

Predictors of Long-Term Social Functioning in Young People with Emerging Severe Mental Illness and Social Disability: A Systematic Review and Secondary Analysis of data from the PRODIGY Trial

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Thesis Portfolio Abstract

Background

Young people experiencing emerging severe mental illness and social disability are at heightened risk for enduring impairments in social functioning. However, predictors of long-term functional outcomes remain poorly understood, particularly across diagnoses. This thesis aimed to identify predictors of social functioning in youth with significant mental health difficulties and social disability.

Method

This thesis comprised two components: (1) a systematic review of longitudinal studies on predictors of socio-occupational functioning in individuals aged 16–25 with complex and/or severe mental illness; and (2) an empirical study examining functioning trajectories and associated baseline predictors through secondary data analysis.

Results

The systematic review identified 24 studies. Consistent predictors of poor functioning included negative symptoms, cognitive impairment, vocational disengagement, and duration of untreated psychosis. In contrast, evidence for demographic and biological predictors was limited and inconsistent. Building on these findings, the empirical study used data from the PRODIGY trial, a multi-site randomised controlled trial evaluating Social Recovery Therapy in young people with emerging severe mental illness and social disability. Latent class growth analysis identified three distinct social functioning trajectories over 24 months: stable low, moderate improvement, and increasing overactive. Higher levels of avolition and being Not in Education, Employment, or Training (NEET) at baseline significantly predicted membership in the stable low functioning group.

Conclusion

This thesis examined the course and predictors of long-term social functioning in young people with emerging severe mental illness, using a transdiagnostic lens. Findings highlight NEET status and negative symptoms, particularly avolition, as key markers of risk for persistent social disability. This disability extends beyond psychotic disorders and often persists despite receiving mental health care, underscoring the need for early, targeted, function-focused care. These findings support a shift in youth mental health care toward prioritising social recovery alongside symptom management to promote sustained and meaningful outcomes.

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Homo sum, humani nihil a me alienum puto.

I am human, and I consider nothing human alien to me.

Terence, *Heauton Timorumenos*, ca. 165 BCE

Chapter One: General Introduction

Adolescence and early adulthood are developmental periods characterised by profound biological, cognitive, psychological, and social transitions (Choudhury et al., 2008). These stages include significant milestones such as entering higher education or employment, establishing greater social independence, and developing a coherent sense of identity (Sawyer et al., 2012). Erikson's theory of psychosocial development (1968) conceptualises this phase as an identity crisis, during which individuals explore and integrate various aspects of self while searching for personally meaningful roles, values, and models (Mouchrek & Benson, 2023).

The magnitude of these developmental challenges may help explain why approximately 50% of all mental disorders emerge by age 14 and 75% by age 25 (Kessler et al., 2005), making youth mental health a global priority (Patel et al., 2007). Untreated mental health difficulties during these formative years can lead to significant lifelong personal and economic costs (Copeland et al., 2015; Gibb et al., 2010), potentially compromising educational achievement, workforce participation, and social engagement (Egan et al., 2016; Fergusson et al., 2007; Kessler et al., 1995). These functional impairments can sometimes persist even after symptom improvement, highlighting the importance of addressing functional recovery in youth mental health care (Fowler et al., 2021). Therefore, a better understanding of functioning trajectories and their correlates can help improve long-term outcomes.

Social functioning, referring to an individual's ability to engage in age-appropriate roles and activities across key life domains including education, employment, interpersonal relationships, and community participation (Yager & Ehmann, 2006), represents one aspect of functioning that can be important to mental health outcomes in youth. When impaired, social disability can lead to persistent difficulties in fulfilling age-appropriate roles in

educational settings, employment contexts, and social relationships, recognised as a hallmark characteristic of severe mental illness (Couture et al., 2006).

The United Nations Convention on the Rights of Persons with Disabilities (2006) frames these difficulties as stemming from the social and economic consequences of poor mental health that impede full societal participation. In conjunction, evidence suggests the consequential impact of poor social functioning on mental health outcomes (Cross et al., 2017; Fowler et al., 2010). Together, these findings imply a bidirectional relationship between social disability and mental illness, amplifying the relevance of early identification and intervention in the prevention of social disability in supporting improved youth mental health outcomes. The urgency of better understanding these factors is further emphasised by the rising number of young people who are Not in Education, Employment, or Training (NEET), a group vulnerable to increased psychiatric morbidity, economic vulnerability, and risk of long-term exclusion (Gariépy et al., 2022; O’Dea et al., 2014).

However, despite the significant development of and investment in youth mental health services, many service users continue to struggle with poor social functioning outcomes (Iorfino et al., 2018, 2022). Traditional diagnostic systems can often struggle to capture the complexity of youth presentations, leading to increased advocacy for transdiagnostic frameworks that account for the shared symptoms and impairments observed across mental health problems (Clarke et al., 2025). The Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2018), the p factor (Caspi et al., 2014), and the Research Domain Criteria (RDoC; Insel et al., 2010) represent examples of such systems, conceptualising mental illness along dimensional, cross-cutting domains, offering a richer understanding of shared mechanisms underlying psychopathology. Such approaches are particularly relevant for youth mental health, where symptoms often emerge in mixed forms and do not always align with diagnostic categories. Functional difficulties such as social

disengagement may arise across a range of conditions and therefore warrant study independent of specific diagnoses.

Moreover, understanding and improving social recovery in youth mental health is a major clinical and policy priority. UK government initiatives such as THRIVE framework (Wolpert et al., 2019) and the NHS Long Term Plan (NHS England, 2019) highlight the need for services that go beyond symptom management to support meaningful social engagement and reduce exclusion. Therefore, examining the factors associated with failure to recover appears critical in supporting service development to encompass individual presentations (De Soet et al., 2023) and to support early risk detection, the tailoring of interventions, and the broader informing of treatment targets beyond symptom remission.

Thesis Overview

This thesis aims to investigate predictors and trajectories of social functioning in young people with severe and/or complex mental health difficulties, across diagnostic categories. Chapter Two, a systematic review, synthesises evidence on predictors of long-term functional outcomes in young people with complex mental health needs and significant functional impairment, across diagnostic categories. Chapter Three features a bridging chapter, followed by a secondary analysis of data from a randomised controlled trial evaluating Social Recovery Therapy (SRT) in youth with emerging severe mental illness and social disability (PRODIGY trial; Berry et al., 2022) (Chapter Four). This is followed by a chapter that provides additional methods from this secondary analysis (Chapter Five). The sixth and final chapter presents a critical appraisal of the thesis portfolio, providing a general discussion, an assessment of strengths and limitations, clinical implications of the findings and suggestions for future research directions.

Chapter Two: Systematic Review

Prepared for submission to PLOS ONE

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Author guidelines are available in Appendix A. Line numbering will be added for journal submission.

Predictors of long-term functioning outcomes in young people, 16–25-year-olds, with severe and/or complex mental health problems: a systematic review and narrative synthesis

Short Title: Systematic review on functioning predictors in youth with mental health problems

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Abstract

Objective: Young people with severe mental health problems face a heightened risk of long-term difficulties in social and occupational functioning. While functional recovery is increasingly recognised as a central goal in youth mental health care, limited evidence exists on predictors of long-term outcomes across diagnostic groups. This systematic review aimed to identify predictors of long-term functioning in this population using a transdiagnostic approach.

Methods: Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, four databases were searched from inception to March 2024 for longitudinal studies involving individuals aged 16 to 25 with significant mental health symptoms and at least moderate functional impairment at baseline. Studies had to examine predictors of functioning over a minimum follow-up of 12 months. Due to heterogeneity in predictor types and outcome measures, a narrative synthesis was conducted.

Results: Twenty-four studies met the inclusion criteria. Most examined individuals with first-episode psychosis or those at clinical high risk for psychosis, while only two studies examined broader transdiagnostic samples. Predictors of functioning were grouped into demographic, clinical, psychosocial, and biological categories. Consistent findings emerged for a few predictors, including negative symptoms, duration of untreated psychosis, cognitive impairment and vocational disengagement. Some evidence also suggested an indirect effect of childhood trauma on functioning through its association with other clinical symptoms. Evidence for demographic and biological predictors was limited and inconsistent.

Conclusion: Findings highlight the importance of early identification of clinical and psychosocial risk factors for long-term functional impairment. Broader research across diagnostic boundaries is needed to support more inclusive and responsive youth mental health

services. Identifying those at highest risk may enable more targeted early interventions and improved long-term functional outcomes. This review was registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD42024497549).

1. Introduction

Mental health disorders are prevalent among young people, with approximately one in four individuals experiencing a mental illness by the age of 25 [1]. A broad spectrum of psychiatric conditions frequently emerges during adolescence and early adulthood. This is a critical developmental period characterised by transitions in education, employment, and social relationships [2,3].

Childhood, adolescent, and young adult mental problems are consistently associated with an increased risk for a wide range of unfavourable clinical and functional outcomes in adulthood, including later mental health problems [4–7], poorer health-related quality of life [6], problems in family and partner relationships [4,8] and lower life satisfaction [6,8]. Additionally, longitudinal population studies have shown that mental health conditions in youth are associated with poorer educational and occupational attainment, including unemployment and financial problems [4,5,7,9,10]. Importantly, these associations might persist even after controlling for childhood adversities and adult psychiatric status, suggesting independent long-term effects of early-life mental health issues [11].

Prospective cohort studies suggest that for many, these mental health conditions can persist, increasing the risk of significant impairments in social and occupational functioning into later adult life. These include lower high school completion, reduced college entry, increased likelihood of being Not in Education, Employment, or Training (NEET) or working without basic educational qualifications [12]. Additionally, persistent mental health issues are associated with lower income, poor psychosocial work conditions, difficulty entering the labour market [13], struggling to meet job demands [14], and an increased risk of long-term unemployment and work disability [15]. Furthermore, longer duration of mental health problems during childhood and adolescence has also been strongly associated with not having paid work in young adulthood [16].

Findings from large-scale longitudinal studies indicate that psychiatric disorders diagnosed in adolescence strongly predict long-term exclusion from education and employment in early adulthood [17,18], even after accounting for socioeconomic factors [18]. The Finnish Birth Cohort study further supports this, showing that nearly half of young adults experiencing long-term NEET had been diagnosed with a psychiatric disorder during adolescence, underscoring the long-term functional consequences of early-onset mental illness [18]. Given these findings, it is evident that severe and enduring mental health problems, manifesting in various forms such as psychotic disorders, mood disorders, and personality disorders, frequently co-occur with social and functional impairments [19].

Despite the well-documented relationship between severe mental health conditions and impaired functional outcomes, clinical research has largely focused on specific diagnostic groups, particularly individuals with first-episode psychosis (FEP) or those identified as at clinically high-risk for psychosis or At Risk Mental State (ARMS) for psychosis [20,21]. Systematic reviews have highlighted various predictors of functioning for FEP and ARMS groups, including cognitive deficits [21–23], symptom remission [21], and duration of untreated psychosis (DUP) [21,24], emphasising the importance of early intervention. However, predictors of long-term functional outcomes across a broader spectrum of severe and complex mental health conditions remain underexplored.

Recent advances in youth mental health frameworks, particularly the clinical staging model, emphasise functional impairment as a key marker of illness progression and prognosis [25–28]. Traditionally, mental disorders have been classified within static diagnostic categories, yet emerging evidence suggests that psychopathology exists along a continuum, with many young people transiting between different stages rather than fitting neatly into a single diagnostic classification [28,29]. The clinical staging model acknowledges this complexity and recognises psychosocial disability as a fundamental aspect of later-stage

illness [30]. Consequently, it has been argued that predictors of functional outcomes should be examined through a transdiagnostic lens, capturing a broader spectrum of severe mental health conditions [29–31]. The Clinical High At-Risk Mental State (CHARMS) criteria, an extension of the ARMS construct within the clinical staging framework, applies this principle by identifying individuals at risk for diverse psychiatric outcomes rather than a single disorder, with socio-occupational functioning playing a central role as a criterion for identifying at-risk individuals and as a relevant factor in characterising and potentially distinguishing between different risk states [31]. Expanding the focus of predictors of functioning beyond psychosis-specific risk groups is therefore essential to better understand functional trajectories, inform early intervention, and improve outcomes for young people with severe and complex mental health conditions.

Given the growing emphasis on early intervention and functional recovery as primary treatment goals in youth mental health services [32–35], identifying predictors of long-term functioning is critical for the identification of those at higher risk of poorer outcomes. However, despite increased research interest in clinical staging models of transdiagnostic mental illness in youth [30], there has been limited synthesis of evidence across diagnostic groups. A more comprehensive understanding of predictors, particularly within a transdiagnostic framework, is necessary to improve prognostic models and inform interventions aimed at preventing long-term social and occupational disability.

Aim of the Review

This systematic review aims to address the gap in the literature by synthesising evidence on the predictors of long-term functional outcomes in young people (16-25 years old) with severe and/or complex mental health problems. These are defined by clinically significant symptom severity and at least moderate functional impairment at baseline, across

diagnostic groups. The review seeks to answer the following research question: What are the predictors of long-term functioning outcomes in young people, 16–25-year-olds, with severe and/or complex mental health problems?

2. Method

2.1 Protocol and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines which include a 27-item checklist (Appendix B) and a four-phase flow diagram illustrating identified, screened, eligible, and included studies [36]. The review protocol was prospectively registered at PROSPERO (CRD42024497549).

2.2 Search Strategy

Electronic systematic searches, from inception until 2nd March 2024, were performed by the primary researcher to find relevant records from the following databases: PubMed (Medline), PsycINFO, EMBASE (Ovid) and Web of Science. The search strategy was informed by the PICOS (Population/Problem, Intervention, Comparison, Outcome, Study design) framework [37,38] used to help formulate the review question. The abstracts and titles of studies were searched using combinations of relevant keywords for the following concepts in the title and abstract of existing records: ‘young people’, ‘mental illness’, ‘severity/complexity’, ‘social functioning/social disability’ and ‘longitudinal’ referring to the study design. Where possible, the search was limited for English language and peer-reviewed articles, using the databases built-in functions. Additional articles were identified by hand-searching all references of retrieved included studies.

Please see Table 1 below for search terms used and Appendix C for the exact search strategies used for each data base.

Table 1. Search terms informed by the PICOS framework [37,38].

PICO terms	Key concept	Search terms used
Population	Young people	juvenile OR "young adult*" OR adolescen* OR "young people*" OR "young person*" OR youth OR student OR undergraduate OR child* OR "emerging adult*" OR "early adult" OR teen* OR pediatric* OR paediatric*
Problem	Mental health problems	"mental health illness*" OR "mental illness*" OR "mental health disorder*" OR "mental disorder*" OR "mental health diagnos*" OR "mental disease*" OR "mental health disease*" OR "psychological disorder*" OR "psychological illness*" OR "psychiatric disorder*" OR "psychiatric diagnos*" OR "psychiatric illness*" OR "psychiatric disease*" OR psychos* OR psychotic OR "personality disorder*" OR schizo* OR bipolar OR depression OR anxiety OR mania OR manic
	Severity /Complexity	"severe" OR "serious" OR "co-morbid*" OR "comorbid*" OR "complex*" OR "stage 1b" OR "attenuated syndromes" OR "stage 2" OR "full-threshold disorder" OR "full-threshold disorders" OR "stage 3" OR "stage 4"
Intervention/Comparison	Not Applicable	
Outcome of interest	Social functioning	functioning OR "functional outcome*" OR "social activit*" OR "social outcome*" OR employment OR "time use" OR "structured activit*" OR "social disability" OR "socially disabled" OR "social impairment" OR "functional impairment" OR "social withdrawal" OR "socially withdrawn" OR "social exclusion" OR "socially excluded" OR "social isolation" OR "socially isolated" OR NEET OR "not in employment, education or training" OR unemploy* OR "economic inactiv*" OR "economically inactiv*" OR "out of work" OR "school attendance" OR "student attendance" OR "college attendance" OR "non-attendance" OR absenteeism OR truan* OR "student withdrawal"
Study type	Longitudinal	"longitudinal" OR "follow-up" OR "follow up" OR "course" OR "trajector*" OR "cohort" OR "prospective" OR "clinical stag*"

2.3 Eligibility Criteria

2.3.1 Inclusion criteria

Participants in the included studies were required to meet the following criteria:

1. Participants should be between the ages of 16 and 25 years and/or the study should present disaggregated data for participants within this age range. Alternatively, studies were included if the mean age of participants fell between 16 and 25 years. The justification for this criterion is that this age range represents a critical period for the emergence of severe mental health problems [25].
2. Participants should present with clinically significant symptoms of one or more severe mental health problems. The minimum level of severity required for inclusion was the presence of 'at-risk mental states' (ARMS) and/or moderate severity of anxiety and/or depression. Additionally, participants were eligible if they had a clinician-rated or research diagnosis of one or more mental health disorders.
3. Participants should have demonstrated at least moderate impairment in social, educational, or occupational domains, or social disability. This included significant social or occupational withdrawal, such as NEET status, school exclusion, or disengagement. To establish at least moderate socio-occupational impairment, validated measurement tools were required, with cut-off scores based on commonly accepted thresholds for moderate impairment. For example, a cut-off of 60 was applied for the Global Assessment of Functioning (GAF; [39]) and Social and Occupational Functioning Assessment Scale (SOFAS; [39]), as this reflects moderate impairment or greater in functioning [39]. The emphasis on an objective measure of baseline functioning was crucial to ensure the inclusion of participants with clear, observable functional difficulties.

The mental health and functional impairment criteria were based on the transdiagnostic clinical staging model [25,40]. Specifically, participants were included if they

presented at stage 1b or above, which indicates emerging but significant mental health concerns with associated significant functional impairment requiring intervention.

The outcome of interest in this review was socio-occupational functioning, broadly conceptualised to include global, social, and/or occupational domains functioning. The focus of the review was on behavioural or objective appraisals of functioning, rather than subjective self-reported measures to ensure a more accurate and observable appraisal of functional outcomes.

To be included, studies should have been primary research, written in English, be peer-reviewed and used quantitative methods. In terms of design, studies needed to be longitudinal, measuring participants' functioning at least two time points with a minimum 12-month timeframe to delineate temporal associations between potential predictors variables and functioning, including both observational and intervention studies. Studies should have been examining one or more predictors of a functional outcome, including sociodemographic, clinical, psychological as well as biological predictors of functioning.

2.3.2 Exclusion criteria

Studies were excluded if they did not meet the inclusion criteria for age, mental health symptom severity, or socio-occupational impairment, or if they failed to report these factors. Studies were also excluded if they did not provide disaggregated data for relevant subgroups when such data were necessary to determine eligibility. Additionally, studies were excluded if participants had co-occurring generalised learning disabilities or pervasive developmental disorders, as these factors may independently influence socio-occupational functioning and confound findings related to emerging mental health conditions.

Non-English language articles, non-peer-reviewed publications, and non-primary research, such as reviews, letters, opinion pieces, editorials, study protocols, books, and book

chapters, were also excluded. Furthermore, abstracts from scientific meetings, conference proceedings, editorials, articles in press, and doctoral dissertations without a corresponding peer-reviewed publication were not included. Case studies focusing on individual participants were similarly excluded to maintain the focus on generalisable findings.

Finally, studies that did not examine any predictors or correlates of socio-occupational functioning were not eligible for inclusion. Specifically, intervention studies that solely assessed the effect of an intervention on functioning, without exploring additional correlates or predictors, were excluded to ensure that the review focused on identifying factors influencing socio-occupational outcomes rather than evaluating treatment effects.

2.4 Selection Process

All studies identified following the search of the databases went through a process involving two steps: title and abstract screening and full-text screening.

All retrieved records were imported into EndNote reference managing software and duplicates were removed manually. One of the reviewers (Aikaterini R.) screened all potentially relevant articles for inclusion based on title and abstract against the inclusion and exclusion criteria. Full text screening of the remaining records was conducted for eligibility. An independent researcher (Alexandros R.) conducted full-text screening on 20% of included studies. There was agreement for 95% of the studies screened, with inter-rater reliability showing moderate agreement ($\kappa = .59$) [41]. Any opposing views that arose regarding the final selection of included studies were discussed until a consensus was reached among the reviewers.

The study selection process was documented in the PRISMA flow chart (Figure 1), which included reasons for including or excluding studies from reviewing records at full-text level.

2.5 Quality Assessment

To assess methodological quality, the Mixed Methods Appraisal Tool (MMAT; [42]) was employed due to its suitability for appraising diverse study designs, including randomised controlled trials, non-randomised, and descriptive studies, using a standardised framework. The MMAT comprises a two-stage process: initial screening for a clearly defined research question and appropriate data collection, followed by a study-specific appraisal of five criteria rated as “Yes,” “No,” or “Can’t tell.” Responses were scored (Yes = 1; No/Can’t tell = 0), yielding a total score from 0 to 5. Studies with attrition rates exceeding 20% were rated “No” on completeness of outcome data (MMAT question 3), reflecting potential bias [43].

All eligible studies were retained regardless of MMAT score to ensure comprehensive evidence synthesis. The MMAT facilitated systematic appraisal of bias risk and enhanced transparency in quality assessment. One reviewer (Aikaterini R.) conducted the initial assessment and 20% of studies were independently cross-checked by a second reviewer (Alexandros R.), with discrepancies resolved through discussion. Inter-rater reliability was $\kappa = .65$, showing substantial agreement [41] with an 84% agreement rate.

2.6 Data Extraction

Data were extracted using a standardised spreadsheet, which was developed and pilot-tested prior to use. One reviewer (AR) conducted the data extraction, capturing key study characteristics, including authorship, publication year, country of origin, study aims, and design. Participant characteristics were recorded, including sample size at baseline, mean age, gender, ethnicity, and follow-up details such as time points and retention rates. Information on socio-occupational functioning was extracted at both baseline and follow-up, where available, including the measure used and mean functioning scores at each time point.

Psychopathology data were documented, including the type of mental health presentation, instruments used to assess symptoms, and the clinical staging classification (e.g., stage 1b “attenuated syndromes” or stage 2 “discrete disorders” or above). Data extraction also included details on key analytical methods and predictors of functioning examined, irrespective of statistical significance. Additionally, any potential confounders accounted for in the analyses were noted. Where studies identified functioning trajectory classes over time, these were also recorded. Finally, key findings relevant to the review question were extracted, including reported effect estimates with 95% confidence intervals, where available.

2.7 Data Synthesis

A narrative synthesis was conducted following the guidance of [44] and Synthesis Without Meta-Analysis (SWiM; [45]), while adhering to the PRISMA [36] reporting guidelines. Given the expected heterogeneity in predictor variables, statistical analyses, and outcome measures, a meta-analysis was not feasible.

First, a preliminary synthesis grouped studies by predictor type. Summary tables were used to organise extracted findings. Second, relationships between predictors and socio-occupational functioning outcomes were explored across different methodologies and study contexts, with attention to effect directions and statistical significance using a vote-counting approach to summarise overall trends, following SWiM guidelines. Effect sizes (e.g., regression coefficients, odds ratios) were reported where available. This approach was chosen over traditional vote counting based solely on statistical significance to avoid misleading interpretations due to small sample sizes or underpowered studies. To ensure transparency and rigor, studies were grouped by predictor type and by functional outcome measure.

Where reported, effect sizes were interpreted using updated empirical guidelines, reflecting concerns that Cohen's original thresholds ([46]) tend to overstate typical effects in psychological and clinical research [47]. For r , effect sizes were interpreted using thresholds proposed by Funder and Ozer [47] with .10 representing a small, .20 a medium, and .30 a large effect. Where standardised regression coefficients (β) were reported, these were interpreted using the same thresholds as Pearson's r , given their comparable scaling in linear models. These estimates align closely with recent empirical benchmarks derived from clinical and psychological research [48–50]. Cohen's d and Hedges' g were interpreted using thresholds of .15 (small), .36 (medium), and .65 (large) as recommended by empirically derived effect size distributions in psychological research [50] aligning closely with estimates from clinical research [48,51]. For odds ratios (ORs), effect size magnitude was interpreted using guidelines proposed by Chen et al. [52], with ORs of 1.5, 2.5, and 4.3 representing small, medium, and large effects respectively when $OR > 1$, and 0.67, 0.40, and 0.23, when $OR < 1$. For hazard ratios (HRs), effect sizes were interpreted using guidelines from Lu et al. [53] who mapped HRs to Cohen's d across a range of baseline event rates in time-to-event data. HRs of approximately 1.16–1.68 were considered small, 1.43–3.43 medium, and 1.73–6.52 large.

Heterogeneity was explored qualitatively by comparing findings across study designs, predictor types, and functioning measures. Since this review did not involve a meta-analysis, the review systematically summarised both significant and non-significant associations and respective effect sizes when reported, ensuring a comprehensive and transparent synthesis of the available evidence.

3. Results

3.1 Study Selection

Database searching identified 7380 records (Figure 1). After removal of duplicates, 3460 articles remained, and titles and abstracts were screened against the eligibility criteria. When it was not explicit that the studies could be excluded, they were included at the full-text screening stage. After screening, 2934 records were excluded, and 526 full texts (15.20%) were retained for full text review. Of these, 512 (97.34%) were excluded.

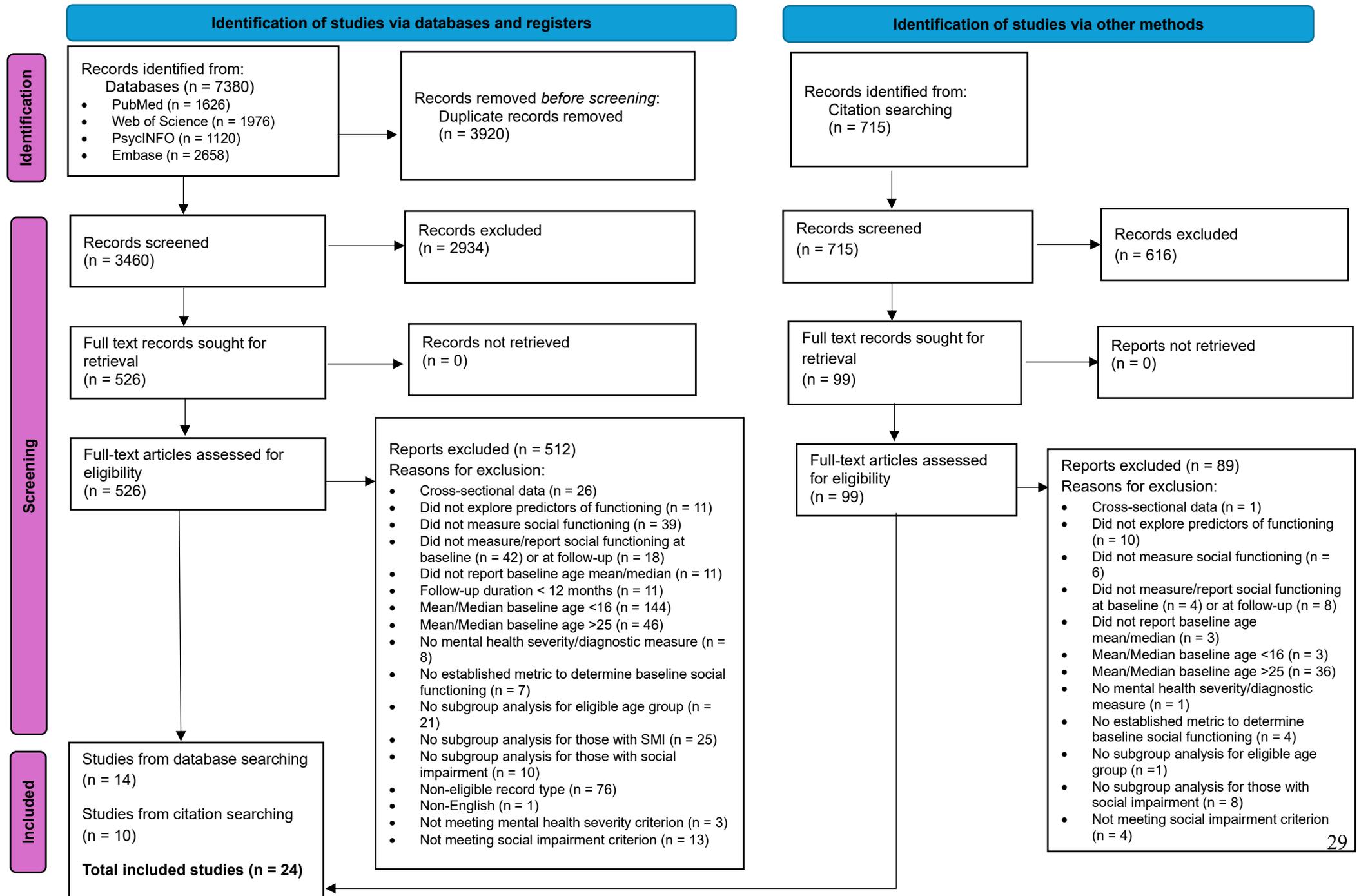
The most common reason for exclusion was age ineligibility, with 144 studies (27.38%) having a mean or median baseline age below 16 and 46 studies (8.75%) exceeding the upper age limit of 25. Other demographic or study design-related exclusions included studies with a follow-up duration of less than 12 months (2.09%), those that did not report a baseline age mean or median (2.09%), and studies that were non-eligible record types, such as reviews or conference abstracts (14.45%). Several studies were excluded due to insufficient measurement of socio-occupational functioning, including those that did not measure social functioning at all (7.41%), lacked social functioning data at baseline (7.98%) or follow-up (3.42%), or did not use an established metric for determining baseline social functioning (1.33%). Similarly, 8 studies (1.52%) did not include a measure of mental health severity or diagnosis, and 3 studies (0.57%) failed to meet the required mental health severity criterion.

Studies that did not investigate predictors of functioning (2.09%) or lacked subgroup analyses for the eligible age group (3.99%), individuals with severe mental illness (4.75%), or those with social impairment (1.90%) were also excluded. Additional exclusions included studies that analysed one-time-point data (4.94%) and studies where samples did not meet the social impairment criterion at baseline (2.47%). Finally, one non-English study (0.19%) was excluded.

A total of 24 studies were included in the final review. Fourteen studies were identified through database searches, while an additional 10 studies were identified through citation searching and screened using the same eligibility criteria.

In the screening process, “baseline” did not necessarily refer to the study’s initial assessment point but could refer to any previous data collection within the eligible age range for the review. Similarly, studies with less than 12 months of follow-up were excluded, but this follow-up period did not always refer to the overall duration of the study; instead, it referred to the time between assessment points that included participants within the age range of interest.

Figure 1. PRISMA Flowchart



3.2 Study Characteristics

The summary of study characteristics is included in Table 2. Appendix D shows supplementary information of the included studies.

Table 2. Characteristics of included studies (N = 24).

