Negative symptoms in first-episode psychosis: clinical correlates and one-year follow-up outcomes in London Early Intervention Services.

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Abstract

Aim: Negative symptoms are associated with poor outcome in patients with schizophrenia but are generally resistant to treatment. There has been growing interest in the role of negative symptoms in the early stages of the illness. In this study, we examine the association between negative symptoms in patients at initial presentation with first episode psychosis and clinical outcome at 1-year.

Methods: Clinical data were utilized from five London Early Intervention Services included in the MiData audit database. The sample comprised 484 first-episode psychosis patients with complete Positive and Negative Syndrome Scale data at baseline and 1-year follow-up. Multiple imputation (N = 50) was conducted to account for missing follow-up data.

Results: Baseline negative symptoms were associated with male gender (B = -1.63, p <. 05), younger age of onset (B = -.15, p <. 05), a higher level of impairment on the Global Assessment of Functioning (disability) scale at baseline (B = -.19, p <. 010), an absence of reported substance misuse prior to baseline assessment (B = -3.05, p <. 001), and unemployment at baseline (B = -.93, p <. 01). At 1-year follow-up, negative symptoms at presentation were associated with worse Global Assessment of Functioning symptom (B = -.28, p <.01) and disability (B = -.27, p <. 05) scales, and with hospital admission (OR= 1.06, p <.01).

Conclusions: Negative symptoms at presentation to Early Intervention Services were associated with worse functioning at entry and poorer outcomes one year later. Future research is required to better understand the aetiology and trajectories of negative symptoms in early psychosis and propose novel targeted interventions.

Introduction

Negative symptoms (NS) remain an unmet therapeutic need for people suffering from psychosis (Chue & Lalonde, 2014; Kirkpatrick, 2014). In first-episode psychosis (FEP) studies NS at onset have been related to poor social functioning after the first year of treatment and at 2 and even 7 years after first presentation to services (Ayesa-Arriola et al., 2013; Best, Grossman, Oyewumi, & Bowie, 2014; Milev, Ho, Arndt, & Andreasen, 2005). Moreover, Best and colleagues (2014) indicated NS as the best symptomatic predictor of functioning both cross-sectionally and longitudinally in a FEP sample, in keeping with other early psychosis (Cacciotti-Saija, Langdon, Ward, Hickie, & Guastella, 2016) and mixed chronicity (Hunter & Barry, 2012; Rabinowitz et al., 2012) studies. Research has also linked NS with symptomatic outcomes and recovery after a FEP. Among other variables, NS were reported as predictors of a continuous illness course at 5-year follow-up (Bertelsen et al., 2008) and were associated with a lower likelihood of achieving recovery (Gee et al., 2016; Novick, Haro, Suarez, Vieta, & Naber, 2009; Schubert, Clark, & Baune, 2015) and clinical remission (Díaz et al., 2013; Gaebel et al., 2014; Levine & Leucht, 2013; Üçok, Serbest, & Kandemir, 2011; Verma, Subramaniam, Abdin, Poon, & Chong, 2012).

Although evidence for the role of negative symptoms in predicting outcome in first episode psychosis is growing, there are relatively few studies at present that investigate this association in real world clinical settings. In this naturalistic study, we investigate the relationship between negative symptoms in patients presenting to specialist Early Intervention Services (EIS) in London to baseline socio-demographic and clinical correlates and to clinical and functional outcomes at 1-year follow-up.

Methods

Setting

This study was a naturalistic cohort of consecutive referrals to seven London EIS in the UK, assessed within one month of entry and followed up after one year. The teams were based in the following National Health Service (NHS) Mental Health Trusts: Camden and Islington (C&I EIS); South London and Maudsley (Lewisham EIS & STEP); East London and the City (EQUIP); Central and North West London (Brent and Kensington, Chelsea & Westminster EIS) and South West London and St. George's (ETHOS).

The patient inclusion criteria for EIS services were: (i) aged between 14 and 35 years old, (ii) presenting to the EIS for the first time with a psychotic episode lasting at least 7 days, and (iii) resident within the EIS catchment area (Fisher et al., 2008). Patients with psychotic symptoms due to acute drug intoxication were excluded.

Data were collected using the MiData audit tool, a standardized computerised assessment package of a minimum set of assessments used in routine clinical practice in EIS. Assessment measures were completed by trained clinicians as part of their routine assessments within 1 month of entry to the EIS (baseline) and at 1 year (follow-up) (Fisher et al., 2008).

Assessment measures.

Socio-demographic information. Basic demographic data were obtained at baseline, including gender, age at onset of psychosis, employment status, ethnicity based on the 2001 UK national census categories, degree of social support ('good', 'limited' or 'none'), and the presence or absence of a history of psychosis in a first-degree relative.

Clinical measures. At baseline, duration of untreated psychosis (DUP) was assessed with a revised version of the Nottingham Onset Schedule (Singh et al., 2005). The following measures were completed at both entry to the service and after 1 year in contact with the service: the Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opler, 1987) including positive (PANSS-P), negative (PANSS-N) and general (PANSS-G) subscales; the Global Assessment of Functioning Scale for

symptoms (GAF-s) and disability (GAF-d) (Endicott, Spitzer, Fleiss, & Cohen, 1976); and the Combined Alcohol and Drug Use Scale (Drake & Wallach, 1989). International Classification of Diseases 10th edition (ICD-10) (World Health Organization, 1993) diagnosis was recorded at 1-year follow-up and was extracted from clinical records and confirmed with EIS consultant psychiatrists. Diagnoses were grouped into schizophrenia-spectrum disorders (ICD-10 codes F20-29), affective psychoses (F30.2, F31.2, F31.5, F32.3, F33.3 or F39), and other disorders (all other codes).

During the 1-year follow-up period, the occurrence of psychiatric admission to an in-patient ward, the use of a crisis or Home Treatment team (HTT), and the occurrence of any suicide attempts or of any violent incidents was determined from the clinical records. Adherence to treatment was ascertained using the treatment adherence subscale of the Service Engagement Scale (Tait, Birchwood, & Trower, 2002), scored on a 4-point Likert-type scale, with higher scores reflecting patients' greater levels of non-compliance.

Two new composite variables were created. PANSS–D yielded presence of depression at baseline when patients had a score greater than 3 for all the following PANSS-G items: somatic concerns (G1), anxiety (G2), guilty feelings (G3) and depression (G6) (Kay & Sevy, 1990; Kjelby, Jørgensen, Kroken, Løberg, & Johnsen, 2011). This measure was created to ensure that the NS explored were not secondary to depression. Based on follow-up PANSS data, overall symptomatic Remission was defined as scores ≤3 on all of the following PANSS items: delusions (P1), unusual thought content (G9), hallucinations (P3), conceptual disorganization (P2), mannerisms and posturing (G5), blunted affect (N1), social withdrawal (N4), and lack of spontaneity (N6). Overall symptomatic Remission was also calculated at baseline, using PANSS baseline data. Positive Symptom Remission was defined as scores ≤3 for the P1, P2, and P3 items at 1-year follow-up (Andreasen et al., 2005).

