurity, lowered confidence and self-esteem,

lack of meaning, and social isolation [4]. Evidence-based supported employment models like Individual Placement and Support (IPS) are effective in supporting people with severe mental illness in obtaining employment [5, 6]. However, a recent review of the effect of IPS according to diagnoses found indications that people with depression did not benefit from IPS to the same extent as people with schizophrenia, bipolar disorder, or substance use disorder [7]. Since depression is one of the most prevalent mental disorders and one of the greatest socioeconomic challenges globally, it is important to support this group of patients, also in their return to work [1]. Bejerholm et al. have proposed that people with depression might benefit from support in strengthening motivation and functional cognitive strategies in order to decrease depressive thoughts and avoidance behavior before attending vocational rehabilitation like IPS [8]. Accordingly, in a randomized trial, they found that the Individual Enabling and Support (IES) model of supported employment, which incorporates training in motivation and cognitive strategies prior to the IPS intervention, was more effective than services as usual [8]. As such, 42%

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of the participants in the IES group had returned to work, compared to only 4% in the control group. IES had good fidelity according to the IPS fidelity scale [9] and could be qualified as an IPS intervention supplemented with enabling strategies.

In a Danish randomized trial, the effect of IPS modified for people with mood or anxiety (IPS-MA) was also investigated [10]. In this case, the modified intervention, based on the IPS principles, consisted of mentor support and career counseling in addition to usual vocational services. The intervention was primarily modified with regards to the principle of integration of mental health and vocational services, which was not possible in a Danish context since people with mood and anxiety disorders are treated in many different settings in Denmark. Instead, mentors and career counsellors were employed in a private company, and IPS-MA mentors had an important role coordinating services provided with mental health-, and vocational services. Fidelity was measured on a modified Supported Employment fidelity scale [29] adapted to measure core elements of the IPS-MA intervention. Good fidelity according to seven of the eight IPS principles was reached. In contrast to most IPS populations, participants in IPS-MA had been employed or in education within the past 3 years; the aim was an early intervention to support participants in their return to work before they drifted too far from the labour market. In this trial, the modified IPS intervention was not found to be superior to standard treatment, as such, 44% in the intervention group had obtained employment after 2 years compared to 38% in the control group [10]. Even though the IES intervention was significantly superior to traditional vocational rehabilitation, in both the above studies only about 40% of the participants had returned to work, which is very low compared to IPS for people with severe mental illness where up to 60% of the participants obtain employment [5, 11]. With this in mind, we need to focus on how better to support people with depression and anxiety in obtaining employment. To do this, we need to know which challenges people face and if differences between those who obtain employment, and those who fail to obtain employment exist. If we could identify predictors of returning to work, we might be able to better target vocational rehabilitation. Some predictors are unchangeable like gender, age, etc.; they can only help us pay attention to specific target groups. However, other predictors are modifiable, like symptom severity, level of function, quality of life, readiness to change, etc. If a modifiable variable was associated with return to work, this could be of valuable knowledge when designing a new intervention.

Previous studies have found older age [12–14], lower level of education [13, 15, 16], gender [13, 17], low socioeconomic status, and living alone [13, 18] to be associated with prolonged return to work among people with depression and anxiety. Health-related predictors were duration of

mental illness, severity of symptoms [19–23], previous sick leave, and comorbidity [20, 24]. Also, job-related factors like low job grades and high job stressors have been found to be associated with prolonged return to work [24]. Factors like self-efficacy [25] and return to work expectancy [26] have also been associated with return to work [27].

The purpose of the present study was to investigate what predicted return to work or education after 2 years, among 289 people with depression or anxiety who had participated in the IPS-MA trial.

Methods

Design and Participants

In the present study, we conducted secondary analyses of data from the Individual Placement and support modified for people with mood and anxiety disorders (IPS-MA) trial [10, 28]. The randomized clinical trial investigated the effectiveness of a supported employment intervention on return to employment or education among people sick-listed with a recent diagnosis of depression or anxiety. Participants were referred by mental health centers and private practicing psychiatrists in the Capital Region of Denmark from October 2011 until February 2014. Participants in the intervention group received mentor support and career counseling in addition to services as usual. The focus was on competitive employment or education, and support was time unlimited. The primary outcome of the trial was returning to competitive employment or education 2 years after enrolment. The control group received vocational services as usual as offered by the job centers. A full description of the intervention and methodology can be found in the trial protocol and effect article [10, 28].

Inclusion criteria were:

- Age between 18 to 60 years;
- A diagnosis of affective disorder (ICD-10: F30-39) or anxiety (ICD-10: F40-41);
- Not having had contact with mental health services for more than the past 3 years;
- Having been employed or enrolled in education at some time during the past 3 years;
- Being motivated to return to work or education;
- Being match group 2 or 3. (The job centers in Denmark use match groups to describe how far from the labor market people are. People in match group 2 are considered able to participate in pre-vocational training, but not able to work and be off public benefits within 3 months. People in match group 3 have more severe long-term problems and are not considered able to work or participate in prevocational training);

- Participants had to be able to read and understand Danish and give informed consent.

Exclusion criteria:

- Somatic comorbidity causing reduced ability to work;
- Primary large-scale alcohol or substance abuse; or
- Having a legal guardian or forensic psychiatric arrangements.

In total 326 participants with mood and anxiety disorders were randomized, of these 37 had a diagnosis of bipolar disorder, and were not included in the present study. Since no difference in return to work or education was found in the original study, we merged the two groups in the present study.

Participants provided written informed consent prior to inclusion. The study was approved by The Regional Ethics Committees of the Capital Region (journal no: H-2-2011-FSP20), reported to the Danish Data Protection Agency (Journal no: 2007-58-0015, local journal no: RHP-2011-20), and registered at www.clinicaltrials.gov (identifier: NCT01721824).

Measures

Participants were assessed by clinician-administered scales in semi-structured interviews by blinded researchers, who were trained in the scales used, as well as by answering online patient-reported outcomes scales at baseline, and after 12 and 24 months. Also, participants were followed in the DREAM database [30], a register including weekly information on all citizens receiving public benefits from 1991 and onwards. The DREAM database is administered by the Danish Agency for Labour Market and Recruitment and based on data from the Ministries of Employment and Education, the Civil Registration System (CPR-register) [31], and the Danish Customs and Tax Administration (SKAT) [32].

The primary outcome of the present study is return to work or education 2 years after baseline; return to work was defined as being competitively employed (a week without government benefits combined with a work-code (indicating attachment to a company since labor market contributions have been paid)), being on rehabilitation benefits, flexible jobs, and wage-subsidized jobs in the private sector which are all competitive jobs (with the possibility of negotiating salary and earn pension) or under education, based on complete data from the highly reliable DREAM database [30].

Based on previous findings and the data available, we examined the following baseline measures as possible predictive factors of return to work or education: study condition (IPS-MA vs. services as usual), age, sex, civil

status, level of education, diagnosis, level of symptoms and function, mental health-related quality of life, apathy, and readiness to seek employment or education. Symptoms of depression were measured by the Hamilton Depression six-item Scale (HAM-D6) [33, 34]. The six items measure core symptoms of depression on a 5-point Likert scale (except the item *tiredness/pain* which is measured on a 3-point Likert scale); 0 equals not present and 4 (2 regarding tiredness/pain) equals very severe. Scores are summed and a score between 0–4 reflects no depression, 5–6: doubtful, 7–8: mild, 9–11: moderate, and 12–22: severe depression. The Hamilton Anxiety six-item Scale (HAM-A6) [33, 35] was used to measure core symptoms of anxiety, also on a 5-point Likert scale (0 equals not present and 4 equals very severe). Scores are summed and scores of 0–4 reflect no anxiety, 5–6: doubtful, 7–8: mild, 9–14: moderate, and 15–24: severe anxiety. Level of functioning was measured by the Personal and Social Performance scale (PSP) [36] where the four sub-dimensions (1) socially useful activities, (2) personal and social relationships, (3) self-care, and (4) disturbing and aggressive behavior were summed to a total score between 0 and 100; a score of 100 indicating perfect functioning. All measures were assessed at baseline interview. Patient-reported measures were answered online at baseline and included: Mental health-related quality of life measured by the WHO-5 well-being index [33] where the scores from the five items are summed and multiplied by four, giving a score between 0 and 100; a higher score indicating better well-being. Apathy was measured by the Diagnostic Apathy scale [37]. The scale consists of six items; (1) difficulties in concentration and memory, (2) difficulties in concentration and decision making, (2) work and interests, (3) somatic general (fatigue and muscle pain), (4) tiredness, (5) lack of energy, and (6) sleep problems (insomnia) which are summed to a total score between 0 and 13, with a higher score indicating higher levels of apathy. Self-reported level of function was measured by The Sheehan Disability Scale (SDS) [38]. The SDS measures functional impairment in three inter-related domains; work/school, social, and family life scored from 0 to 10 and summed into a score from 0 (unimpaired) to 30 (highly impaired). The readiness to seek employment or education was measured by the Change Questionnaire (CQ) [39] consisting of 12 items covering six constructs: desire, ability, reasons, need, commitment, and taking steps towards making the change, each with a score from 0 (definitely not) to 10 (definitely). The scores are summed to a total score from 0 to 120; a higher score indicating higher readiness to change/seek employment or education.

Some of the categorical variables were merged; the three diagnoses were combined to two; (1) depression, and (2) anxiety (phobic and other anxiety); level of education was pooled to (1) maximum high school and (2) higher than high school, and civil status was comprised into (1) cohabitant

(married, registered partnership, co-habitant) and (2) non-cohabitant (divorced, widow, single).

Statistical analyses

Baseline characteristics are presented for those in employment/education after 2 years, those not in employment/education, as well as the total group. Categorical variables are presented with count (n) and percentages and mean and standard deviations (SD) are used for continuous variables. All original analyses were conducted according to the intention-to-treat (ITT) principles. We had complete data on all register and baseline interview data (except for one missing on PSP). Missing data were handled by multiple imputation, predictions were based on variables with full information indicative of missing values; 100 imputations were made. Crude and imputed results are presented.

First, bivariate relationships between independent variables and the outcome variables were tested by Spearman correlation. Univariate logistic regression was used to assess associations of all possible baseline predictors separately with return to employment or education at 24 months follow-up. Only variables associated with the outcome measure with a p-value below 0.1 were included in the multivariate logistic regression. Significant predictors were tested individually for non-linear associations. All numeric predictors were also tested with quadratic terms added to identify non-linear effects. Data were analyzed using SPSS version 25 [40].

Results

Of the 289 participants included in the present study, 118 (41%) had returned to work or education at 24 months follow-up. 144 had originally been randomized to the IPS-MA group and 145 to the SAU group. Almost 70% were women with a mean age of 35 (SD 10.9), most were non-cohabitant (63.7%), and 65.7% had an education that surpassed high school. Most of the participants had depression (77.9%) with a mean score corresponding to a moderate level of depression (mean 10.2, SD 3.0). Participants' self-reported well-being mean score was 32, indicating a rather low level of well-being (below 50 indicates a risk of stress or depression, 30 a high risk of depression). Level of functioning was also low with mean scores of 44 and 20 according to the PSP and SDS respectively, corresponding to moderate or marked impairments. The participants reported a rather high level of readiness to seek employment or education (mean 97.2). See Table 1.