ID	Author(s) /Year	Setting/Recruitment	Sample size (N)	Age (M, SD, Min-Max) in years	Gender (N, % male)	Baseline functioning measure(s)	Baseline functioning level	Clinical stage & presentation	Follow-up time points	Follow-up functioning measure(s)	Functioning predictors examined
1	Abdel-Baki et al. (2017) [54]	EIS FEP programme in Canada. Almost all incident cases from two services.	212	Total: M = 23 (SD not reported), range = 18 – 30 SUD (N= 125): M (SD) = 22.9 (3.5) No SUD (N = 87): M (SD) = 23 (3.6)	Total: 80.2% SUD: 86.4%, no SUD: 71.3% (N not reported)	SOFAS	No exact estimate; M between 30-40 for total, SUD and no SUD subgroups on SOFAS	Stage 2 (FEP)	1 year, 2 years	SOFAS, Employment / study status	SUD persistence
2	Alameda et al. (2015) [55]	EIS FEP programme in Switzerland (TIPP). All eligible patients treated at the programme.	225	M (SE) = 23.94 (0.32), Min-Max = 18 – 35	138 (66.0%)	SOFAS, GAF	No exact estimate; M between 50-60 for total and subgroups on SOFAS	Stage 2 (FEP)	2, 6, 12, 18, 24, 30 and 36 months	SOFAS, GAF	Age of childhood trauma exposure (early vs. late)
3	Alameda et al. (2017) [56]	EIS FEP programme in Switzerland (TIPP). All eligible patients treated at the programme.	209	M (SD) = 24.67 (4.76), Min-Max = 18 – 35	156 (70.27%)	SOFAS, GAF	GAF: M (SD) = 37.72 (15.84) SOFAS: M (SD) = 39.99 (15.27)	Stage 2 (FEP)	2, 6, 12, 18, 24, 30 and 36 months	SOFAS, GAF	Age of childhood trauma exposure (early vs. late)
4	Amminger et al. (2020) [57]	Data from a RCT recruiting from ten EIS in Australia, Asia, and Europe (NEURAPRO trial)	218	M (SD) = 18.8 (4.3), Min- Max = 13 – 40	102 (46.79%)	SOFAS, GF-S and GF-R scales	SOFAS, M (SD) = 53.7 (12) GF-S, M (SD) = 6.5 (61.3) GF-R, M (SD) = 6.0 (61.5)	Stage 1b (ARMS)	6 and 12 months	SOFAS, GF-S and GF-R scales (not mentioned in outcome analysis)	Changes in EPA, DHA, and Omega-3 index (EPA+DHA) levels.
5	Berger et al. (2020) [58]	Data from a RCT recruiting from ten EIS in Australia, Asia, and Europe (NEURAPRO trial)	106	M (SD) = 17.21 (2.37), Min-Max = 15 – 24	36 (33.96%)	SOFAS, GF-S and GF-R scales	SOFAS, M (SD) = 55.70 (10.93) GF-S, M (SD) = 6.61 (1.19)	Stage 1b (ARMS)	6 and 12 months	SOFAS, GF-S and GF-R scales	Allostatic load index

6	Burgher et al. (2023) [59]	Not reported	19 early psychoses (vs. 19 age- and gender-matched HC)	$M (SD) = 21.2 (2.0)$, Min-Max = 17 – 25	12 (63.1%)	SOFAS	GF-R, $(SD) = 6.21 (1.54)$ SOFAS, $M (SD) = 55.70 (15.0)$	Stage 2 (early psychosis)	12 months	SOFAS	Cognitive control (reduced reaction time delta)
7	Cocchi et al. (2008) [60]	EIS programme in Italy (Programma 2000), all eligible FEP and ARMS patients were invited (15 refused)	143 (N = 72 FEP, N = 71 ARMS)	FEP: Male, $M (SD) = 22.49 (3.9)$; Female, $M (SD) = 24 (4.2)$ At-risk: Male, $M (SD) = 21.69 (3.4)$; Female, $M (SD) = 23.09 (3.5)$ Min-Max = 17 – 30	FEP: 56 (77.8%) ARMS: 47 (66.2%)	GAF	FEP: GAF, $M (SD) = 44.09 (8.2)$ At-risk: GAF, $M (SD) = 52.89 (10.5)$	Stages 1b (ARMS) and 2 (FEP)	6 and 12 months	GAF	DUI and DUP
8	Conus et al. (2017) [61]	EIS programme in Australia (EPPIC), file audit considering all admitted patients	584 (N = 108 were 'Never exposed to adequate dose of Antipsychotics' (NA))	Non-NA: $M (SD) = 22.1 (3.4)$ NA: $M (SD) = 21.9 (3.4)$ Min-Max = 15 – 29	Non-NA: 306 (64.3%) NA: 76 (70.4%)	GAF	non-NA: GAF, $M (SD) = 31.6 (9.7)$; NA: GAF, $M (SD) = 32.4 (9.6)$	Stage 2 (FEP)	18 months post initial presentation	Functional recovery as concurrent fulfilment of the following two criteria: 1) having a regular occupational activity based on MVSI; and 2) independent living according to the MLCI (i.e., head of household, living alone, with partner, or with	Age (years), Sex (male), Years in school, Pre-morbid GAF, Duration of prodrome (in days), Duration of untreated psychosis (in days), Age at onset (years), Exposure to traumatic event (Yes/No), Past history of suicide attempt (Yes/No), Past substance use disorder (Yes/No), Forensic history (Yes/No), Baseline variables: Diagnosis at entry, Severity of symptoms at entry (CGI-S, CGI-BP depression, CGI-BP mania), Insight at entry(Yes/No), Employment/occupation (Yes/No), Independent living (Yes/No), GAF, Substance use at entry (Yes/no), Cannabis (Yes/No), Polysubstance (Yes/No)

										peers, and living with family with minimal supervision)	
9	Cotton et al. (2009) [62]	EIS programme in Australia (EPPIC), file audit of consecutive admissions with FEP and available data	661	Male: $M(SD) = 22.2(3.2)$ Female: $M(SD) = 21.7(3.8)$ Min-Max = 15 – 29	43 (65.8%)	GAF, working/ studying at entry	Male: GAF, $M(SD) = 31.4(10.0)$; Working/studying at entry, $N(\%) = 243(56.1\%)$ Female: GAF, $M(SD) = 33.6(9.2)$; Working/studying at entry, $N(\%) = 100(44.2\%)$	Stage 2 (FEP)	18 months	GAF, working/ studying at discharge	Gender
10	Fraguas et al. (2014) [63]	Data from an early onset FEP study (CAFEPS), consecutively recruiting from outpatient and inpatient units at six hospitals in Spain	80	$M(SD) = 16.01(1.78)$ Min-Max = 7 – 17	55 (68.8%)	C-GAF	C-GAF, $M(SD) = 32.83(15.45)$	Stage 2 (FEP)	2 years	C-GAF and C-GAF change score [(C-GAF score at 2 years minus C-GAF score at baseline)/ C-GAF at baseline]	DUP
11	Hall et al. (2019) [64]	Data from the Pittsburgh FEP Longitudinal Cohort Study; considered all admissions for certain period from inpatient and outpatient services of the Western Psychiatric Institute and Clinic in Pittsburgh	129	$M(SD) = 24.42(7.4)$ Min-Max = 15 – 45	83 (64.4%)	GAF at 4–8 weeks (after stabilisation of acute psychotic symptoms)	GAF, $M(SD) = 33.83(9.5)$	Stage 2 (FEP)	4–8 weeks, 6 months, and 1 year	GAF	sex, race, SES, IQ, executive function (WCST Number of perseverative errors), personality, and clinical features (diagnosis, histories of substance use, age of onset, premorbid function, duration of prodromal symptoms, BPRS, HRSD)

12	Iorfino et al. (2018) [65]	Subgroup of patients admitted to youth mental health clinics, primary and secondary care, in Australia (18% of patients in a research register)	Total: 554 Relevant subgroups: serious impairment-deterioration, n = 39; serious impairment-chronic, n = 158; serious impairment-improvement, n = 19	Total: $M (SD) = 19.83 (3.77)$ Relevant subgroups: serious impairment-deterioration: $M (SD) = 20.26 (4.05)$, serious impairment-chronic: $M (SD) = 19.68 (3.70)$, serious impairment-improvement: $M (SD) = 18.37 (4.76)$ Min-Max = 12 – 32 years	Total: 257 (46%) Relevant subgroups: serious impairment - deterioration : 21 (54%), serious impairment -chronic: 81 (48%), serious impairment - improvement: 9 (47%)	SOFAS, NEET status	Total: SOFAS, $M (SD) = 60.45 (9.19)$; NEET: 113 (20%) Relevant subgroups: serious impairment - deterioration SOFAS, $M (SD) = 50.61 (7.25)$, chronic, SOFAS, $M (SD) = 54.90 (5.63)$, improvement, SOFAS, $M (SD) = 43.83 (7.05)$	Stage 1b (attenuated syndromes) and Stage 2 (discrete disorder)	3, 6, 12 months, 2 years, 3 years, 4 years, 5 years, time last seen; Median follow-up duration was 23 months.	SOFAS	Age, sex, receipt of government benefits, NEET status, mental health diagnosis, medical diagnosis, childhood mental health diagnosis, hospitalised (ever), suicide ideation (ever), suicide planning (ever) and suicide attempts
13	Iorfino et al. (2022) [66]	Youth mental health clinics, primary and secondary care in Australia, (Brain and Mind Centre), all eligible participants in a research register	Total: 1510 in total. Relevant subgroups: persistent impairment, n = 237; deteriorating and volatile, n = 733	Total: $M (SD) = 18.1 (3.3)$, Relevant subgroups: Persistent impairment, $M (SD) = 17.9 (3.2)$; Deteriorating and volatile, $M (SD) = 18.0 (3.3)$ Min-Max = 12 – 25	Total: 580 (38.4%), Relevant subgroups: persistent impairment, 95 (40.1%), deteriorating and volatile, 297 (40.5%)	SOFAS, NEET status	Total: SOFAS, $M (SD) = 62.1 (9.6)$ Relevant subgroups: No exact estimate reported.	Stage 1b (attenuated syndromes) and Stage 2 (discrete disorder)	At least 3 data time points between 1 and 24 months after baseline	SOFAS	Age, sex, NEET status, mental health presentation, personal history of mental illness (any childhood disorder, any family history), past psychiatric treatment use (hospitalisation, medication), any major physical illness, self-harm, suicidal ideation, suicide attempts
14	Lambert et al. (2010) [67]	EIS programme in Australia (EPPIC), file audit using available data from an epidemiologically based cohort	605	$M (SD) = 21.6 (3.4)$ Min -Max = 15 – 29	408 (66.1%)	GAF, working/ studying at entry	GAF, $M (SD) = 32.1 (9.8)$; Unemployment at entry, N (%), yes: 312 (51.7)	Stage 2 (FEP)	18 months (or at the point of discharge)	GAF, working/ studying at discharge	Medication adherence (full, partial, persistent refusal)

15	Lévesque et al. (2020) [68]	EIS programme in Canada, all consecutive FEP admissions were considered	167 (N = 44) having experienced homelessness at some point)	Total: $M (SD) = 23.2 (3.7)$ Never homeless: $M (SD) = 23.2 (3.8)$ Homeless: $M (SD) = 23.3 (3.5)$ Min-Max = 18 – 30	Total: 124 (74%) Never homeless: 85 (69%) Homeless: 39 (89%)	SOFAS, GAF	Total: GAF, $M (SD) = 33.7 (10.6)$; SOFAS, $M (SD) = 38.7 (12.1)$ Never Homeless: GAF, $M (SD) = 34.5 (11.03)$, SOFAS, $M (SD) = 40.1 (12.3)$ Homeless: GAF, $M (SD) = 31.3 (9.09)$, SOFAS, $M (SD) = 34.66 (10.9)$	Stage 2 (FEP)	1 year and 2 years	GAF, SOFAS	Homelessness (prior to admission and/ or during the first year of follow-up)
16	Molina-García et al. (2021) [69]	Data from a subsample of eligible participants from two multicentre FEP studies (CAFEPS, PEPs) that recruited patients from psychiatry units at hospitals in Spain	255	$M (SD) = 21.66 (6.06)$ Min- Max = 10 – 36	172 (67.5%)	GAF/ c-GAF	GAF/c-GAF, $M (SD) = 47.10 (21.08)$	Stage 2 (FEP)	2 years	GAF/ c-GAF	Premorbid IQ, age of onset, clinical diagnosis
17	Paillère-Martinot et al. (2000) [70]	Data from consecutive admissions to locked psychiatric wards in a teaching hospital in Paris	36	$M (SD) = 17.5 (1.8)$ Min-Max = 14 – 21	18 (50%)	GAF	For those with schizophreniform disorder, GAF, $M (SD) = 38.0 (10.6)$. For those with schizoaffective disorder), GAF, $M (SD) = 35.1 (18.6)$. For those with psychotic, major depression, GAF, $M (SD) = 35.1 (19.4)$. For those with psychotic,	Stage 2 (FEP or recent-onset psychosis)	At discharge, 1 year after discharge, and subsequently once a year when follow-up was possible. Mean follow up duration was 31 months ($SD = 12$).	GAF	Anhedonia, index GAF score, number of hospital admissions, alogia, MADRS score

18	Pina-Camacho et al. (2022) [71]	Data were drawn from a longitudinal multicentre, naturalistic, prospective FEP imaging study (PEPs) that recruited from outpatient and inpatient units in Spain. No sampling strategy reported.	74 (vs HC, N = 64)	$M (SD) = 23.2 (6.00)$ Min-Max = 15 – 35	50 (67.6%)	GAF/ CGAS	manic episode, GAF, $M (SD) = 35.2 (9.5)$ CGAS/GAF, $M (SD) = 53.5 (23.1)$	Stage 2 (FEP)	24 months	GAF/ CGAS	Temporal lobe cortical thickness change (for specific FEP cluster group with lower baseline temporal lobe cortical thickness)
19	Pruessner et al. (2019) [72]	EIS FEP programme in Canada; Unclear whether all admissions were considered	210	$M (SD) = 23.73 (4.53)$ Min-Max = 14 – 35	146 (68.87%)	GAF	Total: GAF, $M (SD) = 30.06 (8.88)$ Men: GAF, $M (SD) = 29.43 (8.71)$; Women: GAF, $M (SD) = 31.44 (9.16)$	Stage 2 (FEP)	12 and 24 months	GAF	Gender, history of childhood trauma (within gender groups)
20	Pruessner et al. (2021) [73]	EIS FEP programme in Canada; Unclear whether all admissions were considered	210	$M (SD) = 23.73 (4.43)$ Min-Max = 14 – 35	144 (69%)	GAF	Total: 209, GAF, $M (SD) = 30.06 (8.88)$ No-CT, GAF, $M (SD) = 29.35 (7.69)$ CT, GAF, $M (SD) = 30.66 (9.78)$	Stage 2 (FEP)	12 and 24 months	GAF	History of childhood trauma
21	Reniers et al. (2017) [74]	Data from eligible consecutive admissions to an ARMS clinical research programme (PACE) in Australia	109	$M (SD) = 19.5 (3.6)$ Min-Max = 15 – 30	54 (49.54%)	GAF	GAF, $M (SD) = 59.5 (12.3)$	Stage 1b (ARMS)	Between 2.4 and 12.9 years after entry. Median = 9.8 years.	GAF, SOFAS, change in GAF score over time (calculated for each participant relative to their baseline score and constituted of a percentage	Baseline grey and white matter density

											change score and an absolute change score)
22	Schimmelmann et al. (2007) [75]	EIS programme in Australia (EPPIC), file audit using available data from an epidemiologically based cohort	636	$M(SD) = 22.1(3.4)$ Min-Max = 15 – 29	426 (67.0%)	GAF, working/ studying at entry	31.9 (9.6)	Stage 2 (FEP)	18 months	GAF	Early- (age < 18) vs. adult- (≥age 18) psychosis onset
23	Schimmelmann et al. (2008) [76]	EIS programme in Australia (EPPIC), file audit using available data from an epidemiologically based cohort	636	$M(SD) = 22.1(3.4)$ Min-Max = 15 – 29	426 (67.0%)	GAF, working/ studying at entry	31.9 (9.6)	Stage 2 (FEP)	18 months	GAF, working/ studying at discharge	DUP categorised into four groups: short DUP (below 1 month), short-medium DUP (1 month to below 3 months), medium-long DUP (3 months to 12 months), and long DUP (above 12 months).
24	Schlosser et al. (2012) [77]	EIS for ARMS programme in USA (CAPPS); recruited from eligible consecutive admissions to the programme	84 (vs 58 HC)	$M(SD) = 16.9(3.5)$ No age range reported	52 (61.9%)	GF- S and GF- R scales	GF-S, $M(SD) = 5.7(1.7)$ GF-R, $M(SD) = 5.3(2.1)$	Stage 1b (ARMS)	3, 6, 12, and 24 months	Functional recovery (achieving a score of 7 or higher over a 1-month period on both GF-S and GF-R scales)	Positive, negative and mood/anxiety symptom scores

Note. ARMS = At-Risk Mental State; BPRS = Brief Psychiatric Rating Scale; CAFEPS = Child and Adolescent First Episode Psychosis Study; CAPPS = Centre for the Assessment and Prevention of Prodromal States;; CGI-BP = Clinical Global Impression – Bipolar; CGI-S = Clinical Global Impression – Severity; C-GAF = Children's Global Assessment of Functioning; CGAS = Children's Global Assessment Scale; CT = Childhood Trauma; DHA = Docosahexaenoic Acid; DUP = Duration of Untreated Psychosis; DUI = Duration of Untreated Illness; EIS = Early Intervention Service; EPA = Eicosapentaenoic Acid; EPPIC = Early Psychosis Prevention and Intervention Centre; FEP = First Episode Psychosis; GAF = Global Assessment of Functioning; GF-R = Global Functioning - Role; GF-S = Global Functioning - Social; HC = Healthy Controls; HRSD = Hamilton Rating Scale for Depression; ID = Study ID; IQ = Intelligence Quotient; MADRS = Montgomery-Åsberg Depression Rating Scale; MLCI = Modified Location Code Index; MVSI = Modified Vocational Status Index; NEET = Not in Education, Employment, or Training; NEURAPRO = Neuroprotection and Early Psychosis trial; RCT = Randomised Controlled Trial; SD = Standard Deviation; SE = Standard Error; SES = Socioeconomic Status; SUD = Substance Use Disorder; SOFAS = Social and Occupational Functioning Assessment Scale; TIPP = Treatment and Early Intervention in Psychosis Programme; WCST = Wisconsin Card Sorting Test.

Sample size (N) represents participants included at baseline or those with available data (e.g., some studies only included participants with follow-up data). If male descriptives were not reported in the study, they were calculated based on female descriptives to maintain consistency of reporting.

3.2.1 Study sample sizes and participant overlap between studies

Sample sizes across the included studies ranged from 30 [59] to 970 participants [66]. Of the 24 studies, six investigated independent samples, comprising a total of 771 participants [59,60,64,70,74,77]. The remaining 18 studies utilised samples from the same cohorts, clinical programs, or research registers. Due to this overlap, participant numbers were not aggregated. Findings were interpreted with consideration of shared data sources and varying inclusion criteria to avoid double counting and ensure accurate representation of study populations.

3.2.2 Designs

Of the 24 included studies, 22 were observational, employing prospective ($n = 17$) [54–56,59–61,63–66,69–74,77], retrospective ($n = 4$) [62,67,75,76], or combined retrospective-prospective ($n = 1$) longitudinal designs [68]. Two studies were interventional, utilising longitudinal data from the same randomised controlled trial [57,58]. Additionally, three studies included healthy control groups to investigate differences in cognitive functioning, clinical outcomes, and brain structure between clinical and non-clinical populations [59,71,77].

3.2.3 Demographics

The mean age of participants, where reported, ranged from 16.01 [63] to 24.67 years [56]. Gender representation across studies averaged 36.9% female, with individual studies ranging from 19.8% to 66.0% female. Only one study had a perfectly balanced gender distribution [70]. Studies with the largest gender imbalances included one with 80.2% male [54] and another with 74% male [68] highlighting substantial male overrepresentation in certain cohorts.

Participant ethnicity was not collected or reported in 17 out of 24 studies. Among the seven studies that reported ethnicity, six provided specific Caucasian or White percentages, with an average of 69.13%, ranging from 53.0% to 91.9% [63,64,71–73,77]. Additionally, one study [68] reported that 36% of their sample identified as "visible ethnic minority", though no further ethnic classifications were provided. These findings suggest that, when reported, most samples were predominantly White, with inconsistent ethnicity reporting across studies.

3.2.4 *Mental health presentations*

Seventeen studies included FEP samples [54–56,59,61–64,67–73,75,76], four studies focused on ARMS [57,58,74,77] and one study included both ARMS and FEP participants [60]. Participants in 13 studies were recruited from early intervention in psychosis services (EIS), many of which integrate routine research programs [54–56,60–62,67,68,72–76]. An additional four studies recruited FEP participants from general mental health services [63,64,69,71] and two studies used data from an RCT of ARMS individuals which recruited participants from specialised early psychosis treatment centres [57,58]. One study recruited help-seeking ARMS participants from local mental health services, a research mental health provider program, schools, a website, and community advertisements, incorporating both clinical and community-based recruitment [77]. One study [59] included early psychosis participants but did not specify recruitment sources or define the timeframe constituting "early psychosis". Another study [70] recruited participants with FEP or recent-onset psychosis (≤ 3 years) from two inpatient wards at a teaching hospital.

Only two studies recruited transdiagnostic samples of young people with emerging mental health difficulties [65,66], drawing their data from primary care-based early intervention mental health services at the Brain and Mind Centre in Sydney, which caters to individuals aged 12 to 25 years.

3.2.5 *Social functioning measures*

Baseline. To measure baseline functioning, 17 studies measured global functioning using the GAF or CGAS, depending on the participants' age. Nine studies used the Social and Occupational Functioning Assessment Scale (SOFAS), and three studies employed the Global Functioning: Social (GF-S) and Global Functioning: Role (GF-R) scales. Additionally, six studies used a dichotomous measure for engagement in part-time or full-time education, employment, or training. Some studies utilised multiple measures: three reported both SOFAS and GAF scores, two combined SOFAS with the GF-S and GF-R scales, and six studies used the SOFAS or GAF with a dichotomous variable to assess NEET status.

The reported GAF scores ranged from $M = 30.06$ ($SD = 8.88$) [72,73] to $M = 59.5$ ($SD = 12.3$) [74]. SOFAS scores ranged from $M = 38.7$ ($SD = 12.1$) [68] to $M = 55.7$ ($SD = 10.93$) [58]. For the Global Functioning scales, the lower reported baseline GF-S was $M = 5.7$, $SD = 1.7$, and GF-R, $M = 5.3$, $SD = 2.1$ [77] and the highest GF-S was $M = 6.61$, $SD = 1.19$, and GF-R, $M = 6.21$, $SD = 1.54$ [58]. Three studies [54,55,66] indicated baseline SOFAS scores below 60 but did not provide exact values.

Follow-up. Most studies used the same measures as at baseline to measure follow-up functioning. However, there were some exceptions. One study [61] assessed functioning as a binary recovery outcome based on vocational engagement and independent living criteria. Another study [77] dichotomised the GF-S and GF-R scales, defining recovery as achieving scores greater than 7 for at least one month. One study [54] assessed NEET status in addition to SOFAS at follow-up, while another [74] supplemented GAF assessments with SOFAS and reported absolute and percentage changes in GAF scores over time.

Out of the 24 included studies, 15 studies explicitly reported follow-up social functioning outcomes [54,58,59,62–64,67–71,74–77]. Three studies examined functional

trajectories using growth mixture modelling [65,66] or K-means clustering [64]. Iorfino et al. [65,66] identified several distinct social and occupational functioning trajectories among young people in early intervention mental health services, with only a subset of them demonstrating significant social impairment at baseline (SOFAS < 60) and meeting inclusion criteria for this review. In contrast, Hall et al. [64] classified participants into four functional-symptom trajectories—poor, intermediate, good, and catch-up recovery—integrating symptom severity and social functioning.

3.2 Quality Appraisal

The MMAT quality rating findings revealed that the overall quality of the studies was moderate to high. Out of 24 studies, 20 received scores between 3 and 4 out of 5, indicating moderate to high methodological quality, while only three studies received the lowest score of 2, suggesting lower quality.

The lower-scoring studies were primarily affected by three key methodological limitations. First, inadequate adjustment for confounders was a recurring issue, with seven studies (29.2%) failing to sufficiently control for variables such as socioeconomic status, treatment adherence, symptom severity, and comorbidities. This limitation weakened the internal validity of their findings, as the impact of external factors on functional outcomes could not be fully accounted for. Second, 17 out of 24 studies (70.8%) had incomplete functional outcome data or did not report data completeness, raising concerns about missing data bias. Third, high attrition rates posed a challenge for several studies, with nine (37.5%) reporting dropout rates exceeding 30%, thereby increasing the risk of attrition bias. Only three studies (12.5%) met the $\leq 20\%$ dropout threshold, indicating robust follow-up and lower risk of attrition bias [54,68,70].

In addition to these limitations, 45.8% of the studies ($N = 11$) applied a priori selection criteria, requiring participants to have complete data across multiple time points. While this approach ensured greater data consistency in longitudinal analyses, it may have introduced selection bias by overrepresenting participants with better follow-up adherence and excluding those with incomplete data, who may have experienced poorer functional outcomes.

The results of the MMAT quality assessment are presented in tabulated form in Appendix E with justifications for ratings in Appendix F.

3.3 Predictors of Functioning Outcomes

Several predictors were identified and were organised by type (demographic, psychosocial, clinical and biological/neurocognitive). Table 3 presents a summary of findings across different measures of functional outcomes, using the study ID numbers from Table 2. Twenty-one studies examined predictors of functioning outcome whereas only three used trajectory modelling to identify potential predictors of functioning trajectories [64–66]. For this reason, outcomes from these three studies are not included in Table 3.

Table 3. Summary of findings for predictors of functioning outcomes (predictor type, statistical significance, direction).

Predictors	SOFAS			GAF/ C-GAF			Occupational status			Functional recovery		
	P	N	NS	P	N	NS	P	N	NS	P	N	NS
Demographic Predictors												
Age baseline	-	-	-	-	-	-	-	-	-	-	-	8
Gender (male)	-	-	-	-	9 (**)	19	-	9 (*)	-	-	-	8
Years in school	-	-	-	-	-	-	-	-	-	-	-	8
Clinical Predictors												
Premorbid IQ	-	-	-	16 (*)	-	-	-	-	-	-	-	-
Age at onset (early vs. adult)	-	-	-	-	-	22	-	-	22	-	-	-
Age at onset	-	-	-	16 (**)	-	-	-	-	-	-	-	8
DUP	-	-	-	-	23 (***) 10 (**)	7 (FEP)	-	23 (***)	-	-	-	8
DUI	-	-	-	-	7 (*) (ARMS)	7 (FEP)	-	-	-	-	-	-
Duration of prodrome (in days)	-	-	-	-	-	-	-	-	-	-	8 (*)	-
Pre-morbid GAF	-	-	-	-	-	-	-	-	-	-	-	8
Past suicide attempt	-	-	-	-	-	-	-	-	-	-	-	8
Past substance use disorder	-	-	-	-	-	-	-	-	-	-	-	8
Schizophrenia vs. all others psychotic disorders	-	-	-	-	-	17	-	-	-	-	-	8

SSD vs. affective or NOS psychosis	-	-	-	-	16 (***)	-	-	-	-	-	-
Schizophrenia or Schizoaffective vs. Bipolar Disorder	-	-	-	-	17 (*)	-	-	-	-	-	-
Number of hospital admissions					17 (**)						
CGI-S at entry	-	-	-	-	-	-	-	-	-	8 (*)	-
CGI-BP depression at entry	-	-	-	-	-	-	-	-	-	-	8
MADRS at entry				17 (**)	-	-					
CGI-BP mania at entry	-	-	-	-	-	-	-	-	-	-	8
SOPS (Dysphoric Mood)	-	-	-	-	-	-	-	-	-	-	24
Anhedonia baseline	-	-	-	-	17 (**)	-					
Alogia baseline	-	-	-		17 (*)	-					
Negative symptoms baseline (and over time)	-	-	-	-	-	-	-	-	-	24 (***)	-
Insight at entry	-	-	-	-	-	-	-	-	-	-	8
GAF baseline	-	-	-	17 (*)	-	-	-	-	-	-	8
Substance use at entry	-	-	-	-	-	-	-	-	-	-	8
SUD persistence at 1 year	-	1 (**)	-	-	-	-	-	1 (**)	-	-	-
SUD persistence at 2 years	-	1 (**)	-	-	-	-	-	1 (*)	-	-	-
Cannabis use at entry	-	-	-	-	-	-	-	-	-	8 (*)	-
Polysubstance use at entry	-	-	-	-	-	-	-	-	-	-	8

Persistent medication refusal (vs nonadherence and full adherence)	-	-	-	-	14 (***)	-	14 (**)	-	-	-
Psychosocial Predictors										
Exposure to traumatic event	-	-	-	-	-	-	-	-	-	8
CTQ total (in men)	-	-	-	-	19 (** 24m)	19 (12m)	-	-	-	-
Emotional abuse/CTQ (in men)	-	-	-	-	19 (** 24m)	-	-	-	-	-
CTQ overall (in women)	-	-	-	-	-	19	-	-	-	-
CTQ overall	-	-	-	-	-	20	-	-	-	-
Early SPA	-	2 (*), 3 (*)	-	-	2 (*), 3 (*)	-	-	-	-	-
Late SPA	-	-	2, 3	-	-	2, 3	-	-	-	-
Forensic history	-	-	-	-	-	-	-	-	-	8
In employment/occupation baseline	-	-	-	-	-	-	-	-	8 (**)	-
Independent living baseline	-	-	-	-	-	-	-	-	-	8
Homelessness	-	15 (**)	-	-	15 (**)	-	-	-	-	-
Biological/neurocognitive biomarkers										
EPA	4 (*)	-	-	-	-	-	-	-	-	-
DHA	4 (**)	-	-	-	-	-	-	-	-	-
Omega-3 index (EPA+DHA)	4 (**)	-	-	-	-	-	-	-	-	-

Allostatic Load ^a	-	-	5	-	-	-	-	-	-	-	-
Cognitive control (reduced reaction time delta)	6 (*)	-	-	-	-	-	-	-	-	-	-
Temporal lobe cortical thickness change (for specific FEP cluster with lower baseline temporal lobe cortical thickness)	-	-	-	18 (*)	-	-	-	-	-	-	-
Baseline grey matter density	-	21	-	-	21	-	-	-	-	-	-
Baseline white matter density	-	-	21	-	-	-	-	-	-	-	-

Note. 12m = 12-month follow-up; 24m = 24-month follow-up; ARMS = At-Risk Mental State; C-GAF = Children's Global Assessment Scale; CGI-BP = Clinical Global Impression – Bipolar Disorder; CGI-S = Clinical Global Impression – Severity; CTQ = Childhood Trauma Questionnaire; DHA = Docosahexaenoic Acid; DUI = Duration of Untreated Illness; DUP = Duration of Untreated Psychosis; EPA = Eicosapentaenoic Acid; FEP = First-Episode Psychosis; GAF = Global Assessment of Functioning; GF-R = Global Functioning: Role; GF-S = Global Functioning: Social; MADRS = Montgomery–Åsberg Depression Rating Scale; N = negative association (worse functioning); NOS = Not Otherwise Specified; NS = non-significant relationship; P = positive association (better functioning); SOFAS = Social and Occupational Functioning Assessment Scale; SOPS = Scale of Prodromal Symptoms; SPA = Sexual and/or Physical Abuse; SSD = Schizophrenia Spectrum Disorder; SUD = Substance Use Disorder.

The numbers in the table represent the study ID from Table 2. Results reported reflect estimates after corrections for multiple testing and adjusting for covariates or confounding variables where these were carried out. If the same study reported different findings for several time points this is noted. Any variables that were included in relevant analyses as covariates, mediators or confounders were not included in this table.

^aBerger et al (2020) used GF-S and GF-R as functioning outcome measure and thus this measure is not included in the table. The authors found a non-significant relationship between allostatic load and both subscales.

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

3.3.1 Demographic predictors

Demographic factors were examined as potential predictors of functional outcomes in six studies, four focusing on FEP and two on transdiagnostic samples of young people with emerging mental health difficulties.

Three studies examined gender as a predictor of functioning in FEP, with mixed results. Cotton et al. [62], in a treated epidemiological sample ($N = 661$), found that at discharge, males had significantly lower GAF scores than females ($F(1,651) = 7.18, p = .008$) even after controlling for baseline functioning and treatment duration, and were more likely to be unemployed/not studying (Wald $z = 4.24, p = .040$). However, this was not supported in Pruessner et al. [72] ($N = 210$) who showed that global functioning improved over time for both men and women ($p < .001$), with no significant difference between genders at 12- or 24-month follow-up. Similarly, Conus et al. [61] in FEP patients who had not received an adequate dose of antipsychotic medication ($N = 108$) found that gender was not a significant predictor of functional recovery, while adjusting for time in service, occupational and independent living status at service entry. In two transdiagnostic youth samples, Iorfino et al. [65,66] found that gender did not significantly predict membership in any of the functional trajectories that started with moderate to severe functioning, including chronic impairment versus improving trajectories or versus deteriorating trajectories.

Three studies examined age as a demographic predictor. In an inadequately treated FEP sample, Conus et al. [61] reported that age at service entry was not significantly associated with functional recovery ($p < .05$). In contrast, Iorfino et al. [65], using longitudinal trajectory modelling with a median follow-up of 23 months in a transdiagnostic youth sample, found that older age was the only baseline factor predicting membership in a chronic impairment trajectory compared to an improvement trajectory (OR = 0.83, 95%CI [0.71 - 0.98], $p < .05$) among those with baseline serious functioning impairment, representing

a negligible effect size. In a follow-up study, Iorfino et al. [66] did not find age to significantly predict functioning trajectory membership comparing those in the deteriorating and volatile trajectory versus those in the persistent impairment trajectory.