Preliminary analysis

Normality and outliers testing was carried out for all continuous variables used in the analysis. Collinearity between independent variables was tested for with the variance inflation factor (VIF) (Field, 2009). Missing values were imputed using Multiple Imputation (MI) creating 50 imputed data sets.(See the Supplementary materials A, B and C for further details).

Main analyses

Hierarchical linear regression was conducted to explore associations with socio-demographic or key baseline clinical variables and baseline NS, with PANSS-N being the dependent variable. To investigate the relationship of baseline PANSS-N with outcomes at 1-year, multiple linear regressions and binomial logistic regressions were carried out for continuous and categorical outcome variables respectively, using baseline PANSS-N as the predictor in each case. Associations were then adjusted for relevant clinical and demographic covariates, namely ethnicity, social support at baseline, family history of psychosis, gender, age at onset, employment status at baseline, DUP, clinical diagnosis at 1-year follow-up, adherence to medication, and substance abuse or dependence 6 months prior to baseline assessment. PANSS-D, PANSS-P and Remission status at baseline were included as covariates to control for depression and severity of psychotic symptoms at baseline. Lastly, since the data were drawn from different EIS across London, team allocation was also included as a covariate in the adjusted model. All analyses were carried out using SPSS version 22 (IBM).

Ethical Approval

Data collection by each EIS was conducted in accordance with local audit procedures, which do not require patient consent. Any information that could lead to patient identification was removed. Multi-centre ethical approval was obtained from the Wandsworth Research Ethics Committee, which granted permission for secondary research use of the data for a specific set of research questions, including NS and clinical outcomes.

Results

Sample characteristics at baseline assessment

Socio-demographic and clinical characteristics of the sample (N = 484) are summarised in Table 1. Both pooled estimates from the 50 imputed datasets and the original dataset are presented. This sample comprised 315 males (61.5%) and the mean age of psychosis onset was 22.9 years (SD = 5.12).

Baseline Negative Symptoms and characteristics at presentation to EIS

An exploratory forced entry hierarchical linear regression analysis revealed a significant association between baseline PANSS-N score and gender, age of onset, substance use in the preceding 6 months, occupation status and GAF-d score (R^2 =.31, F (21, 462) = 12.75, p < .001; Table 2). Female participants had lower PANSS-N scores at baseline than males (p = .020); those with any substance use in the past 6 months before baseline assessment had lower PANSS-N than those that had not used (p <.001); participants that were employed or in education at baseline scored lower on PANSS-N than those who were unemployed (p = .014); those with more impaired functioning had higher NS (p < .001); and younger age of onset was also associated with higher PANSS-N scores (p = .035). Post-hoc analysis of the relationship between PANSS-N at baseline and individual substance use including opioid, cannabinoid, alcohol, nicotine, cocaine and stimulant use in the model, revealed that only cannabinoid abuse or dependence was associated with lower PANSS-N scores (B = -2.17, B SE = .94, t = -2.39, 95% CI -4.01 – -.33, p =.021; Supplementary Materials D).

Baseline NS and clinical outcomes at 1-year follow-up

PANSS-N at baseline was significantly associated with worse symptoms (GAF-s; B = -.28, p =.007) and impaired functioning (GAF-d; B = -.21, p = .01) at 1-year follow-up (Table 3). PANSS-N at baseline was also associated with higher likelihood of patients being admitted to a psychiatric ward during 1-year follow-up, with one point increase in PANSS-N increasing the odds of being admitted during 1-year

follow-up by 6%, (OR = 1.06, 95% CI 1.03 − 1.10, Wald statistic = 14.77, p =.001; Table 4). The mean (SD) PANSS-N of those who were admitted (N = 206) was 18.70 (9.47) compared to 14.99 (7.34) for those who were not admitted (N = 278). However, no significant associations were found between NS at baseline and Remission of symptoms at 1-year follow-up, nor with risk behaviors or use of HTT or Crisis teams during this period.

Discussion

Negative symptoms: baseline correlates

Participants with higher levels of baseline NS were much more likely to be male, in accordance with previous literature in both cross-sectional (Drake et al., 2016; Thorup et al., 2007) and follow-up FEP studies (Stone et al., 2014; Thorup et al., 2014). Although earlier investigations of gender-specific patterns of negative psychopathology have been contradictory (Ochoa, Usall, Cobo, Labad, & Kulkarni, 2012), most early psychosis studies are consistent with our findings (Köhler et al., 2009; Køster, Lajer, Lindhardt, & Rosenbaum, 2008; Thorup et al., 2014; Thorup et al., 2007; Willhite et al., 2008), including studies of individuals at-risk for psychosis (Rietschel et al., 2015). In our study, severity of baseline NS was related to a younger age of psychosis onset, which is consistent with most (Ballageer, Malla, Manchanda, Takhar, & Haricharan, 2005; Dominguez, Saka, Lieb, Wittchen, & van Os, 2010; Drake et al., 2016; Üçok & Ergül, 2014), but not all (Schultz et al., 1997), previous findings.

We found that patients with a higher level of NS had worse social and vocational functioning at entry to EIS. This is in keeping with previous work in FEP patients by Best *et al.*(Best et al., 2014). Poor premorbid functioning in those with prominent levels of NS at first presentation with psychosis could explain the poor social functioning found at baseline (Chang et al., 2016). Thus, patients with NS might have already suffered functional deterioration during the prodromal phase of psychosis (Corcoran et al., 2011; Kim et al., 2013; Meyer et al., 2014).

We found that substance abuse or dependence in the 6-month period preceding entry to EIS was associated with lower levels of NS at presentation. Although there is a lack of FEP research on this relationship, existing studies are conflicting, with some being in agreement with the present result (J. Addington & Addington, 1998) and others finding no difference in NS symptoms between substance users and non-users (Sevy et al., 2008). In a post-hoc analyses, only abuse of cannabinoids emerged as a significant association with lower baseline NS levels, accounting for other recent substance abuse (opioids, alcohol, nicotine, stimulants, cocaine). It has been suggested that those experiencing a FEP may use cannabis to self-medicate (Khantzian, 1997), possibly alleviating some NS such as anhedonia (Gregg, Barrowclough, & Haddock, 2007; Potvin, Sepehry, & Stip, 2005; Simon, Belzeaux, Adida, & Azorin, 2015), or higher NS could imply less hedonic capacity which in turn could reduce drug-seeking (Compton, Whicker, & Hochman, 2007). Another possible explanation is that those with less severe NS use more cannabis due to better functioning, i.e. are more capable of obtaining substances or more prone to substance abuse, as it has been indicated that FEP patients with cannabis abuse disorder show a stronger premorbid social functioning (Carr et al., 2009; Potvin et al., 2005). Nevertheless, there is still paucity of research, especially in FEP and more research is needed to clarify this association (Seddon et al., 2016; Simon et al., 2015).