Several of the covariates correlated significantly, however, most correlation coefficients were below 0.30, not strong enough to indicate multicollinearity. The strongest correlations were between level of functioning according to PSP and level of depressive symptoms, and level of apathy and depressive symptoms with correlation coefficients of 0.50 and 0.54 respectively. Readiness to change was the only covariate significantly correlated with return to work at 24 months (p < 0.000, rho = 0.266) (see online material for correlation matrix).

In the univariate analysis, a lower level of functioning according to the SDS was associated with a lower chance of being in employment after 24 months (OR = 0.947, 95% CI 0.902–0.995, p = 0.032), and a higher degree of readiness to seek employment or education was significantly associated with a higher chance of being employed or in education after 24 months (OR = 1.028, 95% CI 1.011–1.046, p = 0.001). Higher age was associated with a lower chance of having returned to work or education with a p-value below 0.1 (OR = 0.980, 95% CI 0.959–1.002, p = 0.070) as the only other variable. Hence age, level of functioning according to SDS, and readiness to change were included in the multivariate analysis. In the final model, age, and readiness to change were still significantly associated with being in employment or education. Higher age was significantly associated with a lower chance of having returned to work or education after 24 months follow-up (OR = 0.975, 95% CI 0.952–0.998, p = 0.030), whereas a higher level of readiness to change was associated with a higher chance (OR = 1.027, 95% CI 1.009–1.045, p = 0.003). Both variables were linearly associated with the probability of achieving employment at 24 months. The level of functioning was no longer significant in the final model (OR = 0.961, 95% CI 0.912–1.012, p = 0.130) (Table 2).

Discussion

In this study, including 289 participants with depression or anxiety, we found lower age and a higher level of 'readiness to seek employment or education' to be associated with higher odds of having returned to work or education after 24 months. In the univariate analysis level of functioning measured by SDS was significantly associated with return to work or education at 24 months follow-up, however, in the multivariate model, this association was no longer statistically significant.

Even if the OR is quite small, indicating that the odds of having returned to work is not very much impacted by age each years increase in age, the confidence interval is quite narrow and the association between higher age and less chance of having returned to work is well known and in line with other studies [12, 13, 24, 41]. In a systematic review and meta-analysis of prognostic factors of return to work after depression, a 10-year increase in age was found to be associated with a slower return to work across five

Table 1 Baseline characteristics of 289 participants with depression or anxiety in the IPS-MA trial

	RTW* at 24 mths (n=118)	Non-RTW at 24 mths (n=171)	Total sample (N=289)
Study condition, n (%)			
IPS-MA	62 (52.5)	82 (48.0)	144 (49.8)
Services as usual	56 (47.5)	89 (52.0)	145 (50.2)
Sex, n (%)			
Women	82 (69.5)	118 (69.0)	200 (69.2)
Men	36 (30.5)	53 (31.0)	89 (30.8)
Civil status, n (%)			
Cohabitant	41 (34.7)	64 (37.4)	105 (36.3)
Non-cohabitant	77 (65.3)	107 (62.6)	184 (63.7)
Education, n (%)			
≤ Highschool	36 (30.5)	63 (36.8)	99 (34.3)
> Highschool	82 (69.5)	108 (63.2)	190 (65.7)
Diagnosis, n (%)			
Depression	94 (79.7)	131 (76.6)	225 (77.9)
Anxiety	24 (20.3)	40 (23.4)	64 (22.1)
Match group, n (%)			
2 (1)	75 (63.6)	114 (66.7)	189 (65.4)
3	43 (36.4)	57 (33.3)	100 (34.6)
Age, mean (SD)	34 (10.4)	36 (11.1)	35 (10.9)
PSP[1], mean (SD) (n=288)	45 (7.8)	44 (6.7)	44 (7.2)
Imputed (n=289)	45	44	44
HAM-D6[2] (n=289)	9.97 (3.3)	10.4 (2.7)	10.2 (3.0)
HAM-A6[3] (n=289)	8.0 (3.7)	8.6 (3.5)	8.4 (3.6)
WHO-5[4] (n=242)	35.1 (20.2)	30.1 (17.5)	32.2 (18.8)
Imputed (n=289)	34.5	30.3	32.0
SDS[5] (n=251)	19.3 (5.8)	20.8 (4.7)	20.2 (5.2)
Imputed (n=289)	19.4	20.9	20.3
Apathy[6] (n=229)	8.8 (2.1)	8.9 (1.8)	8.9 (1.9)
Imputed (n=289)	8.5	8.8	8.6
Readiness to change[7] (n=230)	103 (14.1)	93 (19.0)	97.1 (17.7)
Imputed (n=289)	101.7	94.0	97.2

*RTW: return to work

[1]PSP: The Personal and Social Performance scale

[2]HAM-D6: The Hamilton Depression six-item Scale

[3]HAM-A6: The Hamilton Anxiety six-item Scale

[4]WHO-5: The WHO-5 well-being index

[5]SDS: The Sheehan Disability Scale

[6]Apathy: The Diagnostic Apathy scale

[7]Readiness to change: The Change Questionnaire

high-quality studies [24]. However, heterogeneity was high between studies decreasing the strength of the evidence, and other studies have found younger age to be associated with prolonged return to work or long-term unemployment [16, 42]. The association with higher age may be explained by structural factors such as employers being reluctant to hire people of a certain age and it may also become more difficult to be retrained and change profession with age [43]; factors that are all difficult to measure. We found higher age to be correlated with a diagnosis of depression, being cohabitant, higher level of education, and functioning and lower levels of anxiety, however, correlations were not very strong. Identifying factors that moderate the effect of age may be important, in order to modify the negative effect of higher age on return to work chances.

Readiness to change (CQ), in this case, to seek employment or education, was the strongest predictor for having obtained employment or education at 24 months follow-up.

Table 2 Univariate and multivariate logistic regression

	Univarite			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Study condition						
IPS-MA	0.832	0.520–1.331	0.443			
Control (1)	1					
Sex						
Male	1.023	0.615–1.701	0.930			
Female (1)	1					
Civil status						
Cohabitant (1)	1					
Non-cohabitant	0.890	0.546–1.452	0.641			
Education						
≤ Highschool (1)	1					
> Highschool	0.753	0.456–1.241	0.265			
Diagnose						
Depression (1)	1					
Angst	1.196	0.676–2.117	0.539			
Match group						
2 (1)	1					
3	0.872	0.533–1.426	0.585			
Age	0.980	0.959–1.002	**0.070***	0.975	0.952–0.998	**0.030****
PSP[1]	1.025	0.991–1.059	0.147			
HAM-D6[2]	0.954	0.881–1.033	0.247			
HAM-A6[3]	0.955	0.894–1.021	0.175			
WHO-5[4]	1.012	0.998–1.027	0.103			
SDS[5]	0.947	0.902–0.995	**0.032***	0.961	0.912–1.012	0.130
Apathy[6]	0.918	0.809–1.040	0.178			
Readiness to change[7]	1.028	1.011–1.046	**0.001***	1.027	1.009–1.045	**0.003****

[1]PSP: The Personal and Social Performance scale

[2]HAM-D6: The Hamilton Depression six-item Scale

[3]HAM-A6: The Hamilton Anxiety six-item Scale

[4]WHO-5: The WHO-5 well-being index

[5]SDS: The Sheehan Disability Scale

[6]Apathy: The Diagnostic Apathy scale

[7]Readiness to change: The Change Questionnaire

*Statistically significant values are given in bold (p < 0.1)

**Statistically significant values are given in bold (p < 0.5)

Not many studies have used the CQ scale, however, in line with our findings, a study on predictors of return to employment or education among people with severe mental disorders participating in the Individual Placement and Support intervention found a higher score on the CQ to predict return to employment during 18 months follow-up [44]. To some extent, the six constructs of the CQ (desire, ability, reasons, need, commitment, and taking steps) could reflect return to work expectations [45] and return to work self-efficacy [25] which have both been found to predict a shorter time to return to work. Return to work self-efficacy refers to the individual's belief in own capacity to perform a certain behavior, e.g. returning to work. People with high self-efficacy are considered to set higher goals, be more persistent in achieving and maintaining their goals, and be able to cope with setbacks better [46]. Concerning returning to work, domains of return to work self-efficacy like difficulties with concentration, coping with work pressure, dealing with emotionally demanding situations, and energy regulation are important [46] and areas that can be approached by cognitive behavioral therapy. Also, return to work expectations and self-efficacy, as well as the six related constructs of the CQ, are modifiable factors, which can be 'optimized' through therapy. In line with Bejerholm [8] other researchers have proposed to enhance or combine vocational rehabilitation with work-focused cognitive behavioral therapy to support

the return to work of people with common mental disorders [46–48].

Self-reported level of function (SDS) was only significantly associated with return to work in the univariate analyses. Other studies have found higher work functioning, which is one domain of the SDS scale, to be associated with an earlier return to work [24, 49, 50], and higher self-rated workability have been found to have a stronger association with return to work than other health-related measures like symptoms for instance [49]. This might indicate that people's own perception of their ability to work and their health condition is realistic, which may explain why only the self-reported SDS, and not the clinician-rated PSP was significantly associated with return to work in the present study.

In contrast to the findings of a number of studies, where the severity of e.g. depressive symptoms was associated with prolonged return to work [19, 50–52], we did not find the level of symptoms at baseline to be associated with return to work at 24 months. Other studies have found the same lack of association as us though [13, 46, 53], for instance, a study investigating the effect of work-focused cognitive behavioral therapy on return to work found no association between baseline levels of anxiety or depression and return to work [46]. The conflicting findings may indicate that one should be careful to predict time to return to work based on the severity of symptoms of anxiety or depression; firstly, the courses of illness of common mental disorders are heterogeneous and individual [54–56] and levels of symptoms at baseline do not necessarily predict severity of symptoms after 2 years [57], and secondly, people with common mental disorders have been found to have severe symptoms of both anxiety and depression and low level of work function even 1 year after having returned to work [56]. If the proper support is provided in the workplace, some people may be able to work even when not in complete remission. The employers' willingness to adapt working conditions (reduce working hours, provide support, etc.) has been found to influence people's return to work expectations, which, as mentioned, are associated with actual return to work [25, 49]. As such, barriers to return to work could also be related to the workplace/employer, factors that we were not able to measure in the present study.

Studies often define competitive employment differently, which may blur the ability to compare findings across studies. In accordance with the danish IPS-trial [5, 58], we used a rather broad definition of competitive employment, including wage-subsidized jobs in the private sector as well as flexible jobs, which is a dispute in the IPS-field. However, according to danish legislation people are provided financial support when obtaining competitive employment, for instance in wage-subsidized jobs in the private sector and flexible jobs. In both cases both types of employment are in line with the definition of competitive employment, since employees are able to negotiate wages and are paid at least minimum wages, just as jobs are open for everyone.