The only one study that examined ethnicity as a predictor of functional outcomes by Hall et al. [64] found that being Caucasian was associated with a good functional outcome trajectory compared to a poor trajectory in two models that examined the joint evolution of functioning with positive and negative symptom severity ($ps < .05$).

Overall, demographic factors demonstrated mixed associations with functional outcomes. Gender was an inconsistent predictor, with one FEP study identifying poorer functioning in males [62] without reporting an effect size, while two FEP [61,72] and two transdiagnostic studies [65,66] found no relationship. Older age predicted chronic impairment compared to improving trajectories in one transdiagnostic study with minimal effect [65], but not in a follow-up study comparing persistent impairment to deteriorating and volatile trajectories [66], or in FEP samples, suggesting that age may not be a robust predictor of functioning.

3.3.2 Psychosocial predictors

Employment/occupational status. Two studies, one in a FEP [61] and one in a transdiagnostic sample [66] examined occupational status at baseline as predictors of functional outcomes with small to large effect sizes.

Baseline vocational engagement seemed to be a consistent predictor of functional outcomes in both FEP and transdiagnostic samples. In a study of FEP patients who had not received adequate antipsychotic treatment, Conus et al. [61] found that having regular vocational activity at service entry significantly increased the likelihood of functional recovery (OR = 4.29, 95% CI [1.66, 11.08], $p = .003$), representing a large effect. Similarly,

in a transdiagnostic youth sample, Iorfino et al. [66] reported that being not in employment, education, or training (NEET) at baseline significantly increased the odds of belonging to a deteriorating and volatile functional trajectory compared to a persistent impairment trajectory (OR = 1.61, 95% CI [1.05–2.51], $p < .05$), suggesting a small-to-medium effect.

Bringing these findings together, baseline vocational status was consistently predictive of long-term functioning, with effect sizes ranging from small to large. Vocational engagement was associated with better outcomes in FEP, while NEET status predicted poorer functional trajectories in a transdiagnostic youth cohort.

Trauma history. Five studies, all using FEP samples, examined previous exposure to traumatic events as potential predictors of functional outcomes. Two studies [55,56] focused on the timing of sexual and physical abuse (before age 11 vs. ages 12-16), one looked at the presence of previous exposure to trauma [61], one investigated overall childhood trauma (CT) [73] and one explored gender-specific effects [72].

Pruessner et al. [72,73] explored both total CT and gender-specific effects. While one study they found that total CT scores were not associated with functioning at 12 or 24 months [73], another [72] identified gender-specific differences. In males, higher total CT scores were significantly associated with poorer global functioning at 24 months ($\rho = -.29$, $p = .004$, surviving Bonferroni correction) but not at 12 months. Emotional abuse was the only type of CT that remained a significant predictor in regression models, with a medium effect size ($\beta = -.33$, $R^2 = .11$, $p = .001$). No significant associations between CT and functioning outcomes were observed in females.

Alameda et al. [55,56] consistently demonstrated that early-life trauma (before age 12) was significantly associated with poorer functioning outcomes. In their first study ($N = 225$), childhood sexual/physical abuse before age 11 predicted significantly lower GAF ($B =$

−4.75, $SE = 2.10$, $p = .025$) and SOFAS scores ($B = -4.13$, $SE = 2.08$, $p = .048$) over 36 months, while trauma occurring between ages 12–15 showed no significant association ($p > .05$) when compared to those with no trauma history. Their second study [56] ($N = 209$) confirmed this pattern, across multiple time points (12, 18, and 24 months) ($ps < .05$, no effect sizes reported). These effects were further explained through symptom mediation over time: depressive symptoms partially mediated the relationship at 6 months, positive symptoms at 24 months, and depressive symptoms again at 30 and 36 months, with indirect unstandardised effects on GAF and SOFAS ranging from $B = -3.45$ to -5.79 points ($ps < .05$). This pattern indicates that while early trauma initially predicts poorer functioning directly, its long-term impact is primarily mediated by fluctuations in psychotic and depressive symptoms at different stages of illness progression.

In contrast, Conus et al. [61] found no association between trauma exposure and functional recovery at 18-month follow-up in FEP patients who had not received adequate antipsychotic treatment. This null finding may reflect limitations in how trauma was assessed, as a binary presence/absence measure overlooks important factors such as trauma timing, type, severity, which were found to differentiate functional outcomes in other studies.

Overall, findings suggest that CT, particularly when occurring before age 12 and among men, is associated with poorer functional outcomes, with effect sizes ranging from small to medium where reported. These results also highlight that the impact of trauma on functioning depend on how trauma is operationalised, especially in relation to its developmental timing, type, and interaction with other clinical factors.

Other psychosocial predictors. Three additional psychosocial predictors were examined in single FEP studies: independent living status and forensic history at service entry [59], and homelessness at any point during the first year of follow-up [68]. Neither

independent living nor forensic history significantly predicted functional recovery, whereas individuals with a history of homelessness showed poorer functioning at 2-year follow-up, despite comparable baseline scores [66]. Effect sizes were not reported in any of the studies.

3.3.3 *Clinical predictors*

Age of psychosis onset. Age at psychosis onset was examined across three FEP studies with mixed findings. Schimmelmann et al. [75], in a large epidemiological FEP cohort of consecutively admitted patients to an Early Intervention Service (EIS) in psychosis ($N = 636$), found no significant differences in functional outcomes (GAF) or employment rates at 18 months between early-onset (age <18) and adult-onset (age ≥ 18) groups, even after adjusting for baseline functioning and treatment duration. Similarly, in a subgroup of this cohort who had never received adequate treatment ($N = 108$), Conus et al. [61] also found no significant association between age at onset was again and functional recovery. This was further supported in Hall et al. [64] where age of onset did not significantly predict membership in any 1-year functional trajectories ($ps > .05$). In contrast, Molina-García et al. [69], using data from FEP patients recruited from hospital psychiatry units ($N = 255$), found that age of onset was an independent predictor of GAF at a 2-year follow-up with a small effect ($\beta = .19, p = .004$), even after controlling for clinical diagnosis, premorbid IQ, antipsychotic medication exposure, and symptom severity (PANSS subscales).

In summary, only one study [69] identified younger age of onset as a significant predictor of poorer functional outcomes with a small effect, while all other three studies did not [61,64,75]. This discrepancy may reflect sample and recruitment setting differences. Molina-García et al. [69] included a broader age range (10–36 years) with more very early-onset cases (<18 years) potentially associated with greater developmental disruption. In contrast, minimum age in the other three studies was 15 years, with most patients being over 18, potentially limiting power to detect early-onset effects. Additionally, Molina-García et al.

[69] recruited from general psychiatry hospital units, likely reflecting a more clinically severe cohort, while Conus et al. [61] and Schimmelmann et al. [75] recruited from specialised EIS, where patients might benefit from more intensive care, potentially mitigating the impact of younger onset on functioning.

Premorbid IQ. Two FEP studies considered premorbid IQ as a predictor of functional outcomes, both reporting consistent associations with poorer functioning. Molina-García et al. [69] reported that premorbid IQ was significantly associated with GAF at a 2-year follow-up ($\beta = 0.15, p = .02$), indicating a small effect, after controlling for clinical diagnosis, age of onset, antipsychotic medication exposure, and PANSS symptom scores. Subgroup analyses indicated that early-onset individuals with lower premorbid IQ had the poorest functioning at both baseline ($d = 1.29$) and follow-up ($d = 0.82$), reflecting large and medium effects, respectively. Consistent with Molina-García et al. [69], Hall et al. [64] found that lower premorbid IQ was associated with poorer functional outcomes, distinguishing between good and poor functional outcome trajectories ($ps < .05$), although effect sizes were not reported.

Overall, lower premorbid IQ predicted poorer functional outcomes across both studies, with at least small effects where reported, underscoring its relevance as a prognostic marker in FEP.

Duration of untreated illness (DUI) and psychosis (DUP). Four studies examined the role of DUP and DUI as predictors of functional outcomes in FEP samples [60,61,63,76], with one also including ARMS individuals [60]. Findings from studies with greater methodological quality and relevance to the review question consistently showed that longer DUP was associated with poorer functional outcomes, particularly in schizophrenia-spectrum disorders, with effect sizes ranging from small to medium where reported.

In a paediatric FEP sample ($N = 80$), Fraguas et al. [63] found that longer DUP significantly predicted worse global functioning at two years ($r = -.38, p = .001$), particularly in schizophrenia ($r = -.38, p = .008$), indicating medium effects, but not in affective psychosis ($p > .05$). In multiple regression analyses adjusting for premorbid adjustment, PANSS total score, IQ, cumulative antipsychotic dose, diagnosis, baseline mania, age, and gender, DUP remained the only significant predictor of functional outcomes in the whole sample ($\beta = -0.134, 95\%CI [-0.208 \text{ to } -0.060], p = .001$) and the schizophrenia subgroup ($\beta = -0.130, 95\%CI [-0.223 \text{ to } -0.036], p = .008$), both reflecting small but significant effects.. In follow-up analyses, longer DUP predicted smaller functional gains in the whole sample, in those with schizophrenia and with other psychoses, indicating small effects ($\beta s \approx -.01, ps < .05$), though not in affective psychosis or bipolar disorder. Given that all patients in this sample had a DUP of less than six months, findings may not generalise to FEP populations with longer DUP.

Similarly, Schimmelmann et al. [76] ($N = 636$) found that longer DUP predicted lower GAF at discharge ($F(3,588) = 11.9, p < .001$), even after controlling for premorbid adjustment, baseline GAF, age at onset, medication adherence, and persistent substance use, with results remaining significant after excluding bipolar I disorder ($p = .009$). In addition, DUP significantly predicted employment status at discharge ($\chi^2(9) = 85.3, p < .001$, Nagelkerke $R^2 = .21$). However, after excluding bipolar I cases, this effect was no longer significant. Post-hoc analyses revealed that only patients with $DUP < 1$ month had significantly higher odds of employment ($OR = 2.1$), consistent with a small-to-medium effect size, while no additional employment decline was observed beyond three months, suggesting a possible threshold effect.

In contrast, in a subsample of FEP patients who did not receive adequate antipsychotic treatment, Conus et al. [61] found that DUP was not significantly associated

with functional recovery at 18 months ($p < .05$). Cocchi et al. (2008) examined DUI and found in FEP, neither DUI nor DUP predicted follow-up GAF scores, while longer DUI was linked to poorer functioning at six months and one year in the ARMS group ($ps < .05$). However, their primary aim was to describe their service model rather than examine functional predictors in detail, limiting interpretability.

Overall, longer DUP consistently predicted poorer functional outcomes in FEP, particularly in schizophrenia, with small to medium effects where stated and a possible threshold effect at three months. In contrast, findings were less consistent in affective psychosis and bipolar disorder. Notably, Conus et al. [61] found no association between DUP and functioning outcomes in inadequately treated FEP patients, suggesting that treatment adequacy may moderate the impact of prolonged DUP.

Psychopathology. Four studies explored psychopathology variables as predictors of functioning outcomes: three in FEP samples [61,64,70] and one in a transdiagnostic youth sample [66]. Additionally, three studies considered psychopathology variables in regression models primarily to adjust for confounding rather than to assess their predictive utility [56,63,77].

Negative symptoms consistently emerged as predictor of poorer functioning outcomes. In an ARMS cohort ($N = 137$) [77], negative symptoms were the strongest predictor of poorer functional recovery, both as a time-varying predictor ($HR = 0.83$, 95%CI [0.77–0.89], $p < .0001$) with a small-to-medium effect, and a fixed baseline predictor ($p = .0004$), independent of age, gender, and medication use. In a small adolescent inpatient FEP sample, Paillère-Martinot et al. [70] ($N = 36$) reported that specific baseline negative symptoms, specifically anhedonia and alogia, predicted poorer follow-up GAF scores ($ps < .05$), though no effect sizes were reported.

Findings on general psychopathology were mixed. In a FEP sample, Conus et al. [61] found that lower baseline overall illness severity (measured by CGI-S) increased the likelihood of functional recovery (OR = 0.51, 95%CI [0.29, 0.92], $p = .024$), after adjustment for time in service, working/studying status and independent living status at service entry, representing a medium effect size. Fraguas et al. [63], while primarily focused on DUP, found that psychotic symptom severity (PANSS) predicted C-GAF change, but not follow-up C-GAF, only in the subgroup with affective psychosis with a small effect ($\beta = .06$, 95%CI [.02 to .10], $p = .004$), suggesting diagnosis-specific differences. Additionally, in a transdiagnostic youth sample, Iorfino et al. [66] found that the presence of psychosis-like experiences significantly increased the odds of belonging to a deteriorating and volatile trajectory compared to a persistent impairment trajectory (OR = 1.86; 95%CI [1.17–3.06]), with a medium effect.

Mood-related symptoms were inconsistently linked to functional outcomes and no studies reported standardised effect sizes. In Conus et al. [61], depression and mania scores did not predict functional recovery ($ps > .05$) whereas Hall et al. [64] demonstrated that more severe affective symptoms (including anxiety and depression) were consistently associated with poor versus good outcome trajectories ($p < .05$). Alameda et al. [56] also reported that, at 30 and 36 months, depressive symptoms fully mediated the relationship between early trauma and poor functioning, significantly impacting GAF and SOFAS ($ps < .01$). A contrasting finding was found by Paillère-Martinot et al. [70] in a small FEP, inpatient sample, where higher baseline depression scores predicted better follow-up GAF ($p = .005$).

In ARMS, Schlosser et al. [77] found that higher dysphoric mood/anxiety symptoms predicted lower odds of functional recovery (HR = 0.73, 95%CI [0.60–0.90], $p = .004$), though this effect was not significant in fixed baseline models or after covariate adjustment ($p > .05$).

These results highlight negative symptoms as the most reliable psychopathological predictor of functional impairment, with effects in the small-to-medium range. In contrast, broader psychotic symptom severity was mixed, with associations found in affective psychosis or in those not receiving adequate antipsychotic treatment whereas the presence of psychotic-like experiences in a transdiagnostic population seemed to contribute to further functional decline. Mood-related symptoms were inconsistently linked to functioning. While not linked to functional recovery in a FEP sample of inadequately treated patients [61] or in ARMS [77], more severe overall affective symptoms were linked to poorer functional trajectories [64] and depressive symptoms may mediate the relationship between early trauma and functioning outcomes [56]. Notably, several studies did not report effect sizes, limiting the interpretability of findings.

Premorbid and baseline functioning. Three FEP studies [61,63,70] examined premorbid and baseline functioning as predictors of later functional outcomes, with mixed findings.

In a paediatric FEP sample ($N = 80$), Fraguas et al. [63] reported that poorer premorbid adjustment significantly predicted smaller C-GAF improvements over two years, indicating small effects in the whole sample ($\beta = -.092$, 95% CI $[-.180, -.004]$, $p = .041$) and the schizophrenia subgroup ($\beta = -.114$, 95% CI $[-.210, -.019]$, $p = .025$), with a larger effect observed in affective psychosis ($\beta = -.250$, 95% CI $[-.491, -.010]$, $p = .042$). Similarly, in a smaller inpatient sample ($N = 36$), Paillère-Martinot et al. [70] reported that baseline GAF significantly predicted follow-up GAF scores ($p = .030$) alongside negative symptoms and number of hospitalizations. In contrast, Conus et al. [61] found that premorbid GAF and baseline GAF were not significantly associated with functional recovery at 18 months, suggesting that initial functioning may be less predictive in FEP patients without adequate antipsychotic treatment.

Overall, two small FEP studies found that poorer premorbid and baseline functioning generally predicted worse long-term functional outcomes, with small to medium effects where reported. However, the strength of this association appeared to vary depending on treatment access and illness subtype.

Substance use. The predictive role of substance use was examined in two FEP studies [54,61] and one transdiagnostic study [66], with mixed findings.

In FEP studies, Abdel-Baki et al. [54] ($N = 212$) found that persistent SUD over two years, referring to alcohol and/or drug use, was significantly associated with worse functional outcomes, including lower SOFAS scores and poorer employment/study rates, both at 1- and 2-year follow-up points ($ps < .05$). Notably, by two years, functional impairments were significant only when comparing persistent SUD to those who never had SUD, while those who stopped using no longer differed significantly from persistent users ($ps > .05$). This suggests that early cessation of substance use during FEP may mitigate long-term functional impairments. Additionally, in a subgroup of FEP patients who had not received adequate antipsychotic treatment, Conus et al. [61] found that cannabis use at entry increased the likelihood of functional recovery (OR = 0.36, 95%CI [0.14, 0.94], $p = .037$) representing a medium effect. However, past SUD, any substance use at entry, and polysubstance use were not significantly associated with functional recovery ($ps > .05$). This suggests that baseline substance use alone may not reliably predict long-term functioning in inadequately treated patients.

Finally, in a transdiagnostic youth sample, Iorfino et al. [66] ($N = 554$) found that a baseline SUD did not significantly distinguish between functional trajectory groups among individuals with low baseline functioning.

Overall, while baseline substance use alone does not appear to reliably predict functional outcomes in FEP [61], persistent SUD may be more predictive of poorer

functioning outcomes [54]. However, effect sizes were not reported in these studies, limiting the ability to quantify the magnitude of these associations.

Psychiatric diagnoses. Six studies examined psychiatric diagnostic categories as predictors of functional outcomes: four in FEP samples [59, 62, 67, 68], and two in transdiagnostic youth cohorts [63, 64].

In FEP research, consistent evidence indicated that schizophrenia-spectrum disorders (SSD) were associated with poorer long-term functional outcomes compared to affective psychoses. Molina-García et al. [69] ($N = 255$) reported that SSD was a significant predictor of worse GAF scores at follow-up compared to affective or Non-Otherwise Specified psychosis ($\beta = -0.30, p < 0.001$), indicating a medium effect even after adjusting for IQ, age at onset, and medication exposure. Similarly, Hall et al. [64] ($N = 129$) showed that a schizophrenia diagnosis was more prevalent in the poor outcome trajectory compared to affective psychosis ($p < .05$). Paillère-Martinot et al. [70] further demonstrated that diagnostic category was significantly associated with GAF scores at follow-up ($p = .007$), though the small inpatient sample limits generalisability. Post-hoc analyses revealed that bipolar disorder was associated with significantly better GAF outcomes than schizophrenia ($p = .02$, effect size = 1.20) and schizoaffective disorder ($p = .01$, effect size = 1.00), reflecting large effects, albeit in the context of limited statistical power. Conversely, Conus et al. [61] found that diagnostic category at entry (schizophrenia vs. all other psychotic disorder diagnoses) was not significantly associated with functional recovery in a cohort of individuals with FEP who were not adequately treated with antipsychotics ($p > .05$).

In transdiagnostic samples, findings were mixed. In a large sample ($N = 1510$) Iorfino et al. [66] found that only bipolar disorder increased the odds of belonging to a deteriorating and volatile trajectory compared to a persistent impairment trajectory (OR = 2.37, 95%CI

[1.08–5.40]), indicating a small-to-medium effect. However, in a similar cohort, Iorfino et al. [65] did not find any diagnosis to significantly predict trajectory membership.

In summary, across FEP samples, diagnostic category had medium-to-large effects on functioning, with SSD being associated with poorer functional outcomes compared to affective psychoses [64,69,70]. However, findings from Conus et al. [61] suggest that in the absence of adequate treatment diagnostic effects may be attenuated. In transdiagnostic youth, Iorfino et al. [66] found that bipolar disorder was linked to a deteriorating and volatile trajectory compared to the persistent impairment trajectory showing a small-to-medium effect, while Iorfino et al. [65] found no diagnostic effects on trajectory membership. These discrepancies may reflect differences between transdiagnostic and FEP samples, as well as the potential influence of comorbidities and heterogeneity in symptom presentations.

Other clinical variables. A number of additional clinical variables were examined in single studies only, including medication adherence [67], number of past hospital admissions [70], duration of prodromal symptoms, past suicide attempts and insight at service entry [61] in FEP samples, as well as comorbid physical illness in a transdiagnostic sample [66]. Given these predictors were only examined in single studies, no consistent patterns could be drawn to be integrated into the narrative synthesis. Further details can be found in Table 3.

3.3.4 Biological and neurocognitive biomarkers

Five studies investigated biological and neurocognitive markers as predictors of functioning. three in ARMS and two in FEP/early psychosis samples, each exploring distinct predictors.

Omega-3 Fatty Acids & Allostatic Load. Two studies used data from the same ARMS RCT, combining control and intervention groups. Amminger et al. [57] ($N = 218$) found that increases in Omega-3 index, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)

levels significantly predicted higher socio-occupational functioning (SOFAS) scores at 12 months, with effect sizes ranging from small to medium ($\beta = .17-.23$ $ps < .05$). Conversely, Berger et al. [58] ($N = 106$) reported that higher allostatic load (AL), a physiological measure of the cumulative burden of stress on the body, was associated with lower functioning (SOFAS, GF-S, GF-R) at 6 months, with small to medium negative effects ($\beta s = -0.19$ to -0.25 , $ps < .05$), but not at 12 months, suggesting only short-term impact.

Cognitive control. In a functional MRI study, Burgher et al. [59] ($N = 38$) found that, when early psychosis participants were compared to healthy controls, improvements in cognitive control measured by reaction time delta (RT Δ ; interference condition reaction time minus neutral condition reaction time) were significantly associated with improved SOFAS over 12 months (repeated-measures correlation = $-.53$, $p = .017$), indicating a large effect.

Structural brain changes. Two studies investigated structural MRI markers as predictors of functional outcomes in FEP and ARMS individuals respectively. Pina-Camacho et al. [71] ($N = 74$ FEP patients) identified two FEP subgroups based on baseline cortical thickness (CT), with comparisons made against healthy controls. In the low baseline CT group ($n = 43$), smaller temporal lobe CT changes were associated with worse functional outcomes (GAF/CGAS scores, $p < .05$), indicating a medium association, although no exact estimate was reported. This suggested that minimal cortical thinning may be maladaptive in this group. Conversely, no associations were found in the high baseline CT group ($n = 31$), who also received lower antipsychotic doses and were younger, pointing to possible developmental differences. Furthermore, in an ARMS sample with a mean of 9.2 years follow-up, Reniers et al. [74] found that lower baseline grey matter density (GMD) in the middle and inferior frontal gyri predicted greater GAF decline and lower-than-average baseline GMD in key regions, including the medial prefrontal cortex, right cingulate gyrus,

left anterior cingulate, and left cerebellar declive, was significantly associated with lower SOFAS scores at follow-up ($ps < .05$, family-wise error corrected). This was independent of transition to psychosis, and after adjusting for age, sex, scanner strength, and follow-up length. These associations were attenuated when controlling for symptom severity (SANS and BPRS psychotic subscale scores), suggesting potential confounding.

Overall, biological and neurocognitive markers show promise in predicting functional outcomes in early psychosis although most studies were not explicitly designed to assess predictors of functional outcomes. In ARMS, omega-3 fatty acids emerged as promising long-term predictors of socio-occupational functioning with small-to-medium effects on functioning over time whereas lower GMD in frontal and limbic regions predicted long-term functional decline in ARMS individuals, regardless of transition to psychosis, although no effect sizes were reported. In FEP, cognitive control improvements were linked to better functioning outcomes but only in individuals with low baseline CT. These findings underscore the potential of integrating behavioural, biological and cognitive markers when evaluating predictors of functional outcomes.

4. Discussion

4.1 Summary of Key Findings

This systematic review synthesised evidence on predictors of long-term functional outcomes among young people (16–25 years old) with severe and/or complex mental health problems with significantly impaired functioning. Eighteen identified studies used FEP, five ARMS, and only two transdiagnostic samples. A range of demographic, clinical, psychosocial, and biological predictors were examined, with considerable variability across studies. Despite heterogeneity in predictor variables, several key findings emerged.

Among clinical factors, diagnostic category consistently predicted functioning in FEP, with SSD associated with poorer outcomes compared to affective psychoses [64,69,70], with medium to large effect sizes. Lower IQ [64,69] and negative symptoms also robustly predicted poorer functioning, with negative symptoms showing consistent associations in both ARMS [77] and FEP samples [70], with small to medium effect reported. In contrast, mood-related symptoms showed inconsistent associations with functioning outcomes, and the lack of effect sizes reported limited interpretability. However, in FEP, more severe affective symptoms predicted poor versus good functional trajectories in FEP [64], and depressive symptoms were found to mediate the relationship between early life trauma and functioning outcomes [56].

Additionally, in all but one study, longer DUP predicted poorer functional outcomes with effect sizes, with small to moderate effects, particularly in schizophrenia. This relationship was less evident in affective psychoses and was absent in those who had not received adequate antipsychotic treatment [61]. Similarly, longer DUI was linked to poorer global functioning outcomes in ARMS, although this was investigated only in one study [60].

Regarding psychosocial factors, childhood trauma was consistently linked to poorer functional outcomes, particularly when experienced before age 12 [55], with later research indicating that this effect is largely mediated by depressive and psychotic symptoms over time [56], or may operate indirectly through elevated negative symptoms rather than via a direct effect on functioning [73]. Some evidence also indicated gender-specific effects, with higher childhood trauma exposure predicting poorer functioning in males but not females [72]. Additionally, vocational engagement also emerged as a significant predictor, with small to large effects, in both FEP [61] and a transdiagnostic sample, where NEET status predicted a deteriorating functional course [66].

No demographic factor was consistently associated with functional outcomes across studies. A range of other psychosocial, clinical, and biological factors showed potential associations with functioning outcomes, but these were examined in single studies, limiting generalisability.

Taken together, while some predictors demonstrated consistent associations with functional outcomes, others showed mixed or context-dependent effects. These findings underscore the complexity of predicting functional outcomes in young people with mental illness and significant social impairment and highlight the need for further high-quality, longitudinal research to clarify the prognostic value of less consistently supported and researched factors.

4.2 Limitations of the Evidence Included in the Review

A number of key limitations were evident across the studies included in this review, many of which constrain the strength and generalisability of conclusions that could be drawn.

First, although this review applied stringent inclusion criteria to ensure consistent baseline definitions of functional impairment—restricting studies to those using observer-rated measures—functioning was nonetheless conceptualised and operationalised in diverse ways at follow-up.

Second, most included studies relied on observational methodologies and assessed outcomes at a single follow-up time point. Only three studies applied trajectory or growth mixture modelling to examine within-individual variation over time [64–66], limiting the capacity to capture nuanced functional change over time despite increasing evidence for the heterogeneous nature of functional outcomes. Additionally, attrition was a pervasive concern, with 11 studies reported dropout rates exceeding 20% [55,57–60,63,64,70,72,73,77] yet relatively few employed imputation methods or sensitivity analyses to address missing data

and potential for bias. Although several included studies limited analyses to participants with complete data, systematic differences between retained and lost participants remain plausible, potentially reducing generalisability and undermining the robustness of reported effects.

Third, although this review aimed to investigate predictors of functioning in youth with complex mental health needs and moderate to severe baseline impairment, the existing evidence base was heavily skewed towards individuals with FEP, drawing on both epidemiological and treatment-seeking cohorts. As a result, the findings are disproportionately informed by psychosis-focused cohorts and may have limited applicability to the wider population of help-seeking youth, particularly those presenting with attenuated symptoms or non-psychotic disorders.

Fourth, limited demographic reporting and sample diversity constrain the generalisability of findings. Only 7 of the 24 included studies reported participant ethnicity and most samples were drawn from high-income countries in Europe, Australia, or North America, with participant groups that were predominantly White. Additionally, few studies explicitly tested the representativeness of their samples or compared those included with participants excluded or lost to follow-up, undermining the external validity of their findings. Some studies also appeared to draw on the same clinical cohorts, raising questions about sample independence and the breadth of the evidence base.

Fifth, the handling of confounding variables was inconsistent, limiting the internal validity of findings. While several studies adjusted for key clinical and sociodemographic covariates such as baseline functioning and symptom severity, others did not report any statistical control for potential confounders. Although most studies were conducted within mental health services reflecting real-world clinical practice, the naturalistic nature of the designs introduces additional interpretive complexity. Participants typically received varied

combinations of pharmacological and psychosocial treatments, and only a minority of studies explicitly attempted to isolate the effects of specific exposures, such as by focusing on antipsychotic-naïve participants [61] or adjusting for pharmacological treatment [63,69]. Without consistent control for treatment heterogeneity or related clinical variables, it remains difficult to draw firm conclusions about the independent effects of predictors on functioning.

Finally, two additional limitations constrained the synthesis and interpretation of findings. Effect sizes were not consistently reported, limiting the ability to compare the strength of associations across studies or to synthesise findings quantitatively. Moreover, many predictors were examined in single studies only, precluding confident conclusions about their generalisability or clinical relevance. This highlights the need for replication and more standardised reporting in future research to strengthen the evidence base on this topic.

4.3 Strengths and Limitations of the Review

This review has several notable strengths. It is the first to date to systematically synthesise predictors of functional outcomes in youth with moderate to severe functional impairment at baseline, irrespective of diagnosis. This transdiagnostic focus reflects contemporary youth mental health frameworks that view functioning as a dynamic indicator of illness progression and prognosis, while acknowledging the diagnostic heterogeneity typical of early-stage presentations [28–31]. By moving beyond disorder-specific groupings, the review offers insights more reflective of real-world clinical complexity. A comprehensive search strategy was applied across multiple databases, with dual independent screening and quality appraisal. Importantly, full-text screening was undertaken even when functioning was not the primary outcome, enabling the inclusion of secondary analyses that addressed relevant predictors. The application of strict eligibility baseline functioning criteria to be able to assess moderate to severe impairment ensured consistency in defining baseline impairment and reliably identify individuals with significant functional difficulties. Finally, the use of a

structured quality appraisal tool facilitated systematic evaluation of methodological limitations across diverse study designs.

Nonetheless, several limitations should be acknowledged. The decision to include only studies using observer-rated functioning measures with clearly defined severity thresholds led to the exclusion of studies employing alternative tools, such as self-report measures or quality-of-life scales, that may have provided richer insight into subjective or domain-specific functioning. For instance, three studies using the Strauss - Carpenter Scale [78] or the Functioning Assessment Short Test [79] were excluded due to the absence of validated severity thresholds [80–82]. Similarly, one potentially relevant study was excluded because it reported only age of onset, not age at baseline [83]. Moreover, although global functioning measures promote consistency, they may lack sensitivity to detect domain-specific changes, especially when used in isolation, and may obscure within-sample heterogeneity when reporting only mean scores. For example, studies like Iorfino et al. [65,66] demonstrated that low-functioning subgroups can be masked within samples with overall modest impairment.

Furthermore, “baseline” functioning was typically assessed at the point of service entry, which may not reflect the chronicity or duration of impairment across individuals, potentially ranging from longstanding disability to more transient disruptions. Many included studies assessed functioning as a secondary rather than primary outcome, limiting the granularity of analysis. Finally, narrative synthesis, while necessary due to heterogeneity in design and outcomes, introduces interpretive subjectivity.

4.4 Clinical and Theoretical Implications

The findings of this review have direct clinical relevance for early identification and intervention efforts in youth mental health services. They align with contemporary youth

mental health frameworks that emphasise functional impairment as a core marker of clinical need [28,29,31]. Moderate-to-severe functional impairment at service entry may indicate heightened risk for persistent disability, even in the absence of a formal diagnosis. This underscores the value of embedding function-based risk formulations, such as those advocated in the clinical staging [28] and Clinical High At Risk Mental State (CHARMS) models [31], into routine care. The high prevalence of enduring social and occupational disability in transdiagnostic cohorts identified in this review highlights that enduring impairment is not exclusive to psychosis. For example, the 65% of participants in Iorfino et al. [66] who began with moderate/severe impairment, either remained impaired or deteriorated. This supports youth care models that conceptualise functional impairment as a distinct assessment and treatment target rather than simply a byproduct of symptoms [26]. In this direction, prognostic tools are being developed in youth mental health services [84] to enable early identification of functional risk, based on emerging evidence around key risk factors including NEET status, physical comorbidities, and subthreshold psychotic symptoms. Integrating such tools into routine assessment may facilitate stratified intervention and help prevent long-term disability.

Negative symptoms and cognitive impairment emerged as particularly robust predictors of long-term functional outcomes across both FEP and ARMS populations. The association between negative symptoms and persistent disability is well established in FEP [85–87] and ARMS [88,89] underscoring the need for systematic assessment from the outset of care. Their enduring impact may also be compounded by potential co-occurring cognitive impairments that limit recovery and adaptation [90], with cognitive impairment, including low premorbid IQ, consistently predicting poor outcomes in FEP [22,23].