Negative symptoms: clinical and functional outcomes

Baseline NS were related to higher possibility of admission to a psychiatric ward, used as a proxy of deterioration or relapse (Addington, Patten, McKenzie, & Addington, 2013). Previous studies generally support this finding (Morgan, Korten, & Jablensky, 2006; Patel et al., 2015; Sipos, 2001), although one study did not replicate this finding (Addington et al., 2010). We found baseline NS were also associated with worse symptoms at 1-year follow-up, as reflected in GAF-s and did not predict symptomatic remission at follow-up, being in accordance with previous studies (Cesková, Radovan, Tomás, & Hana, 2007)(Chang et al., 2012).

Risk behaviours, i.e. suicidality and violence incidents, were not predicted by NS levels. Our results are consistent with another FEP study that failed to find an association between NS and suicide attempts (Bertelsen et al., 2007) and studies that have linked mainly positive (Foley et al., 2007; Winsper et al., 2013) or manic symptoms (Dean et al., 2007; Large & Nielssen, 2011) to violent behavior during FEP.

Higher NS at baseline were associated with worse functioning at 1-year follow-up as reflected by the GAF-d scores. This finding is consistent with most FEP studies to date that show NS as a critical determinant of both global and social functioning (Cacciotti-Saija et al., 2016) as well as real-world functioning (Robertson et al., 2014), for at least 2 years after the FEP (Bergé et al., 2016). Recent research has supported this link at the at-risk for psychosis stage as well (Meyer et al., 2014). Thus, it could be that those with high negative symptoms at presentation, even when these symptoms decrease, are less likely to achieve recovery, which could be explained by highly disrupted premorbid functioning (Gee et al., 2016).

Strengths and limitations

This study has several strengths. The FEP sample was large, naturalistic, from different EIS within well-defined catchment areas, with minimal confounding effects of chronicity, institutionalization and prolonged exposure to antipsychotic treatment. Previous studies have indicated that FEP patients with higher NS might be at greater risk of dropping out (AlAqeel & Margolese, 2012; Thompson et al., 2011; Üçok & Ergül, 2014). Thus, although there was a considerable amount of missing data due to the naturalistic follow-up study design, MI was applied in order to correct for biases due to non-completion (Schafer & Graham, 2002). The differences between the original dataset and the pooled estimates showed that MI considered that those with missing follow-up data might have had high NS scores.

Nonetheless, a few caveats need to be considered. Firstly, due to the design of this study, some ethnic minorities and clinical subgroups might have been over/under-represented, which potentially limits the

generalizability of the findings. Patients with lower severity of positive symptoms were more likely to have a fully completed PANSS at baseline, leading to over-representation of cases with lower positive symptoms. However, their mean difference was less than 3 points, possibly not representing a clinically significant difference. Additionally, cross-sectional remission rate estimation at baseline and follow-up tends to be more vulnerable to confounding variables and lacks specificity. Lastly, regarding controlling for secondary NS, although this study controlled for positive symptoms and depression, it did not take into account extra-pyramidal side-effects (EPS) since there was no measure available (Millan et al., 2014).

Clinical implications

The present findings suggest that NS are associated poorer global functioning and symptomatic outcomes and increased likelihood of admission, leading to several clinical implications. This is noteworthy since social and occupational functioning have been indicated as the most important recovery markers by both field experts (Kane et al., 2003) and experts by lived experience (Pitt, Kilbride, Nothard, Welford, & Morrison, 2007). Based on the relative fluctuation of NS in FEP and their increasing stability after the first year (Chang et al., 2011; Ventura et al., 2015), this period might be a therapeutic window to ameliorate negative symptomatology, prevent disability and maximize functional outcome. Further investigations should examine the prognostic significance of timely, intensive and integrated intervention in NS during this potential critical period in preventing emergence of persistence. Careful monitoring of those showing higher NS at presentation warrants the attention of EIS (Gee et al., 2016), if possible from the at-risk stage of the illness when NS often occur (Fusar-Poli et al., 2013). While emphasizing the need for specific treatment approaches for reducing the burden of NS (Schennach-Wolff et al., 2011; Verdoux et al., 2001), it might be important to distinguish between primary NS and secondary NS, as the latter can be subject to treatment changes (Carbon & Correll, 2014).

Conclusion

Negative symptoms in FEP are a significant problem, leading to worse functional and clinical outcomes even amongst patients treated by specialist services. Since pharmacological treatments (Fusar-Poli et al., 2015) and psychosocial interventions (Jauhar et al., 2014; Østergaard Christensen et al., 2014) have shown to have little or no effect, further studies are needed in order to tackle NS, early and effectively, maximizing the long-term recovery for FEP patients.

References

Addington, D. E., Beck, C., Wang, J., Adams, B., Pryce, C., Zhu, H., … McKenzie, E. (2010). Predictors of admission in first-episode psychosis: developing a risk adjustment model for service comparisons. *Psychiatric Services (Washington, D.C.)*, *61*(5), 483–488. https://doi.org/10.1176/appi.ps.61.5.483

Addington, D. E., Patten, S. B., McKenzie, E., & Addington, J. (2013). Relationship Between Relapse and Hospitalization in First-Episode Psychosis. *Psychiatric Services*, *64*(8), 796–799. https://doi.org/10.1176/appi.ps.201200440

Addington, J., & Addington, D. (1998). Effect of substance misuse in early psychosis. *The British Journal of Psychiatry. Supplement*, *172*(33), 134–136.

AlAqeel, B., & Margolese, H. C. (2012). Remission in schizophrenia: critical and systematic review. *Harvard Review of Psychiatry*, *20*(6), 281–297. https://doi.org/10.3109/10673229.2012.747804

Albert, N., Bertelsen, M., Thorup, A., Petersen, L., Jeppesen, P., Le Quack, P., … Nordentoft, M. (2011). Predictors of recovery from psychosis. *Schizophrenia Research*, *125*(2–3), 257–266. https://doi.org/10.1016/j.schres.2010.10.013

Andreasen, N. C., Carpenter, W. T., Kane, J. M., Lasser, R. A., Marder, S. R., & Weinberger, D. R. (2005). Remission in schizophrenia: proposed criteria and rationale for consensus. *The American Journal of Psychiatry*, *162*(3), 441–449. https://doi.org/10.1176/appi.ajp.162.3.441

Ayesa-Arriola, R., Manuel Rodríguez-Sánchez, J., Pérez-Iglesias, R., González-Blanch, C., Pardo-García, G., Tabares-Seisdedos, R., … Crespo-Facorro, B. (2013). The relevance of cognitive, clinical and premorbid variables in predicting functional outcome for individuals with first-episode psychosis: A 3 year longitudinal study. *Psychiatry Research*, *209*(3), 302–308. https://doi.org/10.1016/j.psychres.2013.01.024