Strengths and Limitations

The present study is based on a large sample of clinically ill participants. Analyses are based on complete data from valid nationwide, Danish registers. We have complete data on clinician-administered patient-reported outcome data as well. For self-reported online measures, multiple imputations have been applied to make up for missing data.

A limitation is that we did not have data on several factors possibly associated with return to work or education, for instance; personal factors like general- or return-to-work self-efficacy, workability, expectations about time to return to work, and personality traits; and work-related factors such as previous work history, need for workplace accommodations, employers' willingness to hire or adapt working conditions for people with mental disorders, and also the stigma associated with having a mental disorder. Hence, many factors besides the ones reported in our study may impact people's return to work or education.

Furthermore, the associations reported are not causal relationships that suggest the endpoint status to be a function of the predictor. Instead, the predictors either facilitate or inhibit the return to employment or education.

Conclusion

Lower age and higher readiness to change at baseline predicted return to work or education at 24 months among people with depression and anxiety, included in a randomized clinical trial investigating the effect of individual placement and support modified for people with mood, and anxiety disorders.

Our study adds to the mixed evidence regarding the predictive value of age, supporting higher age to be associated with prolonged return to work. Future studies should investigate which factors moderate the effect of age; both personal, health-related, and workplace-related factors, including structural barriers.

Readiness to change is modifiable and future interventions should focus on how to increase people's readiness to change, maybe by adding work-focused cognitive behavioral therapy to vocational rehabilitation. Just as expectancy of future workability and self-efficacy, factors somewhat corresponding with readiness to change, should be focal

points in the development of interventions to support the return to work of people with common mental disorders.

An important finding is the lack of association between levels of symptoms and return to work or education, which indicates, that it may be important to measure readiness to change or related constructs like workability, and general-, or return to work self-efficacy, and not solely focus on symptoms when trying to predict the return to work of people with common mental disorders.

Declarations

Conflict of interest All authors declare no conflicts of interest.

Ethical Approval The IPS-MA trial was approved by The Regional Ethics Committees of the Capital Region (journal no: H-2-2011-FSP20), reported to the Danish Data Protection Agency (Journal no: 2007-58-0015, local journal no: RHP-2011-20), and registered at www.clinicaltrials.gov (identifier: NCT01721824).

Consent to Participate In the original trial all participants provided written and oral consent.

Consent for Publication Consent to participate was obtained from all participants, and the study was reported to the Danish Data Protection Agency (Journal no: 2007-58-0015, local journal no: RHP-2011-20).

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Predictors of Return to Work for People with Anxiety or Depression Participating in a Randomized Trial Investigating the Effect of a Supported Employment Intervention

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Abstract

Purpose Common mental disorders have a severe impact on society and individuals; rates of unemployment and disability pensions are high. Knowing which factors facilitate or hinder people's return to work is important when designing effective vocational rehabilitation interventions. *Methods* We conducted secondary analyses on data from 289 participants with depression or anxiety included in the Individual Placement and Support modified for people with mood and anxiety disorders (IPS-MA) trial. Associations of baseline characteristics and employment or education after 24 months were tested in univariate logistic regression analyses, variables with a p-value below 0.1 were included in multivariate analyses. *Results* In the univariate analyses, self-reported level of functioning ($p = 0.032$), higher age ($p = 0.070$), and higher level of readiness to change ($p = 0.001$) were associated with the outcome and included in the multivariate analysis. Only age ($p = 0.030$) and readiness to change ($p = 0.003$) remained significantly associated with return to work or education after 24 months in the multivariate analysis. *Conclusion* Higher age and lower readiness to change were associated with a lower chance of having returned to work or education. Factors modifying the effect of higher age should be identified, just as vocational rehabilitation should focus on improving factors related to people's readiness to change.

Keywords Predictors · Return to work · Depression · Anxiety

Background

Globally, people with common mental disorders like depression and anxiety are estimated to cost 1 trillion US Dollars per year in lost productivity alone [1]. In Denmark, the unemployment rate among people with mental disorders is more than 60%, and of those receiving long-term sickness benefits, 70% have a mental illness [2]. Moreover, anxiety is the number one reason for being granted a disability pension [3]. Besides the impact on society, unemployment may also have serious consequences for the individual with regards to economic insecurity, lowered confidence and self-esteem,

lack of meaning, and social isolation [4]. Evidence-based supported employment models like Individual Placement and Support (IPS) are effective in supporting people with severe mental illness in obtaining employment [5, 6]. However, a recent review of the effect of IPS according to diagnoses found indications that people with depression did not benefit from IPS to the same extent as people with schizophrenia, bipolar disorder, or substance use disorder [7]. Since depression is one of the most prevalent mental disorders and one of the greatest socioeconomic challenges globally, it is important to support this group of patients, also in their return to work [1]. Bejerholm et al. have proposed that people with depression might benefit from support in strengthening motivation and functional cognitive strategies in order to decrease depressive thoughts and avoidance behavior before attending vocational rehabilitation like IPS [8]. Accordingly, in a randomized trial, they found that the Individual Enabling and Support (IES) model of supported employment, which incorporates training in motivation and cognitive strategies prior to the IPS intervention, was more effective than services as usual [8]. As such, 42%

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of the participants in the IES group had returned to work, compared to only 4% in the control group. IES had good fidelity according to the IPS fidelity scale [9] and could be qualified as an IPS intervention supplemented with enabling strategies.

In a Danish randomized trial, the effect of IPS modified for people with mood or anxiety (IPS-MA) was also investigated [10]. In this case, the modified intervention, based on the IPS principles, consisted of mentor support and career counseling in addition to usual vocational services. The intervention was primarily modified with regards to the principle of integration of mental health and vocational services, which was not possible in a Danish context since people with mood and anxiety disorders are treated in many different settings in Denmark. Instead, mentors and career counsellors were employed in a private company, and IPS-MA mentors had an important role coordinating services provided with mental health-, and vocational services. Fidelity was measured on a modified Supported Employment fidelity scale [29] adapted to measure core elements of the IPS-MA intervention. Good fidelity according to seven of the eight IPS principles was reached. In contrast to most IPS populations, participants in IPS-MA had been employed or in education within the past 3 years; the aim was an early intervention to support participants in their return to work before they drifted too far from the labour market. In this trial, the modified IPS intervention was not found to be superior to standard treatment, as such, 44% in the intervention group had obtained employment after 2 years compared to 38% in the control group [10]. Even though the IES intervention was significantly superior to traditional vocational rehabilitation, in both the above studies only about 40% of the participants had returned to work, which is very low compared to IPS for people with severe mental illness where up to 60% of the participants obtain employment [5, 11]. With this in mind, we need to focus on how better to support people with depression and anxiety in obtaining employment. To do this, we need to know which challenges people face and if differences between those who obtain employment, and those who fail to obtain employment exist. If we could identify predictors of returning to work, we might be able to better target vocational rehabilitation. Some predictors are unchangeable like gender, age, etc.; they can only help us pay attention to specific target groups. However, other predictors are modifiable, like symptom severity, level of function, quality of life, readiness to change, etc. If a modifiable variable was associated with return to work, this could be of valuable knowledge when designing a new intervention.

Previous studies have found older age [12–14], lower level of education [13, 15, 16], gender [13, 17], low socio-economic status, and living alone [13, 18] to be associated with prolonged return to work among people with depression and anxiety. Health-related predictors were duration of

mental illness, severity of symptoms [19–23], previous sick leave, and comorbidity [20, 24]. Also, job-related factors like low job grades and high job stressors have been found to be associated with prolonged return to work [24]. Factors like self-efficacy [25] and return to work expectancy [26] have also been associated with return to work [27].

The purpose of the present study was to investigate what predicted return to work or education after 2 years, among 289 people with depression or anxiety who had participated in the IPS-MA trial.

Methods

Design and Participants

In the present study, we conducted secondary analyses of data from the Individual Placement and support modified for people with mood and anxiety disorders (IPS-MA) trial [10, 28]. The randomized clinical trial investigated the effectiveness of a supported employment intervention on return to employment or education among people sick-listed with a recent diagnosis of depression or anxiety. Participants were referred by mental health centers and private practicing psychiatrists in the Capital Region of Denmark from October 2011 until February 2014. Participants in the intervention group received mentor support and career counseling in addition to services as usual. The focus was on competitive employment or education, and support was time unlimited. The primary outcome of the trial was returning to competitive employment or education 2 years after enrolment. The control group received vocational services as usual as offered by the job centers. A full description of the intervention and methodology can be found in the trial protocol and effect article [10, 28].

Inclusion criteria were:

- Age between 18 to 60 years;
- A diagnosis of affective disorder (ICD-10: F30-39) or anxiety (ICD-10: F40-41);
- Not having had contact with mental health services for more than the past 3 years;
- Having been employed or enrolled in education at some time during the past 3 years;
- Being motivated to return to work or education;
- Being match group 2 or 3. (The job centers in Denmark use match groups to describe how far from the labor market people are. People in match group 2 are considered able to participate in pre-vocational training, but not able to work and be off public benefits within 3 months. People in match group 3 have more severe long-term problems and are not considered able to work or participate in prevocational training);

- Participants had to be able to read and understand Danish and give informed consent.

  Exclusion criteria:

- Somatic comorbidity causing reduced ability to work;
- Primary large-scale alcohol or substance abuse; or
- Having a legal guardian or forensic psychiatric arrangements.

In total 326 participants with mood and anxiety disorders were randomized, of these 37 had a diagnosis of bipolar disorder, and were not included in the present study. Since no difference in return to work or education was found in the original study, we merged the two groups in the present study.

Participants provided written informed consent prior to inclusion. The study was approved by The Regional Ethics Committees of the Capital Region (journal no: H-2-2011-FSP20), reported to the Danish Data Protection Agency (Journal no: 2007-58-0015, local journal no: RHP-2011-20), and registered at www.clinicaltrials.gov (identifier: NCT01721824).

Measures

Participants were assessed by clinician-administered scales in semi-structured interviews by blinded researchers, who were trained in the scales used, as well as by answering online patient-reported outcomes scales at baseline, and after 12 and 24 months. Also, participants were followed in the DREAM database [30], a register including weekly information on all citizens receiving public benefits from 1991 and onwards. The DREAM database is administered by the Danish Agency for Labour Market and Recruitment and based on data from the Ministries of Employment and Education, the Civil Registration System (CPR-register) [31], and the Danish Customs and Tax Administration (SKAT) [32].

The primary outcome of the present study is return to work or education 2 years after baseline; return to work was defined as being competitively employed (a week without government benefits combined with a work-code (indicating attachment to a company since labor market contributions have been paid)), being on rehabilitation benefits, flexible jobs, and wage-subsidized jobs in the private sector which are all competitive jobs (with the possibility of negotiating salary and earn pension) or under education, based on complete data from the highly reliable DREAM database [30].