Given the limited responsiveness of negative symptoms to existing treatments in both FEP and ARMS populations [91–93], they remain an urgent therapeutic target, highlighting

the need for large-scale trials specifically addressing this domain. Moreover, although cognitive difficulties are a key contributor to poor functional outcomes, a recent meta-analysis concluded that standalone cognitive remediation approaches do not significantly improve functioning in early psychosis [94], emphasising the need for integrated, multimodal strategies that embed cognitive support within broader recovery models.

Occupational disengagement, particularly NEET status at entry, also emerged as a potent and modifiable predictor of deteriorating functional outcomes in both psychosis-specific [61] and transdiagnostic samples [66]. Given the links between NEET status, clinical complexity, and long-term social exclusion [18,95], routine assessment of vocational engagement may assist in stratifying intervention needs and identifying those requiring more intensive vocational and psychosocial support. The association between NEET status youth and other functional risk factors such as longer DUP, poorer premorbid functioning, and more severe negative symptoms, suggest that NEET status may act as both a marker and mechanism of functional decline [95]. Early identification of NEET youth within clinical settings may therefore provide a critical window to reduce treatment delays, enhance engagement, and improve prognosis. There is growing support for targeted vocational interventions, such as Individual Placement and Support, which has shown promising outcomes for young people with severe mental illness [96]. Embedding IPS and similar approaches within youth services may improve long-term functional trajectories and aligns with calls to shift early intervention priorities toward employment, education, and training outcomes [97].

In addition to the factors mentioned above, childhood trauma may indirectly affect functioning by increasing vulnerability to depressive, positive psychotic [56] and negative symptoms [73], as found in this review, and it is also linked with prolonged the duration of untreated psychosis [98]. This supports the need to recognise the complex interplay between

developmental adversity and functional outcomes in youth and also provides support for an affective pathway to psychosis, in which trauma-related affective disturbances may drive later functional impairment [99–102]. Thus, clinically, incorporating trauma-informed assessments into early care models may enhance prediction of functional risk.

Overall, these findings support the case for early, function-focused formulation and intervention strategies, and align with broader service reform priorities, including stepped-care approaches and the expansion of early intervention services that address functional impairment as a central outcome. This may include systematically assessing and prioritising negative symptoms, cognitive deficits, vocational status at service entry, as well as offering tailored interventions to at-risk subgroups such as NEET youth and those with early life trauma histories. These approaches represent a significant evolution from symptom-focused care models toward recovery-oriented frameworks that emphasise functional outcomes as central to meaningful clinical improvement [26].

4.5 Research Implications and Future Directions

The findings and limitations of this review point to several important directions for future research. One key priority is the need for longitudinal studies that investigate functional trajectories in transdiagnostic youth populations with emerging or complex mental health difficulties. To date, most longitudinal work has focused on psychosis-specific cohorts, leaving a gap in understanding how functional outcomes unfold in broader clinical populations. Expanding recruitment beyond traditional mental health care to include community-based and youth support services may improve the detection of at-risk individuals who are not yet engaged in specialist services but already show significant social and occupational impairment.

Another critical consideration is the continued reliance on global functioning scales, which may fail to detect changes in specific domains such as social or vocational functioning [103]. Future studies would benefit from incorporating validated multi-domain instruments and applying standardised thresholds to enhance both comparability and sensitivity to change.

Furthermore, the use of mean functioning scores in many studies risks obscuring individual variability, particularly for those who remain chronically impaired. Longitudinal designs using advanced statistical approaches, such as growth mixture modelling or latent class analyses, could help to identify distinct functional trajectories and clarify the modifiable predictors that shape these different courses over time.

Lastly, incorporating the perspectives of young people themselves through qualitative methods could enrich our understanding of how clinical, cognitive, and social factors intersect to shape functional outcomes. These insights may improve the development of predictive models and enhance the design of interventions by grounding them more firmly in lived experience, ultimately supporting more tailored and developmentally informed approaches to care.

4.6 Conclusion

This review is the first to systematically synthesise evidence on predictors of long-term functional outcomes in young people aged 16–25 with moderate to severe functional impairment across mental health diagnoses. It responds to a key gap in the literature and aligns with contemporary models of youth mental health that emphasise functional impairment as a core clinical concern. Despite this, the current evidence base remains skewed toward FEP populations, with limited representation of other clinical presentations. The marked heterogeneity in functioning trajectories and persistence of poor functioning for some

in broader youth populations underscores the importance of expanding prognostic research beyond diagnostic boundaries.

Key predictors of poor functional outcomes included negative symptoms, cognitive impairment, and vocational disengagement, reinforcing the importance of early identification and intervention. However, methodological limitations, such as inconsistent outcome measures, short follow-up periods, limited reporting of effect sizes and limited replication of findings, constrain the strength of current conclusions.

Moving forward, the integration of multidimensional functional assessments, youth-informed qualitative data, and longitudinal modelling tools may offer a path toward more personalised care capable of improving long-term outcomes for young people with complex mental health needs. Addressing these gaps in future research and clinical practice could enhance our ability to identify high-risk individuals of persistent functional impairment and support the development of tailored interventions aimed to improve long-term outcomes in youth mental health care.

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6. Supporting Information

Appendix B. PRISMA checklist

Appendix C. Search Strategies for each database

Appendix D. Additional Characteristics of Included Studies

Appendix E. MMAT Ratings

Appendix F. Detailed quality assessment of included studies based on MMAT

Chapter Three: Bridging Chapter

Understanding the long-term functional outcomes of young people with emerging severe mental illness is crucial for informing early intervention and improving recovery pathways. The preceding systematic review aimed to address this need by synthesising evidence on predictors of long-term functional outcomes in young people aged 16-25, across diagnostic categories. The review highlighted consistent associations between certain clinical factors—particularly negative symptoms—and poorer functional trajectories, especially within first-episode psychosis (FEP) and At-Risk Mental State (ARMS) for psychosis populations. However, it also underscored notable gaps in the literature, particularly regarding transdiagnostic samples and youth experiencing persistent social disability outside of psychosis-specific contexts.

A key limitation across the reviewed studies was the underrepresentation of young people with complex mental health needs outside of psychosis. Most included samples were drawn from FEP or ARMS cohorts, limiting generalisability to broader clinical populations. Only two studies investigated transdiagnostic samples (Iorfino et al., 2018, 2022), and even these focused on heterogeneity in mental health presentations rather than explicitly examining individuals with significant pre-existing social functioning impairment at service entry. This leaves a critical gap in our understanding of how functional recovery unfolds in young people who begin with established social disability, regardless of diagnostic classification.

To address this gap, the empirical paper presented in the next chapter uses data from the PRODIGY trial (Berry et al., 2022), a multi-centre, single-blind, parallel-group, superiority randomised controlled trial investigating the effectiveness of Social Recovery Therapy (SRT) combined with Enhanced Standard Care (ESC), compared to ESC alone, in young people with emerging severe mental illness and social disability. The trial recruited

individuals aged 16–25 from both NHS mental health services and community-based youth-facing services, including employment, education, and voluntary sector organisations. All participants met criteria for persistent social disability, defined by engagement in fewer than 30 hours of structured activity per week over at least six months. Importantly, the trial’s inclusion criteria allowed for a range of severe mental health presentations, including but not limited to individuals meeting criteria for an At-Risk Mental State (ARMS). Participants with active or past psychotic disorders were excluded, offering a unique opportunity to study functional recovery in a non-psychosis population. The trial protocol and findings can be found elsewhere (Berry et al., 2022; Fowler et al., 2017).

The primary trial hypothesis proposed that SRT plus ESC would be superior to ESC alone in improving social recovery, measured by hours in structured activity on an adapted version of the Office for National Statistics Time Use Survey (TUS; Short, 2006, adapted by Hodgekins, French, et al., 2015), over a 15-month follow-up period. However, the published results of the trial found no statistically significant differences in functional outcomes between intervention and control groups at follow-up (Berry et al., 2022). Considering these null findings, the empirical study in this thesis (Chapter 4) conducted a secondary analysis that pooled participants from both the SRT and ESC arms to examine broader patterns of functioning over time, rather than treatment effects.

This secondary analysis used data from four time points, baseline, nine months (post-treatment), 15 months, and 24 months post-entry. Specifically, it explored social functioning trajectories over 24 months and examined baseline predictors of trajectory group membership. This analysis extends prior research by focusing on a transdiagnostic cohort of young people with severe and persistent social impairment, an underrepresented group in the literature, as identified by the systematic review. The use of structured behavioural data and standardised assessments collected as part of a randomised controlled trial adds

methodological rigour, while the focus on functioning trajectories allows for a more nuanced, person-centred understanding of change over time.

Chapter Four: Empirical Paper

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Exploring social recovery for young people with emerging severe mental illness
and social disability: A secondary data analysis of the PRODIGY trial data

Short title: Social recovery in youth with emerging severe mental illness

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Abstract

Objective: This study aimed to identify distinct trajectories of social functioning in a sample of young people with persistent social disability and emerging severe mental illness, and to examine baseline demographic and clinical predictors of trajectory membership.

Methods: Secondary data analysis was conducted using the ‘Prevention of long-term social disability among young people with emerging psychological difficulties’ (PRODIGY) trial dataset, including 270 individuals aged 16–25 years with social disability and emerging severe mental illness. Latent Class Growth Analysis modelled structured activity across four time points (baseline, 9, 15, and 24 months). Multinomial logistic regression was used to examine baseline predictors of trajectory membership.

Results: Three distinct trajectories of social functioning were identified: Stable Low (64.8%, $n = 175$), Moderate Improvement (29.3%, $n = 79$), and Increasing Overactive (5.9%, $n = 16$). Not in Education, Employment, or Training (NEET) status and avolition-apathy severity significantly predicted class membership. Individuals in the Moderate Improvement group were more likely to be non-NEET than those in the Stable Low group (OR = 2.34, 95%CI [1.21, 4.54], $p = .012$). Higher avolition-apathy severity predicted lower odds of being in the Moderate Improvement (OR = 0.47, 95%CI [0.35, 0.64], $p < .001$) or Increasing Overactive group (OR = 0.50, 95%CI [0.30, 0.85], $p = .011$) compared to Stable Low.

Conclusions: Findings highlight the impact of motivational deficits and NEET status on persistent impairment, suggesting current interventions may be insufficient and that early, targeted approaches addressing avolition, vocational exclusion, and social participation are needed to improve long-term outcomes.

1. Introduction

Adolescence and early adulthood represent a critical developmental window marked by increased vulnerability to mental health difficulties [1]. Around 50% of mental disorders emerge by age 14, and 75% by age 25 [2]. Mental health difficulties during this period can have significant social and functional consequences, including disengagement from education, employment, and social activities [3] with many young people with emerging severe mental illness experiencing persistent severe social functioning impairment [4]. Research has also linked Not being in Education, Employment, or Training (NEET) as almost twice as common in youth seeking mental health care (19%) compared to the general population (11%) [5]. A recent meta-analysis has provided further evidence on the link between being NEET and mental illness in youth, showing that mental health problems predicted later onset of being NEET, while the evidence of the inverse relationship was sparse [6]. Additionally, social functioning difficulties might be observable before the onset of mental health problems [7], and when persistent, can lead to long-term problems of diagnostic severity [3,8] and further social impairment [9]. Social withdrawal and disengagement may contribute to worsening symptoms by reinforcing avoidance patterns, reducing social support, while exacerbating low self-efficacy and hopelessness [10].

Severe social functioning impairment is recognised as a transdiagnostic issue affecting young people across various mental health conditions [11], including those at risk of developing psychosis [12,13], with nearly half of ultra-high-risk individuals meeting criteria for social disability [4] as well as a substantial proportion of young people with emerging mental health disorders, regardless of diagnosis [14].

Despite engagement with mental health services, functional recovery remains elusive for many young people, with up to 82% continuing to experience significant global functioning impairment at discharge [15]. Observational studies from general mental health

services have also suggested that for a substantial subgroup of young people, social disability persists over the course of treatment, even among those with subthreshold symptoms of severe mental illness [9,14]. This highlights the urgent need to examine why some individuals fail to improve, particularly those with severe and enduring social disability [16].

Research using longitudinal modelling that could help examine social functioning trajectories in young people with mental health difficulties is limited. However, a few key studies provide insight into the patterns of functional recovery and predictors of persistent social disability. First-episode psychosis research in youth has identified that, within the first year from service entry, the largest group of patients are located in a persistently poor functioning trajectory (66% in [17]; 48.1% in [18]). Regarding young people at-risk for psychosis, the only study to date using trajectory modelling [19] identified two groups of young people with distinct functioning trajectories, both with potential improvement over two years, despite having different starting points in terms of their functioning levels. Nevertheless, individuals in the largest group (56%) started with lower functioning and despite some improvement, did not reach the threshold for non-clinical social functioning. Furthermore, two naturalistic studies have described the longitudinal course of social functioning of young people with emerging complex mental problems using data from mental health clinics that are not diagnosis-specific and attract young people with a broad range of emerging anxiety, depressive, mania-like, psychosis-like, and comorbid syndromes. Iorfino et al. [14] indicated that during the five years of early intervention care from youth mental health clinics, 40% of the sample had serious functional impairment at entry, with 29% remaining persistently impaired over time, 7% deteriorating further and 4% demonstrating improvement to non-clinical levels. In a larger naturalistic study using data from the same clinics, Iorfino et al. [20] found further evidence for the existence of a large group of young people who deteriorated (49%) or reported persistent impairment (16%) over two years of

early intervention care. These findings show that social functioning, especially for those who enter services with severe impairment, can fail to significantly improve, highlighting a need for targeted intervention.

Predictors of persistent social functioning impairment or deterioration over time vary across studies. In first episode psychosis (FEP) studies, persistent poor social functioning has been associated with multiple clinical and demographic factors. Ethnic minority status, younger age at onset of psychosis, increased negative symptoms, poor premorbid adjustment [17], lower educational attainment, a diagnosis of schizophrenia-spectrum disorder, inpatient treatment at initial presentation [18] and male gender [17,18] have been linked to persistent functional impairment. In the study of young people at risk for psychosis by Hartmann et al. (2020), no significant predictors of functioning trajectories were identified, highlighting the need for further investigation of this population.

In contrast, transdiagnostic studies have identified a range of factors associated with persistent functional impairment and deterioration over time. Comparing trajectories of functioning between those who present to services with moderate to severe impairment, older age at service entry has been found to increase the likelihood of belonging to a stable low trajectory rather than an improving trajectory [14], whereas a follow-up study did not find an improving trajectory [20]. They only indicated that compared to those who remained persistently impaired, membership in deteriorating and volatile trajectory was significantly predicted by physical illness, NEET status, bipolar disorder, and psychosis-like experiences, indicating that these factors may contribute to an increased risk of worsening functional outcomes despite engagement with early intervention services.

Given the limited longitudinal research in transdiagnostic youth populations, the present study aimed to explore social functioning trajectories in youth with severe and complex mental health problems and investigate predictors of different trajectories. Unlike

previous naturalistic studies [14,20], which examined mixed-functioning clinical populations engaged in youth mental health services, the present study focuses on a transdiagnostic sample of young people with persistent social disability at baseline, recruited from both mental health services and wider youth-facing community settings. It also uses structured behavioural outcome measures collected as part of a clinical trial, allowing for a more standardised and focused examination of functional outcomes. Identifying those at greatest risk of long-term social disability despite receiving support can inform early intervention efforts to mitigate maladaptive functional trajectories [21,22] and improve mental health service provision for this population.

This study is a secondary analysis of the PRODIGY trial dataset [23], a randomised controlled trial for the prevention and treatment of long-term social disability among young people with emerging severe mental illness. Specifically, this study aimed to:

1. Explore the social functioning trajectories over a 24-month period in help-seeking young people with severe and complex mental health problems who presented with poor baseline social functioning.
2. Investigate the demographic and clinical characteristics that predict membership in different social recovery trajectories.

2. Method

2.1 Design

This study conducted a secondary analysis of data originally collected as part of the PRODIGY trial, a multi-centre, single-blind, parallel-group, superiority randomised controlled trial. The trial investigated the effectiveness of Social Recovery Therapy (SRT) combined with Enhanced Standard Care (ESC), compared to ESC alone, in young people with emerging severe mental illness and social disability. Assessments were conducted at four time points: baseline, nine months (post-treatment), 15 months, and 24 months post-entry.

The trial protocol and findings have been previously published [23,24]. The present analysis involved two stages: i) the use of Latent Class Growth Analysis (LCGA) to identify social functioning trajectories in this sample; and then ii) the use of multinomial logistic regression to explore predictors of trajectory membership.

2.2 Participants

Participants were recruited from NHS mental health services as well as third-sector youth, employment, and education organisations and met the following inclusion criteria: aged 16 to 25, experiencing severe and complex mental health problems, and exhibiting persistent social disability. Persistent social impairment was defined as engaging in fewer than 30 hours of structured activity per week, as measured by the Time Use Survey (TUS; [25]), with social functioning difficulties persisting for at least six months. Severe and complex mental health problems were operationalised as attenuated psychotic symptoms meeting criteria for an At-Risk Mental State for psychosis (ARMS) and/or a Global Assessment of Functioning (GAF; [26]) score of 50 or below, with at least moderate symptoms persisting for over six months.

Exclusion criteria included the presence of active positive psychotic symptoms or a history of psychosis, severe learning disability, non-English speaking status, or physical health conditions that could limit participation.

The final sample comprised 270 young people, with a mean age of 19.50 years ($SD = 2.6$). Of these, 133 met criteria for ARMS but had no history of psychosis, while the remaining 137 did not meet ARMS criteria but had a GAF score of 50 or lower, indicating the presence of at least two of the following conditions: depression, anxiety, substance misuse, or behavioural/thinking difficulties.

2.3 Power Considerations

Determining the appropriate sample size for LGCA is subject to ongoing debate [27]. Adequate sample size depends on both the number of indicators and the degree of class separation [28,29] as insufficient power may reduce the ability to detect distinct trajectories [30]. While some suggest 300 or more participants is ideal, smaller samples may be sufficient when models are simpler (fewer indicators and classes) and classes are well separated [31]. The present sample ($N = 270$) was considered adequate for conducting LCGA in this context.

To assess power for multinomial logistic regression, a post-hoc power analysis was conducted using the *pwr* package in R [32], assuming a dependent variable with three categories (Iorfino et al., 2018) and 16 predictor variables. At $\alpha = .05$, the sample had sufficient power to detect medium ($f^2 = .15$) and large ($f^2 = .35$) effects, but limited power for small effects ($f^2 = .02$) [33] (see Appendix G). To improve model parsimony, only predictors showing significant trajectory group differences at baseline were included in the final model.

2.4 Ethical Considerations

Participants provided informed consent for their anonymised data to be used in secondary analyses. The PRODIGY dataset was fully anonymised, and this secondary analysis aligned with the trial's original aims of identifying social recovery patterns and associated factors to inform support for young people with mental health difficulties. The participant information sheet and consent form used in the PRODIGY trial can be found in Appendices H and I.

The PRODIGY trial obtained ethics approvals from the Norfolk Research Ethics Committee, 07/09/2012, ref: 12/EE/0311 for the internal pilot phase and the Preston Research Ethics Committee North West, 24/07/2015, ref: 15/NW/0590, for its extended phase. This study was approved by the Faculty of Medicine and Health at the University of East Anglia (ETH2324-0183; Appendix J).

2.5 Measures

A comprehensive list of all measures administered in the PRODIGY trial, including time points for data collection, are provided in Appendix K. The outcome measure and key potential predictor variables selected for the secondary analysis are listed below. Potential predictor variables were chosen from the wider group of study measures based on previous literature. Psychometric properties and rationale for inclusion are available in the Additional Methods chapter. Copies of non-copyrighted measures used in the analysis are available in Appendices L to S.

2.5.1 Outcome measures

Social functioning. Social functioning was assessed using an adapted version of the Office for National Statistics Time Use Survey (TUS; [25], adapted by [4]), a semi-structured interview that captures weekly hours spent in structured activities that captures the total hours per week spent in structured activities, including employment, education, voluntary work, household chores, childcare, and structured leisure activities. This measure was selected as a proxy for behavioural aspects of functional recovery.

2.5.2 Predictor variables

Demographics. Participants completed a self-report questionnaire covering age, gender, ethnicity, and NEET status

Psychopathology. The Comprehensive Assessment of At-Risk Mental States for psychosis (CAARMS; [34]), a semi-structured interview, was used to assess levels of attenuated psychotic symptoms, ARMS (At-Risk Mental State) status and associated psychopathology. In addition to total psychotic symptom severity, the suicidality subscale was included as a separate variable. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; [35]) was used to assess baseline comorbidity. Participants were categorised into low (0–3 diagnoses) and high comorbidity (3–6 diagnoses) groups based on

the median number of diagnoses in the sample. Social anxiety was measured using the 20-item self-report Social Interaction Anxiety Scale (SIAS; [36]), and depressive symptoms were assessed using the 21-item self-report Beck Depression Inventory–II (BDI-II; [37]). Negative symptoms were evaluated using the Scale for the Assessment of Negative Symptoms (SANS; [38]), capturing affective flattening, alogia, avolition, anhedonia, and attentional impairment, symptoms commonly observed in psychosis.

Substance use. Alcohol and drug use were measured using the self-report Alcohol Use Disorders Identification Test (AUDIT; [39]) and Drug Use Disorders Identification Test (DUDIT; [40]), respectively.

Neurocognition. Neurocognitive functioning was assessed using two standardised tasks: the Logical Memory I (LM-I) subtest from the Wechsler Memory Scale [41], specifically immediate recall scaled scores, and the Controlled Oral Word Association Test (COWAT; [42]) to evaluate verbal fluency.

2.6 Data Analysis

All analyses adhered to the Guidelines for Reporting on Latent Trajectory Studies (GRoLTS checklist; [27]) (Appendix T). Prior to modelling, data were screened for outliers, normality, and missingness. A missing value analysis compared completers and non-completers on key demographic and clinical variables. No significant differences were found after Bonferroni correction ($\alpha = .007$), and pairwise deletion was applied in subsequent analyses.

To identify distinct social functioning trajectories (Aim 1), Latent Class Growth Analysis (LCGA; [43]) was conducted in Mplus version 8 [44], using structured activity hours from the TUS at baseline, 9, 15, and 24 months. LCGA, a constrained variant of Growth Mixture Modelling, was selected due to its emphasis on identifying homogeneous trajectory groups with minimal within-class variance [45].

Model fit was evaluated using the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), sample-size adjusted BIC (aBIC), entropy values, and likelihood ratio tests (Lo-Mendell-Rubin, Vuong-Lo-Mendell-Rubin, and bootstrap). Solutions were compared incrementally from one to several classes. Linear, quadratic, and cubic models were explored. Selection was guided by model fit indices, classification accuracy (entropy > .80), and theoretical interpretability [45]. If fit indices were comparable across models, average posterior probabilities (> .70) were used to determine class reliability [46]. Final syntax is available in Appendix U.

Sensitivity analyses were conducted on the top three solutions, repeating analyses with and without extreme values ($z > 3.29$) for 9-, 15-, and 24-month TUS data and within each trial arm to examine model robustness.

Once the best-fitting solution was identified, trajectory class membership was saved and merged with the main dataset. To examine group differences at baseline, chi-square tests and one-way ANOVAs were conducted across demographic and clinical variables. Holm-Bonferroni correction was applied to adjust for multiple comparisons (adjusted for 20 comparisons). Post-hoc pairwise comparisons with Bonferroni correction were used to interpret significant effects.

To examine predictors of social functioning trajectories (aim 2), multinomial logistic regression was performed, with trajectory membership as the outcome variable. Predictor variables included key demographic variables (age, gender, ethnicity), trial arm allocation, and any baseline variables that significantly differed between trajectory groups in the initial comparisons ($p < .05$). Multicollinearity was assessed using variance inflation factors (VIF), with all values < 5 indicating acceptable levels [47]. Analyses were conducted in IBM SPSS Statistics (Version 28).

Further details of LCGA and initial analysis procedures are provided an Additional Methods chapter (Chapter Five).

3. Results

3.1 Missing Data

Missing data for TUS Structured Activity were 10.7% at 9 months ($N = 29$), 13.0% at 15 months ($N = 35$), and 24.1% at 24 months post-randomisation ($N = 65$). A missing value analysis indicated that data were Missing Completely At Random (MCAR), Little's MCAR test, $\chi^2(310) = 340.24, p = .114$ (see Appendix V for further details).

LCGA in Mplus 8 handled missing data using Full Information Maximum Likelihood (FIML) estimation with the robust maximum likelihood estimator (MLR). This was deemed appropriate [49] as it allows all available data to contribute to the estimation of model parameters, yielding unbiased estimates under the Missing at Random (MAR) assumption [50]. Given that data were most likely MCAR, a more restrictive condition than MAR, FIML remained suitable.

3.2 Latent Class Growth Analysis

Visual and statistical inspection of the TUS data distribution at all time points showed significant positive skewness and kurtosis ($z > 3.29$), indicating non-normality. Seven cases exhibited extreme values ($z > 3.29$) at follow-up time points, though none were present at baseline. As these cases may represent meaningful clinical differences, they were retained in the analysis rather than being removed as statistical outliers. Sensitivity analyses examined the impact of extreme cases on model solutions by running LCGA with and without these cases. Model stability was also assessed within each trial arm, comparing for the top three best-fitting class solutions found for the overall sample as well as $k-1$ class solutions to ensure model convergence and interpretability. See Appendices W and Y for further details.

All models successfully converged using FIML estimation with MLR, which accounts for missing data and non-normality. Descriptive analyses showed that 72.95% ($N = 197$) of participants had complete TUS data across all time points, while FIML effectively incorporated available data for the remaining participants.

3.3 Model Selection & Retained Class Solution

The best three-class solutions from linear, quadratic, and cubic models were evaluated based on model fit indices and interpretability (see Appendix Z, Table Z1). Table 4 presents the top three solutions based on these criteria. The quadratic three-class model was retained, as it provided the best balance of model fit (AIC, BIC, aBIC), classification accuracy (entropy), and theoretical interpretability. The average posterior probabilities for each class were .89 (Class 1), .94 (Class 2), and .93 (Class 3), indicating good classification certainty.

Table 4. Goodness-of-fit statistics of LCGA models for the three top best-fitting class solutions of functional trajectories.

Type of method	Classes	AIC	BIC	aBIC	Entropy	VLMR	BLRT	Class sizes (N s)	Min-Max average posterior probabilities
Quadratic	3	7719.448	7773.425	7725.864	.832	-3893.290 *	-3893.290 ***	175, 79, 16	.888 - .943
Quadratic	4	7690.265	7758.635	7698.392	.875	-3844.724 *	-3844.724 ***	173, 80, 10, 7	.890 - .986
Cubic	4	7640.573	7723.336	7650.411	.882	-3832.929	-3832.929 ***	171, 79, 17, 3	.893 - 1.000

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; aBIC = Sample-Size Adjusted Bayesian Information Criterion; VLMR = Vuong-Lo-Mendell-Rubin Likelihood Ratio Test; BLRT = Bootstrap Likelihood Ratio Test. The AIC, BIC, and aBIC are fit indices used to compare model performance, with lower values indicating a better model fit. Entropy represents classification certainty, where values closer to 1 indicate greater accuracy in class assignment. VLMR and BLRT compare a model with k classes to a $k-1$ class model. A significant p -value ($p < .05$) indicates that the k -class model provides a better fit. Classes refers to the number of latent classes requested in each model. Average posterior probabilities indicate the probability of correct class membership assignment, with values closer to 1 reflecting better classification accuracy. Solution in bold indicates the best-fitting model.

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

3.4 Trajectory Classes

The final class solution identified three distinct trajectory groups. Table 5 presents the descriptive statistics for TUS structured activity for the whole sample and within each trajectory class.

Class 1, the Moderate Improvement group ($n = 79$, 29.3%), exhibited a gradual and meaningful increase in structured activity over time. Although participants in this group did not quite reach the clinical threshold of 45 hours per week, their improvement was substantial, with average activity levels almost doubling between baseline and follow-up. Class 2, the Stable Low group ($n = 175$, 64.8%), was the largest group and demonstrated consistently low levels of structured activity across all time points, with minimal improvement. This suggests that participants in this group maintained a persistently low level of engagement in structured activities over the 24-month period. Class 3, the Increasing Overactive group ($n = 16$, 5.9%), showed a substantial and continuous increase in structured activity over time. By the 15-month follow-up, participants in this class had already surpassed the 45-hour clinical threshold, and their activity levels continued to rise at the 24-month mark, indicating sustained increases, with some exceeding typical activity levels, potentially raising concerns about over-engagement or imbalance in daily functioning.

As shown in Figure 2, the quadratic nature of these trajectories suggests non-linear patterns of change, where rates of improvement varied over time. Figure 2 presents the group-level quadratic trajectories, with line thickness indicating relative class size.

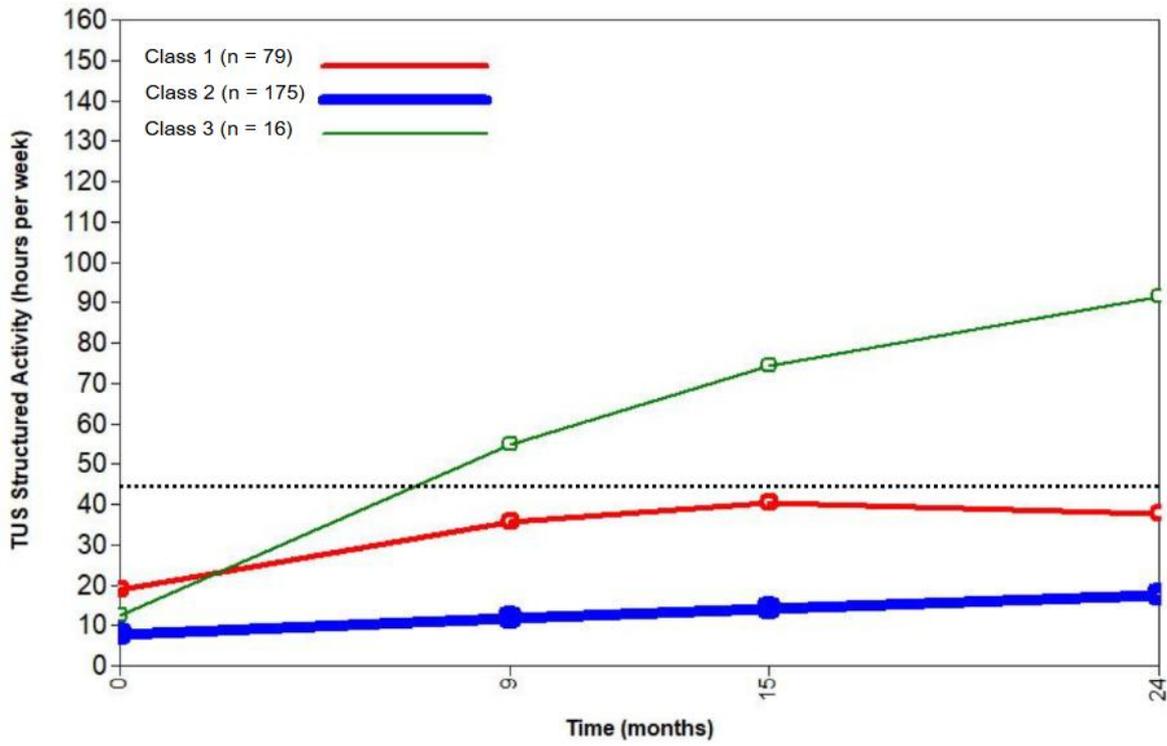
Table 5. Descriptive and distribution statistics of the observed Time Use Structured

Activity at each time point for the whole sample and within each class.