Ballageer, T., Malla, A., Manchanda, R., Takhar, J., & Haricharan, R. (2005). Is adolescent-onset first-episode psychosis different from adult onset? *Journal of the American Academy of Child and Adolescent Psychiatry*, *44*(8), 782–789. https://doi.org/10.1097/01.chi.0000164591.55942.ea

Bergé, D., Mané, A., Salgado, P., Cortizo, R., Garnier, C., Gomez, L., … Pérez, V. (2016). Predictors of Relapse and Functioning in First-Episode Psychosis: A Two-Year Follow-Up Study. *Psychiatric Services*, *67*(2), 227–233. https://doi.org/10.1176/appi.ps.201400316

Bertelsen, M., Jeppesen, P., Petersen, L., Thorup, A., OHLENSCHLAeGER, J., Quach, P. L., … Nordentoft, M. (2007). Suicidal behaviour and mortality in first-episode psychosis: the OPUS trial. *The British Journal of Psychiatry*, *191*(51), s140–s146. https://doi.org/10.1192/bjp.191.51.s140

Bertelsen, M., Jeppesen, P., Petersen, L., Thorup, A., Øhlenschlaeger, J., le Quach, P., … Nordentoft, M. (2008). Five-year follow-up of a randomized multicenter trial of intensive early intervention vs standard treatment for patients with a first episode of psychotic illness: the OPUS trial. *Archives of General Psychiatry*, *65*(7), 762–771. https://doi.org/10.1001/archpsyc.65.7.762

Best, M. W., Grossman, M., Oyewumi, L. K., & Bowie, C. R. (2014). Examination of the Positive and Negative Syndrome Scale factor structure and longitudinal relationships with functioning in early psychosis: PANSS factor structure and functioning. *Early Intervention in Psychiatry*, n/a-n/a. https://doi.org/10.1111/eip.12190

Cacciotti-Saija, C., Langdon, R., Ward, P. B., Hickie, I. B., & Guastella, A. J. (2016). Clinical symptoms predict concurrent social and global functioning in an early psychosis sample: Clinical symptoms predict functioning in early psychosis. *Early Intervention in Psychiatry*, n/a-n/a. https://doi.org/10.1111/eip.12295

Carbon, M., & Correll, C. U. (2014). Thinking and acting beyond the positive: the role of the cognitive and negative symptoms in schizophrenia. *CNS Spectrums*, *19*(S1), 35–53. https://doi.org/10.1017/S1092852914000601

Carr, J. A. R., Norman, R. G. M., & Manchanda, R. (2009). Sociodemographic and clinical characteristics of patients presenting with first-episode psychosis and concurrent substance misuse. *Early Intervention in Psychiatry*, *3*(1), 75–79. https://doi.org/10.1111/j.1751-7893.2008.00100.x

Cesková, E., Radovan, P., Tomás, K., & Hana, K. (2007). One-year follow-up of patients with first-episode schizophrenia (comparison between remitters and non-remitters). *Neuropsychiatric Disease and Treatment*, *3*(1), 153–160.

Chang, W. C., Hui, C. L. M., Tang, J. Y. M., Wong, G. H. Y., Lam, M. M. L., Chan, S. K. W., & Chen, E. Y. H. (2011). Persistent negative symptoms in first-episode schizophrenia: a prospective three-year follow-up study. *Schizophrenia Research*, *133*(1–3), 22–28. https://doi.org/10.1016/j.schres.2011.09.006

Chang, W. C., Tang, J. Y., Hui, C. L., Lam, M. M., Chan, S. K., Wong, G. H., … Chen, E. Y. (2012). Prediction of remission and recovery in young people presenting with first-episode psychosis in Hong Kong: A 3-year follow-up study. *Australian and New Zealand Journal of Psychiatry*, *46*(2), 100–108. https://doi.org/10.1177/0004867411428015

Chang, W. C., Lau, C. F. C., Chan, S. S. I., Hui, C. L. M., Chan, S. K. W., Lee, E. H. M., … Chen, E. Y. H. (2016). Premorbid, clinical and cognitive correlates of primary negative symptoms in first-episode psychosis. *Psychiatry Research*, *242*, 144–149. https://doi.org/10.1016/j.psychres.2016.05.045

Chue, P., & Lalonde, J. (2014). Addressing the unmet needs of patients with persistent negative symptoms of schizophrenia: emerging pharmacological treatment options. *Neuropsychiatric Disease and Treatment*, 777. https://doi.org/10.2147/NDT.S43404

Compton, M. T., Whicker, N. E., & Hochman, K. M. (2007). Alcohol and cannabis use in Urban, African American, first-episode schizophrenia-spectrum patients: associations with positive and negative symptoms. *The Journal of Clinical Psychiatry*, *68*(12), 1939–1945.

Corcoran, C. M., Kimhy, D., Parrilla-Escobar, M. A., Cressman, V. L., Stanford, A. D., Thompson, J., … Malaspina, D. (2011). The relationship of social function to depressive and negative symptoms in individuals at clinical high risk for psychosis. *Psychological Medicine*, *41*(02), 251–261. https://doi.org/10.1017/S0033291710000802

Dean, K., Walsh, E., Morgan, C., Demjaha, A., Dazzan, P., Morgan, K., … Murray, R. M. (2007). Aggressive behaviour at first contact with services: findings from the AESOP First Episode Psychosis Study. *Psychological Medicine*, *37*(04), 547–557. https://doi.org/10.1017/S0033291706008920

Díaz, I., Pelayo-Terán, J. M., Pérez-Iglesias, R., Mata, I., Tabarés-Seisdedos, R., Suárez-Pinilla, P., … Crespo-Facorro, B. (2013). Predictors of clinical remission following a first episode of non-affective psychosis: Sociodemographics, premorbid and clinical variables. *Psychiatry Research*, *206*(2–3), 181–187. https://doi.org/10.1016/j.psychres.2012.10.011

Dominguez, M.-G., Saka, M. C., Lieb, R., Wittchen, H.-U., & van Os, J. (2010). Early Expression of Negative/Disorganized Symptoms Predicting Psychotic Experiences and Subsequent Clinical Psychosis: A 10-Year Study. *American Journal of Psychiatry*, *167*(9), 1075–1082. https://doi.org/10.1176/appi.ajp.2010.09060883

Drake, R. E., & Wallach, M. A. (1989). Substance abuse among the chronic mentally ill. *Hospital & Community Psychiatry*, *40*(10), 1041–1046.

Drake, R. J., Addington, J., Viswanathan, A. C., Lewis, S. W., Cotter, J., Yung, A. R., & Abel, K. M. (2016). How Age and Gender Predict Illness Course in a First-Episode Nonaffective Psychosis Cohort. *The Journal of Clinical Psychiatry*, e283–e289. https://doi.org/10.4088/JCP.14m09369

Endicott, J., Spitzer, R. L., Fleiss, J. L., & Cohen, J. (1976). The global assessment scale. A procedure for measuring overall severity of psychiatric disturbance. *Archives of General Psychiatry*, *33*(6), 766–771.