Based on previous findings and the data available, we examined the following baseline measures as possible predictive factors of return to work or education: study condition (IPS-MA vs. services as usual), age, sex, civil status, level of education, diagnosis, level of symptoms and function, mental health-related quality of life, apathy, and readiness to seek employment or education. Symptoms of depression were measured by the Hamilton Depression six-item Scale (HAM-D6) [33, 34]. The six items measure core symptoms of depression on a 5-point Likert scale (except the item *tiredness/pain* which is measured on a 3-point Likert scale); 0 equals not present and 4 (2 regarding tiredness/pain) equals very severe. Scores are summed and a score between 0–4 reflects no depression, 5–6: doubtful, 7–8: mild, 9–11: moderate, and 12–22: severe depression. The Hamilton Anxiety six-item Scale (HAM-A6) [33, 35] was used to measure core symptoms of anxiety, also on a 5-point Likert scale (0 equals not present and 4 equals very severe). Scores are summed and scores of 0–4 reflect no anxiety, 5–6: doubtful, 7–8: mild, 9–14: moderate, and 15–24: severe anxiety. Level of functioning was measured by the Personal and Social Performance scale (PSP) [36] where the four sub-dimensions (1) socially useful activities, (2) personal and social relationships, (3) self-care, and (4) disturbing and aggressive behavior were summed to a total score between 0 and 100; a score of 100 indicating perfect functioning. All measures were assessed at baseline interview. Patient-reported measures were answered online at baseline and included: Mental health-related quality of life measured by the WHO-5 well-being index [33] where the scores from the five items are summed and multiplied by four, giving a score between 0 and 100; a higher score indicating better well-being. Apathy was measured by the Diagnostic Apathy scale [37]. The scale consists of six items; (1) difficulties in concentration and memory, (2) difficulties in concentration and decision making, (2) work and interests, (3) somatic general (fatigue and muscle pain), (4) tiredness, (5) lack of energy, and (6) sleep problems (insomnia) which are summed to a total score between 0 and 13, with a higher score indicating higher levels of apathy. Self-reported level of function was measured by The Sheehan Disability Scale (SDS) [38]. The SDS measures functional impairment in three inter-related domains; work/school, social, and family life scored from 0 to 10 and summed into a score from 0 (unimpaired) to 30 (highly impaired). The readiness to seek employment or education was measured by the Change Questionnaire (CQ) [39] consisting of 12 items covering six constructs: desire, ability, reasons, need, commitment, and taking steps towards making the change, each with a score from 0 (definitely not) to 10 (definitely). The scores are summed to a total score from 0 to 120; a higher score indicating higher readiness to change/seek employment or education.

Some of the categorical variables were merged; the three diagnoses were combined to two; (1) depression, and (2) anxiety (phobic and other anxiety); level of education was pooled to (1) maximum high school and (2) higher than high school, and civil status was comprised into (1) cohabitant

(married, registered partnership, co-habitant) and (2) non-cohabitant (divorced, widow, single).

Statistical analyses

Baseline characteristics are presented for those in employment/education after 2 years, those not in employment/education, as well as the total group. Categorical variables are presented with count (n) and percentages and mean and standard deviations (SD) are used for continuous variables. All original analyses were conducted according to the intention-to-treat (ITT) principles. We had complete data on all register and baseline interview data (except for one missing on PSP). Missing data were handled by multiple imputation, predictions were based on variables with full information indicative of missing values; 100 imputations were made. Crude and imputed results are presented.

First, bivariate relationships between independent variables and the outcome variables were tested by Spearman correlation. Univariate logistic regression was used to assess associations of all possible baseline predictors separately with return to employment or education at 24 months follow-up. Only variables associated with the outcome measure with a p-value below 0.1 were included in the multivariate logistic regression. Significant predictors were tested individually for non-linear associations. All numeric predictors were also tested with quadratic terms added to identify non-linear effects. Data were analyzed using SPSS version 25 [40].

Results

Of the 289 participants included in the present study, 118 (41%) had returned to work or education at 24 months follow-up. 144 had originally been randomized to the IPS-MA group and 145 to the SAU group. Almost 70% were women with a mean age of 35 (SD 10.9), most were non-cohabitant (63.7%), and 65.7% had an education that surpassed high school. Most of the participants had depression (77.9%) with a mean score corresponding to a moderate level of depression (mean 10.2, SD 3.0). Participants' self-reported well-being mean score was 32, indicating a rather low level of well-being (below 50 indicates a risk of stress or depression, 30 a high risk of depression). Level of functioning was also low with mean scores of 44 and 20 according to the PSP and SDS respectively, corresponding to moderate or marked impairments. The participants reported a rather high level of readiness to seek employment or education (mean 97.2). See Table 1.

Several of the covariates correlated significantly, however, most correlation coefficients were below 0.30, not strong enough to indicate multicollinearity. The strongest correlations were between level of functioning according to PSP and level of depressive symptoms, and level of apathy and depressive symptoms with correlation coefficients of 0.50 and 0.54 respectively. Readiness to change was the only covariate significantly correlated with return to work at 24 months (p < 0.000, rho = 0.266) (see online material for correlation matrix).

In the univariate analysis, a lower level of functioning according to the SDS was associated with a lower chance of being in employment after 24 months (OR = 0.947, 95% CI 0.902–0.995, p = 0.032), and a higher degree of readiness to seek employment or education was significantly associated with a higher chance of being employed or in education after 24 months (OR = 1.028, 95% CI 1.011–1.046, p = 0.001). Higher age was associated with a lower chance of having returned to work or education with a p-value below 0.1 (OR = 0.980, 95% CI 0.959–1.002, p = 0.070) as the only other variable. Hence age, level of functioning according to SDS, and readiness to change were included in the multivariate analysis. In the final model, age, and readiness to change were still significantly associated with being in employment or education. Higher age was significantly associated with a lower chance of having returned to work or education after 24 months follow-up (OR = 0.975, 95% CI 0.952–0.998, p = 0.030), whereas a higher level of readiness to change was associated with a higher chance (OR = 1.027, 95% CI 1.009–1.045, p = 0.003). Both variables were linearly associated with the probability of achieving employment at 24 months. The level of functioning was no longer significant in the final model (OR = 0.961, 95% CI 0.912–1.012, p = 0.130) (Table 2).

Discussion

In this study, including 289 participants with depression or anxiety, we found lower age and a higher level of 'readiness to seek employment or education' to be associated with higher odds of having returned to work or education after 24 months. In the univariate analysis level of functioning measured by SDS was significantly associated with return to work or education at 24 months follow-up, however, in the multivariate model, this association was no longer statistically significant.

Even if the OR is quite small, indicating that the odds of having returned to work is not very much impacted by age each years increase in age, the confidence interval is quite narrow and the association between higher age and less chance of having returned to work is well known and in line with other studies [12, 13, 24, 41]. In a systematic review and meta-analysis of prognostic factors of return to work after depression, a 10-year increase in age was found to be associated with a slower return to work across five

Table 1 Baseline characteristics of 289 participants with depression or anxiety in the IPS-MA trial

	RTW* at 24 mths (n=118)	Non-RTW at 24 mths (n=171)	Total sample (N=289)
Study condition, n (%)			
IPS-MA	62 (52.5)	82 (48.0)	144 (49.8)
Services as usual	56 (47.5)	89 (52.0)	145 (50.2)
Sex, n (%)			
Women	82 (69.5)	118 (69.0)	200 (69.2)
Men	36 (30.5)	53 (31.0)	89 (30.8)
Civil status, n (%)			
Cohabitant	41 (34.7)	64 (37.4)	105 (36.3)
Non-cohabitant	77 (65.3)	107 (62.6)	184 (63.7)
Education, n (%)			
≤Highschool	36 (30.5)	63 (36.8)	99 (34.3)
>Highschool	82 (69.5)	108 (63.2)	190 (65.7)
Diagnosis, n (%)			
Depression	94 (79.7)	131 (76.6)	225 (77.9)
Anxiety	24 (20.3)	40 (23.4)	64 (22.1)
Match group, n (%)			
2 (1)	75 (63.6)	114 (66.7)	189 (65.4)
3	43 (36.4)	57 (33.3)	100 (34.6)
Age, mean (SD)	34 (10.4)	36 (11.1)	35 (10.9)
PSP[1], mean (SD) (n=288)	45 (7.8)	44 (6.7)	44 (7.2)
Imputed (n=289)	45	44	44
HAM-D6[2] (n=289)	9.97 (3.3)	10.4 (2.7)	10.2 (3.0)
HAM-A6[3] (n=289)	8.0 (3.7)	8.6 (3.5)	8.4 (3.6)
WHO-5[4] (n=242)	35.1 (20.2)	30.1 (17.5)	32.2 (18.8)
Imputed (n=289)	34.5	30.3	32.0
SDS[5] (n=251)	19.3 (5.8)	20.8 (4.7)	20.2 (5.2)
Imputed (n=289)	19.4	20.9	20.3
Apathy[6] (n=229)	8.8 (2.1)	8.9 (1.8)	8.9 (1.9)
Imputed (n=289)	8.5	8.8	8.6
Readiness to change[7] (n=230)	103 (14.1)	93 (19.0)	97.1 (17.7)
Imputed (n=289)	101.7	94.0	97.2

*RTW: return to work

[1]PSP: The Personal and Social Performance scale

[2]HAM-D6: The Hamilton Depression six-item Scale

[3]HAM-A6: The Hamilton Anxiety six-item Scale

[4]WHO-5: The WHO-5 well-being index

[5]SDS: The Sheehan Disability Scale

[6]Apathy: The Diagnostic Apathy scale

[7]Readiness to change: The Change Questionnaire

high-quality studies [24]. However, heterogeneity was high between studies decreasing the strength of the evidence, and other studies have found younger age to be associated with prolonged return to work or long-term unemployment [16, 42]. The association with higher age may be explained by structural factors such as employers being reluctant to hire people of a certain age and it may also become more difficult to be retrained and change profession with age [43]; factors that are all difficult to measure. We found higher age to be correlated with a diagnosis of depression, being cohabitant, higher level of education, and functioning and lower levels of anxiety, however, correlations were not very strong. Identifying factors that moderate the effect of age may be important, in order to modify the negative effect of higher age on return to work chances.

Readiness to change (CQ), in this case, to seek employment or education, was the strongest predictor for having obtained employment or education at 24 months follow-up.