Time point	Sample	<i>N</i>	<i>M</i>	<i>SD</i>	Median	Skewness (<i>SD</i>)	Kurtosis (<i>SD</i>)	Min-Max
Baseline								
	Total	270	11.29	8.29	9.39	.65 (.15)	-.66 (.30)	.05 - 31.38
	Class 1	79	19.24	7.73	19.82	-.47 (.27)	-.87 (.54)	1.85 - 31.38
	Class 2	175	7.61	5.77	6.71	.90 (.18)	.26 (.37)	.05 - 26.20
	Class 3	16	12.25	6.55	11.54	1.29 (.56)	1.92 (1.09)	3.50 - 29.04
9 months								
	Total	241	21.83	17.89	16.67	1.17 (.16)	1.04 (.31)	.00 - 86.02
	Class 1	68	37.76	13.51	36.12	.95 (.29)	1.45 (.57)	13.55 - 85.77
	Class 2	157	11.95	8.31	11.59	.86 (.19)	.67 (.39)	.00 - 41.35
	Class 3	16	51.18	22.33	60.00	-.59 (.56)	-.59 (1.09)	11.15 - 86.02
15 months								
	Total	235	24.83	23.97	17.62	2.22 (.16)	7.17 (.32)	.00 - 153.91
	Class 1	68	38.72	16.43	37.87	.51 (.29)	-.44 (.57)	11.54 - 81.44
	Class 2	153	13.45	9.58	11.52	.86 (.20)	.45 (.39)	.00 - 47.93
	Class 3	14	81.65	38.88	72.63	.67 (.60)	-.10 (1.15)	18.25 - 153.91
24 months								
	Total	205	27.94	24.07	21.13	1.62 (.17)	3.83 (.34)	.04 - 147.35
	Class 1	59	38.39	16.43	37.87	.13 (.31)	-.97 (.61)	9.62 - 72.21
	Class 2	134	17.79	11.67	13.82	1.28 (.21)	1.82 (.42)	.04 - 79.54
	Class 3	12	89.91	26.28	78.45	1.09 (.64)	.40 (1.23)	63.82 - 147.35

Note. *N* = Sample size; *M* = Mean; *SD* = Standard deviation; Min-Max = Minimum and Maximum values. Skewness and kurtosis are presented with their respective standard errors in parentheses. Class 1 = Moderate Improvement; Class 2 = Stable Low; Class 3 = Increasing Overactive.

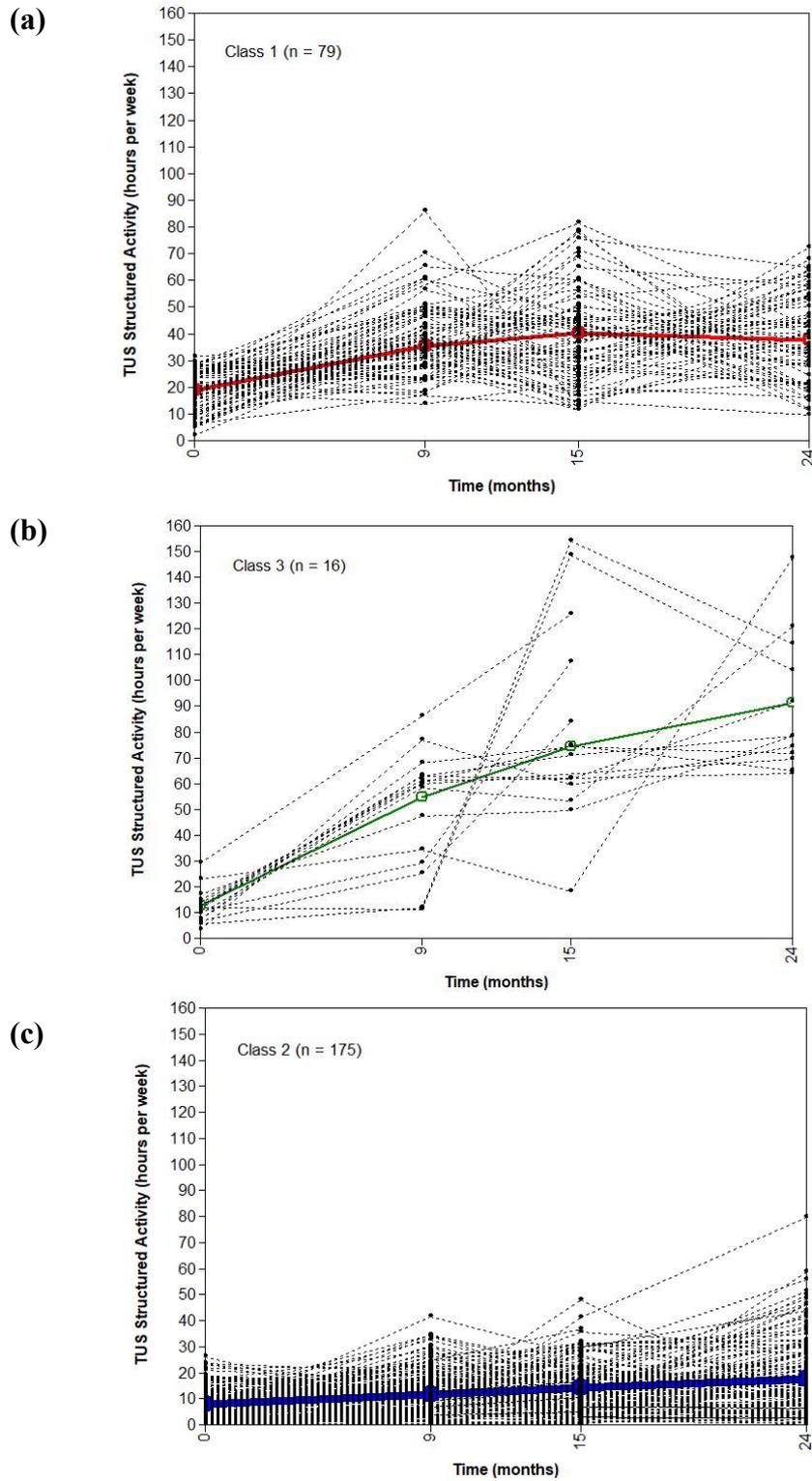
Figure 2. The three distinct quadratic trajectories identified for Time Use Survey Structured Activity score over a 24-month period.



Note. The thickness of each line represents the sample size of that particular trajectory, relative to all others. The dotted line represents the TUS structured activity score of 45 hours per week that differentiates clinical from non-clinical populations [4].

Figure 3 provides individual-level observed trajectories within each of the three quadratic trajectory classes. Panel (a) shows that most participants in Class 1 (Moderate Improvement) exhibited substantial increases in structured activity, though individual variability was apparent. While some individuals showed slight improvements, others maintained relatively stable levels, highlighting individual variability within this group. Panel (b) illustrates that in Class 2 (Stable Low), a large proportion of participants remained stable at low activity levels, with minimal fluctuation. Finally, in Panel (c) (Class 3 – Increasing Overactive), individual trajectories show rapid and substantial increases in structured activity, though some participants experienced fluctuations before stabilising at higher levels.

Figure 3. Panels (a) (b) (c) show the observed individual trajectories of Time Use Survey Structured Activity for each quadratic class over a 24-month period.



Note. The solid lines represent the estimated means for each trajectory group, providing an aggregate view of overall patterns.

3.5 Baseline Characteristics and Differences Between Trajectory Groups

Baseline demographic and clinical characteristics were examined across the three trajectory groups as shown in Table 6.

The distribution of SCID diagnoses varied somewhat across trajectory groups. In Class 1 (Moderate Improvement), the most common diagnoses were Major Depressive Disorder (76.0%) and Major Depressive Episode (51.9%). Anxiety-related conditions were also prevalent, including Social Phobia (40.5%) and Generalised Anxiety Disorder (27.9%). In Class 2 (Stable Low), MDD (66.3%) and MDE (47.4%) were again the most frequent diagnoses, with Social Phobia (44.0%) and Generalised Anxiety Disorder (31.4%) also common. In Class 3 (Increasing Overactive), MDE (81.3%) and MDD (75.0%) were the most prevalent, alongside Social Phobia (43.8%) and Panic Disorder with Agoraphobia (31.3%). Additional baseline characteristics are available in Appendix AA, Table AA1.

Normality testing and visual inspection of the data indicated that all variables, except for LM-I Scaled Total and BDI-II, significantly deviated from normality, as evidenced by z-scored skewness or kurtosis values exceeding ± 1.96 in at least one trajectory group. Consequently, analyses with these variables were conducted using the non-parametric equivalent of a one-way ANOVA, the Kruskal-Wallis one-way ANOVA.

After applying Holm-Bonferroni correction for multiple comparisons, only employment status and avolition/apathy remained statistically significant. A significant association was found between trajectory group and employment status (NEET vs. non-NEET), $\chi^2(2, N = 269) = 17.16, p < .001, V = .25$, indicating a moderate effect size. Similarly, a significant group difference emerged for avolition-apathy, $H(2) = 36.26, p < .001, \eta^2 = .13$.

Post hoc comparisons for both variables are summarised in Table 6 using superscript Greek letters.

Table 6. Baseline Demographic and Clinical Characteristics for the Three Trajectory Groups.

Sample Characteristic	Class 1 Moderate Improvement (<i>N</i> = 79)	Class 2 Stable Low (<i>N</i> = 175)	Class 3 Increasing Overactive (<i>N</i> = 16)	Test statistic	<i>p</i> - value	Effect size
<i>M</i> (Min-Max; <i>SD</i>) / <i>N</i> (Valid %)						
Age	19.32 (16-25; 2.46)	19.55 (16-25; 2.67)	20.13 (16- 25; 2.60)	H(2) = 1.25	.535	$\eta^2 = .00$
Trial arm				$\chi^2(2, 270) = 3.10$.208	<i>V</i> = .11
ESC	40 (50.6)	81 (46.3)	11(68.8)			
SRT	39 (49.4)	94 (53.1)	5 (31.3)			
Gender				$\chi^2(2, 270) = 1.11$.615	<i>V</i> = .06
Male	40 (50.6)	101 (57.7)	9 (56.3)			
Female	39 (49.4)	74 (42.3)	7 (43.8)			
Ethnicity				$\chi^2(2, 270) = 5.08$.079	<i>V</i> = .14
White British	66 (83.5)	159 (90.9)	16 (100)			
Black and minority ethnic	12 (16.5)	16 (9.1)	0			
Employment status ^a				$\chi^2(2, 269) = 17.16$	<.001	<i>V</i> = .25
Non-NEET	38 (48.1) ^α	39 (22.4) ^β	6 (37.5) ^{α,β}			
NEET	41 (51.9)	135 (77.6)	10 (62.5)			
ARMS status				$\chi^2(2, 270) = 3.17$.213	<i>V</i> = .11
No	34 (43.0)	93 (53.1)	10 (62.5)			
Yes	45 (57.0)	82 (46.9)	6 (37.5)			
CAARMS overall symptom severity ^b	24.62 (0-64; 14.03)	26.36 (0-72; 16.85)	31.67 (0-67; 18.18)	H(2) = 1.72	.424	$\eta^2 = .00$
CAARMS suicidality subscale severity ^c	6.19 (0-24; 5.47)	6.35 (0-36; 6.93)	6.87 (0-15; 5.79)	H(2) = .73	.695	$\eta^2 = .00$
Comorbidity severity ^d				$\chi^2(2, 269) = 5.97$.050	<i>V</i> = .15
Low comorbidity (0-3)	48 (61.5)	118 (67.43)	6 (37.5)			
High Comorbidity (4-6)	30 (38.5)	57 (32.6)	10 (62.5)			
SIAS Total ^e	49.48 (14-78; 15.38)	50.90 (8-80; 14.59)	45.64 (10- 74; 20.59)	H(2) = .79	.675	$\eta^2 = .00$
BDI-II Total ^f	32.72 (5-57; 11.28)	28.68 (0-62; 12.88)	36.50 (13- 54; 11.98)	F(2, 258) = 4.920	.008	<i>Partial</i> $\eta^2 = .037$
SANS Total ^g	22.77 (4-76; 12.26)	28.49 (10-73; 12.54)	28.63 (5- 48; 13.37)	H(2) = 11.72	.003	$\eta^2 = .04$

Sample Characteristic	Class 1 Moderate Improvement (N = 79)	Class 2 Stable Low (N = 175)	Class 3 Increasing Overactive (N = 16)	Test statistic	p- value	Effect size
SANS Affective Flattening	0.82 (0-5; 1.09)	1.11 (0-5; 1.29)	1 (0-3; 1.03)	H(2) = 2.51	.285	$\eta^2 = .01$
SANS Alogia	0.65 (0-3; 0.85)	0.79 (0-5; 1.04)	0.50 (0-2; 0.63)	H(2) = 0.91	.635	$\eta^2 = .00$
SANS Avolition/Apathy	2.72 (0-5; 1.10) ^α	3.58 (1-5; 0.92) ^β	2.94 (1-4; 1.12) ^{α, β}	H(2) = 36.26	<.001	$\eta^2 = .14$
SANS Anhedonia/Asociality ^a	2.63 (0-4; 1.21)	2.95 (0-5; 1.11)	2.88 (0-5; 1.31)	H(2) = 3.01	.212	$\eta^2 = .01$
SANS Attention ^h	0.72 (0-3; 0.85)	0.89 (0-5; 1.03)	1 (0-4; 1.32)	H(2) = 1.01	.603	$\eta^2 = .01$
AUDIT Total	6.71 (0-34; 7.96)	4.10 (0-31; 5.37)	5.38 (0-14; 4.00)	H(2) = 7.75	.021	$\eta^2 = .02$
DUDIT Total	4.63 (0-31; 8.36)	2.91 (0-36; 6.29)	7.88 (0-41; 12.37)	H(2) = 7.24	.027	$\eta^2 = .02$
COWAT Total ^a	30.48 (5-63; 12.25)	29.32 (7-58; 10.55)	32.88 (25- 56; 7.69)	H(2) = 2.67	.263	$\eta^2 = .00$
LM-I Scaled Total ^a	8.41 (2-17; 3.27)	8.66 (1-17; 3.28)	9.25 (3-15; 3.77)	F(2, 266) = .467	.627	Partial η^2 = .003

Note. M = Mean; SD = Standard Deviation; Valid % represents the percentage of participants with available data; SRT = Social Recovery Therapy; ESC = Enhanced Standard Care; ARMS = At-Risk Mental State for Psychosis; SCID = Structured Clinical Interview for DSM-IV Axis I Disorders; NEET = Not in Education, Employment, or Training; CAARMS = Comprehensive Assessment of At-Risk Mental States; SIAS = Social Interaction Anxiety Scale; SANS = Scale for the Assessment of Negative Symptoms; AUDIT = Alcohol Use Disorders Identification Test; DUDIT = Drug Use Disorders Identification Test; COWAT = Controlled Oral Word Association Test; LM-I scaled = scaled Logical Memory Immediate Recall total score; BDI-II = Beck Depression Inventory-II.

Missing data is noted where applicable. Percentages are calculated based on available data.

^a Missing N=1 in Class 2; ^b Missing N= 1 in all Classes; ^c Missing N = 1 in Class 1, Missing N = 6 in Class 2, Missing N = 1 in Class 3; ^d Missing N= 1 in Class 2; ^e Missing N = 2 in Class 1, Missing N = 7 in Class 2, Missing N = 2 in Class 3; ^f Missing N = 1 in Class 1, Missing N = 8 in Class 2; ^g Missing N = 2 in Class 1, Missing N = 5 in Class 2; ^h Missing N = 1 in Class 1 and Missing N = 1 in Class 2.

Effect sizes are reported where applicable: partial eta squared (η^2) for one-way ANOVA, eta squared (η^2) for Kruskal-Wallis, and Cramér's V for chi-square tests.

For employment status and avolition/apathy, groups sharing a superscript Greek letter do not differ significantly ($p > .05$). Standardised residuals were used for chi-square post hoc tests; Kruskal-Wallis post hoc comparisons used mean ranks pairwise comparisons with Bonferroni correction.

3.6 Baseline Predictors of Trajectory Membership

A multinomial logistic regression was conducted to examine baseline predictors of trajectory group membership. Based on the above group comparisons, NEET status and

SANS Avolition/Apathy were entered as primary predictors. Although age, gender, ethnicity, trial allocation, and neurocognitive performance (COWAT Total and Logical Memory scaled scores) did not differ significantly across groups, they were included as covariates to control for potential confounding. All assumptions for multinomial logistic regression were met (see Appendix AB for details).

Model fit was assessed using likelihood ratio tests, and pseudo- R^2 values (Nagelkerke $R^2 = .25$) indicated that the final model provided a moderate fit to the data. Likelihood ratio tests indicated that NEET status, $\chi^2(2) = 6.37, p = .041$, and avolition-apathy, $\chi^2(2) = 28.94, p < .001$, significantly improved model fit.

As shown in Table 7, individuals in Class 1 (Moderate Improvement) were 2.34 times more likely to be non-NEET compared to Class 2 (Stable Low), Wald $\chi^2(1) = 6.36, p = .012$. Avolition-apathy severity also significantly predicted group membership, with higher symptom scores associated with lower odds of being in Class 1 compared to Class 2, Wald $\chi^2(1) = 23.73, p < .001$. Avolition-apathy also significantly distinguished Class 3 (Increasing Overactive) from Class 2 (Stable Low), Wald $\chi^2(1) = 6.54, p = .011$, with higher symptom scores associated with lower odds of being in Class 3. Finally, trial arm allocation significantly predicted class membership, such that participants assigned to the Social Recovery Therapy (SRT) condition had increased odds of being classified in Class 3 (Increasing Overactive) relative to Class 2 (Stable Low), Wald $\chi^2(1) = 3.89, p = .049$.

These results suggest that individuals in the Moderate Improvement group were more likely to be engaged in education, employment, or training, and to have lower avolition-apathy than those in the Stable Low group. Those in the Increasing Overactive group also experienced lower levels of avolition-apathy and were more likely to have received SRT compared to the Stable Low group.

No other predictors significantly distinguished trajectory classes ($ps > .05$).

Table 7. Multinomial Logistic Regression Predicting Social Functioning Trajectory

Group Membership.

	<i>b</i> (SE)	Odds Ratio	95%CI for Odds Ratio	
			Lower Limit	Upper Limit
Class 1 vs. Class 2^a				
Intercept	1.00 (1.36)			
Age	0.03 (0.06)	1.03	0.91	1.16
Gender (female)	-0.33 (0.31)	0.72	0.39	1.32
Trial allocation (SRT)	0.20 (0.30)	1.22	0.67	2.21
Ethnicity (White British)	0.39 (0.45)	1.48	0.61	3.58
COWAT Total	0.10 (0.02)	1.01	0.98	1.04
LM-I Scaled Total	-0.03 (0.05)	0.88	0.00	1.07
SANS Avoliton/Apathy	-0.75 (0.15) ^{***}	0.47	0.35	0.64
NEET status	.85 (0.34) [*]	2.34	1.21	4.54
Class 3 vs. Class 2^a				
Intercept	-3.65 (2.38)			
Age in years	0.09 (0.11)	1.10	0.88	1.36
Gender (female)	-.22 (0.57)	0.80	0.26	2.46
Trial allocation (SRT)	1.17 (0.59) [*]	3.21	1.01	10.24
Ethnicity (White British)	-19.36 (0.00)	0.00	0.00	0.00
COWAT Total	0.02 (0.03)	1.02	0.97	1.08
LM-I Scaled Total	0.04 (0.09)	1.04	0.87	1.24
SANS Avoliton/Apathy	-0.69 (0.27) [*]	0.50	0.30	0.85
NEET status (NEET)	0.40 (0.61)	1.49	0.45	4.94

Note. Class 1 = Moderate Improvement; Class 2 = Stable Low (reference category); Class 3 = Increasing Overactive; COWAT = Controlled Oral Word Association Test; LM-I Scaled Total = Logical Memory Recall Scaled Score; SANS Total = Scale for the Assessment of Negative Symptoms total score; NEET status = Not in Education, Employment, or Training at baseline; SRT = Social Recovery Therapy. Comparison categories for the dummy variables are in brackets. $R^2 = .20$ (Cox–Snell), $.25$ (Nagelkerke). Model $\chi^2(16) = 59.59, p < .001$. $*p < .05, **p < .01, ***p < .001$.

4. Discussion

This study examined baseline predictors of trajectory group membership in young individuals with complex and severe mental health difficulties. Latent Class Growth Analysis identified three distinct trajectory groups based on social functioning, measured by structured activity engagement: the Stable Low group (64.8%), characterised by persistent functional impairment; the Moderate Improvement group (29.3%), which demonstrated modest but meaningful functional gains over time despite remaining below typical non-clinical levels; and the Increasing Overactive group (5.9%), which exhibited the most substantial improvement but may have exceeded the optimal level of engagement by the final time point.

Key baseline predictors of trajectory classification were negative symptom severity, specifically apathy and avolition, and NEET status. Higher avolition-apaty scores were associated with significantly lower odds of belonging to either the Moderate Improvement or Increasing Overactive group compared to the Stable Low group. Additionally, baseline NEET status significantly distinguished the Moderate Improvement group from the Stable Low group, with individuals in education, employment, or training more likely to show moderate functional gains. No other clinical, cognitive, or demographic predictors significantly distinguished class membership.

It is important to note that, despite all participants receiving at least enhanced standard care, and half receiving specialised intervention, the largest subgroup remained Stable Low. Findings may reflect the enduring impact of baseline NEET status and motivational deficits, both of which may signal more entrenched functional difficulties that are harder to reverse through existing interventions, especially if they have been longstanding. Given this, the timing of intervention may be critical, with the possibility that earlier psychosocial input could shift longer-term trajectories. Notably, these two predictors of persistent social disability in this sample were transdiagnostic and were not confined to psychosis risk

syndromes. This supports previous findings that such factors independently predict poorer illness trajectories across diagnostic categories [3].

4.1 Comparison with Existing Literature

These findings align with earlier studies demonstrating heterogeneous functional trajectories among youth receiving mental health support [14,20]. The three-class solution identified here mirrors patterns in previous longitudinal modelling studies, including subgroups of persistently impaired individuals, those with modest improvements, and a smaller subset showing substantial recovery. Specifically, Allswede et al. [51] found similarly three trajectories, one of rapid symptomatic and functional improvement, with high rates, one of moderate gains in symptomatic and functional improvement, with ongoing need for support and one of stable, chronic impairment in symptoms and functioning, using two independent ARMS youth samples. Considering the trajectories of those starting with severe impairment, Iorfino et al. [14] found that nearly 30% of their sample remained persistently impaired over five years, with a very small portion showing marked substantial increase to the highest functioning levels, in alignment with a more recent study [20], where more than half either deteriorated or showed no meaningful improvement. The present study extends these findings to a broader, transdiagnostic youth population with complex mental health needs.

4.1.1 Negative Symptoms and Functioning Outcomes

Negative symptoms, specifically avolition and apathy characterised by reduced initiation and persistence in goal-directed activity, emerged as the strongest predictor of persistent social disability. These results highlight that specific negative symptom, even in the absence of psychosis, may act as early markers of long-term social disability.

Prior studies in ARMS populations have consistently identified that negative symptoms significantly correlate with poor functioning [52,53]. Importantly, higher severity

of negative symptoms at baseline has been found to be a robust predictor of poor functioning outcomes [54,55]. Several studies have also identified specifically social amotivation and avolition to predict functioning in ARMS at 1 year [56,57] and at 2-year follow-ups [58]. This has also been repeatedly found in FEP research with negative symptoms predicting functional and symptomatic recovery at 5 years [59] and functional remission at 2 years [60]. In FEP, avolition seems to also be more predictive of functioning than expressive deficits [61].

Evidence about predictors of functioning trajectories come from FEP studies primarily to this date, suggesting that baseline negative symptoms predict poorer functional trajectories, both in the short term [17] and over extended follow-up with more severe baseline symptoms linked to the most impaired functional group at 20 years [62], with one study finding a near-significant link between baseline negative symptoms distinguishing between gradually improved and persistently poor trajectories, possibly due to less specific negative symptoms measurement [18].

Importantly, this study contributes to the validation of negative symptom constructs beyond psychosis-specific populations, reinforcing their broader clinical relevance. The transdiagnostic nature of negative symptoms has been increasingly recognised, as they are observed across a range of first psychiatric episodes in adolescents and young adults [67]. Prior research suggests that negative symptoms may exist along a continuum from the general population to fully developed clinical syndromes [68] as attenuated forms are detectable in community youth samples [69,70].

4.1.2 NEET Status and Social Disability

NEET status was associated with a greater likelihood of belonging to the Stable Low group, consistent with prior research highlighting its role as a marker of persistent functional

impairment across clinical youth populations, in transdiagnostic [14,20], ARMS [71] and FEP [72].

NEET status could predict persistent social disability due to its link with multiple factors that impact on socio-occupational functioning. NEET status has been strongly associated with poorer mental health outcomes across youth populations, such as transitioning from sub-threshold to full syndrome mental disorders [3], poorer social functioning at baseline, greater disability and economic hardship, and a more advanced stage of mental illness than those engaged in education, training or work [73], and higher levels of depression [73,74] compared to those engaged in education, training or work. In a cohort of 20,293 young adults treated primary mental health services, those with NEET status had higher scores across all symptom measures pre-treatment, were more likely to report having a comorbid long-term physical health condition, waited longer between both referral and assessment, and assessment and treatment, and had worse treatment outcomes than their not-NEET peers [75]. Further supporting this, Iyer et al. [76], in a FEP cohort, found that NEET youth presented with several risk factors for poorer outcomes, such as higher negative symptoms, worse premorbid adjustment from late adolescence, and longer duration of untreated psychosis despite more frequent help-seeking compared to their non-NEET peers, suggesting a subgroup marked by both psychosocial disadvantage and clinical vulnerability. Overall, being NEET may both reflect and reinforce a cycle of functional decline, where lack of structure and engagement limits opportunities for social recovery [6].

4.2 Strengths and Limitations

The present study used LCGA to identify subgroups based on social functioning change, offering a data-driven, person-centred approach to modelling heterogeneity. To our knowledge, it is the first study to apply this approach in a sample of youth with complex and severe mental health difficulties characterised by persistent social disability from the outset,

unlike previous studies [14,20]. This provided an opportunity to focus on change within a high-risk subgroup rather than across a full spectrum of functioning. Importantly, it examined the trajectories of functioning in young people with complex and severe mental health difficulties outside the context of psychosis, which is the focus of most existing literature. Additionally, the sample included participants recruited from both mental health and wider youth-facing services, not all of whom had prior access to formal mental health support. This allowed for the inclusion of a more functionally impaired yet service-diverse sample, enhancing ecological validity and potentially capturing unmet needs among hard-to-reach populations who might face mental health problems but not access mental health services. Furthermore, data were drawn from a randomised controlled trial, ensuring standardised assessment procedures and minimising bias in outcome measurement, due to blind ratings compared to previous studies in transdiagnostic samples that were based on clinical audits [14,20].

However, several limitations must be acknowledged. Treatment exposures beyond trial arm allocation were not systematically captured, and it remains unclear how differences in the type or quality of support influenced outcomes. Additionally, although the trial ensured a minimum level of support via enhanced standard care in the control group, the contribution of non-mental health community services remains underexplored and could be a valuable target in future research. Because baseline assessments were conducted at study entry, participants may have been at different stages of symptom progression or duration of NEET status when they enrolled. As a result, the trajectories observed may reflect variation in timing of recovery, rather than uniform change from a shared starting point. This is a known limitation in the trajectory literature and can complicate comparisons across individuals. Moreover, the two-year follow-up period of this study may also be insufficient to capture longer-term patterns of functioning, especially given the chronicity of social disability in this

population. Although missing value analysis indicated no significant baseline differences between participants with and without complete follow-up data on age, ethnicity, gender, NEET status, ARMS status, comorbidity, and trial allocation, the 24-month TUS data were missing for 24.1% of the sample. It remains possible that unmeasured factors, such as marked improvement or deterioration in functioning, may have influenced continued participation, potentially introducing bias into the estimated trajectories. Finally, the Time Use Survey, while a valuable behavioural measure, does not capture the quality or meaningfulness of activities, which could offer a more comprehensive view of recovery [77].

4.3 Clinical Implications

The findings of this study have several clinical implications. Firstly, NEET status and negative symptoms should be considered as potential predictive markers of longer-term social disability, especially in young people with complex mental health needs, irrespective of diagnosis. Within mental health services, this could guide the identification of those in need of additional support with motivational deficits and re-engagement with education, training or work to increase structured activity. Additionally, avolition should be considered as a transdiagnostic marker of social disability and not only conceptualised within those presenting with psychotic experiences. Given the strong link between avolition and poor functional recovery, as well as its potential to persist and impact broader clinical outcomes [55], early intervention may offer significant long-term benefits. However, evidence for effective treatments targeting negative symptoms remains limited [78].

From a life course perspective, early mental health difficulties that disrupt entry into employment or education may set young people on long-term trajectories of social and economic exclusion [79], highlighting the importance of timely, preventive interventions that address both mental health and vocational engagement. Thus, there is also an argument for mental health services being mindful that mental health difficulties, especially during youth

[80], predict becoming NEET [6] and that these individuals are at increased risk of failing to make the transition from school to employment [81].

Since NEET status is both a predictor and consequence of poor functional and clinical outcomes, integrated vocational and social interventions may also help break the cycle of functional stagnation. Evidence supports embedding employment and education support, such as Individual Placement and Support (IPS) and vocational specialists, within youth mental health services [82]. However, research from early psychosis populations suggests that vocational engagement remains low for many young people with FEP and ARMS, even after receiving specialised care and may not be directly influenced by symptom change [83]. While IPS has demonstrated effectiveness in supporting job acquisition and stability among individuals with severe mental illness [84], its impact on education and its generalisability beyond psychosis and its impact on educational outcomes remain unclear [85]. Critically, motivation is often required to access such interventions posing a challenge for those experiencing severe negative symptoms.

4.4 Future Directions

While this study examined a broad range of clinical and demographic factors potentially important predictors such as support access, treatment quality and adherence were not available. Future research should include systematic assessments of engagement with community services, mental health treatment, and medication to better understand how these influence functional outcomes. Longer-term trajectory studies are also needed to assess whether gains are sustained, plateau, or decline over time, and to identify modifiable factors that could inform interventions. Incorporating measures of personal recovery, such as activity meaningfulness and social connectedness [77], could provide a more holistic understanding of meaningful change in this population.

A critical area for future research is the longitudinal course of negative symptoms in this population, as it may offer insight into their link with persistent social disability. Present in up to 80% of ARMS individuals [55], negative symptoms often persist [86], regardless of transition to psychosis [87]. Their persistence predicts poorer clinical, functional, and intervention outcomes in ARMS samples [55], even when controlling for depressive symptoms and independent of transition to psychosis [88,89]. Emerging research has begun to identify early predictors of persistent negative symptoms, such as poor premorbid functioning in late adolescence [90], and suggests that early symptom improvements, particularly within the first six months, may mark a critical intervention window before symptoms plateau [91]. Extending this work to transdiagnostic youth samples, future studies should explore whether specific symptom trajectories, such as avolition, predict functional outcomes, and investigate early factors associated with the development and maintenance of negative symptoms to enhance the detection of youth at risk for enduring social disability.

Future research should prioritise identifying factors that contribute to and sustain NEET status in youth, given the bidirectional relationship of NEET status with mental health difficulties in youth [92,93]. Evaluating community-based interventions embedded in schools, job centres, or youth-facing services may inform scalable, preventative strategies that complement or operate alongside specialist care.

4.5 Conclusion

This study provides novel insights into the predictors of functional trajectories among young people with complex and severe mental health difficulties and social disability, emphasising the importance of NEET status and negative symptoms—particularly apathy and avolition— as key predictors of persistent low functioning. Using latent class growth analysis, the findings indicated that a large proportion of participants remained functionally impaired over two years, suggesting that existing interventions may be insufficient to address

entrenched social disengagement. These results call for the development and evaluation of integrated, targeted interventions that address motivational barriers and vocational exclusion, as well as the broader social contexts in which young people live. Future research should aim to investigate long-term functional outcomes in non-psychosis populations and explore preventative and intervention strategies across both clinical and non-clinical settings to improve functional trajectories for this vulnerable group.

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6. Supporting Information

Appendix G. Code and Outputs of Power Calculations

Appendix H. Participant Information Sheet for the PRODIGY Trial

Appendix I. Participant Consent Form for the PRODIGY Trial

Appendix J. Ethics Approval Letter

Appendix K. PRODIGY Trial List of Measures

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Appendix T. GRoLTS Checklist

Appendix U. Final Mplus Syntax for the Latent Class Growth Analysis

Appendix V. Missing Value Analysis Details

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Appendix AB. Multinomial Logistic Regression Assumptions Check

Chapter Five: Empirical Paper Extended Methodology

This chapter provides additional methodological details for the empirical study presented in Chapter Four. It provides a detailed description of the outcome and predictor variable measures, describes the Latent Class Growth Analysis approach used to identify trajectory subgroups, outlines the procedures for handling missing data and details how baseline characteristics were examined across these groups.