Field, A. P. (2009). *Discovering statistics using SPSS: (and sex, drugs and rock "n" roll)* (3rd ed). Los Angeles: SAGE Publications.

Fisher, H., Theodore, K., Power, P., Chisholm, B., Fuller, J., Marlowe, K., … Johnson, S. (2008). Routine evaluation in first episode psychosis services: feasibility and results from the MiData project. *Social Psychiatry and Psychiatric Epidemiology*, *43*(12), 960–967. https://doi.org/10.1007/s00127-008-0386-1

Foley, S. R., Browne, S., Clarke, M., Kinsella, A., Larkin, C., & O'Callaghan, E. (2007). Is violence at presentation by patients with first-episode psychosis associated with duration of untreated psychosis? *Social Psychiatry and Psychiatric Epidemiology*, *42*(8), 606–610. https://doi.org/10.1007/s00127-007-0217-9

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., … Yung, A. (2013). The Psychosis High-Risk State: A Comprehensive State-of-the-Art Review. *JAMA Psychiatry*, *70*(1), 107. https://doi.org/10.1001/jamapsychiatry.2013.269

Fusar-Poli, P., Papanastasiou, E., Stahl, D., Rocchetti, M., Carpenter, W., Shergill, S., & McGuire, P. (2015). Treatments of Negative Symptoms in Schizophrenia: Meta-Analysis of 168 Randomized Placebo-Controlled Trials. *Schizophrenia Bulletin*, *41*(4), 892–899. https://doi.org/10.1093/schbul/sbu170

Gaebel, W., Riesbeck, M., Wölwer, W., Klimke, A., Eickhoff, M., von Wilmsdorff, M., … Möller, H.-J. (2014). Rates and predictors of remission in first-episode schizophrenia within 1year of antipsychotic maintenance treatment. Results of a randomized controlled trial within the German

Research Network on Schizophrenia. *Schizophrenia Research*, *152*(2–3), 478–486.

https://doi.org/10.1016/j.schres.2013.04.012

Gee, B., Hodgekins, J., Fowler, D., Marshall, M., Everard, L., Lester, H., … Birchwood, M. (2016). The

course of negative symptom in first episode psychosis and the relationship with social recovery.

Schizophrenia Research, *174*(1–3), 165–171. https://doi.org/10.1016/j.schres.2016.04.017

Gregg, L., Barrowclough, C., & Haddock, G. (2007). Reasons for increased substance use in psychosis.

Clinical Psychology Review, *27*(4), 494–510. https://doi.org/10.1016/j.cpr.2006.09.004

Hadden, K. L., LeDrew, K., Hogan, K., & Thomas, B. (2016). Impact of comorbid cannabis use on

outcome in first episode psychosis: Cannabis use in first-episode psychosis. *Early Intervention in

Psychiatry*. https://doi.org/10.1111/eip.12377

Hafner, H., Maurer, K., Loffler, W., & Riecher-Rossler, A. (1993). The influence of age and sex on the

onset and early course of schizophrenia. *The British Journal of Psychiatry*, *162*(1), 80–86.

https://doi.org/10.1192/bjp.162.1.80

Harvey, P. D., Koren, D., Reichenberg, A., & Bowie, C. R. (2006). Negative Symptoms and Cognitive

Deficits: What Is the Nature of Their Relationship? *Schizophrenia Bulletin*, *32*(2), 250–258.

https://doi.org/10.1093/schbul/sbj011

Hunter, R., & Barry, S. (2012). Negative symptoms and psychosocial functioning in schizophrenia:

Neglected but important targets for treatment. *European Psychiatry*, *27*(6), 432–436.

https://doi.org/10.1016/j.eurpsy.2011.02.015

Jauhar, S., McKenna, P. J., Radua, J., Fung, E., Salvador, R., & Laws, K. R. (2014). Cognitive-

behavioural therapy for the symptoms of schizophrenia: systematic review and meta-analysis

with examination of potential bias. *The British Journal of Psychiatry*, *204*(1), 20–29.

https://doi.org/10.1192/bjp.bp.112.116285

Kane, J. M., Leucht, S., Carpenter, D., Docherty, J. P., & Expert Consensus Panel for Optimizing

Pharmacologic Treatment of Psychotic Disorders. (2003). The expert consensus guideline series.

Optimizing pharmacologic treatment of psychotic disorders. Introduction: methods, commentary, and summary. *The Journal of Clinical Psychiatry*, *64 Suppl 12*, 5–19.

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, *13*(2), 261–276.

Kay, S. R., & Sevy, S. (1990). Pyramidical Model of Schizophrenia. *Schizophrenia Bulletin*, *16*(3), 537–545. https://doi.org/10.1093/schbul/16.3.537

Khantzian, E. J. (1997). The Self-Medication Hypothesis of Substance Use Disorders: A Reconsideration and Recent Applications. *Harvard Review of Psychiatry*, *4*(5), 231–244. https://doi.org/10.3109/10673229709030550

Kim, K. R., Song, Y. Y., Park, J. Y., Lee, E. H., Lee, M., Lee, S. Y., … Kwon, J. S. (2013). The relationship between psychosocial functioning and resilience and negative symptoms in individuals at ultra-high risk for psychosis. *Australian & New Zealand Journal of Psychiatry*, *47*(8), 762–771. https://doi.org/10.1177/0004867413488218

Kirkpatrick, B. (2014). Progress in the Study of Negative Symptoms. *Schizophrenia Bulletin*, *40*(Suppl 2), S101–S106. https://doi.org/10.1093/schbul/sbt158

Kjelby, E., Jørgensen, H. A., Kroken, R. A., Løberg, E.-M., & Johnsen, E. (2011). Anti-depressive effectiveness of olanzapine, quetiapine, risperidone and ziprasidone: a pragmatic, randomized trial. *BMC Psychiatry*, *11*(1). https://doi.org/10.1186/1471-244X-11-145

Köhler, S., van der Werf, M., Hart, B., Morrison, G., McCreadie, R., Kirkpatrick, B., … Allardyce, J. (2009). Evidence that better outcome of psychosis in women is reversed with increasing age of onset: A population-based 5-year follow-up study. *Schizophrenia Research*, *113*(2–3), 226–232. https://doi.org/10.1016/j.schres.2009.05.017

Køster, A., Lajer, M., Lindhardt, A., & Rosenbaum, B. (2008). Gender differences in first episode psychosis. *Social Psychiatry and Psychiatric Epidemiology*, *43*(12), 940–946. https://doi.org/10.1007/s00127-008-0384-3