Table 2 Univariate and multivariate logistic regression

	Univarite			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Study condition						
IPS-MA	0.832	0.520–1.331	0.443			
Control (1)	1					
Sex						
Male	1.023	0.615–1.701	0.930			
Female (1)	1					
Civil status						
Cohabitant (1)	1					
Non-cohabitant	0.890	0.546–1.452	0.641			
Education						
≤Highschool (1)	1					
>Highschool	0.753	0.456–1.241	0.265			
Diagnose						
Depression (1)	1					
Angst	1.196	0.676–2.117	0.539			
Match group						
2 (1)	1					
3	0.872	0.533–1.426	0.585			
Age	0.980	0.959–1.002	**0.070***	0.975	0.952–0.998	**0.030****
PSP[1]	1.025	0.991–1.059	0.147			
HAM-D6[2]	0.954	0.881–1.033	0.247			
HAM-A6[3]	0.955	0.894–1.021	0.175			
WHO-5[4]	1.012	0.998–1.027	0.103			
SDS[5]	0.947	0.902–0.995	**0.032***	0.961	0.912–1.012	0.130
Apathy[6]	0.918	0.809–1.040	0.178			
Readiness to change[7]	1.028	1.011–1.046	**0.001***	1.027	1.009–1.045	**0.003****

[1]PSP: The Personal and Social Performance scale

[2]HAM-D6: The Hamilton Depression six-item Scale

[3]HAM-A6: The Hamilton Anxiety six-item Scale

[4]WHO-5: The WHO-5 well-being index

[5]SDS: The Sheehan Disability Scale

[6]Apathy: The Diagnostic Apathy scale

[7]Readiness to change: The Change Questionnaire

*Statistically significant values are given in bold (p < 0.1)

**Statistically significant values are given in bold (p < 0.5)

Not many studies have used the CQ scale, however, in line with our findings, a study on predictors of return to employment or education among people with severe mental disorders participating in the Individual Placement and Support intervention found a higher score on the CQ to predict return to employment during 18 months follow-up [44]. To some extent, the six constructs of the CQ (desire, ability, reasons, need, commitment, and taking steps) could reflect return to work expectations [45] and return to work self-efficacy [25] which have both been found to predict a shorter time to return to work. Return to work self-efficacy refers to the individual's belief in own capacity to perform a certain behavior, e.g. returning to work. People with high self-efficacy are considered to set higher goals, be more persistent in achieving and maintaining their goals, and be able to cope with setbacks better [46]. Concerning returning to work, domains of return to work self-efficacy like difficulties with concentration, coping with work pressure, dealing with emotionally demanding situations, and energy regulation are important [46] and areas that can be approached by cognitive behavioral therapy. Also, return to work expectations and self-efficacy, as well as the six related constructs of the CQ, are modifiable factors, which can be 'optimized' through therapy. In line with Bejerholm [8] other researchers have proposed to enhance or combine vocational rehabilitation with work-focused cognitive behavioral therapy to support

the return to work of people with common mental disorders [46–48].

Self-reported level of function (SDS) was only significantly associated with return to work in the univariate analyses. Other studies have found higher work functioning, which is one domain of the SDS scale, to be associated with an earlier return to work [24, 49, 50], and higher self-rated workability have been found to have a stronger association with return to work than other health-related measures like symptoms for instance [49]. This might indicate that people's own perception of their ability to work and their health condition is realistic, which may explain why only the self-reported SDS, and not the clinician-rated PSP was significantly associated with return to work in the present study.

In contrast to the findings of a number of studies, where the severity of e.g. depressive symptoms was associated with prolonged return to work [19, 50–52], we did not find the level of symptoms at baseline to be associated with return to work at 24 months. Other studies have found the same lack of association as us though [13, 46, 53], for instance, a study investigating the effect of work-focused cognitive behavioral therapy on return to work found no association between baseline levels of anxiety or depression and return to work [46]. The conflicting findings may indicate that one should be careful to predict time to return to work based on the severity of symptoms of anxiety or depression; firstly, the courses of illness of common mental disorders are heterogeneous and individual [54–56] and levels of symptoms at baseline do not necessarily predict severity of symptoms after 2 years [57], and secondly, people with common mental disorders have been found to have severe symptoms of both anxiety and depression and low level of work function even 1 year after having returned to work [56]. If the proper support is provided in the workplace, some people may be able to work even when not in complete remission. The employers' willingness to adapt working conditions (reduce working hours, provide support, etc.) has been found to influence people's return to work expectations, which, as mentioned, are associated with actual return to work [25, 49]. As such, barriers to return to work could also be related to the workplace/employer, factors that we were not able to measure in the present study.

Studies often define competitive employment differently, which may blur the ability to compare findings across studies. In accordance with the danish IPS-trial [5, 58], we used a rather broad definition of competitive employment, including wage-subsidized jobs in the private sector as well as flexible jobs, which is a dispute in the IPS-field. However, according to danish legislation people are provided financial support when obtaining competitive employment, for instance in wage-subsidized jobs in the private sector and flexible jobs. In both cases both types of employment are in line with the definition of competitive employment, since employees are able to negotiate wages and are paid at least minimum wages, just as jobs are open for everyone.

Strengths and Limitations

The present study is based on a large sample of clinically ill participants. Analyses are based on complete data from valid nationwide, Danish registers. We have complete data on clinician-administered patient-reported outcome data as well. For self-reported online measures, multiple imputations have been applied to make up for missing data.

A limitation is that we did not have data on several factors possibly associated with return to work or education, for instance; personal factors like general- or return-to-work self-efficacy, workability, expectations about time to return to work, and personality traits; and work-related factors such as previous work history, need for workplace accommodations, employers' willingness to hire or adapt working conditions for people with mental disorders, and also the stigma associated with having a mental disorder. Hence, many factors besides the ones reported in our study may impact people's return to work or education.

Furthermore, the associations reported are not causal relationships that suggest the endpoint status to be a function of the predictor. Instead, the predictors either facilitate or inhibit the return to employment or education.

Conclusion

Lower age and higher readiness to change at baseline predicted return to work or education at 24 months among people with depression and anxiety, included in a randomized clinical trial investigating the effect of individual placement and support modified for people with mood, and anxiety disorders.

Our study adds to the mixed evidence regarding the predictive value of age, supporting higher age to be associated with prolonged return to work. Future studies should investigate which factors moderate the effect of age; both personal, health-related, and workplace-related factors, including structural barriers.

Readiness to change is modifiable and future interventions should focus on how to increase people's readiness to change, maybe by adding work-focused cognitive behavioral therapy to vocational rehabilitation. Just as expectancy of future workability and self-efficacy, factors somewhat corresponding with readiness to change, should be focal

points in the development of interventions to support the return to work of people with common mental disorders.

An important finding is the lack of association between levels of symptoms and return to work or education, which indicates, that it may be important to measure readiness to change or related constructs like workability, and general-, or return to work self-efficacy, and not solely focus on symptoms when trying to predict the return to work of people with common mental disorders.

Declarations

Conflict of interest All authors declare no conflicts of interest.

Ethical Approval The IPS-MA trial was approved by The Regional Ethics Committees of the Capital Region (journal no: H-2-2011-FSP20), reported to the Danish Data Protection Agency (Journal no: 2007-58-0015, local journal no: RHP-2011-20), and registered at www.clinicaltrials.gov (identifier: NCT01721824).

Consent to Participate In the original trial all participants provided written and oral consent.

Consent for Publication Consent to participate was obtained from all participants, and the study was reported to the Danish Data Protection Agency (Journal no: 2007-58-0015, local journal no: RHP-2011-20).

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Trajectories of symptoms of anxiety and depression among people on sick leave with mood or anxiety disorders: Secondary analysis from a randomized controlled trial

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A B S T R A C T

Background: Depression and anxiety are heterogenous disorders often combined into one entity in studies. Few studies have compared trajectories of depression and anxiety among clinically ill. We aimed to identify specific trajectories of depression, and anxiety and predictors of trajectory membership.
Methods: Latent growth mixture modelling was carried out on data from the IPS-MA trial (n = 261), a supported employment intervention for people with mood or anxiety, to identify trajectories of depression and anxiety. Logistic regression was used to estimate predictors for trajectory membership. Associations between trajectory class and remission of comorbid depression or anxiety and return to work were also tested.
Results: We identified three trajectories of depression and anxiety symptoms respectively; moderate-decreasing (60%), moderate-stable (26%), and low-stable (14%) depression and mild-decreasing (59%), moderate-decreasing (33%), and moderate-stable (8%) anxiety. The depression model showed low precision in class separation (entropy 0.66), hence, predictors of class membership were not estimated. For anxiety, lower age and higher levels of depressive symptoms were associated with a less desirable trajectory. Remission of comorbid depressive symptoms after two years differed significantly between classes (p < 0.000). Fewer had returned to work in the two moderate classes compared to the mild-decreasing anxiety class.
Limitations: Depression model not reliable. Only 80% of participants from original study included. Not able to distinguish between anxiety disorders.
Conclusion: Trajectories of anxiety confirm that, even after two years, a rather large proportion in the moderate-stable class had symptoms of moderate anxiety, moderate comorbid depressive symptoms, and less probability of having returned to work.
Trial registration: ClinicalTrials.govNCT01721824.

1. Introduction

Clinical and growing epidemiological evidence agree that depression and anxiety are heterogenous disorders(Nandi et al., 2009); anxiety is associated with a longer time to remission, a more chronic course with lower rates of recovery, and relatively high rates of recurrence, compared to depression (Hendriks et al., 2013; Penninx et al., 2011). Nevertheless, studies often treat the disorders as one homogeneous entity (Nandi et al., 2009). In doing so, variations in the effect of interventions or treatments across diagnostic groups may be overlooked. Furthermore, within each of the two disorders different trajectories of course of illness have been identified (Merikangas et al., 2003; Batelaan

et al., 2014; Arends et al., 2019) and the literature suggests that factors generally associated with course of depression or anxiety may vary by trajectory subtype (Nandi et al., 2009). Ignoring this may mask an effect, or lack of effect, of an intervention for a subgroup of people(Nandi et al., 2009). Hence, in order to translate research into effective interventions it is important to distinguish outcomes between depression and anxiety, and to acknowledge that membership of a certain trajectory-class may be associated with different prognostic factors. Few studies have compared trajectories of depression and anxiety in the same study (Nandi et al., 2009; Penninx et al., 2011) and among clinically ill participants (Musliner et al., 2016). Studies are often limited to specific groups (young adults, mothers, caregivers etc.) which decreases

generalizability(Nandi et al., 2009). Furthermore, number of trajectories identified vary between studies (Batelaan et al., 2014; Wardenaar et al., 2014; Rhebergen et al., 2012) and in contrast to earlier studies (Nandi et al., 2009; Penninx et al., 2011; Merikangas et al., 2003), a recent study found four rather identical trajectories of depression and anxiety (Arends et al., 2019). Further research is needed to establish the evidence of unique trajectories of depression and anxiety.