Additional Measures Details

Outcome Measures

Social Functioning. Social functioning was assessed using an adapted version of the Office for National Statistics Time Use Survey (TUS; Short, 2006, adapted by Hodgekins, French, et al., 2015). This measure captures the total hours per week spent in structured activities, including employment, education, voluntary work, household chores, childcare, and structured leisure activities such as sports and hobbies. Data were collected through a semi-structured interview conducted by trained assessors. The TUS was chosen as a proxy for social functioning as it provides an operationalised assessment of the behavioural aspects of functional recovery (Hodgekins, French, et al., 2015) and has been associated with reduced mental health symptoms and improved well-being (Eklund et al., 2009; Gershuny, 2011). This measure has demonstrated sensitivity in distinguishing clinical from non-clinical groups in youth mental health populations (Hodgekins, French, et al., 2015). TUS has also shown convergent validity with measures of quality of life and social functioning (Fowler et al., 2009), reinforcing its utility as an indicator of functional recovery in youth mental health research.

Predictor Variables

Demographic Information. All participants completed a questionnaire capturing key demographic information. Based on previous research, ethnicity, gender (Chang, Chu, et al.,

2018; Hodgekins, Birchwood, et al., 2015a), being NEET (Iorfino et al., 2018; 2022) and age (Bright et al., 2018; Iorfino et al., 2018, 2022) were examined as potential predictors of social functioning trajectory membership.

Psychopathology. The Comprehensive Assessment of At-Risk Mental States for psychosis (CAARMS; Yung et al., 2005), a semi-structured interview, was used to assess levels of attenuated psychotic symptoms and associated psychopathology.

The CAARMS was used both as a categorical measure to determine At-Risk Mental State (ARMS) status (yes/no) and as a continuous measure of overall symptom severity. It has demonstrated good to excellent concurrent, discriminant, and predictive validity, along with excellent inter-rater reliability (Yung et al., 2005). Previous research has shown that the presence (Iorfino et al., 2018; 2022) and severity of psychotic-like experiences are associated with poor social functioning in clinical samples of young people (Brandizzi et al., 2015). Additionally, given the indicated link between self-harm, suicidality, and long-term social impairment (Iorfino et al., 2018, 2022), the CAARMS suicidality subscale was also examined as a potential predictor of social functioning trajectories.

Social anxiety was assessed using the Social Interaction Anxiety Scale (SIAS; Mattick & Clarke, 1998) which is a 20-item self-report measure, which evaluates symptoms of anxiety in social situations over the past week. Items are rated on a five-point scale, from 0 to 4 and overall scores range from 0 to 80. The SIAS has been used in clinical samples of young people (McEnery et al., 2021) demonstrating good internal consistency (Rodebaugh et al., 2011). Previous research suggests that higher levels of social anxiety in youth are associated with impaired social functioning throughout development (Swan & Kendall, 2016) and in young people at risk for psychosis (Bright et al., 2018; Cotter et al., 2019), and thus it was examined as a potential predictor of social functioning trajectories in this study.

Depressive symptom severity was assessed using the Beck Depression Inventory-II (BDI-II; Beck et al., 1996), a 21-item self-report measure evaluating the severity of depressive symptoms over the past two weeks. Items are rated on a scale from 0 to 3, with total scores ranging from 0 to 63. BDI-II has been used in several studies with young people, and it has demonstrated good psychometric properties (Krefetz et al., 2002, 2003; Steer et al., 1998) including young people at risk for psychosis (DeVylder et al., 2014). Prior research has indicated that higher depressive symptoms are associated with poorer functional recovery (Schlosser et al., 2012) and lower depressive symptoms at baseline have been linked to more favourable outcome trajectories (Polari et al., 2018) in ARMS populations. Given these findings, depression was examined as a potential predictor of social functioning trajectories in this study.

Comorbidity. The Structured Clinical Interview for DSM-IV for Axis -I disorders (SCID-I; First et al., 2002) was administered at baseline to determine whether participants met diagnostic criteria for any mood, anxiety, somatoform, or eating disorder, or for any episode, within the past month. To capture comorbidity severity, a binary variable was created using the median number of diagnoses in the sample, categorising participants into two groups: low (0–3 diagnoses) and high comorbidity (3–6 diagnoses). Previous research suggests that persistence or recurrence of comorbid disorders has been associated with an increased chance of severe functional impairment at long term follow-up in ARMS (Rutigliano et al., 2016), lower comorbidity burden has been associated with an improving functional trajectory (Iorfino et al., 2022), and increasing symptom burden (including anxious-depressive, somatic, and psychotic-like symptoms, irrespective of symptom dimension) increases the likelihood of socio occupational functional impairments in transdiagnostic samples of young people (Iorfino et al., 2022). Given these findings,

comorbidity was examined as a potential predictor of social functioning trajectories in this study.

Negative symptoms were assessed using the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1989), which captures affective flattening, alogia, avolition, anhedonia, and attentional impairment, symptoms commonly observed in psychosis. The scale consists of 25 items, rated from 0 to 5, with internal consistency ranging from high ($\alpha > .90$) to modest ($\alpha = .60$) (Levine & Leucht, 2013). The sum of individual items was used as a measure of symptom severity, ranging from 0 to 125, with higher scores showing higher symptom severity. Negative symptoms have been associated with poor functioning outcomes in youth at risk for psychosis (Devoe et al., 2020, 2021; Hodgekins, Birchwood, et al., 2015b; Schlosser et al., 2012) and thus, severity of these symptoms was considered as a potential predictor of social functioning trajectories in this study.

Substance and Alcohol Use. As substance use (Iorfino et al., 2018; 2022) has been associated with worse long-term social functioning outcomes in youth, the total scores from the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) ranging from 0 to 40, and the Drug Use Disorders Identification Test (DUDIT; Berman et al., 2005), ranging from 0 to 44, were considered as potential predictors. Both self-report measures assess alcohol and drug-related problems, with higher scores indicating more severe substance use issues. Both measures have been used with young people and have good psychometric properties (De Meneses-Gaya et al., 2009; Hildebrand, 2015).

Neurocognition. Neurocognitive functioning was assessed using the Logical Memory I (LM-I) subtest of the Wechsler Memory Scale (Wechsler, 1997) and the Controlled Oral Word Association Test (COWAT; Benton & Hamsher, 1976). The total COWAT verbal fluency score and the scaled Logical Memory Immediate Recall total score were used as potential predictors, given that poorer neurocognitive functioning has been associated with

worse functioning outcomes in young people at risk for psychosis (Eslami et al., 2011; Haining et al., 2021).

Additional Data Analysis Details

Missing Values Analysis

Completers and non-completers of variables with missing data were compared on key demographic characteristics (age, ethnicity, gender, NEET status) and clinical variables (ARMS status, comorbidity, and trial allocation).

Latent Class Growth Analysis

LCGA (Muthén, 2004) is a variant of Growth Mixture Modelling that restricts within-class variance to zero, ensuring that all individuals within a class follow the same trajectory shape (Jung & Wickrama, 2008). This method assumes minimal within-group variability, making it particularly suitable for identifying homogeneous subgroups based on developmental patterns (Berlin et al., 2014; Muthén, 2004). The metric of time was specified in months. This approach was selected to align with the study's aim of classifying youth into distinct social functioning trajectory subgroups rather than examining within-group variability.

Model selection was informed by both data-driven indices and pragmatic considerations, including model parsimony, entropy, and interpretability (Berlin et al., 2014; Losina & Collins, 2016; Van De Schoot et al., 2017). Models were fitted sequentially, beginning with a one-class solution and increasing incrementally. Entropy values closer to 1 indicate greater classification accuracy, with values above .80 generally accepted as reflecting adequate class separation (Clark & Muthén, 2009). When multiple models demonstrated similar fit indices, decisions were guided by entropy and average posterior probabilities. Posterior probabilities above .70 were considered indicative of reliable class membership

assignment (Nagin, 2005). Directionality of fit indices was also considered, with lower AIC, BIC, and aBIC values indicating improved model fit (Nylund et al., 2007).

Linear, quadratic, and cubic growth models were explored to assess different potential shapes of social functioning trajectories over time. A linear model assumes a constant rate of change across time, whereas a quadratic model introduces one inflection point, allowing for acceleration or deceleration. A cubic model allows for two inflection points, capturing more complex non-linear patterns such as increase followed by plateau or decline. Including these model specifications provides greater flexibility in identifying distinct and theoretically meaningful trajectory shapes within the data (Nagin, 2005).

Baseline Characteristics and Differences Between Trajectory Groups

The baseline variables used to examine trajectory group differences were the following: ethnicity (White British vs other), gender (female, male), NEET status (yes/no), age, ARMS status (yes/no), CAARMS overall psychotic symptom severity, CAARMS suicidality subscale score, social anxiety (SIAS total score), depressive symptom severity (BDI-II total score), Comorbidity severity (0-3 diagnoses, 3-6 diagnoses), negative symptoms (SANS total score, SANS affective flattening, SANS alogia, SANS avolition, SANS anhedonia, SANS attentional impairment), alcohol use (AUDIT total score), drug use (DUDIT total score), neurocognition (scaled Logical Memory Immediate Recall total score, COWAT total score).

Chapter Six: General Discussion and Critical Evaluation

The overarching aim of this thesis was to contribute to the current understanding of social disability in youth mental health by identifying predictors and mapping the long-term trajectories of social functioning in young people with severe and complex mental health difficulties and social functioning impairments. This aim was approached through two complementary components. First, a systematic review synthesised evidence on predictors of long-term functioning across diagnoses. Second, a secondary data analysis used the PRODIGY trial to model functioning trajectories and examined their baseline predictors in a transdiagnostic sample with persistent social disability.

This chapter brings together and critically appraises the findings from both studies. It begins with a brief summary of results from each study, followed by an integrated interpretation of the main findings in light of existing theory and research. The chapter then evaluates key methodological strengths and limitations, explores clinical implications, and concludes with recommendations for future research.

Overview of Findings

Systematic Review Findings

The systematic review (Chapter Two) synthesised evidence on predictors of long-term functional outcomes in young people aged 16–25 with severe and/or complex mental health problems and significant social impairment at baseline. Twenty-four studies were included in the synthesis, which predominantly focused on youth with first-episode psychosis (FEP) or at-risk mental state (ARMS) for psychosis, with only two studies examining transdiagnostic samples.

Where measured, findings from two studies consistently identified negative symptoms as predictors of poor functioning. Other key predictors included longer duration of untreated psychosis and NEET status at baseline, with some evidence also pointing to lower IQ and

poor premorbid functioning, although these were examined in fewer studies of lesser methodological quality. Demographic factors, such as age, gender and ethnicity, showed inconsistent associations with functioning outcomes, and evidence for psychosocial factors was limited. It is worth noting that very few of the studies used objective behavioural measures of functioning, such as NEET status, and instead relied on global clinician-rated scales. This is important because clinician-rated scales, while widely used, may introduce subjectivity and fail to capture real-world functional outcomes, such as employment or social participation, which are more reflective of an individual's actual ability to navigate daily life.

The review identified a gap in research focused on factors relating to social functioning in youth with mental health difficulties outside the psychosis spectrum, emphasising the need for further investigation of this underexplored vulnerable group.

Empirical Paper Findings

The empirical paper of this thesis (Chapter Four) addressed the gap identified in the review by conducting a secondary analysis of data from the PRODIGY trial (Berry et al., 2022), a randomised controlled trial investigating Social Recovery Therapy (SRT) for young people aged 16–25 with emerging severe mental illness and persistent social disability. Participants were recruited from both NHS and community-based services and assessed at four time points over 24 months.

Significant functional impairment at entry was operationalised as engaging in fewer than 30 hours per week of structured activity for at least six months. Importantly, the sample was transdiagnostic, including individuals meeting ARMS criteria and/or those with non-psychosis-related complex mental health difficulties, but excluding those with a history of psychotic disorder. This offered a unique opportunity to explore the course of social functioning in a non-psychosis population.

Latent Class Growth Analysis (LCGA) identified three distinct social functioning trajectories: a large group who exhibited persistently low levels of structured activity (Stable Low, $n = 175$, 64.8%, $M = 17.79$ hours/week at 24 months), a group who demonstrated gradual gains but remained below the clinical recovery threshold (Moderate Improvement, $n = 79$, 29.3%, $M = 38.39$ hours/week at 24 months) and a small group with marked functional gains (Marked Increase, $n = 16$, 5.9%, $M = 89.91$ hours/week at 24 months) exceeding typical clinical thresholds for functional recovery (Hodgekins, French, et al., 2015). Multinomial logistic regression revealed that baseline NEET status and avolition significantly predicted poorer functional trajectories. This study is the first to characterise long-term functional trajectories in a transdiagnostic sample of youth with persistent social disability at baseline, offering novel insights into an under-researched group and highlighting the importance of motivational and vocational factors in predicting social recovery.

Integrated Overview of Findings

Taken together, the systematic review and empirical paper offer converging insights into the central role of negative symptoms and particularly motivational impairment (avolition) and occupational disengagement (NEET status) as predictors of long-term social functioning in youth with complex mental health difficulties who present with significantly low functioning.

While the systematic review highlighted these factors primarily within psychosis-specific populations, the empirical paper extended their relevance across a broader transdiagnostic sample and highlighted their potential relevance as transdiagnostic markers of long-term social impairment in young people with complex mental health difficulties and social disability. Overall, both studies underscore that functional recovery is not guaranteed by symptom reduction alone and must be targeted directly through assessment, formulation, and intervention.

Interpretation of Main Findings

Findings from this thesis confirm that in young people with a range of emerging severe mental health problems, a large proportion experience persistent social disability despite receiving some form of mental health support (Heinze et al., 2018; Hodgekins, Birchwood, et al., 2015; Iorfino et al., 2018, 2022). This supports the view that social disability is a transdiagnostic issue among young people affected by mental health difficulties (Hickie et al., 2019).

They also indicate that severe functional impairment present at service entry is often persistent throughout treatment, suggesting that for many, these difficulties may be enduring. This thesis contributes to an emerging body of evidence focused on identifying prognostic markers of functioning trajectories in youth mental health. This line of work aims to enable stratified care by identifying young people at highest risk of long-term functional impairment and guiding the allocation of targeted interventions (Delgadillo & Lutz, 2020; Fusar-Poli et al., 2018) Such an approach facilitates personalised, proactive care that prioritises not only symptom reduction but also functional recovery and improved quality of life from an early stage (Colizzi et al., 2020).

Though research into prediction models for functioning in youth mental health remains limited (Iorfino et al., 2024; Koutsouleris et al., 2018), the importance of functioning as a key outcome is widely recognised by service users and researchers alike (Hickie et al., 2019).

While prior studies have focused on early intervention to prevent functional decline shortly after service entry (Iorfino et al., 2024), this thesis examines predictors of persistent social disability once it is already established.

In this context, the two key predictors identified across both studies, negative symptoms and NEET status, are highly relevant. Specifically, this thesis underscores the role

of negative symptoms, particularly avolition, as risk markers for poor functional outcomes in young people with ARMS, FEP, and other emerging complex mental health difficulties who present with significant social impairment.

Negative symptoms may contribute to persistent functional impairment observed in youth with complex mental health difficulties through specific psychological mechanisms. According to the cognitive model of negative symptoms (Beck et al., 2009; Grant & Beck, 2009), individuals with neurocognitive vulnerabilities may encounter discouraging early experiences in domains such as education, employment, or relationships, which can contribute to the formation of dysfunctional beliefs, such as defeatist performance beliefs, involving overgeneralised negative assumptions about one's capacity to successfully perform tasks (Grant & Beck, 2009). These beliefs are proposed to play a central role in the emergence and maintenance of negative symptoms (Beck et al., 2009) and contribute to maladaptive behavioural responses, such as avoidance of effortful or goal-directed activity and social withdrawal.

According to the model, negative symptoms arise from the interaction of the dysfunctional beliefs and subsequent behavioural choices. Although withdrawal may initially serve as a protective strategy against anticipated failure or poor performance, over time, reduced engagement may limit opportunities to challenge these beliefs, reinforcing amotivation and functional impairment (Couture et al., 2011; Perivoliotis et al., 2009). This aligns with literature indicating that defeatist beliefs are associated with experiential negative symptoms such as diminished motivation, which in turn predict poorer functional outcomes (Campellone et al., 2016; Green et al., 2012). In a non-clinical sample, Luther et al., (2018) showed that these beliefs were significantly associated with negative symptoms, independently of depressive symptoms, suggesting they may represent a transdiagnostic cognitive factor rather than mere byproducts of illness.

In addition to defeatist beliefs, diminished self-efficacy – the belief in one’s capacity to execute behaviours necessary to produce specific performance attainments (Bandura, 1978) – has been associated with negative symptoms (Kurtz et al., 2013; Ventura et al., 2014). While distinct, self-efficacy may interact with defeatist beliefs, potentially contributing to reduced initiation of goal-directed activity. Recent findings suggest that the relationship between self-efficacy and negative symptoms may be mediated by defeatist performance beliefs (Luther et al., 2018). The association between these cognitive variables tied to negative symptoms and functional impairment may be particularly relevant in youth, where identity formation and engagement in structured activity are key developmental tasks. Qualitative research by Cotter et al. (2019) provides converging evidence, showing that young people with ARMS identified self-stigmatising beliefs and unhelpful metacognitive beliefs – such as rumination, and heightened self-focus in social contexts – as barriers to social and occupational participation. These beliefs were linked to negative symptoms, but also to poor self-efficacy and in turn, to social withdrawal further contributing to impaired functioning. While causal pathways remain to be established, existing evidence suggests that these cognitive factors may maintain reduced functioning and represent potential therapeutic targets for avolition in youth mental health.

Additionally, NEET status may function as a risk factor, an expression, and a consequence of functional impairment. Disengagement from education, employment, or training may contribute to the development of dysfunctional beliefs that underlie avolition and to the maintenance of functional impairment. Lack of involvement in structured roles limits opportunities to develop skills, establish social roles, and form connections during a critical developmental period. Prolonged vocational inactivity may also reduce access to experiences that could challenge defeatist beliefs, contributing to diminished perceived competence and confidence. In turn, this may reinforce avoidance of goal-directed behaviour.

Taken together, negative symptoms and NEET status may therefore act as mutually reinforcing factors in the persistence of social disability.

This thesis also adds to the limited literature addressing the transdiagnostic nature of negative symptoms (Mallet et al., 2020), suggesting that such symptoms may exist along a continuum from the general population (Barragan et al., 2011; Métivier et al., 2024; Rodríguez-Testal et al., 2019; Ronald et al., 2014) to fully developed disorders (Kaiser et al., 2011). Despite this, little is known about how these symptoms relate to functional outcomes in non-psychosis related contexts.

A promising direction involves conceptualising negative symptoms within dimensional frameworks of psychopathology. Models such as the Hierarchical Taxonomy of Psychopathology (HiTOP) (Cowan & Mittal, 2021; Kotov et al., 2018; Stevanovic et al., 2024) which moves beyond categorical diagnoses to identify shared symptom dimensions and underlying mechanisms across disorders, and the Research Domain Criteria (RDoC) (Insel et al., 2010) which focuses on transdiagnostic psychological processes, offer valuable conceptual tools. When integrated with the clinical staging model (Hickie et al., 2013; Scott et al., 2013), which maps illness progression over time, these frameworks can offer a transdiagnostic perspective on how negative symptoms emerge and influence functioning, supporting early identification and targeted intervention strategies.

Furthermore, the findings of this thesis further support the notion that young people who are NEET are at increased risk of remaining in a persistent social disability trajectory, extending prior evidence from transdiagnostic (Iorfino et al., 2018, 2022), ARMS (Brandizzi et al., 2015) and FEP populations (Strassnig et al., 2018), including being predictive of being NEET at follow-up (Lee et al., 2017; O’Dea et al., 2016).

It is important to consider NEET status as both an antecedent of early mental health problems (Lindblad et al., 2024), an indicator of the severity of concurrent mental health

difficulties (Hickie et al., 2019), and a factor that can also precede them (Cross et al., 2017; Fowler et al., 2010). Furthermore, its co-occurrence with even subthreshold affective symptoms increases the risk of progression to enduring mental illness (Cross et al., 2017). These findings suggest that intervening early to prevent disengagement, or to mitigate its impact, could help reduce long-term social disability.

Together, this thesis offers a cohesive narrative: from identifying what is known (and unknown) about predictors of poor social functioning in young people with emerging mental illness and social disability, to applying this understanding in a clinical trial dataset to better understand trajectories of functioning and identify factors associated with recovery or stagnation. Overall, this work contributes to ongoing efforts to effectively identify and support young people who are at most risk of long-term social exclusion (Fowler et al., 2019, 2021; Iorfino et al., 2024; Vella et al., 2023)

Overall Strengths and Limitations

A key strength of this thesis lies in its focus on an underrepresented but clinically important population - young people with severe and complex mental health difficulties and persistent social disability. Both the systematic review and empirical paper prioritised this subgroup, addressing a critical gap in the literature which has historically focused on diagnosis-specific cohorts, particularly those with psychosis. The empirical work adopted a person-centred approach through Latent Class Growth Analysis (LCGA) to capture the heterogeneity of functional outcomes in this population. This aligns with broader calls for youth mental health services to shift toward recovery-oriented care that prioritises social engagement and quality of life alongside symptom reduction (van Os et al., 2019).

Another strength is the ecological validity and policy relevance of the outcome measure used in the empirical paper. In line with recent recommendations for more specific and objective indicators of functioning (Cowman et al., 2024), the empirical paper utilised the

Time Use Survey (TUS) (Short, 2006) to measure structured activity, an ecologically valid measure that has been validated as a proxy for social disability and recovery thresholds (Hodgekins, French, et al., 2015). The PRODIGY trial dataset also offered a rich and rare opportunity to explore functioning over two years in a large, multi-site sample of help-seeking youth. The recruitment strategy, which included participants from both NHS and third-sector services across urban and rural sites, enhanced the generalisability of the findings to youth with complex needs in real-world service settings.

Nonetheless, the thesis has several limitations that warrant consideration. While the empirical paper provided a novel application of trajectory modelling in a functionally impaired transdiagnostic sample, the selection of predictors was constrained by the availability of variables in the existing trial dataset. Important factors such as socioeconomic status and premorbid adjustment were not available, which may have limited the scope of the analysis. The thesis overall relied on objective or clinician-rated measures of social functioning, and it did not capture the subjective meaning or quality of the structured activities, which are central to recovery as defined by lived experience research (Leamy et al., 2011).

Across both the systematic review and empirical paper, generalisability is a key consideration. While the empirical paper included individuals recruited from both specialist mental health and community-based services, all participants were engaged with some form of care, which may exclude those not accessing services. Similarly, most studies included in the review were conducted within specialist clinical settings, often with diagnostically specific cohorts, limiting applicability to broader, more diverse youth populations. Finally, in the systematic review, few studies reported on ethnicity or explored its association with functional outcomes, while the empirical sample was predominantly White British (83.5%), potentially restricting the applicability of results to more diverse cultural contexts.

Clinical Implications

Shifting Focus Toward Functional Recovery

Contemporary youth mental health frameworks increasingly call for a broader focus beyond symptom remission toward supporting functional and personal recovery. Models such as the THRIVE (Wolpert et al., 2019) and Connectedness, Hope, Identity, Meaning, Empowerment (CHIME; Leamy et al., 2011) frameworks underscore the importance of a needs-led approach in mental health, and of domains like connectedness, hope, and meaning. The findings of this thesis further support this shift by highlighting that many young people experience persistent social disability despite clinical care. Embedding functioning as a central outcome in routine assessment and care planning could help services better identify unmet needs and target support more effectively.

Identification of Those At Risk of Persistent Social Disability

The findings also reinforce the value of identifying early indicators of poor functional trajectories. Negative symptoms, particularly avolition, and NEET status were indicated to be robust predictors of long-term social impairment, aligning with earlier findings in psychosis and transdiagnostic youth samples (Brandizzi et al., 2015; Iorfino et al., 2018, 2022; Mallet et al., 2020). Routine screening for these markers during assessment could support early stratification of individuals at higher risk, prompting more proactive and targeted intervention efforts.

Interventions for Those At Risk of Persistent Social Disability

Findings from this thesis reinforce a critical need to move beyond symptom-focused models of care in youth mental health. Although symptom severity is important, studies have consistently shown that functional impairment may persist despite symptomatic improvement (Cotter et al., 2017; O’Dea et al., 2016; Schlosser et al., 2012). The identification of large groups of young people with entrenched social disability—even within early intervention

services—suggests that existing treatments may be insufficient for restoring everyday functioning. Consequently, service models must prioritise social recovery, including vocational engagement and community participation, as core outcomes from the point of assessment through to intervention and follow-up (Hickie et al., 2019; van Os et al., 2019).

Psychosocial interventions hold promise in addressing these functional impairments. Evidence supports the use of social skills training (Turner et al., 2018), cognitive remediation (Ventura et al., 2019) and cognitive behavioural therapy (Mayer et al., 2024) in targeting negative symptoms.

Interventions such as Groups 4 Health (Haslam et al., 2016) may help mitigate social disability and mental health problems (Cruwys et al., 2013) by increasing structured activity and facilitating meaningful group memberships (Berry et al., 2019). Furthermore, embedding Individual Placement and Support (IPS) into youth mental health services has shown promising early outcomes in improving vocational outcomes (Simmons et al., 2023).

Additionally, interventions focusing on preventing NEET status among youth might be another area worth exploring. Several initiatives have been instigated with this focus, such as dual apprenticeship systems that integrate schooling with paid work to facilitate school-to-work transitions (Eichhorst et al., 2015) and implementation plans of the EU's Youth Guarantee aiming to provide all youth with an offer of employment, education, or training within four months of becoming unemployed or leaving education (European Commission, n.d.).

It is important to note that most young people experiencing this profile may never access mental health services. The Children's Commissioner for England (2024) report estimates that only 21.7% of youth access treatment from NHS mental health services. This raises important questions about who gets help and how. Many young people who are NEET

or functionally impaired may instead engage with other community or third-sector services which may offer untapped opportunities for both early intervention and long-term support. Nevertheless, these services have been increasingly threatened by significant state funding cuts, with local authority expenditure on youth services having fallen by 73% in England and 27% in Wales since 2010-11 (YMCA England and Wales, 2025). This has resulted in the closure of many youth clubs and community support services. Despite this, findings from this thesis suggest that these services remain a worthy area for investment, particularly given their potential to address gaps in mental health care thus reducing the long-term burden on NHS services. It is noteworthy, however, that these services may lack expertise in managing mental health needs, pointing to the importance of building strong interfaces between clinical and non-clinical systems. Youth support services embedded in schools, job centres, and local community hubs could play a critical role in identifying early signs of social disability and facilitating referrals to appropriate care pathways (Mawn et al., 2017; Richter & Hoffmann, 2019).

Future Research Directions

Although this thesis identified key predictors and patterns of social disability in youth with emerging severe and complex mental health difficulties, several areas remain underexplored.

First, qualitative research is needed to complement quantitative findings by capturing the lived experiences of young people with social disability. While quantitative methods are effective in identifying predictors, they often overlook the nuanced, subjective realities that shape individuals' engagement with social and occupational roles. For instance, Cotter et al. (2019) used qualitative interviews with ARMS youth and found that participants attributed their social disability to clinical symptoms, cognitive difficulties, trauma, self-stigmatising beliefs and maladaptive metacognitive beliefs as key obstacles to social and vocational

participation, factors that are underexplored in quantitative literature. Exploring young people's perceptions of what contributes to, maintains, or alleviates their functional difficulties could offer vital direction for the design of person-centred and acceptable interventions.

Second, larger, longer-term studies are needed to capture the complexity and heterogeneity of social functioning trajectories over time in young people with emerging mental health difficulties and social functioning impairment. Future studies should recruit from both clinical and community-facing services to include harder-to-reach populations, such as young people who are NEET but not engaged with mental health services. Extending follow-up periods beyond two years would allow researchers to detect delayed improvements, relapses, or enduring functional impairments.

Third, there is a growing need to refine the measurement of social functioning in youth mental health. Most studies in the systematic review relied on global tools like the GAF and SOFAS due to their established severity thresholds, but these measures have notable limitations including low sensitivity to change and conflation with symptom severity (Cowman et al., 2024). Cowman et al. recommend using more domain-specific or objective measures such as NEET status or validated tools that capture distinct aspects of social functioning. Thus, there is a clear need to incorporate more domain-specific and objective tools, such as the Time Use Survey (TUS), into youth mental health research. When accompanied by validated cut-offs, such tools would improve comparability and allow more precise identification of change.

Fourth, future studies should validate tools designed to assess negative symptoms in transdiagnostic youth populations. Although this thesis highlighted the role of negative symptoms in predicting poor functioning, most available scales have been developed for psychosis-specific contexts and may miss important manifestations in broader clinical groups

(Strauss et al., 2020). Ensuring the validity of these tools in diverse youth samples is essential to accurately identify and target negative symptoms beyond psychosis-risk cohorts.

Another significant gap relates to neurodevelopmental disorders (NDDs), which were not reported or accounted for in most studies included in the systematic review. NDDs, such as autism and ADHD, can have a substantial impact on social functioning (Bölte, 2025) and may influence how young people engage with interventions. Lindblad et al. (2024) found that both early-life mental health problems and NDDs increased the likelihood of becoming NEET. Future research should examine how co-occurring NDDs affect social disability trajectories and whether tailored interventions are needed for this subgroup.

Additionally, the importance of modelling functional trajectories should be emphasised in intervention studies. For example, although the original PRODIGY trial found no significant group differences between treatment and control arms with both groups improving (Berry et al., 2022), trajectory modelling in the present thesis revealed that most participants remained in a persistently impaired group. This suggests that average treatment effects may mask individual variation and points to the value of person-centred approaches to outcome evaluation and to identify reasons for non-response to treatment.

Lastly, future research should explore what works for whom. It is likely that distinct subgroups of young people, particularly those with non-psychotic severe and complex mental health difficulties, respond differently to standard care. Identifying these subgroups, including those who may be “treatment resistant,” could inform the development of more specialised or intensive interventions. A recent review by De Soet et al. (2023) argued that existing evidence-based treatments may be poorly matched to the needs of young people due to their focus on single disorders and narrow treatment targets (Chorpita et al., 2011; Weisz et al., 2013). Better understanding the mechanisms and predictors of treatment non-response could guide more adaptive and personalised models of care.

Conclusion

This thesis set out to investigate the course and predictors of long-term social functioning in young people with emerging severe mental illness and social disability using a transdiagnostic focus to address an under-researched but clinically important area. This work contributes to this research area by indicating that being NEET and presenting with negative symptoms—specifically avolition—could be markers for identifying those at risk of persistent social disability. The findings also indicate that persistent social disability is not limited to psychosis-specific populations and often endures despite access to early intervention services, reinforcing the importance of employing targeted, function-focused interventions early in care. Importantly, the thesis supports a paradigm shift in youth mental health services that prioritises social functioning alongside symptom reduction, to support young people in achieving meaningful and sustained recovery.

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Appendices

Appendix A. Submission Guidelines for PLOS ONE

Guidelines on scientific subjects unrelated to the thesis have been removed.

Style and Format

File format	Manuscript files can be in the following formats: DOC, DOCX, or RTF. Microsoft Word documents should not be locked or protected. LaTeX manuscripts must be submitted as PDFs. Read the LaTeX guidelines.
Length	Manuscripts can be any length. There are no restrictions on word count, number of figures, or amount of supporting information. We encourage you to present and discuss your findings concisely.
Font	Use a standard font size and any standard font, except for the font named “Symbol”. To add symbols to the manuscript, use the Insert → Symbol function in your word processor or paste in the appropriate Unicode character.
Headings	Limit manuscript sections and sub-sections to 3 heading levels. Make sure heading levels are clearly indicated in the manuscript text.
Layout and spacing	Manuscript text should be double-spaced. Do not format text in multiple columns.
Page and line numbers	Include page numbers and line numbers in the manuscript file. Use continuous line numbers (do not restart the numbering on each page).
Footnotes	Footnotes are not permitted. If your manuscript contains footnotes, move the information into the main text or the reference list, depending on the content.
Language	Manuscripts must be submitted in English. You may submit translations of the manuscript or abstract as supporting information. Read the supporting information guidelines.
Abbreviations	Define abbreviations upon first appearance in the text. Do not use non-standard abbreviations unless they appear at least three times in the text. Keep abbreviations to a minimum.
Reference style	PLOS uses “Vancouver” style, as outlined in the ICMJE sample references . See reference formatting examples and additional instructions below.

Equations We recommend using MathType for display and inline equations, as it will provide the most reliable outcome. If this is not possible, Equation Editor or Microsoft's Insert→Equation function is acceptable.