Large, M. M., & Nielssen, O. (2011). Violence in first-episode psychosis: A systematic review and meta-analysis. *Schizophrenia Research*, *125*(2–3), 209–220. https://doi.org/10.1016/j.schres.2010.11.026

Levine, S. Z., & Leucht, S. (2013). Attaining and sustaining remission of predominant negative symptoms. *Schizophrenia Research*, *143*(1), 60–64. https://doi.org/10.1016/j.schres.2012.11.010

Mané, A., Fernández-Expósito, M., Bergé, D., Gómez-Pérez, L., Sabaté, A., Toll, A., … Perez, V. (2015). Relationship between cannabis and psychosis: Reasons for use and associated clinical variables. *Psychiatry Research*, *229*(1–2), 70–74. https://doi.org/10.1016/j.psychres.2015.07.070

Meyer, E. C., Carrion, R. E., Cornblatt, B. A., Addington, J., Cadenhead, K. S., Cannon, T. D., … the NAPLS group. (2014). The Relationship of Neurocognition and Negative Symptoms to Social and Role Functioning Over Time in Individuals at Clinical High Risk in the First Phase of the North American Prodrome Longitudinal Study. *Schizophrenia Bulletin*, *40*(6), 1452–1461. https://doi.org/10.1093/schbul/sbt235

Milev, P., Ho, B.-C., Arndt, S., & Andreasen, N. C. (2005). Predictive Values of Neurocognition and Negative Symptoms on Functional Outcome in Schizophrenia: A Longitudinal First-Episode Study With 7-Year Follow-Up. *American Journal of Psychiatry*, *162*(3), 495–506. https://doi.org/10.1176/appi.ajp.162.3.495

Millan, M. J., Fone, K., Steckler, T., & Horan, W. P. (2014). Negative symptoms of schizophrenia: Clinical characteristics, pathophysiological substrates, experimental models and prospects for improved treatment. *European Neuropsychopharmacology*, *24*(5), 645–692. https://doi.org/10.1016/j.euroneuro.2014.03.008

Morgan, V., Korten, A., & Jablensky, A. (2006). Modifiable risk factors for hospitalization among people with psychosis: evidence from the National Study of Low Prevalence (Psychotic) Disorders. *Australian and New Zealand Journal of Psychiatry*, *40*(8), 683–690. https://doi.org/10.1080/j.1440-1614.2006.01868.x

Novick, D., Haro, J. M., Suarez, D., Vieta, E., & Naber, D. (2009). Recovery in the outpatient setting: 36-month results from the Schizophrenia Outpatients Health Outcomes (SOHO) study. *Schizophrenia Research*, *108*(1–3), 223–230. https://doi.org/10.1016/j.schres.2008.11.007

Ochoa, S., Usall, J., Cobo, J., Labad, X., & Kulkarni, J. (2012). Gender Differences in Schizophrenia and First-Episode Psychosis: A Comprehensive Literature Review. *Schizophrenia Research and Treatment*, *2012*, 1–9. https://doi.org/10.1155/2012/916198

Østergaard Christensen, T., Vesterager, L., Krarup, G., Olsen, B. B., Melau, M., Gluud, C., & Nordentoft, M. (2014). Cognitive remediation combined with an early intervention service in first episode psychosis. *Acta Psychiatrica Scandinavica*, *130*(4), 300–310. https://doi.org/10.1111/acps.12287

Patel, R., Jayatilleke, N., Broadbent, M., Chang, C.-K., Foskett, N., Gorrell, G., … Stewart, R. (2015). Negative symptoms in schizophrenia: a study in a large clinical sample of patients using a novel automated method. *BMJ Open*, *5*(9), e007619. https://doi.org/10.1136/bmjopen-2015-007619

Pitt, L., Kilbride, M., Nothard, S., Welford, M., & Morrison, A. P. (2007). Researching recovery from psychosis: a user-led project. *Psychiatric Bulletin*, *31*(2), 55–60. https://doi.org/10.1192/pb.bp.105.008532

Potvin, S., Sepehry, A. A., & Stip, E. (2005). A meta-analysis of negative symptoms in dual diagnosis schizophrenia. *Psychological Medicine*, *36*(04), 431. https://doi.org/10.1017/S003329170500574X

Rabinowitz, J., Levine, S. Z., Garibaldi, G., Bugarski-Kirola, D., Berardo, C. G., & Kapur, S. (2012). Negative symptoms have greater impact on functioning than positive symptoms in schizophrenia: Analysis of CATIE data. *Schizophrenia Research*, *137*(1–3), 147–150. https://doi.org/10.1016/j.schres.2012.01.015

Rietschel, L., Lambert, M., Karow, A., Zink, M., Müller, H., Heinz, A., … PREVENT study group. (2015). Clinical high risk for psychosis: gender differences in symptoms and social functioning: Gender differences in HR for psychosis. *Early Intervention in Psychiatry*, n/a-n/a. https://doi.org/10.1111/eip.12240

Robertson, B. R., Prestia, D., Twamley, E. W., Patterson, T. L., Bowie, C. R., & Harvey, P. D. (2014). Social competence versus negative symptoms as predictors of real world social functioning in schizophrenia. *Schizophrenia Research*, *160*(1–3), 136–141. https://doi.org/10.1016/j.schres.2014.10.037

Schafer, J. L., & Graham, J. W. (2002). Missing data: our view of the state of the art. *Psychological Methods*, *7*(2), 147–177.

Schennach-Wolff, R., Jäger, M., Mayr, A., Meyer, S., Kühn, K.-U., Klingberg, S., … Riedel, M. (2011). Predictors of response and remission in the acute treatment of first-episode schizophrenia patients — Is it all about early response? *European Neuropsychopharmacology*, *21*(5), 370–378. https://doi.org/10.1016/j.euroneuro.2010.10.003

Schubert, K. O., Clark, S. R., & Baune, B. T. (2015). The use of clinical and biological characteristics to predict outcome following First Episode Psychosis. *Australian & New Zealand Journal of Psychiatry*, *49*(1), 24–35. https://doi.org/10.1177/0004867414560650

Schultz, S. K., Miller, D. D., Oliver, S. E., Arndt, S., Flaum, M., & Andreasen, N. C. (1997). The life course of schizophrenia: age and symptom dimensions. *Schizophrenia Research*, *23*(1), 15–23. https://doi.org/10.1016/S0920-9964(96)00087-4

Seddon, J. L., Birchwood, M., Copello, A., Everard, L., Jones, P. B., Fowler, D., … Singh, S. P. (2016). Cannabis Use Is Associated With Increased Psychotic Symptoms and Poorer Psychosocial Functioning in First-Episode Psychosis: A Report From the UK National EDEN Study. *Schizophrenia Bulletin*, *42*(3), 619–625. https://doi.org/10.1093/schbul/sbv154