In general, common mental disorders like depression and anxiety are associated with high levels of long-term sick leave and a subsequent struggle to return to work (RTW)(Oecd, 2019). It is likely that specific trajectory classes may be associated with distal outcomes like remission or RTW. Being able to identify factors associated with membership of a certain trajectory-class based on sociodemographic or disease specific characteristics, may help identify individuals at risk of a less favorable course of illness. In the literature poor symptom trajectory outcomes are associated with severity and duration of index episode, early age of onset, older age (Penninx et al., 2011), sex (Nandi et al., 2009), education (Nandi et al., 2009), and functional disability (Batelaan et al., 2014). Comorbidity of depression and anxiety is substantial (Merikangas et al., 2003) and often associated with a more chronic course of illness, and people with comorbid anxiety-depression often experience a higher degree of work disability compared to people without comorbidity (Hendriks et al., 2015). General predictors of prolonged RTW following depression or anxiety are older age (Lammerts et al., 2015; Vemer et al., 2013; Dewa et al., 2003), female gender (Vemer et al., 2013; Koopmans et al., 2008), low level of education (Ervasti et al., 2014), being married or cohabitant (Vemer et al., 2013; Tolman et al., 2009), as well as severity of depression and anxiety symptoms (Dewa et al., 2003; Banerjee et al., 2014; Druss et al., 2001; Nielsen et al., 2012; Bultmann et al., 2006). In contrast, a recent study found a high RTW among patients in moderate or high anxiety trajectories, high depressive symptom trajectory, and moderate to low workfunctioning trajectory (Arends et al., 2019). If membership of a certain trajectory of depression or anxiety is associated with a lower chance of RTW, being able to predict this would be valuable and could guide carers and social workers in providing the adequate support. However, few studies have studied this association (Arends et al., 2019).

The aim of this study is to describe trajectories of symptoms of depression and anxiety including if and how they differ. Secondly, we wish to investigate whether baseline characteristics or comorbid depression-anxiety are related to class membership. Finally, we will investigate if remission of symptoms or RTW are associated with membership of a certain trajectory class.

RTWHypotheses are:

1. Unique trajectories of symptoms of depression and anxiety exist. Trajectories of anxiety are characterized by a more chronic course, lower rates of recovery, and higher rates of recurrence, compared to trajectories of depression
2. Comorbid depression-anxiety, higher symptom severity, older age, male gender, lower education, and low level of function predict membership of a less desireable trajectory class.
3. Remission of comorbid symptoms of anxiety or depression is associated with a more favorable trajectory class-membership
4. RTW is associated with a more favorable trajectory class-membership

2. Methods

2.1. Study design and participants

Participants were included in the Individual Placement and Support modified for people with mood and anxiety disorders (IPS-MA) trial (Hellstrom et al., 2013; Hellström et al., 2017), a randomized trial evaluating the effect of a supported employment intervention on RTW or education for participants on sick leave with recently diagnosed mood or anxiety disorders. Participants were referred by mental health centres and private practicing psychiatrists in the Capital Region of Denmark from October 2011 until February 2014. The IPS-MA trial has previously been described in detail(Hellstrom et al., 2013; Hellström et al., 2017). In short, the intervention group received support from a mentor and career counselling in addition to services as usual. Focus was on competitive employment and education; support was time unlimited. The control group received vocational services as usual as offered by the jobcentres. The primary outcome of the trial was return to competitive employment or education two years after enrolment in the study.

2.2. Inclusion criteria

- Age 18–60 years,
- A diagnosis of affective disorder (F30-39) or anxiety (F40-41) according to the International Classification of Disease 10th version (World Health Organization (WHO), 2016)
- Exclusively had contact with mental health services in the past three years, i.e. no contact prior to this,
- Employed or enrolled in education at some point in the past three years,
- Motivated to return to work or education.
- Match-group 2 or 3. (Match-groups describe 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: more severe long-term problems and not able to work or participate in prevocational training).
- Able to read and understand Danish and give informed consent.

Exclusion criteria:

- Somatic comorbidity causing reduced ability to work;
- Large-scale alcohol or substance abuse;
- Legal guardian or forensic psychiatric arrangements.

Participants provided written informed consent prior to inclusion. The study was approved by The Regional Ethics Committees of the Capital Region (journal no: H-2-2011-FSP20), reported to the Danish Data Protection Agency (Journal no: 2007-58-0015, local journal no: RHP-2011-20), and registered at www.clinicaltrials.gov (identifier: NCT01721824).

2.3. Procedures

Participants were interviewed and answered online patient-reported outcome scales. Furthermore, participants were followed in the DREAM database (The Danish Agency for Lab, 2015), a register administered by the Danish Agency for Labour Market and Recruitment, containing weekly information on all citizens receiving public benefits from 1991, based on data from the Ministries of Employment and Education, the Civil Registration System (The Civil Registration Sy, 2018) and the Danish Customs and Tax Administration (The Danish Customs and Ta, 2017).

2.4. Measures

Symptoms of anxiety were measured by The Hamilton Anxiety Scale (HAM-A6)(Maier et al., 1988; Bech, 2012). The six items measure core symptoms of anxiety on a 5-point Likert scale (0 equals not present and 4 equals very severe). Scores are summed and scores of 0–4 reflect no anxiety, 5–6: doubtful, 7–8: mild, 9–14: moderate and 15–24: severe anxiety(Bech, 2012).

The Hamilton Depression Scale (HAM-D6) was used to measure symptoms of depression(Bech, 2012; O'Sullivan et al., 1997). Six items measure core symptoms of depression on a 5- point Likert scale (the item tiredness/pain is measured on a 3-point Likert scale); 0 equals not

present and 4 (2 regarding tiredness/pain) equals very severe. Scores are summed and 0–4 reflects no depression, 5–6: doubtful, 7–8: mild, 9–11: moderate, and 12–22: severe depression(Bech, 2012; Timmerby et al., 2017; Carrozzino et al., 2020).

Participants were interviewed at baseline and after 12 and 24 months, providing three measurement points. At 12- and 24- month follow-up 26% and 30% respectively had missing data on HAM-A6 and HAM-D6. Only participants with at least two measures were included, leaving 261 participants (80%) in the analysis. Responders and non-responders were compared on all baseline measures; non -responders were significantly more likely to be men and non-cohabitant.

Based on previous findings (Nandi et al., 2009; Penninx et al., 2011; Batelaan et al., 2014) and data available, the following baseline measures were examined as possible trajectory membership predictors: gender, age, diagnosis (mood disorders (depression and bipolar disorder) vs. anxiety (phobic and other anxiety)), level of education (high school or lower vs. higher than high school), civil status (cohabitant (married, registered partnership, co-habitant) vs. non-cohabitant (divorced, widowed, single)), as well as level of symptoms and function. Information on diagnosis was provided by mental health professionals on referral and confirmed by the MINI International Neuropsychiatric Interview(Sheehan et al., 1998). Information on level of education, and civil status was gathered by asking the participants. Level of functioning was measured by The Global Assessment of Functioning (GAF-F)(Pedersen and Karterud, 2012), which measures social and occupational functioning. The scale is scored from 0 (severely impaired) – 100 (best possible level of functioning).

In additional analyses, we examined whether a certain trajectory was associated with remission of comorbid depression or anxiety or RTW at two-year follow-up. Remission was defined as a score below 7 on both HAM-D6 or HAM-A6. RTW was defined as being competitively employed (a week without government benefits combined with a work code (indicating attachment to a company since labour market contributions have been paid), being on rehabilitation benefits, flexible jobs, and wage-subsidized jobs in the private sector which are all competitive jobs on ordinary terms, with the possibility of negotiating salary and earn pension) or under education, based on data from the DREAM database (The Danish Agency for Lab, 2015).

2.5. Statistical analysis

Two separate analyses were conducted on symptoms of depression and anxiety respectively. In Mplus statistical software, we applied latent growth mixture modelling (LGMM) to identify unique patterns of course in symptoms of depression or anxiety (Jung and Wickrama, 2008). LGMM is a data-driven person-centered approach, that identifies population subgroups (classes) based on prototypical patterns in intercepts and slopes(Muthén and Muthén, 2000).

To enhance precision of analyses, we included all participants with at least two measures of symptoms of depression (n = 261) and anxiety (n = 261) in the LGMM and handled missing data by application of Full Information Maximum Likelihood (FIML)(Muthen and Muthen, 2012). Initially, a series of LGMM-models were estimated for symptoms of depression and anxiety ranging from one to four classes. These models were evaluated based on Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC), and the Sample-Size adjusted BIC (adj. BIC). Also, entropy of the model, class accuracy and model fit improvement with addition of an extra class tested by Lo-Mendell-Rubin, Vuong-Lo--Mendell-Rubin, and the Bootstrap likelihood ratio tests, respectively, were applied to evaluate models. Lastly, model selection was also based on subjective evaluation parsimony and theoretical meaningfulness of the models. We tested predictors of class membership by applying the Three-Step approach. In this approach, covariates are not included in the model but treated as auxiliary variables, thus, covariates do not influence the formation of classes, but their association with the latent classes is tested based on the probabilistic nature of class assignments.

Therefore, class membership is established first, and subsequently predictors for membership of identified latent classes are examined (Asparouhov and Muthén, 2014). Predictors were first tested univariately, and secondly in a multivariable model including all variables from the univariable analyses with a p-value below 0.10. Level of significance was set to p < 0.05. All analyses were carried out in Mplus version 7.

In additional analyses, we tested distal outcomes. By applying the Lanza method(Asparouhov and Muthén, 2014; Wickrama et al., 2016) we estimated each class' mean for depression level and looked into the probability of being remitted and for RTW at 2-year follow-up.

3. Results

Baseline characteristics of 261 participants included in the analysis are shown in Table 1.

3.1. Trajectories of depressive symptoms

Linear LGMM models were estimated for one to four classes with free variance around the intercept and slope, however models displayed warnings for the two- and four-class models regarding both intercept and slope. Hence, we ran models with fixed variance around the intercept and the slope, respectively. Both models converged with no warnings in one to four classes estimation. Of these two different models the fit estimates in the models with variance fixed around the slope were slightly lower than fit estimates in the models with fixed variance around the intercept, thus indicating that models with variance fixed around the slope had a slightly better statistical fit of the data. In Table 2 the fit estimates, p-values for n-1 class fit and entropy's for models of depression trajectories with variance fixed around the slope are presented from one to four classes. The fit estimates drop when adding classes, however in the four-class model the BIC estimate is higher than in the three-class model indicating that the four-class model is inferior. This is supported by the p-values for adding a fourth class being non-significant in all three tests hereof. Thus the three-class model indicated the best statistical fit of data, however based on the entropy on .66

Table 1
Baseline characteristics of 261 participants included in the trajectory analysis.

Variables	All included participants (n = 261)
Age - Mean (sd)	38 (10.9)
Intervention	
IPS-MA – n (%)	141 (54)
Control – n (%)	120 (Schneider et al., 2014)
Sex	
Female – n (%)	186 (71)
Male – n (%)	75 (Bech, 2012)
Level of education	
≤Highschool – n (%)	90 (34.5)
>Highschool – n (%)	171 (60.2)
Civil status	
Cohabitant – n (%)	104 (39.8)
Non-cohabitant – n (%)	157 (60.2)
Diagnosis	
Affective – n (%)	206 (78.9)
Anxiety - n (%)	55 (21.1)
Symptoms (HAM[a] > 6 at baseline)	
Depression - n (%)	207 (79,3)
Anxiety - n (%)	154 (59)
RTW[b] at 2 years follow-up	
Non RTW – n (%)	150 (57.5)
RTW – n (%)	111 (42.5)
Remission of depression at two-year follow-up	
Remission – n (%)	152 (58.2)
Non-remission – n (%)	77 (29.5)
Missing – n (%)	32 (12.3)

[a] The Hamilton anxiety or depression 6 items scale.
[b] RTW: returned to work.