Avoid using MathType, Equation Editor, or the Insert→Equation function to insert single variables (e.g., “ $a^2 + b^2 = c^2$ ”), Greek or other symbols (e.g., β , Δ , or ' [prime]), or mathematical operators (e.g., x , \geq , or \pm) in running text. Wherever possible, insert single symbols as normal text with the correct Unicode (hex) values.

Do not use MathType, Equation Editor, or the Insert→Equation function for only a portion of an equation. Rather, ensure that the entire equation is included. Equations should not contain a mix of different equation tools. Avoid “hybrid” inline or display equations, in which part is text and part is MathType, or part is MathType and part is Equation Editor.

Copyediting manuscripts

Prior to submission, authors who believe their manuscripts would benefit from professional editing are encouraged to use language-editing and copyediting services. Obtaining this service is the responsibility of the author, and should be done before initial submission. These services can be found on the web using search terms like “scientific editing service” or “manuscript editing service.”

Submissions are not copyedited before publication.

Submissions that do not meet the [PLOS ONE publication criterion for language standards](#) may be rejected.

Manuscript Organization

Manuscripts should be organized as follows. Instructions for each element appear below the list.

Beginning section	<p><i>The following elements are required, in order:</i></p> <ul style="list-style-type: none"> • Title page: List title, authors, and affiliations as first page of the manuscript • Abstract • Introduction
Middle section	<p><i>The following elements can be renamed as needed and presented in any order:</i></p> <ul style="list-style-type: none"> • Materials and Methods • Results • Discussion • Conclusions (optional)

Ending section *The following elements are required, in order:*

- Acknowledgments
- References
- Supporting information captions (if applicable)

Other elements

- Figure captions are inserted immediately after the first paragraph in which the figure is cited. Figure files are uploaded separately.
- Tables are inserted immediately after the first paragraph in which they are cited.
- Supporting information files are uploaded separately.

Refer to our downloadable sample files to ensure that your submission meets our formatting requirements:

- [Download sample title, author list, and affiliations page \(PDF\)](#)
- [Download sample manuscript body \(PDF\)](#)

Viewing Figures and Supporting Information in the compiled submission PDF

The compiled submission PDF includes low-resolution preview images of the figures after the reference list. The function of these previews is to allow you to download the entire submission as quickly as possible. Click the link at the top of each preview page to download a high-resolution version of each figure. Links to download Supporting Information files are also available after the reference list.

Parts of a Submission

Title

Include a full title and a short title for the manuscript.

Title	Length	Guidelines	Examples
Full title	250 characters	Specific, descriptive, concise, and comprehensible to readers outside the field	Impact of cigarette smoke exposure on innate immunity: A <i>Caenorhabditis elegans</i> model Solar drinking water disinfection (SODIS) to reduce childhood diarrhoea in rural Bolivia: A cluster-randomized, controlled trial
Short title	100 characters	State the topic of the study	Cigarette smoke exposure and innate immunity SODIS and childhood diarrhoea

Titles should be written in sentence case (only the first word of the text, proper nouns, and genus names are capitalized). Avoid specialist abbreviations if possible. For clinical trials, systematic reviews, or meta-analyses, the subtitle should include the study design.

Author list

Authorship requirements

All authors must meet the criteria for authorship as outlined in the [authorship policy](#). Those

who contributed to the work but do not meet the criteria for authorship can be mentioned in the Acknowledgments. [Read more about Acknowledgments.](#)

The corresponding author must provide an ORCID iD at the time of submission by entering it in the user profile in the submission system. [Read more about ORCID.](#)

Author names and affiliations

Enter author names on the title page of the manuscript and in the online submission system.

On the title page, write author names in the following order:

- First name (or initials, if used)
- Middle name (or initials, if used)
- Last name (surname, family name)

Each author on the list must have an affiliation. The affiliation includes department, university, or organizational affiliation and its location, including city, state/province (if applicable), and country. Authors have the option to include a current address in addition to the address of their affiliation at the time of the study. The current address should be listed in the byline and clearly labeled “current address.” At a minimum, the address must include the author’s current institution, city, and country.

If an author has multiple affiliations, enter all affiliations on the title page only. In the submission system, enter only the preferred or primary affiliation. Author affiliations will be listed in the typeset PDF article in the same order that authors are listed in the submission.

Author names will be published exactly as they appear in the manuscript file. Please double-check the information carefully to make sure it is correct.

Corresponding author

The submitting author is automatically designated as the corresponding author in the submission system. The corresponding author is the primary contact for the journal office and the only author able to view or change the manuscript while it is under editorial consideration.

The corresponding author role may be transferred to another coauthor. However, note that transferring the corresponding author role also transfers access to the manuscript. (To designate a new corresponding author while the manuscript is still under consideration, watch the video tutorial below.)

Only one corresponding author can be designated in the submission system, but this does not restrict the number of corresponding authors that may be listed on the article in the event of publication. Whoever is designated as a corresponding author on the title page of the manuscript file will be listed as such upon publication. Include an email address for each corresponding author listed on the title page of the manuscript.

Consortia and group authorship

If a manuscript is submitted on behalf of a consortium or group, include its name in the manuscript byline. Do not add it to the author list in the submission system. You may include the full list of members in the Acknowledgments or in a supporting information file.

PubMed only indexes individual consortium or group author members listed in the article byline. If included, these individuals must qualify for authorship according to our [criteria](#).

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Author contributions

Provide at minimum one contribution for each author in the submission system. Use the CRediT taxonomy to describe each contribution. [Read the policy and the full list of roles.](#)

Contributions will be published with the final article, and they should accurately reflect contributions to the work. The submitting author is responsible for completing this information at submission, and we expect that all authors will have reviewed, discussed, and agreed to their individual contributions ahead of this time.

PLOS ONE will contact all authors by email at submission to ensure that they are aware of the submission.

Cover letter

Upload a cover letter as a separate file in the online system. The length limit is 1 page.

The cover letter should include the following information:

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- Relate the study to previously published work
- Specify the type of article (for example, research article, systematic review, meta-analysis, clinical trial)
- Describe any prior interactions with PLOS regarding the submitted manuscript
- Suggest appropriate Academic Editors to handle your manuscript ([see the full list of Academic Editors](#))
- List any opposed reviewers

IMPORTANT: Do not include requests to reduce or waive publication fees in the cover letter. This information will be entered separately in the online submission system.

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Title page

The title, authors, and affiliations should all be included on a title page as the first page of the manuscript file.

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Abstract

The Abstract comes after the title page in the manuscript file. The abstract text is also entered in a separate field in the submission system.

The Abstract should:

- Describe the main objective(s) of the study
- Explain how the study was done, including any model organisms used, without methodological detail
- Summarize the most important results and their significance
- Not exceed 300 words

Abstracts should not include:

- Citations

- Abbreviations, if possible

Introduction

The introduction should:

- Provide background that puts the manuscript into context and allows readers outside the field to understand the purpose and significance of the study
- Define the problem addressed and why it is important
- Include a brief review of the key literature
- Note any relevant controversies or disagreements in the field
- Conclude with a brief statement of the overall aim of the work and a comment about whether that aim was achieved

Materials and Methods

The Materials and Methods section should provide enough detail to allow suitably skilled investigators to fully replicate your study. Specific information and/or protocols for new methods should be included in detail. If materials, methods, and protocols are well established, authors may cite articles where those protocols are described in detail, but the submission should include sufficient information to be understood independent of these references.

Supporting reproducibility with protocols

To enhance the reproducibility of your results, we recommend and encourage you to make your protocols public. There are several options:

Protocols associated with Research Articles

Protocol documents may be uploaded as Supporting Information or linked from the Methods section of the article. For laboratory protocols, we recommend protocols.io. Include the DOI link in the Methods section of your manuscript using the following format:

[http://dx.doi.org.uea.idm.oclc.org/10.17504/protocols.io.\[PROTOCOL DOI\]](http://dx.doi.org.uea.idm.oclc.org/10.17504/protocols.io.[PROTOCOL DOI]). This allows editors and reviewers to consult the detailed step-by-step protocol when evaluating your manuscript. You can choose to keep the protocol private on the protocols.io platform until your article is published—at which time it will be published automatically.

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PLOS ONE offers two options for publishing stand-alone protocol articles: Lab Protocols that describe reusable methodologies and Study Protocols that describe detailed plans and proposals for research projects. Specific guidelines apply to the submission of [Lab Protocol](#) and [Study Protocol](#) manuscripts. Read the detailed instructions for submitting [Lab Protocols](#) and [Study Protocols](#).

Results, Discussion, Conclusions

These sections may all be separate, or may be combined to create a mixed Results/Discussion section (commonly labeled “Results and Discussion”) or a mixed Discussion/Conclusions section (commonly labeled “Discussion”). These sections may be further divided into subsections, each with a concise subheading, as appropriate. These sections have no word limit, but the language should be clear and concise.

Together, these sections should describe the results of the experiments, the interpretation of these results, and the conclusions that can be drawn.

Authors should explain how the results relate to the hypothesis presented as the basis of the study and provide a succinct explanation of the implications of the findings, particularly in relation to previous related studies and potential future directions for research.

PLOS ONE editorial decisions do not rely on perceived significance or impact, so authors should avoid overstating their conclusions. See the [PLOS ONE Criteria for Publication](#) for more information.

Acknowledgments

Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution.

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PLOS journals publicly acknowledge the indispensable efforts of our editors and reviewers on an annual basis. To ensure equitable recognition and avoid any appearance of partiality, do not include editors or peer reviewers—named or unnamed—in the Acknowledgments.

Do not include funding sources in the Acknowledgments or anywhere else in the manuscript file. Funding information should only be entered in the financial disclosure section of the submission system.

References

Any and all available works can be cited in the reference list. Acceptable sources include:

- Published or accepted manuscripts
- Manuscripts on preprint servers, providing the manuscript has a citable DOI or arXiv URL.

Do not cite the following sources in the reference list:

- Unavailable and unpublished work, including manuscripts that have been submitted but not yet accepted (e.g., “unpublished work,” “data not shown”). Instead, include those data as supplementary material or deposit the data in a publicly available database.
- Personal communications (these should be supported by a letter from the relevant authors but not included in the reference list)
- Submitted research should not rely upon retracted research. You should avoid citing retracted articles unless you need to discuss retracted work to provide historical context for your submitted research. If it is necessary to discuss retracted work, state the article’s retracted status in your article’s text and reference list.

Ensure that your reference list includes full and current bibliography details for every cited work at the time of your article’s submission (and publication, if accepted). If cited work is corrected, retracted, or marked with an expression of concern before your article is published, and if you feel it is appropriate to cite the work even in light of the post-publication notice, include in your manuscript citations and full references for both the affected article and the post-publication notice. Email the journal office if you have questions.

References are listed at the end of the manuscript and numbered in the order that they appear in the text. In the text, cite the reference number in square brackets (e.g., “We used the techniques developed by our colleagues [19] to analyze the data”). PLOS uses the numbered citation (citation-sequence) method and first six authors, et al.

Do not include citations in abstracts.

Make sure the parts of the manuscript are in the correct order *before* ordering the citations.

Formatting references

Because all references will be linked electronically as much as possible to the papers they cite, proper formatting of references is crucial.

PLOS uses the reference style outlined by the International Committee of Medical Journal Editors (ICMJE), also referred to as the “Vancouver” style. Example formats are listed below. Additional examples are in the [ICMJE sample references](#).

A reference management tool, EndNote, offers a current [style file](#) that can assist you with the formatting of your references. If you have problems with any reference management program, please contact the source company's technical support.

Journal name abbreviations should be those found in the [National Center for Biotechnology Information \(NCBI\) databases](#).

Source	Format
Published articles	<p>Hou WR, Hou YL, Wu GF, Song Y, Su XL, Sun B, et al. cDNA, genomic sequence cloning and overexpression of ribosomal protein gene L9 (rpL9) of the giant panda (<i>Ailuropoda melanoleuca</i>). <i>Genet Mol Res</i>. 2011;10: 1576-1588.</p> <p>Devaraju P, Gulati R, Antony PT, Mithun CB, Negi VS. Susceptibility to SLE in South Indian Tamils may be influenced by genetic selection pressure on TLR2 and TLR9 genes. <i>Mol Immunol</i>. 2014 Nov 22. pii: S0161-5890(14)00313-7. doi: 10.1016/j.molimm.2014.11.005.</p> <p>Note: A DOI number for the full-text article is acceptable as an alternative to or in addition to traditional volume and page numbers. When providing a DOI, adhere to the format in the example above with both the label and full DOI included at the end of the reference (doi: 10.1016/j.molimm.2014.11.005). Do not provide a shortened DOI or the URL.</p>
Accepted, unpublished articles	Same as published articles, but substitute “Forthcoming” for page numbers or DOI.
Online articles	Huynen MMTE, Martens P, Hilderlink HBM. The health impacts of globalisation: a conceptual framework. <i>Global Health</i> . 2005;1: 14. Available from: http://www.globalizationandhealth.com/content/1/1/14
Books	Bates B. <i>Bargaining for life: A social history of tuberculosis</i> . 1st ed. Philadelphia: University of Pennsylvania Press; 1992.
Book chapters	Hansen B. New York City epidemics and history for the public. In: Harden VA, Risse GB, editors. <i>AIDS and the historian</i> . Bethesda: National Institutes of Health; 1991. pp. 21-28.
Deposited articles (preprints, e-prints, or arXiv)	Krick T, Shub DA, Verstraete N, Ferreiro DU, Alonso LG, Shub M, et al. Amino acid metabolism conflicts with protein diversity. arXiv:1403.3301v1 [Preprint]. 2014 [cited 2014 March 17]. Available from: https://128.84.21.199/abs/1403.3301v1

Source	Format
	Kording KP, Mensh B. Ten simple rules for structuring papers. BioRxiv [Preprint]. 2016 bioRxiv 088278 [posted 2016 Nov 28; revised 2016 Dec 14; revised 2016 Dec 15; cited 2017 Feb 9]: [12 p.]. Available from: https://www.biorxiv.org/content/10.1101/088278v5 doi: 10.1101/088278
Published media (print or online newspapers and magazine articles)	Fountain H. For Already Vulnerable Penguins, Study Finds Climate Change Is Another Danger. The New York Times. 2014 Jan 29 [Cited 2014 March 17]. Available from: http://www.nytimes.com/2014/01/30/science/earth/climate-change-taking-toll-on-penguins-study-finds.html
New media (blogs, web sites, or other written works)	Allen L. Announcing PLOS Blogs. 2010 Sep 1 [cited 17 March 2014]. In: PLOS Blogs [Internet]. San Francisco: PLOS 2006 - . [about 2 screens]. Available from: http://blogs.plos.org.uea.idm.oclc.org/plos/2010/09/announcing-plos-blogs/ .
Masters' theses or doctoral dissertations	Wells A. Exploring the development of the independent, electronic, scholarly journal. M.Sc. Thesis, The University of Sheffield. 1999. Available from: http://cumincad.scix.net/cgi-bin/works/Show?2e09
Databases and repositories (Figshare, arXiv)	Roberts SB. QPX Genome Browser Feature Tracks; 2013 [cited 2013 Oct 5]. Database: figshare [Internet]. Available from: http://figshare.com/articles/QPX_Genome_Browser_Feature_Tracks/701214
Multimedia (videos, movies, or TV shows)	Hitchcock A, producer and director. Rear Window [Film]; 1954. Los Angeles: MGM.

Supporting information

Authors can submit essential supporting files and multimedia files along with their manuscripts. All supporting information will be subject to peer review. All file types can be submitted, but files must be smaller than 20 MB in size.

Authors may use almost any description as the item name for a supporting information file as long as it contains an “S” and number. For example, “S1 Appendix” and “S2 Appendix,” “S1 Table” and “S2 Table,” and so forth.

Supporting information files are published exactly as provided, and are not copyedited.

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List supporting information captions at the end of the manuscript file. Do not submit captions in a separate file.

The file number and name are required in a caption, and we highly recommend including a one-line title as well. You may also include a legend in your caption, but it is not required.

Example caption

S1 Text. Title is strongly recommended. Legend is optional.

In-text citations

We recommend that you cite supporting information in the manuscript text, but this is not a requirement. If you cite supporting information in the text, citations do not need to be in numerical order.

Read the [supporting information guidelines](#) for more details about submitting supporting information and multimedia files.

Figures and tables

Figures

Do not include figures in the main manuscript file. Each figure must be prepared and submitted as an individual file.

Cite figures in ascending numeric order at first appearance in the manuscript file.

[Read the guidelines for figures](#) and [requirements for reporting blot and gel results](#).

Figure captions

Figure captions must be inserted in the text of the manuscript, immediately following the paragraph in which the figure is first cited (read order). Do not include captions as part of the figure files themselves or submit them in a separate document.

At a minimum, include the following in your figure captions:

- A figure label with Arabic numerals, and “Figure” abbreviated to “Fig” (e.g. Fig 1, Fig 2, Fig 3, etc). Match the label of your figure with the name of the file uploaded at submission (e.g. a figure citation of “Fig 1” must refer to a figure file named “Fig1.tif”).
- A concise, descriptive title

The caption may also include a legend as needed.

[Read more about figure captions](#).

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Tables require a label (e.g., “Table 1”) and brief descriptive title to be placed above the table. Place legends, footnotes, and other text below the table.

[Read the guidelines for tables](#).

Statistical reporting

Manuscripts submitted to *PLOS ONE* are expected to report statistical methods in sufficient detail for others to replicate the analysis performed. Ensure that results are rigorously reported in accordance with community standards and that statistical methods employed are appropriate for the study design.

Consult the following resources for additional guidance:

- [SAMPL guidelines](#), for general guidance on statistical reporting
- [PLOS ONE guidelines](#), for clinical trials requirements
- [PLOS ONE guidelines](#), for systematic review and meta-analysis requirements

- [EQUATOR](#), for specific reporting guidelines for a range of other study types

Reporting of statistical methods

In the methods, include a section on statistical analysis that reports a detailed description of the statistical methods. In this section:

- List the name and version of any software package used, alongside any relevant references
- Describe technical details or procedures required to reproduce the analysis
- Provide the repository identifier for any code used in the analysis (See our [code-sharing policy](#).)

Statistical reporting guidelines:

- Identify research design and independent variables as being between- or within-subjects
- For pre-processed data:
 - Describe any analysis carried out to confirm the data meets the assumptions of the analysis performed (e.g. linearity, co-linearity, normality of the distribution).
 - If data were transformed include this information, with a reason for doing so and a description of the transformation performed
- Provide details of how outliers were treated and your analysis, both with the full dataset and with the outliers removed
- If relevant, describe how missing/excluded data were handled
- Define the threshold for significance (alpha)
- If appropriate, provide sample sizes, along with a description of how they were determined. If a sample size calculation was performed, specify the inputs for power, effect size and alpha. Where relevant, report the number of independent replications for each experiment.
- For analyses of variance (ANOVAs), detail any post hoc tests that were performed
- Include details of any corrections applied to account for multiple comparisons. If corrections were not applied, include a justification for not doing so
- Describe all options for statistical procedures. For example, if t-tests were performed, state whether these were one- or two-tailed. Include details of the type of t-test conducted (e.g. one sample, within-/between-subjects).
- For step-wise multiple regression analyses:
 - Report the alpha level used
 - Discuss whether the variables were assessed for collinearity and interaction
 - Describe the variable selection process by which the final model was developed (e.g., forward-stepwise; best subset). [See SAMPL guidelines](#).
- For Bayesian analysis explain the choice of prior trial probabilities and how they were selected. Markov chain Monte Carlo settings should be reported.

Reporting of statistical results

Results must be rigorously and appropriately reported, in keeping with community standards.

- **Units of measurement.** Clearly define measurement units in all tables and figures.
- **Properties of distribution.** It should be clear from the text which measures of variance (standard deviation, standard error of the mean, confidence intervals) and central tendency (mean, median) are being presented.
- **Regression analyses.** Include the full results of any regression analysis performed as a supplementary file. Include all estimated regression coefficients, their standard error, p-values, and confidence intervals, as well as the measures of goodness of fit.
- **Reporting parameters.** Test statistics (F/t/r) and associated degrees of freedom should be provided. Effect sizes and confidence intervals should be reported where appropriate. If percentages are provided, the numerator and denominator should also be given.
- **P-values.** Report exact p-values for all values greater than or equal to 0.001. P-values less than 0.001 may be expressed as $p < 0.001$, or as exponentials in studies of genetic associations.

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Data reporting

All data and related metadata underlying the findings reported in a submitted manuscript should be deposited in an appropriate public repository, unless already provided as part of the submitted article.

See [instructions on providing underlying data to support blot and gel results](#).

[Read our policy on data availability](#).

Repositories may be either subject-specific (where these exist) and accept specific types of structured data, or generalist repositories that accept multiple data types. We recommend that authors select repositories appropriate to their field. Repositories may be subject-specific (e.g., GenBank for sequences and PDB for structures), general, or institutional, as long as DOIs or accession numbers are provided and the data are at least as open as CC BY. Authors are encouraged to select repositories that meet accepted criteria as trustworthy digital repositories, such as criteria of the Centre for Research Libraries or Data Seal of Approval. Large, international databases are more likely to persist than small, local ones.

[See our list of recommended repositories](#).

To support data sharing and author compliance of the PLOS data policy, we have integrated our submission process with a select set of data repositories. The list is neither representative nor exhaustive of the suitable repositories available to authors. Current repository integration partners include [Dryad](#) and [FlowRepository](#). Please contact data@plos.org to make recommendations for further partnerships.

Instructions for PLOS submissions with data deposited in an integration partner repository:

- Deposit data in the integrated repository of choice.
- Once deposition is final and complete, the repository will provide you with a dataset DOI (provisional) and private URL for reviewers to gain access to the data.
- Enter the given data DOI into the full Data Availability Statement, which is requested in the Additional Information section of the PLOS submission form. Then provide the URL passcode in the Attach Files section.

If you have any questions, please [email us](#).

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All appropriate data sets, images, and information should be deposited in an appropriate public repository. [See our list of recommended repositories](#).

Accession numbers (and version numbers, if appropriate) should be provided in the Data Availability Statement. Accession numbers or a citation to the DOI should also be provided when the data set is mentioned within the manuscript.

In some cases authors may not be able to obtain accession numbers of DOIs until the manuscript is accepted; in these cases, the authors must provide these numbers at acceptance. In all other cases, these numbers must be provided at full submission.

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As much as possible, please provide accession numbers or identifiers for all entities such as genes, proteins, mutants, diseases, etc., for which there is an entry in a public database, for example:

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- [Entrez Gene](#)
- [FlyBase](#)
- [InterPro](#)
- [Mouse Genome Database \(MGD\)](#)
- [Online Mendelian Inheritance in Man \(OMIM\)](#)
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Additional Information Requested at Submission

Financial Disclosure Statement

This information should describe sources of funding that have supported the work. It is important to gather these details prior to submission because your financial disclosure statement cannot be changed after initial submission without journal approval. If your manuscript is published, your statement will appear in the Funding section of the article.

Enter this statement in the Financial Disclosure section of the submission form. Do not include it in your manuscript file.

The statement should include:

- Specific grant numbers
- Initials of authors who received each award
- Full names of commercial companies that funded the study or authors
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- URLs to sponsors’ websites

Also state whether any sponsors or funders (other than the named authors) played any role in:

- Study design
- Data collection and analysis
- Decision to publish
- Preparation of the manuscript

If they had no role in the research, include this sentence: “The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.”

If the study was unfunded, include this sentence as the Financial Disclosure statement: “The author(s) received no specific funding for this work.”

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Competing interests

This information should not be in your manuscript file; you will provide it via our submission system.

All potential competing interests must be declared in full. If the submission is related to any patents, patent applications, or products in development or for market, these details, including patent numbers and titles, must be disclosed in full.

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Manuscripts disputing published work

For manuscripts disputing previously published work, it is *PLOS ONE* policy to invite a signed review by the disputed author during the peer review process. This procedure is aimed at ensuring a thorough, transparent, and productive review process.

If the disputed author chooses to submit a review, it must be returned in a timely fashion and contain a full declaration of all competing interests. The Academic Editor will consider any such reviews in light of the competing interest.

Authors submitting manuscripts disputing previous work should explain the relationship between the manuscripts in their cover letter, and will be required to confirm that they accept the conditions of this review policy before the manuscript is considered further.

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Upon submission, authors must confirm that the manuscript, or any related manuscript, is not currently under consideration or accepted elsewhere. If related work has been submitted to *PLOS ONE* or elsewhere, authors must include a copy with the submitted article. Reviewers will be asked to comment on the overlap between related submissions.

We strongly discourage the unnecessary division of related work into separate manuscripts, and we will not consider manuscripts that are divided into “parts.” Each submission to *PLOS ONE* must be written as an independent unit and should not rely on any work that has not already been accepted for publication. If related manuscripts are submitted to *PLOS ONE*, the authors may be advised to combine them into a single manuscript at the editor's discretion.

Read our policies on [related manuscripts](#).

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Authors submitting manuscripts in the life and health sciences to *PLOS ONE* may choose to have PLOS forward their submission to bioRxiv or medRxiv, depending on the scope of the paper, for consideration for posting as a preprint.

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Guidelines for Specific Study Types

Study design, reporting, and analyses are assessed against all relevant research and methodological technique standards held by the community. Guidelines for specific study types are outlined below.

Registered Reports

Submission and format requirements for [Registered Report Protocols and Registered Reports](#) are similar to those for a regular submission and may be specific to your study type. For instance, if your Registered Report Protocol submission is about a Clinical Trial or a Systematic Review, follow the appropriate guidelines.

For Registered Report Protocols:

- Provide enough methodological detail to make the study reproducible and replicable
- Confirm that data will be made available upon study completion in keeping with the [PLOS Data policy](#)
- Include ethical approval or waivers, if applicable
- Preliminary or pilot data may be included, but only if necessary to support the feasibility of the study or as a proof of principle
- For meta-analyses or Clinical Trials, use the protocol-specific reporting guidelines [PRISMA-P](#) or [SPIRIT](#) respectively

For more guidance on format and presentation of a protocol, consult the [sample template hosted by the Open Science Framework](#). [Discipline-specific and study-specific templates](#) are also available.

If data need to be collected, modified or processed specifically for your study, or if participants need to be recruited specifically for your study, then it should occur only after your Registered Report Protocol is accepted for publication.

For Registered Report Research Articles:

- Report the results of all planned analyses and, if relevant, detail and justify all deviations from the protocol.
- The manuscript may also contain exploratory, unplanned analyses.

[Read more about Registered Report framework.](#)

Human subjects research

All research involving human participants must have been approved by the authors' Institutional Review Board (IRB) or by equivalent ethics committee(s), and must have been conducted according to the principles expressed in the [Declaration of Helsinki](#). Authors should be able to submit, upon request, a statement from the IRB or ethics committee indicating approval of the research. We reserve the right to reject work that we believe has not been conducted to a high ethical standard, even when formal approval has been obtained.

Subjects must have been properly instructed and have indicated that they consent to participate by

signing the appropriate informed consent paperwork. Authors may be asked to submit a blank, sample copy of a subject consent form. If consent was verbal instead of written, or if consent could not be obtained, the authors must explain the reason in the manuscript, and the use of verbal consent or the lack of consent must have been approved by the IRB or ethics committee.

All efforts should be made to protect patient privacy and anonymity. Identifying information, including photos, should not be included in the manuscript unless the information is crucial and the individual has provided written consent by completing the [Consent Form for Publication in a PLOS Journal \(PDF\)](#). Download additional translations of the form [here](#). More information about patient privacy, anonymity, and informed consent can be found in the [International Committee of Medical Journal Editors \(ICMJE\) Privacy and Confidentiality guidelines](#).

Manuscripts should conform to the following reporting guidelines:

- Studies of diagnostic accuracy: [STARD](#)
- Observational studies: [STROBE](#)
- Microarray experiments: [MIAME](#)
- Other types of health-related research: Consult the [EQUATOR](#) web site for appropriate reporting guidelines

Methods sections of papers on research using human subjects or samples must include ethics statements that specify:

- **The name of the approving institutional review board or equivalent committee(s).** If approval was not obtained, the authors must provide a detailed statement explaining why it was not needed
- **Whether informed consent was written or oral.** If informed consent was oral, it must be stated in the manuscript:
 - Why written consent could not be obtained
 - That the Institutional Review Board (IRB) approved use of oral consent
 - How oral consent was documented

For studies involving humans categorized by race/ethnicity, age, disease/disabilities, religion, sex/gender, sexual orientation, or other socially constructed groupings, authors should:

- Explicitly describe their methods of categorizing human populations
- Define categories in as much detail as the study protocol allows
- Justify their choices of definitions and categories, including for example whether any rules of human categorization were required by their funding agency
- Explain whether (and if so, how) they controlled for confounding variables such as socioeconomic status, nutrition, environmental exposures, or similar factors in their analysis

In addition, outmoded terms and potentially stigmatizing labels should be changed to more current, acceptable terminology. Examples: “Caucasian” should be changed to “white” or “of [Western] European descent” (as appropriate); “cancer victims” should be changed to “patients with cancer.”

For papers that include identifying, or potentially identifying, information, authors must [download the Consent Form for Publication in a PLOS Journal](#), which the individual, parent, or guardian must sign once they have read the paper and been informed about the terms of PLOS open-access license. The signed consent form should not be submitted with the manuscript, but authors should securely file it in the individual's case notes and the methods section of the manuscript should explicitly state that consent authorization for publication is on file, using wording like:

The individual in this manuscript has given written informed consent (as outlined in PLOS consent form) to publish these case details.

For more information about *PLOS ONE* policies regarding human subjects research, see the [Publication Criteria](#) and [Editorial Policies](#).

Manuscripts describing observational clinical studies are subject to all policies regarding [human research](#) and community standards for reporting observational research as outlined by the [STROBE](#) statement. Furthermore, authors submitting work of this nature should pay special attention to the following requirements:

- If the submitted manuscript is very similar to previous work, authors must provide a sound scientific rationale for the submitted work and clearly reference and discuss the existing literature.
- The sampling strategy and eligibility criteria of enrolled subjects should be described in sufficient detail.
- Sample size calculations should be justified with relevant inputs defined.
- Independent and dependent variables considered for statistical analysis should be clearly defined and justified.
- The validity and reliability testing of self-developed data collection tools should be reported.
- Conclusions should be appropriate for the study design, with indications on how the study results will contribute to the base of academic knowledge.

Clinical trials

Clinical trials are subject to all [policies regarding human research](#). *PLOS ONE* follows the [World Health Organization's \(WHO\) definition of a clinical trial](#):

A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes [...] Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc.

All clinical trials must be registered in one of the publicly-accessible registries approved by the [WHO](#) or [ICMJE](#) (International Committee of Medical Journal Editors). Authors must provide the trial registration number. Prior disclosure of results on a clinical trial registry site will not affect consideration for publication. We reserve the right to inform authors' institutions or ethics committees, and to reject the manuscript, if we become aware of unregistered trials.

PLOS ONE supports prospective trial registration (i.e. before participant recruitment has begun) as recommended by the ICMJE's [clinical trial registration policy](#). **Where trials were not publicly registered before participant recruitment began**, authors must:

- Register all related clinical trials and confirm they have done so in the Methods section
- Explain in the Methods the reason for failing to register before participant recruitment

Clinical trials must be reported according to the relevant reporting guidelines, i.e. [CONSORT](#) for randomized controlled trials, [TREND](#) for non-randomized trials, and [other specialized guidelines](#) as appropriate. The intervention should be described according to the requirements of the [TIDieR checklist and guide](#). Submissions must also include the study protocol as supporting information, which will be published with the manuscript if accepted.

Authors of manuscripts describing the results of clinical trials must adhere to the [CONSORT](#) reporting guidelines appropriate to their trial design, available on the [CONSORT Statement web site](#). Before the paper can enter peer review, authors must:

- The name of the registry and the registration number must be included in the Abstract.

- Provide a copy of the trial protocol as approved by the ethics committee and a completed [CONSORT checklist](#) as supporting information (which will be published alongside the paper, if accepted). This should be named S1 CONSORT Checklist.
- Include the [CONSORT flow diagram](#) as the manuscript's "Fig 1"

Any deviation from the trial protocol must be explained in the paper. Authors must explicitly discuss informed consent in their paper, and we reserve the right to ask for a copy of the patient consent form.

The name of the registry and the registry number must be provided in the Abstract. If the trial is registered in more than one location, please provide all relevant registry names and numbers.