Sevy, S., Robinson, D. G., Holloway, S., Alvir, J. M., Woerner, M. G., Bilder, R., … Kane, J. (2008). Correlates of substance misuse in patients with first-episode schizophrenia and schizoaffective disorder: Substance misuse in schizophrenia. *Acta Psychiatrica Scandinavica*, *104*(5), 367–374. https://doi.org/10.1111/j.1600-0447.2001.00452.x

Simon, N., Belzeaux, R., Adida, M., & Azorin, J.-M. (2015). Symptômes négatifs dans la schizophrénie et addiction. *L'Encéphale*, *41*(6), 6S27-6S31. https://doi.org/10.1016/S0013-7006(16)30007-0

Singh, S. P. (2010). Early intervention in psychosis. *The British Journal of Psychiatry: The Journal of Mental Science*, *196*(5), 343–345. https://doi.org/10.1192/bjp.bp.109.075804

Singh, S. P., Cooper, J. E., Fisher, H. L., Tarrant, C. J., Lloyd, T., Banjo, J., … Jones, P. (2005). Determining the chronology and components of psychosis onset: The Nottingham Onset Schedule (NOS). *Schizophrenia Research*, *80*(1), 117–130. https://doi.org/10.1016/j.schres.2005.04.018

Sipos, A. (2001). Patterns and predictors of hospitalisation in first-episode psychosis: Prospective cohort study. *The British Journal of Psychiatry*, *178*(6), 518–523. https://doi.org/10.1192/bjp.178.6.518

Stone, J. M., Fisher, H. L., Major, B., Chisholm, B., Woolley, J., Lawrence, J., … Young, A. H. (2014). Cannabis use and first-episode psychosis: relationship with manic and psychotic symptoms, and with age at presentation. *Psychological Medicine*, *44*(03), 499–506. https://doi.org/10.1017/S0033291713000883

Tait, L., Birchwood, M., & Trower, P. (2002). A new scale (SES) to measure engagement with community mental health services. *Journal of Mental Health*, *11*(2), 191–198. https://doi.org/10.1080/09638230020023570-2

Thompson, J., Berk, M., Dean, O., Kohlmann, K., Jeavons, S., Bush, A., & Copolov, D. (2011). Who's left? Symptoms of schizophrenia that predict clinical trial dropout. *Human Psychopharmacology*, *26*(8), 609–613. https://doi.org/10.1002/hup.1253

Thorup, A., Albert, N., Bertelsen, M., Petersen, L., Jeppesen, P., Le Quack, P., … Nordentoft, M. (2014). Gender differences in first-episode psychosis at 5-year follow-up – two different courses of disease? Results from the OPUS study at 5-year follow-up. *European Psychiatry*, *29*(1), 44–51. https://doi.org/10.1016/j.eurpsy.2012.11.005

Thorup, A., Petersen, L., Jeppesen, P., Ohlenschlaeger, J., Christensen, T., Krarup, G., … Nordentoft, M. (2007). Gender differences in young adults with first-episode schizophrenia spectrum disorders at baseline in the Danish OPUS study. *The Journal of Nervous and Mental Disease*, *195*(5), 396–405. https://doi.org/10.1097/01.nmd.0000253784.59708.dd

Üçok, A., & Ergül, C. (2014). Persistent negative symptoms after first episode schizophrenia: A 2-year follow-up study. *Schizophrenia Research*, *158*(1–3), 241–246. https://doi.org/10.1016/j.schres.2014.07.021

Üçok, A., Serbest, S., & Kandemir, P. E. (2011). Remission after first-episode schizophrenia: Results of a long-term follow-up. *Psychiatry Research*, *189*(1), 33–37. https://doi.org/10.1016/j.psychres.2010.11.013

Ventura, J., Subotnik, K. L., Gitlin, M. J., Gretchen-Doorly, D., Ered, A., Villa, K. F., … Nuechterlein, K. H. (2015). Negative symptoms and functioning during the first year after a recent onset of schizophrenia and 8years later. *Schizophrenia Research*, *161*(2–3), 407–413. https://doi.org/10.1016/j.schres.2014.10.043

Verdoux, H., Liraud, F., Gonzales, B., Assens, F., Abalan, F., & van Os, J. (2001). Predictors and outcome characteristics associated with suicidal behaviour in early psychosis: a two-year follow-up of first-admitted subjects. *Acta Psychiatrica Scandinavica*, *103*(5), 347–354. https://doi.org/10.1034/j.1600-0447.2001.00202.x

Verma, S., Subramaniam, M., Abdin, E., Poon, L. Y., & Chong, S. A. (2012). Symptomatic and functional remission in patients with first-episode psychosis: Remission in first-episode psychosis. *Acta Psychiatrica Scandinavica*, *126*(4), 282–289. https://doi.org/10.1111/j.1600-0447.2012.01883.x

Willhite, R. K., Niendam, T. A., Bearden, C. E., Zinberg, J., O'Brien, M. P., & Cannon, T. D. (2008). Gender differences in symptoms, functioning and social support in patients at ultra-high risk for developing a psychotic disorder. *Schizophrenia Research*, *104*(1–3), 237–245. https://doi.org/10.1016/j.schres.2008.05.019

Winsper, C., Singh, S. P., Marwaha, S., Amos, T., Lester, H., Everard, L., … Birchwood, M. (2013). Pathways to Violent Behavior During First-Episode Psychosis: A Report From the UK National EDEN Study. *JAMA Psychiatry*, *70*(12), 1287. https://doi.org/10.1001/jamapsychiatry.2013.2445

World Health Organization (Ed.). (1993). *The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research*. Geneva: World Health Organization.

Table 1. *Socio-demographic and baseline clinical characteristics of the sample, for both pooled estimates from imputed data and original data*

Variable	Pooled		Original		
	N (%)	M (SD)	N (%)	M (Min-Max; SD)	N of missing cases (%)
Gender					0
Male	315 (65.1)		315 (65.1)		
Female	169 (34.9)		169 (34.9)		
Ethnicity					0
White British	96 (19.8)		96 (19.8)		
White Other	61 (12.6)		61 (12.6)		
Black Caribbean	48 (9.9)		48 (9.9)		
Black African	126 (26.0)		126 (26.0)		
Black Other	22 (4.5)		22 (4.5)		
Asian	72 (14.9)		72 (14.9)		
Mixed	44 (9.1)		44 (9.1)		
Other	15 (3.1)		15 (3.1)		
Family history of psychosis	120.6 (24.7)		120 (24.8)		2 (0.4)
Social Support					5 (1)