Table 2
Goodness-of-Fit Statistics for 1 to 4 class Solutions of symptoms of depression (HAM-D6) and anxiety (HAM-A6).

	Fit estimates[a]			P-values[b]			Entropy[j]	class size (%)[c]	Accuracy[k]
	AIC[d]	BIC[e]	Adj. BIC[f]	Vuong-Lo-Mendell-Rubin likelihood ratio test[g]	adj. Lo-Mendell-Rubin likelihood ratio test[h]	Bootstrapped likelihood ratio test[i]			
Depression trajectories									
1 class	3841	3862	3843					100	
2 class	3820	3852	3824	0.0218	0.0265	0.0000	0.61	70;30	0.90; 0.83
3 class	3805	3848	3810	0.0087	0.0111	0.0000	0.66	58; 26; 14	0.86; 0.82; 0.81
4 class	3802	3856	3808	0.3255	0.3842	0.1071	0.67	46; 29; 12; 13	0.86; 0.72; 0.85; 0.80
Anxiety trajectories									
1 class	3852	3877	3866					100	
2 class	3831	3867	3835	0.0039	0.0052	0.0000	0.72	72; 28	0.94; 0.85
3 class	3820	3866	3825	0.0844	0.0946	0.000	0.78	8; 33; 59	0.92; 0.87; 0.85
4 class	3822	3879	3828	0.206	0.2209	0.6667	0.68	19; 16; 56; 8	0.71; 0.61; 0.90; 0.84

[a] Statistical information criteria. A lower value indicates a better fit.
[b] A significant P-value indicates that the model with n number of classes is a better t of the data compared to a model with n – 1 number of classes.
[c] Distribution of the total sample into identified classes based on the posterior probability.
[d] Akaike Information Criteria – a lower value indicates better model-fit.
[e] Bayesian Information Criteria – a lower value indicates better model-fit.
[f] Sample size adjusted BIC – a lower value indicates better model-fit.
[g] The Vuong Lo Mendell Rubin likelihood ratio test.
[h] The Lo Mendell Rubin adjusted likelihood ratio test.
[i] Bootstrap Likelihood Ratio Test.
[j] Entropy is estimated based on the average posterior probability and ranges from 0 to 1 where higher estimates represent greater classification accuracy for the overall model.
[k] Expresses the average accuracy of membership classification in each class. As the entropy measure it ranges from 0 to 1 where higher estimates represent greater classification accuracy.

and on the estimated means and observed individual values plot (see online Fig. 1) it did not represent a model that indicates clear class separation, i.e. the precision of individual classification is low.

Fig. 1 shows the three trajectories of symptoms of depression. In the largest class, the moderate-decreasing class (60% (156/261)), participants had symptoms of a moderate depression at baseline (HAM-D6 scores between 10 and 11) ending with a score of 4 (no depression) after two years. The moderate-stable class (26% (69/261)) had a stable course of moderate depressive symptoms (between nine and 11) during the two-year follow-up. The smallest class, the low-stable class (14% (36/261)), consisted of participants with a score between five and six throughout the two-year follow-up, corresponding to doubtful symptoms of depression (Fig. 1). Even though entropy is not a measure of fit, when the aim is to identify homogenous classes of people with distinctive changes in symptom profiles, then a low entropy (such as 0.66) indicates reduced reliability in class separation (Nagin and Carnegie Mellon, 1999; Feldman et al., 2009) and thus low precision in individual class membership. Therefore, we decided not to estimate predictors of depression class membership and to only present the identified trajectories of depression symptoms.

3.2. Trajectories of anxiety symptoms

Goodness-of-fit statistics for the LGMM analyses of anxiety are shown in Table 2. We estimated linear term LGMM models from one to four classes with free variance around the intercept and slope. Based on goodness-of-fit statistics we decided on the three-class model to best present data on symptoms of anxiety. All fit estimates (AIC, BIC and adj. BIC) drop until the four-class model where they start increasing. The p-values, especially the Bootstrap likelihood ratio test, indicate that adding a third class improved the model, whereas a fourth class did not add value to the model according to the presented p-values in Table 2. Also, the entropy score was highest in the three-class model with an estimate of 0.77 indicating a great classification accuracy for the whole model and the individual class accuracy scores in the three-class model also expressed great classification accuracy all above 0.85.

The three prototypical classes representing subgroups with different trajectories of anxiety symptoms over the 2-year follow-up are presented in Fig. 2. The mild-decreasing class had most members (59% (153/261)) and started with a mean score of 7.1 on the HAM-A6 (intercept) corresponding to mild anxiety and ended with a mean score of 2.3 in the 'no-anxiety' area in the figure (slope = −2.3, p < 0.001). The moderate-decreasing class (33% (86/261)) started with a higher intercept (9.9), corresponding to moderate anxiety, but also had a significant improvement (slope = −1.3; p < 0.001) in symptoms ending their trajectory course in the mild area with a score of 7.2. The smallest class, the moderate-stable class, consisting of 8% (22/261) had a stable course of anxiety (slope p-value = 0.269) staying in the moderate area throughout the two-year follow-up starting with a mean score of 11.0, ending at 12.5 at the last follow-up. Fig. 3 illustrates each class with observed individual values. The figure illustrates that the data-driven prototypical classes seems especially defined by the slopes, and the HAM-A6 score at the two-year follow-up, thus in all classes the individual variation in HAM-A6 score is very wide-ranged at baseline whereas at two-year follow-up the individual observed variation around the mean for each class is smaller.

3.3. Predictors

In the univariable analyses only age, symptoms of depression, and level of function had a p < 0.10 and were included in the multivariable model (Table 3). None of the predictors were significant when the moderate-stable class was reference, presumably due to the small sample (online Table 1). Older age was associated with lower odds of being in the moderate-decreasing class compared to the mild-decreasing class (OR 0.96, 95% CI 0.93–1.00, p = 0.033). Higher levels of depressive
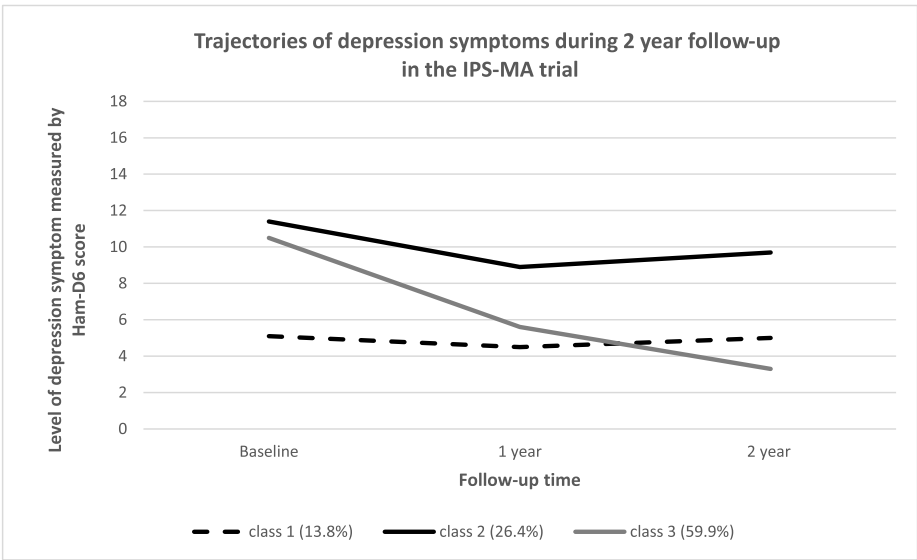
Fig. 1. Trajectories of symptoms of depression during 2-year follow-up of participants in the IPS-MA trial.
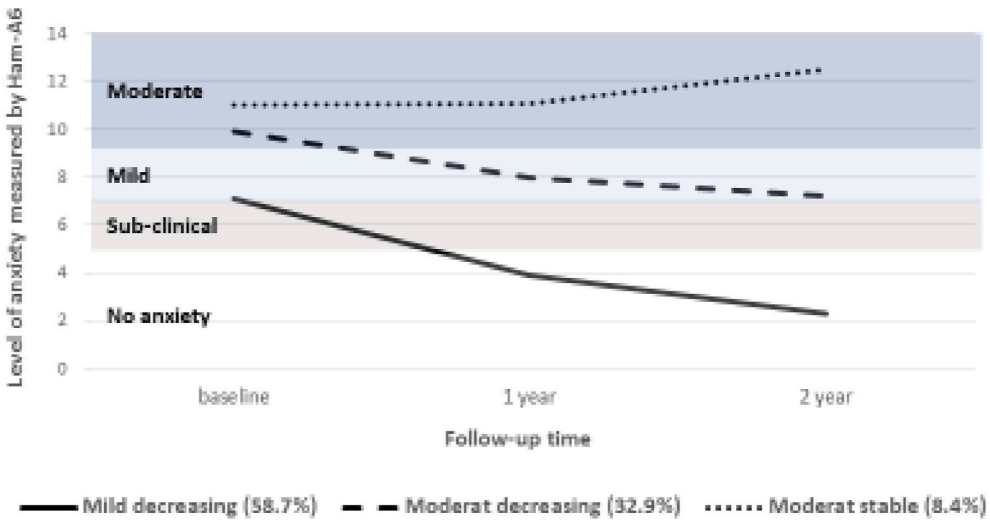

Fig. 2. Trajectories of symptoms of anxiety (HAM-A6) during two-year follow-up of 261 participants in the IPS-MA trial.
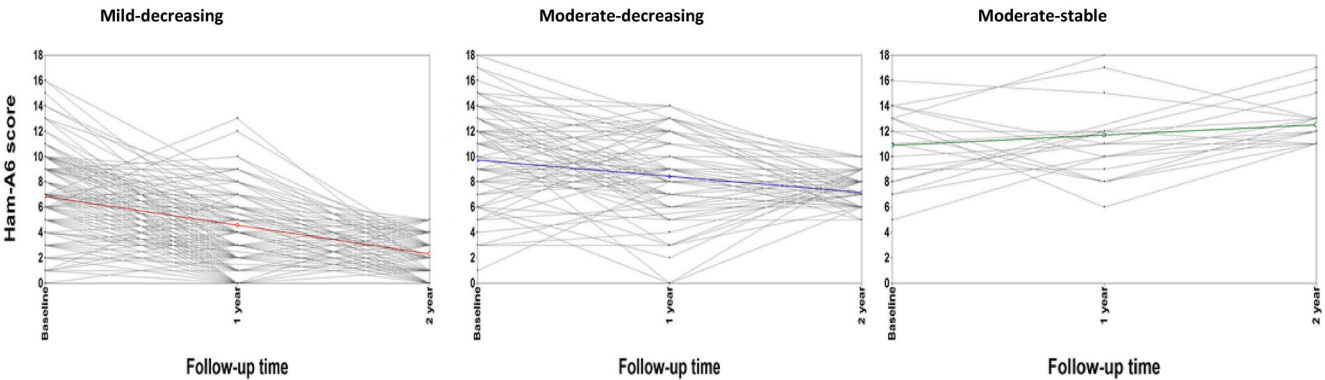

Fig. 3. Three trajectory classes with individual observed trajectories of symptoms of anxiety.

symptoms at baseline was associated with higher odds of being in the moderate-decreasing class compared to the mild-decreasing class (OR 1.12, 95% CI 1.03–1.41, p = 0.018).

3.4. Additional analyses

Associations between class-membership and remission of symptoms

Table 3
Univariable and multivariable associations of baseline predictors with anxiety trajectory classes in 261 participants.

	Univariable[a]				Multivariable[a,b]			
	Moderate decreasing versus mild decreasing		Moderate stable versus mild decreasing		Moderate decreasing versus mild decreasing		Moderate stable versus mild decreasing	
	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value
Age	0.96 (0.93–1.00)	**0.030**	0.97 (0.92–1.02)	0.224	0.96 (0.93–1.00)	**0.033**	0.97 (0.92–1.02)	0.267
Gender								
Female (ref)	1		1					
Male	0.53 (0.24–1.17)	0.115	0.48 (0.13–1.78)	0.271				
Civil status								
Cohabitant (ref)	1							
Non-cohabitant	1.53 (0.75–3.14)	0.243	0.85 (0.29–2.47)	0.768				
Education								
≤Highschool (ref)	1		1					
>Highschool	0.76 (0.37–1.56)	0.46	0.41 (0.14–1.20)	0.105				
HAM-D6[c] baseline	1.19 (1.03–1.37)	**0.017**	1.12 (0.96–1.30)	0.171	1.21 (1.03–1.41)	**0.018**	1.09 (0.93–1.28)	0.273
GAF[¶] - baseline	0.96 (0.90–1.01)	0.14	0.94 (0.88–1.01)	**0.091**	1.00 (0.94–1.07)	0.964	0.97 (0.91–1.03)	0.313

[¶]GAF: Global assessment of functioning scale.
[a] Mild decreasing is reference.
[b] Variables with a p-value<0.100 in the univariable analysis was included in the multivariable analysis.
[c] HAM-D6: The Hamilton Depression Scale – 6 items.

of depression were also tested. In the moderate-stable class none had remission, whereas there was a 41% probability in the moderate-decreasing class, and 94% probability of remission in the mild-decreasing class. The probability of remission was significantly different when comparing all classes pairwise (p < 0.001 in all three comparisons). The mean level of depression at two-year follow-up was 11 in the moderate-stable class (corresponding to moderate depression), 7 in the moderate-decreasing class (mild depression), and 3 in the mild-decreasing class (no depression), also these means differed significantly (Table 4).

Furthermore, we tested if a certain class was associated with RTW at two year follow-up (Table 4). In the moderate-stable and moderate-decreasing classes there were a 25% probability of RTW at two-year follow-up, whereas the probability was 55% in the mild-decreasing class. Comparing the three classes pairwise, there was no difference between the moderate-stable and decreasing groups (p = 0.990), or the moderate-stable group and the mild-decreasing group (p = 0.51). This could be explained by the very small moderate-stable class. Comparing the moderate-decreasing group with the mild-decreasing the probability of RTW was significantly different (p = 0.001).

Table 4
Probability of RTW and remission of depression at two-year follow-up according to trajectory class in 261 participants.

	Class 1 Moderate stable	Class 2 Moderate decreasing	Class 3 Mild decreasing	Chi-square test between classes
Distal outcome 2 year follow-up	Probability	Probability	Probability	p-value
RTW				Overall < 0.001
Non-RTW	0.748	0.746	0.451	
RTW	0.252	0.254	0.549	
Remission HAM-D6[a]				Overall < 0.001
Non-remission	1.000	0.586	0.064	
Remission	<0.001	0.414	0.936	

[a] Remission of HAM-D6: Hamilton Depression Scale – 6 item, with a score below 7.

4. Discussion

In our sample, we found three trajectories of depressive symptoms; moderate-decreasing, moderate-stable, and low-stable. However, the relatively low entropy (0.66) indicated a poor model for individual classification. Hence, we could not reliably confirm if unique trajectories of depressive symptoms exist, nor could we compare the trajectories of depressive symptoms with those of anxiety or look at predictors of being in a certain class. The high percentage of non-cohabitant participants in our sample may have affected the model of depression trajectories since being cohabitant is associated with depression(Schneider et al., 2014). However, the association is quite complex and differs for men and women and depends on whether they are married, cohabitant or in a relationship, hence, it is difficult to say how and if it has affected the model.

We found three trajectories of symptoms of anxiety: moderate-stable, moderate-decreasing, and mild-decreasing. Lower age and higher level of depressive symptoms were associated with being in the moderate-decreasing class when compared to the mild-decreasing class. After two years, significantly more people experienced a remission of depression in the mild-decreasing group compared to the other two groups. In addition, more people had returned to work in the mild-decreasing class. No difference was found between the two moderate groups.

Our findings are in accordance with previous findings (Batelaan et al., 2014; Arends et al., 2019). Batelaan et al. also found three trajectory classes; mild (42%), moderate (43%), and severe, chronic anxiety(15%) (Batelaan et al., 2014). Contrary to Batelaan, we did not find baseline severity of anxiety to predict course of illness. Arends et al. found four trajectories; three had very similar trajectories as ours (stable high (17.6%), high decreasing (53.8%), low decreasing (13.3%)). However, they found a fourth trajectory (stable low (15.3%)), possibly because their participants were ready to RTW and may have been further in their recovery process. The trajectories found in our study are characterised by very heterogene within-class levels of anxiety at baseline (range:5–16 in the moderate-stable class, 1–18 in the moderate-decreasing, and 0–16 in the mild-decreasing class), and more homogene within-class levels of symptoms after two years (range 10–17 moderate-stable, 5–10 moderate-decreasing, and 0–5 in the mild-decreasingclass). The trajectories seem to be defined by their slope and the level of anxiety symptoms two years after basline. Our results

indicate that practitioners should be careful to predict the outcome of the anxiety disorder based on initial symptom severity.

Contrary to other studies (Penninx et al., 2011; Boer et al., 2019), we found older age to be associated with being in a more favorable trajectory class (mild-vs moderate-decreasing), maybe because people benefit more from treatment and gain more beneficial coping strategies with age.

In accordance with other studies(Penninx et al., 2011; Batelaan et al., 2014), we found that comorbid anxiety-depression was associated with the worst course of illness; significantly more people experienced a remission of depression in the mild-decreasing group compared to the other two groups after two years. Penninx et al. found that 47.6% of patients with depression and 46.0% with anxiety had remission after two years, whereas only 25.1% of patients with comorbid anxiety-depression had remitted (Penninx et al., 2011). Batelaan found co-morbid depression at baseline to be associated with being in the severe-chronic class compared to the mild, and moderate, chronic anxiety classes(Batelaan et al., 2014).

We did not find any associations between trajectory class and gender, level of education or function, which may be due to power.

We found a lower probability of RTW in the two moderate classes, compared to the mild-decreasing class, which is in accordance with other studies where people with comorbid anxiety-depression reported most workdisability(Hendriks et al., 2015). Even when patients are free of symptoms of anxiety and improve in social functioning and cognition, work functioning can still be affected (Iancu et al., 2014).

4.1. Strengths and limitations

Strengths of our study are that data was gathered by trained interviewers and that we had complete data on employment from highly reliable registers.

A clear limitation is that we could not produce a reliable model of trajectories of depressive symptoms.

Participants had all been admitted to mental health care as in- or outpatients, were quite ill and a selected group, hence, results may not be generalizable to less severely ill patients. Furthermore, there is a risk that carers recruiting participants did not inform the most ill patients about the trial since the focus was RTW, which would also compromise generalizability.

Only 261 of the 326 participants had at least two measurement points, which may have affected the results. If those not showing up for follow-up were the most ill, results may have been underestimated with regards to the size of the moderate classes, resulting in differences between classes probably being easier to detect. Fewer would probably have experienced remission in the moderate classes just as the proportion who had RTW at two-year follow-up would be smaller. When comparing responders to non-responders, the only significant difference was that non-responders were more likely to be men and non-cohabitant.

More frequent measurement points might have produced more detailed trajectories and strengthened the results. It would also have been interesting to investigate variables that could have had an impact on depression or anxiety between timepoints. This was not possible in these secondary analyses, due to the limited numbers of follow-ups and measures gathered at these time points.

It is a limitation that we did not consider type and amount of treatment which could be associated with trajectory class. However, participants were primarily referred from mental health centres, receiving outpatient standard treatment, and amount of treatment did not differ between intervention groups in the original trial (data not shown). Information on use of psychologists or private practicing psychiatrists was not available. It is also a limitation that we did not take time out of work before baseline into account, since this could vary from a few days till three years and could very well be associated with membership of a certain class.

Studies have found that trajectories differ across anxiety disorders (Hendriks et al., 2013; Batelaan et al., 2014). We did not have power to differentiate between different anxiety disorders but had to focus on anxiety in general.

The moderate-stable class was quite small, and we may not have had power enough to establish a significant difference between mild-decreasing and moderate-stable regarding RTW after 2 years. Overall, it is a limitation that the sample size of our study is in the lower end in order to conduct trajectory analyses.

5. Conclusion

We identified three trajectories of depression but could not reliably separate participants into the respective classes. A larger sample is probably needed to produce a more solid model of trajectories of depressive symptoms.

We found that anxiety is indeed a disorder associated with individual and heterogeneous courses of illness. An important finding is that initial severity of symptoms did not seem to be associated with course of illness, which could be of valuable knowledge when trying to encourage hope in patients in the acute phase.

We confirmed that people with comorbid symptoms of depression had a less favorable course of illness. Furthermore, non-remission of depressive symptoms two years after baseline was associated with the less favorable trajectory classes; practically none in the moderate-stable class had reached remission of depressive symptoms after two years. Professionals need to pay attention to this group of patients which might need more intensive care.

RTW two years after study enrolment was highest in the mild-decreasing class compared to the two moderate classes.

Data availability

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

Authors contributions

All authors participated in the planning and design of the study, interpretation of the results, and have read and critically revised the manuscript. TM conducted the data analysis and drafting of the figures. LH wrote the manuscript.

Compliance with ethical standards.

Ethical approval

The study was approved by The Regional Ethics Committees of the Capital Region (journal no: H-2-2011-FSP20), reported to the Danish Data Protection Agency (Journal no: 2007-58-0015, local journal no: RHP-2011-20), and registered at www.clinicaltrials.gov (identifier: NCT01721824).

Informed consent

All participants provided oral and written informed consent prior to inclusion in the study.

Declaration of competing interest

We declare no conflict of interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2021.02.040.

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