Variable	Pooled		Original		
	N (%)	M (SD)	N (%)	M (Min-Max; SD)	N of missing cases (%)
Good	345.9 (71.5)		345 (71.3)		
Limited/none	115.7 (23.9)		84 (17.4)		
GAF- s		46.9 (20.08)		46.8 (8-90; 20.09)	13 (2.7)
GAF- d		50.82 (17.07)		50.71 (1-95; 17.07)	13 (2.7)
PANSS-P		17.91 (7.76)		17.91 (7-42; 7.76)	0
PANSS-N		16.57 (8.28)		16.57 (7-43; 8.28)	0
PANSS-G		36.84 (12.50)		36.84 (16-75; 12.50)	0
PANSS total		71.32 (24.25)		71.32 (30-149; 24.25)	0
Age of psychosis onset		22.97 (5.12)		23.07 (6.06-35.63; 5)	39 (8.1)
Any substance abuse/ dependence in past 6 months	159.3 (32.9)		133 (27.5)		75 (15.5)
Employed/ student	177.8 (36.7)		168 (34.7)		28 (5.8)
Long DUP (>=3 months)	252.9 (52.3)		222 (45.9)		63 (13)

Note. M = mean, SD = standard deviation, N = number of patients, DUP = duration of untreated psychosis, GAF = Global Assessment of Functioning scale, GAF-d = disability subscale, GAF-s = symptom subscale, PANSS = Positive and Negative Syndrome Scale, PANSS-P = positive subscale, PANSS-N = negative subscale, PANSS-G = general psychopathology subscale.

Table 2. *Multiple linear regression results for the predictor variables of PANSS-N scores at baseline*

Predictor baseline variables		B	SE B	95% CI for B	t
Team		.16	.21	-.25 – .58	.76
Gender		-1.63	.70	-3.00 – -.26	-2.33*
Age of Onset		-.15	.07	-.29 – -.01	-2.10*
Ethnicity[a]					
	White Other	-.14	1.21	-2.51 – 2.23	-.12
	Mixed	2.14	1.32	-.44 – 4.72	1.63
	Asian	-.25	1.15	-2.50 – 2.01	-.21
	Black Caribbean	1.67	1.29	-.85 – 4.19	1.30
	Black African	1.38	.99	-.54 – 3.32	1.41
	Black Other	1.60	1.70	-1.73 – 4.93	.94
	Other	3.13	2.00	-.80 – 7.06	1.56
Family history of psychosis		.012	.77	-1.49 – 1.52	.02
Social support[b]					
	Limited	-1.11	.89	-2.85 – .63	-1.25
	None	.88	1.42	-1.91 – 3.67	.62
Employed/Student		-1.76	.72	-3.17 – .35	-2.45*
Dichotomised DUP		.14	.70	-1.24 – 1.52	.20
GAF-s		.003	.03	-.05 –.06	.10
GAF-d		-.19	.03	-.24 – -.13	-6.42***

Predictor baseline variables	B	SE B	95% CI for B	t
Substance abuse in the past 6 months	-3.05	.78	-4.58 – -1.52	-3.91***

Note. B = unstandardized regression coefficient, SE = standard error, R^2 = proportion of the variance explained, F = F-ratio, t = t-test, CI = confidence intervals, GAF = Global Assessment of Functioning scale, GAF-d = disability subscale, GAF-s = symptom subscale, PANSS-N = Positive and Negative Syndrome Scale – negative subscale score, df = degrees of freedom, DUP = duration of untreated psychosis (DUP was dichotomized at 3 months).

[a] All ethnic groups were compared to White British; [b] Level of support were compared to Good Level

Model R^2= .31; Model Adjusted R^2= .28; F(df)= 12.75 (462), p < .001

Model's constant, B= 28.38; B SE= 3.09; t= 9.18; p<.001; 95% CI 22.32 – 34.45.

The model was controlled for PANSS Depression factor and PANSS positive subscale score.

* p < .05, **p < .01, ***p < .001.

Table 3. *Summary of linear regressions examining the effect of the level of baseline negative symptoms on continuous outcome variables at 1-year follow-up.*

Variables at 1-year follow-up	B (SE)	95% CI for B	R^2	Adjusted [a] R^2	Durbin Watson d	F (df1, df2)	t
GAF-s	-.28 (.10)	-.49 – -.08	.02	.57	2.16	24.48 (15, 277)***	-2.70**
GAF-d	-.27 (.11)	-.48– -.06	.02	.49	2.01	17.90 (15, 277)***	-2.57*

Note. B = unstandardized regression coefficient, SE = standard error, R^2 = proportion of the variance explained, Durbin Watson d = test statistic of autocorrelation, F = F-ratio, t = t-test, CI = confidence intervals, GAF = Global Assessment of Functioning scale, GAF-d = disability subscale, GAF-s = symptom subscale, df1 = regression degrees of freedom, df2 = residual degrees of freedom.

[a] adjusted for team, age at psychosis onset, ethnicity, family history of psychosis, social support at baseline, employed/student at baseline, dichotomized duration of untreated psychosis, Positive and Negative Syndrome Scale (PANSS) depression factor at baseline, PANSS positive subscale score at baseline, remission at baseline, diagnosis at 1-year follow-up, treatment adherence at 1-year follow-up, any substance

Variables at 1-year follow-up	B (SE)	95% CI for B	R^2	Adjusted [a] R^2	Durbin Watson d	F (df1, df2)	t

abuse or dependence in the 6 months prior to baseline.

* $p < .05$, **$p < .01$, ***$p < .001$.

Table 4. *Summary of binary logistic regressions examining the effect of the level of baseline negative symptoms on categorical outcome variables at 1-year follow-up.*

Variables at 1-year follow-up	B (SE)	Wald statistic	Unadjusted OR (95% CI)	Adjusted [a] OR (95% CI)
Remission	-.01 (.02)	.40	.99 (.96 -1.01)	.99 (.96-1.03)
Positive Symptom Remission	.02 (.02)	1.18	1.00 (97 -1.02)	1.02 (.98- 1.06)
Admitted to a psychiatric ward	.06 (.02)	11.09	1.06 (1.03 -1.08)***	1.06 (1.02-1.10)**
Used HTT or Crisis team	.001 (.02)	.11	1.00 (.97-1.02)	1.00 (.96-1.04)

Variables at 1-year follow-up	B (SE)	Wald statistic	Unadjusted OR (95% CI)	Adjusted [a] OR (95% CI)
Any suicide attempts	-.004 (.05)	.26	.98 (.94-1.04)	1.00 (.90-1.10)
Any violent incident towards others	.01 (.03)	.25	1.01 (.98-1.04)	1.01 (.96-1.06)

Note. PANSS = Positive and Negative Syndrome Scale, HTT = Home Treatment Team, OR = odds ratio, B = regression coefficient on the independent variable, CI = confidence interval.

[a] adjusted for team, age at psychosis onset, ethnicity, family history of psychosis, social support at baseline, employed/student at baseline, duration of untreated psychosis median split (<3 is short, > or =3 months is long), PANSS-D (depression subscale) at baseline, PANSS-P (positive subscale) at baseline, remission at baseline, diagnosis at 1-year follow-up, treatment adherence at 1-year follow-up, any substance abuse or dependence in the 6 months prior to baseline.

* $p < .05$, ** $p < .01$, *** $p < .001$.