Study Protocols

[Study Protocols](#) describe plans for conducting research projects and consist of a single article on *PLOS ONE*.

Study Protocols must comply with the *PLOS ONE* general submission guidelines (detailed above in this article) and any guidelines specific to the related research study type. In addition, the protocol must:

- Relate to a research study that has not yet generated results.
- Be submitted before recruitment of participants or collection of data for the study is complete.
- Meet the same standards for [ethics of experimentation and research integrity](#) as the research study. If it involves [human](#) or [animal](#) subjects, [cell lines](#) or [field sampling](#), or has [potential biosafety implications](#), prior approval from the relevant ethics body must be obtained prior to submission. Please contact us if you have a valid reason for not obtaining approval.

Additional prerequisites apply for these study types:

- [Clinical trials](#):
 - The trial must be registered prior to submission of your protocol in one of the publicly accessible registries approved by the WHO or ICMJE (International Committee of Medical Journal Editors).
 - The name of the registry and the trial or study registration number must be included in the Abstract.
 - A copy of the protocol that was approved by the ethics committee must be submitted as a supplementary information file. Please provide an additional English translation if the original document is not in English. Please note that the protocol will be published with the manuscript if accepted.
 - A SPIRIT [schedule of enrollment, interventions, and assessments](#) must be included as the manuscript's Figure 1, and a completed [SPIRIT checklist](#) must be uploaded as Supporting Information file S1.
- [Systematic reviews and meta-analyses](#):
 - A completed [PRISMA-P checklist](#) must be provided as a supporting information (SI) file. See [PRISMA-P Explanation and Elaboration](#) for more information on completing your checklist.

Study Protocols must also comply with general *PLOS ONE* [criteria for publication](#) and in addition you should:

- include the word "Protocol" in your Title.
- include a detailed description of the planned study in the Materials and Methods section. This should provide sufficient methodological detail for the protocol to be reproducible and replicable. Your description should cover all relevant and applicable facts and hypothesis, including:

- the aim, design, and settling
- the sample size calculation
- how data saturation will be determined (for qualitative studies)
- the characteristics of participants e.g., inclusion and exclusion criteria, sample selection criteria, variables to be measured, randomization and blinding criteria (where applicable), and how informed consent will be obtained
- how materials will be selected and used e.g., where and how they will be sourced, the processes, interventions, or comparisons to be used, the outcomes to be measured, and when and how they will be measured
- the data management plan
- safety considerations
- the type of data and statistical analyses to be used
- the status and timeline of the study, including whether participant recruitment or data collection has begun
- where and when the data will be made available. See our [Data Availability policy](#) for more.
- include an analysis of preliminary or pilot data, only if it is necessary to support the feasibility of the study or as a proof of principle. This is optional.
- we encourage authors you to register with [OSF](#) and provide the your registration number in the Materials and Methods section. This is optional.
- optionally add any other SI files, figures or tables that elaborate or authenticate the protocol: e.g., any reporting checklists applicable to your study type.

Read the [supporting information guidelines](#) for more details about adding SI files.

Download [our sample Study Protocol template](#) or an OSF [discipline or study-specific template](#).

Study Protocols are subject to the same [editorial](#) and [peer review](#) process as all other articles, and are eligible for both [signed and published peer review](#).

You can expedite the review process by providing:

- proof of external funding. This is typically your funding approval letter and a list of the names and credentials of the funders who conducted the external peer review of the protocol. Include an English translation if needed.
- proof of ethics approval (if required). This is typically the approval or waiver letter from the relevant ethics body and a copy of the protocol approved by this body.

The proof of external funding and approval or waiver letter are used for internal purposes and do not form part of the published Study Protocol.

Expedited review is conducted by an internal Staff Editor only and bypasses the external review process.

If the Study Protocol describes a replication study or involves re-analysis of published work, we will invite the author of the initial or replicated study to provide a signed review.

We encourage you to share your Study Protocol with other researchers, either before or after submission. You can publish it on your website or [protocols.io](#), or submit it for posting on [medRxiv](#) or another preprint server.

Observational and field studies

Methods sections for submissions reporting on any type of field study must include ethics statements that specify:

- Permits and approvals obtained for the work, including the full name of the authority that approved the study; if none were required, authors should explain why

- Whether the land accessed is privately owned or protected
- Whether any protected species were sampled
- Full details of animal husbandry, experimentation, and care/welfare, where relevant

Systematic reviews and meta-analyses

A systematic review paper, as defined by [The Cochrane Collaboration](#), is a review of a clearly formulated question that uses explicit, systematic methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review. These reviews differ substantially from narrative-based reviews or synthesis articles. Statistical methods (meta-analysis) may or may not be used to analyze and summarize the results of the included studies.

Reports of systematic reviews and meta-analyses should include a completed [PRISMA \(Preferred Reporting Items for Systematic Reviews and Meta-Analyses\)](#) checklist and flow diagram to accompany the main text. Blank templates are available here:

- Checklist: [PDF](#) or [Word document](#)
- Flow diagram: [PDF](#) or [Word document](#)

Authors must also state in their “Methods” section whether a protocol exists for their systematic review, and if so, provide a copy of the protocol as supporting information and provide the registry number in the abstract.

If your article is a systematic review or a meta-analysis you should:

- State this in your cover letter
- Select “Research Article” as your article type when submitting
- Include the PRISMA flow diagram as Fig 1 (required where applicable)
- Include the PRISMA checklist as supporting information

Meta-analysis of genetic association studies

Manuscripts reporting a meta-analysis of genetic association studies must report results of value to the field and should be reported according to the guidelines presented in [Systematic Reviews of Genetic Association Studies](#) by Sagoo *et al.*

On submission, authors will be asked to justify the rationale for the meta-analysis and how it contributes to the base of scientific knowledge in the light of previously published results. Authors will also be asked to complete a [checklist \(DOCX\)](#) outlining information about the justification for the study and the methodology employed. Meta-analyses that replicate published studies will be rejected if the authors do not provide adequate justification.

Personal data from third-party sources

For all studies using personal data from internet-based and other third-party sources (e.g., social media, blogs, other internet sources, mobile phone companies), data must be collected and used according to company/website Terms and Conditions, with appropriate permissions. All data sources must be acknowledged clearly in the [Materials and Methods section](#).

[Read our policy on data availability.](#)

In the Ethics Statement, authors should declare any potential risks to individuals or individual privacy, or affirm that in their assessment, the study posed no such risks. In addition, the following Ethics and Data Protection requirements must be met.

For interventional studies, which impact participants' experiences or data, the study design must have been prospectively approved by an Ethics Committee, and informed consent is required. The Ethics Committee may waive the requirement for approval and/or consent.

For observational studies in which personal experiences and accounts are not manipulated, consultation with an Ethics or Data Protection Committee is recommended. Additional requirements apply in the following circumstances:

- If information used could threaten personal privacy or damage the reputation of individuals whose data are used, an Ethics Committee should be consulted and informed consent obtained or specifically addressed.
- If authors accessed any personal identifying information, an Ethics or Data Protection Committee should oversee data anonymization. If data were anonymized and/or aggregated before access and analysis, informed consent is generally not required.

Note that Terms of Use contracts do not qualify as informed consent, even if they address the use of personal data for research.

[See our reporting guidelines for human subjects research.](#)

Methods, software, databases, and tools

PLOS ONE will consider submissions that present new methods, software, databases, or tools as the primary focus of the manuscript if they meet the following criteria:

Utility

The tool must be of use to the community and must present a proven advantage over existing alternatives, where applicable. Recapitulation of existing methods, software, or databases is not useful and will not be considered for publication. Combining data and/or functionalities from other sources may be acceptable, but simpler instances (i.e. presenting a subset of an already existing database) may not be considered. For software, databases, and online tools, the long-term utility should also be discussed, as relevant. This discussion may include maintenance, the potential for future growth, and the stability of the hosting, as applicable.

Validation

Submissions presenting methods, software, databases, or tools must demonstrate that the new tool achieves its intended purpose. If similar options already exist, the submitted manuscript must demonstrate that the new tool is an improvement over existing options in some way. This requirement may be met by including a proof-of-principle experiment or analysis; if this is not possible, a discussion of the possible applications and some preliminary analysis may be sufficient.

Availability

If the manuscript's primary purpose is the description of new software or a new software package, this software must be open source, deposited in an appropriate archive, and conform to the [Open Source Definition](#). If the manuscript mainly describes a database, this database must be open-access and hosted somewhere publicly accessible, and any software used to generate a database should also be open source. If relevant, databases should be open for appropriate deposition of additional data. Dependency on commercial software such as Mathematica and MATLAB does not preclude a paper from consideration, although complete open source solutions are preferred. In these cases, authors should provide a direct link to the deposited software or the database hosting site from within the paper. If the primary focus of a manuscript is the presentation of a new tool, such as a newly

developed or modified questionnaire or scale, it should be openly available under a license no more restrictive than CC BY.

Software submissions

Manuscripts whose primary purpose is the description of new software must provide full details of the algorithms designed. Describe any dependencies on commercial products or operating system. Include details of the supplied test data and explain how to install and run the software. A brief description of enhancements made in the major releases of the software may also be given. Authors should provide a direct link to the deposited software from within the paper.

Database submissions

For descriptions of databases, provide details about how the data were curated, as well as plans for long-term database maintenance, growth, and stability. Authors should provide a direct link to the database hosting site from within the paper.

[Read the PLOS policy on sharing materials, software and code.](#)

Appendix B. PRISMA Checklist (Paige et al., 2020)

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			Pages
Title	1	Identify the report as a systematic review.	13
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	14,15
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	16-18
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	18,19
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	21-23. 25
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	19
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	19,20, 194-198
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	23
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	24,25
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	24,25
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	24,25
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	23,24
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	25
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	25
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	25
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias	14	Describe any methods used to assess risk of bias due to missing results in a synthesis	23,24

Section and Topic	Item #	Checklist item	Location where item is reported
assessment		(arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	26-28
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	N/A
Study characteristics	17	Cite each included study and present its characteristics.	30-36
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	204,205
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	42-44
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	37-62
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	41-62
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	40,41, 204,205
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	67-70
	23b	Discuss any limitations of the evidence included in the review.	64-66
	23c	Discuss any limitations of the review processes used.	66,67
	23d	Discuss implications of the results for practice, policy, and future research.	67-71
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	19
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	19
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	N/A
Competing interests	26	Declare any competing interests of review authors.	Not reported
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not reported

Appendix C. Search Strategies for Each Database

Table C1.

Search Strategy used in PubMed.

(("longitudinal"[Title/Abstract] OR "follow-up"[Title/Abstract] OR "follow-up"[Title/Abstract] OR "course"[Title/Abstract] OR "trajector*"[Title/Abstract] OR "cohort"[Title/Abstract] OR "prospective"[Title/Abstract] OR "clinical stag*"[Title/Abstract]) AND (("mental health illness*"[Title/Abstract] OR "mental illness*"[Title/Abstract] OR "mental health disorder*"[Title/Abstract] OR "mental disorder*"[Title/Abstract] OR "mental health diagnos*"[Title/Abstract] OR "mental disease*"[Title/Abstract] OR "mental health disease*"[Title/Abstract] OR "psychological disorder*"[Title/Abstract] OR "psychological illness*"[Title/Abstract] OR "psychiatric disorder*"[Title/Abstract] OR "psychiatric diagnos*"[Title/Abstract] OR "psychiatric illness*"[Title/Abstract] OR "psychiatric disease*"[Title/Abstract] OR "psychos*"[Title/Abstract] OR "psychotic"[Title/Abstract] OR "personality disorder*"[Title/Abstract] OR "schizo*"[Title/Abstract] OR "bipolar"[Title/Abstract] OR "depression"[Title/Abstract] OR "anxiety"[Title/Abstract] OR "mania"[Title/Abstract] OR "manic"[Title/Abstract]) AND ("severe"[Title/Abstract] OR "serious"[Title/Abstract] OR "co morbid*"[Title/Abstract] OR "comorbid*"[Title/Abstract] OR "complex*"[Title/Abstract] OR "stage 1b"[Title/Abstract] OR "attenuated syndromes"[Title/Abstract] OR "stage 2"[Title/Abstract] OR "full-threshold disorder"[Title/Abstract] OR "full-threshold disorders"[Title/Abstract] OR "stage 3"[Title/Abstract] OR "stage 4"[Title/Abstract])) AND ("functioning"[Title/Abstract] OR "functional outcome*"[Title/Abstract] OR "social activit*"[Title/Abstract] OR "social outcome*"[Title/Abstract] OR "employment"[Title/Abstract] OR "time use"[Title/Abstract] OR "structured activit*"[Title/Abstract] OR "social disability"[Title/Abstract] OR "socially disabled"[Title/Abstract] OR "social impairment"[Title/Abstract] OR "functional impairment"[Title/Abstract] OR "social withdrawal"[Title/Abstract] OR "socially withdrawn"[Title/Abstract] OR "social exclusion"[Title/Abstract] OR "socially excluded"[Title/Abstract] OR "social isolation"[Title/Abstract] OR "socially isolated"[Title/Abstract] OR "NEET"[Title/Abstract] OR "unemploy*"[Title/Abstract] OR "economic inactiv*"[Title/Abstract] OR "economically inactiv*"[Title/Abstract] OR "out of work"[Title/Abstract] OR "student attendance"[Title/Abstract] OR "college attendance"[Title/Abstract] OR "non-attendance"[Title/Abstract] OR "absenteeism"[Title/Abstract] OR "student withdrawal"[Title/Abstract]) AND ("juvenile"[Title/Abstract] OR "young adult*"[Title/Abstract] OR "adolescen*"[Title/Abstract] OR "young people*"[Title/Abstract] OR "young person*"[Title/Abstract] OR "youth"[Title/Abstract] OR "student"[Title/Abstract] OR "undergraduate"[Title/Abstract] OR "child*"[Title/Abstract] OR "emerging adult*"[Title/Abstract] OR "early adult"[Title/Abstract] OR "teen*"[Title/Abstract] OR "pediatric*"[Title/Abstract] OR "paediatric*"[Title/Abstract]) Filters: English

Table C2.*Search Strategy used in Web of Science.*

1: (TI=(“mental health illness*” OR “mental illness*” OR “mental health disorder*” OR “mental disorder*” OR “mental health diagnos*” OR “mental disease*” OR “mental health disease*” OR "psychological disorder*" OR “psychological illness*” OR “psychiatric disorder*” OR “psychiatric diagnos*” OR “psychiatric illness*” OR “psychiatric disease*” OR psychos* OR psychotic OR “personality disorder*” OR schizo* OR bipolar OR depression OR anxiety OR mania OR manic)) OR AB=(“mental health illness*” OR “mental illness*” OR “mental health disorder*” OR “mental disorder*” OR “mental health diagnos*” OR “mental disease*” OR “mental health disease*” OR "psychological disorder*" OR “psychological illness*” OR “psychiatric disorder*” OR “psychiatric diagnos*” OR “psychiatric illness*” OR “psychiatric disease*” OR psychos* OR psychotic OR “personality disorder*” OR schizo* OR bipolar OR depression OR anxiety OR mania OR manic)
2: (TI=(“severe” OR “serious” OR “co-morbid*” OR “comorbid*” OR “complex*” OR “stage 1b” OR “attenuated syndromes” OR “stage 2” OR “full-threshold disorder” OR “full-threshold disorders” OR “stage 3” OR “stage 4”)) OR AB=(“severe” OR “serious” OR “co-morbid*” OR “comorbid*” OR “complex*” OR “stage 1b” OR “attenuated syndromes” OR “stage 2” OR “full-threshold disorder” OR “full-threshold disorders” OR “stage 3” OR “stage 4”)
3: #1 AND #2
4: (TI=(“longitudinal” OR “follow-up” OR “follow up” OR “course” OR “trajector*” OR “cohort” OR “prospective” OR “clinical stag*”)) OR AB=(“longitudinal” OR “follow-up” OR “follow up” OR “course” OR “trajector*” OR “cohort” OR “prospective” OR “clinical stag*”)
5: (TI=(functioning OR “functional outcome*” OR “social activit*” OR “social outcome*” OR employment OR “time use” OR “structured activit*” OR “social disability” OR “socially disabled” OR “social impairment” OR “functional impairment” OR “social withdrawal” OR “socially withdrawn” OR “social exclusion” OR “socially excluded” OR “social isolation” OR “socially isolated” OR NEET OR “not in employment, education or training” OR unemploy* OR “economic inactiv*” OR “economically inactiv*” OR “out of work” OR “school attendance” OR “student attendance” OR “college attendance” OR “non-attendance” OR absenteeism OR truan* OR “student withdrawal”)) OR AB=(functioning OR “functional outcome*” OR “social activit*” OR “social outcome*” OR employment OR “time use” OR “structured activit*” OR “social disability” OR “socially disabled” OR “social impairment” OR “functional impairment” OR “social withdrawal” OR “socially withdrawn” OR “social exclusion” OR “socially excluded” OR “social isolation” OR “socially isolated” OR NEET OR “not in employment, education or training” OR unemploy* OR “economic inactiv*” OR “economically inactiv*” OR “out of work” OR “student attendance” OR “college attendance” OR “non-attendance” OR absenteeism OR “student withdrawal”)
6: (TI=(juvenile OR "young adult*" OR adolescen* OR "young people*" OR "young person*" OR youth OR student OR undergraduate OR child* OR “emerging adult*” OR “early adult” OR teen* OR p?ediatic*)) OR AB=(juvenile OR "young adult*" OR adolescen* OR "young people*" OR "young person*" OR youth OR student OR undergraduate OR child* OR “emerging adult*” OR “early adult” OR teen* OR p?ediatic*)

Table C3.*Search Strategy used in PsycInfo.*

#	Query	Limiters/Expanders
S1	TI (juvenile OR "young adult*" OR adolescen* OR "young people*" OR "young person*" OR youth OR student OR undergraduate OR child* OR "emerging adult*" OR "early adult" OR teen* OR pediatric* OR paediatric*) OR AB (juvenile OR "young adult*" OR adolescen* OR "young people*" OR "young person*" OR youth OR student OR undergraduate OR child* OR "emerging adult*" OR "early adult" OR teen* OR pediatric* OR paediatric*)	Limiters - Peer Reviewed; English language Search modes - Boolean/Phrase
S2	TI (functioning OR "functional outcome*" OR "social activit*" OR "social outcome*" OR employment OR "time use" OR "structured activit*" OR "social disability" OR "socially disabled" OR "social impairment" OR "functional impairment" OR "social withdrawal" OR "socially withdrawn" OR "social exclusion" OR "socially excluded" OR "social isolation" OR "socially isolated" OR NEET OR "not in employment, education or training" OR unemploy* OR "economic inactiv*" OR "economically inactiv*" OR "out of work" OR "student attendance" OR "college attendance" OR "non-attendance" OR absenteeism OR "student withdrawal") OR AB (functioning OR "functional outcome*" OR "social activit*" OR "social outcome*" OR employment OR "time use" OR "structured activit*" OR "social disability" OR "socially disabled" OR "social impairment" OR "functional impairment" OR "social withdrawal" OR "socially withdrawn" OR "social exclusion" OR "socially excluded" OR "social isolation" OR "socially isolated" OR NEET OR "not in employment, education or training" OR unemploy* OR "economic inactiv*" OR "economically inactiv*" OR "out of work" OR "student attendance" OR "college attendance" OR "non-attendance" OR absenteeism OR "student withdrawal")	Limiters - Peer Reviewed; English language Search modes - Boolean/Phrase
S3	TI ("mental health illness*" OR "mental illness*" OR "mental health disorder*" OR "mental disorder*" OR "mental health diagnos*" OR "mental disease*" OR "mental health disease*" OR "psychological disorder*" OR "psychological illness*" OR "psychiatric disorder*" OR "psychiatric diagnos*" OR "psychiatric illness*" OR "psychiatric disease*" OR psychos* OR psychotic OR "personality disorder*" OR schizo* OR bipolar OR depression OR anxiety OR mania OR manic) OR AB ("mental health illness*" OR "mental illness*" OR "mental health disorder*" OR "mental disorder*" OR "mental health	Limiters - Peer Reviewed; English language Search modes - Boolean/Phrase

	diagnos*" OR "mental disease*" OR "mental health disease*" OR "psychological disorder*" OR "psychological illness*" OR "psychiatric disorder*" OR "psychiatric diagnos*" OR "psychiatric illness*" OR "psychiatric disease*" OR psychos* OR psychotic OR "personality disorder*" OR schizo* OR bipolar OR depression OR anxiety OR mania OR manic)	
S4	TI ("severe" OR "serious" OR "co-morbid*" OR "comorbid*" OR "complex*" OR "stage 1b" OR "attenuated syndromes" OR "stage 2" OR "full-threshold disorder" OR "full-threshold disorders" OR "stage 3" OR "stage 4") OR AB ("severe" OR "serious" OR "co-morbid*" OR "comorbid*" OR "complex*" OR "stage 1b" OR "attenuated syndromes" OR "stage 2" OR "full-threshold disorder" OR "full-threshold disorders" OR "stage 3" OR "stage 4")	Limiters - Peer Reviewed; Language: English Search modes - Boolean/Phrase
S5	TI ("longitudinal" OR "follow-up" OR "follow up" OR "course" OR "trajector*" OR "cohort" OR "prospective" OR "clinical stag*") OR AB ("longitudinal" OR "follow-up" OR "follow up" OR "course" OR "trajector*" OR "cohort" OR "prospective" OR "clinical stag*")	Limiters - Peer Reviewed; English language Search modes - Boolean/Phrase
S6	S3 AND S4	Limiters - Peer Reviewed; English language Search modes - Boolean/Phrase
S7	S1 AND S2 AND S5 AND S6	Limiters - Peer Reviewed; English language Search modes - Boolean/Phrase

Table C4.

Search Strategy used in EMBASE.

1	(juvenile or "young adult*" or adolescen* or "young people*" or "young person*" or youth or student or undergraduate or child* or "emerging adult*" or "early adult" or teen* or pediatric* or paediatric*).ab. or (juvenile or "young adult*" or adolescen* or "young people*" or "young person*" or youth or student or undergraduate or child* or "emerging adult*" or "early adult" or teen* or pediatric* or paediatric*).ti.
2	(functioning or "functional outcome*" or "social activit*" or "social outcome*" or employment or "time use" or "structured activit*" or "social disability" or "socially disabled" or "social impairment" or "functional impairment" or "social withdrawal" or "socially withdrawn" or "social exclusion" or "socially excluded" or "social isolation" or "socially isolated" or NEET or "not in employment, education or training" or unemploy* or "economic inactiv*" or "economically inactiv*" or "out of work" or "student attendance" or "college attendance" or "non-attendance" or absenteeism or "student withdrawal").ab. or (functioning or "functional outcome*" or "social activit*" or "social outcome*" or employment or "time

	use" or "structured activit*" or "social disability" or "socially disabled" or "social impairment" or "functional impairment" or "social withdrawal" or "socially withdrawn" or "social exclusion" or "socially excluded" or "social isolation" or "socially isolated" or NEET or "not in employment, education or training" or unemploy* or "economic inactiv*" or "economically inactiv*" or "out of work" or "student attendance" or "college attendance" or "non-attendance" or absenteeism or "student withdrawal").ti.
3	("mental health illness*" or "mental illness*" or "mental health disorder*" or "mental disorder*" or "mental health diagnos*" or "mental disease*" or "mental health disease*" or "psychological disorder*" or "psychological illness*" or "psychiatric disorder*" or "psychiatric diagnos*" or "psychiatric illness*" or "psychiatric disease*" or psychos* or psychotic or "personality disorder*" or schizo* or bipolar or depression or anxiety or mania or manic).ab. or ("mental health illness*" or "mental illness*" or "mental health disorder*" or "mental disorder*" or "mental health diagnos*" or "mental disease*" or "mental health disease*" or "psychological disorder*" or "psychological illness*" or "psychiatric disorder*" or "psychiatric diagnos*" or "psychiatric illness*" or "psychiatric disease*" or psychos* or psychotic or "personality disorder*" or schizo* or bipolar or depression or anxiety or mania or manic).ti.
4	("severe" or "serious" or "co-morbid*" or "comorbid*" or "complex*" or "stage 1b" or "attenuated syndromes" or "stage 2" or "full-threshold disorder" or "full-threshold disorders" or "stage 3" or "stage 4").ab. or ("severe" or "serious" or "co-morbid*" or "comorbid*" or "complex*" or "stage 1b" or "attenuated syndromes" or "stage 2" or "full-threshold disorder" or "full-threshold disorders" or "stage 3" or "stage 4").ti.
5	("longitudinal" or "follow-up" or "follow up" or "course" or "trajector*" or "cohort" or "prospective" or "clinical stag*").ab. or ("longitudinal" or "follow-up" or "follow up" or "course" or "trajector*" or "cohort" or "prospective" or "clinical stag*").ti.
6	3 and 4
7	1 and 2 and 5 and 6
8	limit 7 to English language

Appendix D. Additional Characteristics of Included Studies

Table D1.

Additional Characteristics of Included Studies (N = 24).

ID	Author(s)	Aims	Mental Health Diagnostic & Symptom Measures	Retention and Attrition Details
1	Abdel-Baki et al. (2017)	To examine the influence of substance-use disorders course on functional and symptomatic outcomes as well as service use in FEP.	DSM-IV criteria for psychotic disorder diagnosis Symptoms: PANSS, CDSS	Among 268 patients admitted to the EIS, 56 (20.9%) declined to participate. Of the 212 FEP patients in the study, 21 (9.9%) were lost to follow-up at 1 year and 36 (17%) at 2 years. Final samples: at 1 year, n = 187; at 2 years, n = 166
2	Alameda et al. (2015)	To examine whether traumatic experiences occurring at an earlier age would induce a more severe and longer lasting impairment of functional level than trauma occurring later in early psychosis patients.	CAARMS for meeting psychosis threshold and diagnosis based on DSM-IV criteria	Follow-up data were available for 169 out of 225 patients (75%) during 36-month follow-up.
3	Alameda et al. (2017)	To investigate the mediating role of depressive symptoms on the relationship between childhood trauma and functional outcomes in early psychosis patients.	CAARMS for meeting psychosis threshold and diagnosis based on DSM-IV criteria Symptoms: MADRS, PANSS	Does not report attrition rates or the specific number of participants who completed each assessment point. Of the first 221 patients for which data was available at the time of the study, 12 patients were excluded due to age at exposure to trauma not being available, first exposure to trauma occurred during their prodromal phase, after psychosis onset or after age 16, resulting in the remaining data of 209 patients.
4	Amminger et al. (2020)	To investigate to determine whether changes in cell membrane n-3 PUFA levels predicted clinical outcomes at 6 months and 12 months in individuals at ultra-high risk for psychosis.	CAARMS criteria for ARMS status and transition to psychosis; Diagnoses (both psychotic and nonpsychotic) based on the Structured Clinical Interview for DSM-IV-TR Axis I Disorders Symptoms: CGI, BPRS, SANS, MADRS, YMRS CAARMS criteria for ARMS status	Of the 304 RCT participants, 285 (93.8%) had fatty acid data at baseline, and 218 (71.7%) had fatty acid data at baseline and a subsequent time point (209 at month 6; 9 at point of transition to psychosis). Participants with fatty acid data at 2 time points comprised the study sample of this biomarker analysis.
5	Berger et al. (2020)	To investigate the relationship between allostatic load and clinical outcomes in individuals at ultra-high risk for psychosis.	Symptoms: CGI, BPRS, SANS, MADRS, YMRS Diagnostic Interview for Psychosis for psychosis and substance use diagnoses	106 participants of the NEURAPRO study with allostatic load measure data; 6 months (n = 90); 12 months (n = 74) (69.8% of 106)
6	Burgher et al. (2023)	To investigate longitudinal changes in the cognitive control system in early psychosis participants comparing them to healthy controls.	Symptoms: PANSS	63.33% (N=19) with follow-up data were included in the study, compared to the N =30 recruited initially.

7	Cocchi et al. (2008)	To describe the structure and the organisation of an Italian programme specifically targeted at the early detection of and interventions for people with an onset of or at high risk of psychosis.	ICD-10 and DSM-IV criteria for FEP diagnoses; ERIRaos for early recognition of psychosis risk Symptoms and disability: HoNOS, BPRS and the CBA 2.0 (personality traits, neurotic symptoms, somatisation, anxiety, depression) DSM-IV criteria for both psychosis and non-psychosis diagnoses	70.83% (51/ 72) patients at FEP, and 70.42% (50/71) of those at high risk of psychosis were retained at follow-up.
8	Conus et al. (2017)	To identify predictors of symptomatic and functional outcome in those who are not exposed to an adequate dose of antipsychotic medication in FEP patients.	Symptoms: CGI-severity of illness scale DSM-IV criteria for initial psychosis diagnosis	Included data only from patients with existing files for the follow-up points. No report of the overall sample size of patients that were screened for inclusion.
9	Cotton et al. (2009)	To explore gender differences in premorbid, entry, treatment, and outcome characteristics in a treated epidemiological sample of patients with FEP.	Symptoms: CGI-Severity of Illness Scale, CGI-Severity of Illness Scale — Bipolar Illness Diagnosis based on DSM-IV criteria	82 of the initial files had been transferred to other services and 43 patients were excluded because they had a non-psychotic diagnosis at discharge. Data was therefore available on 661 patients.
10	Fraguas et al. (2014)	To estimate the influence of DUP on functional and clinical outcome at 2-year follow-up in subjects with early-onset FEP.	using the K-SADS, Present and Lifetime Version Symptoms: PANSS	110 patients initially considered. A subsample of 80 patients completed both the baseline and the 2-year follow-up functional and clinical evaluations and were therefore included in the study.
11	Hall et al. (2019)	To identify homogeneous function outcome trajectories in patients with FEP using objective data-driven methods and considering three separate predictors (positive symptoms, negative symptoms, and soft neurological signs) and to explore the potential risk /protective factors associated with each trajectory.	Diagnosis based on clinical data and the SCID-P interview for DSM-IV Symptoms: SAPS, SANS, affective items from the BPRS, HRSD and the Personality Disorder Evaluation.	Among the 369, 129 patients (35%) with at least 3 assessment data points were included in the trajectory analyses.
12	Iorfino et al. (2018)	To describe the longitudinal course of social and occupational functioning of young people attending primary care-based, early intervention services.	Diagnoses based on DSM-5 criteria	Not specified
13	Iorfino et al. (2022)	To identify trajectories of social and occupational functioning in young people during the two years after presenting for early intervention mental health care and identify demographic and clinical factors that influence these trajectories.	Diagnoses based on DSM-5 criteria and at-risk mental states (clusters of symptoms deemed to be risk factors for progression to more severe mental disorders).	Not specified
14	Lambert et al. (2010)	To assess the rates of persistent medication refusal, nonadherence, and full adherence in a cohort of first-episode psychosis patients, to identify pretreatment and baseline predictors of medication refusal and	DSM-IV criteria for both psychosis and non-psychosis diagnoses	This sample was derived from a larger cohort of 786 patients, with some exclusions due to file unavailability, being transferred or discharged to other services, a non-psychotic diagnosis at the end of the study, missing or non-assessable adherence ratings, ended treatment

		nonadherence, and to evaluate the association between medication refusal and illness outcomes.	Symptoms: CGI-severity of illness scale	early within the first 6 weeks after entry, related to transfer to other services.
15	Lévesque et al. (2020)	To compare the characteristics (socio-demographic, clinical and functional) at baseline and at 2 years after admission to an between FEP individuals who experienced homelessness (prior to admission and/ or during the first year of follow-up) and those who never experienced homelessness.	Diagnoses (psychotic disorders, SUD and cluster B personality trait/disorder) based on DSM-IV-TR) diagnoses Symptoms: PANSS, CDS, CGI-severity of illness scale	Attrition: 19.8% and not significantly different between studied groups. 167 FEP patients were approached: 12.6% (n = 21) declined to participate (but were eventually included in retrospective file review of partial data). At 2 years, 19.8% (n = 33) were lost-to-follow up, either because they moved to another town, quit treatment or were transferred to a Program for Assertive Community Treatment (PACT) team because of illness severity. In patients lost-to-follow up at 2 years (compared to patients still followed-up), no differences were observed on all baseline variables. No baseline differences were observed between the complete protocol group (with interview, n = 107) and the partial protocol group (without interview, n =60) on all baseline variables.
16	Molina-García et al. (2021)	To investigate the combined effect of premorbid IQ and age of onset of psychotic symptoms on psychotic symptomatology and functioning over two years of follow-up on a FEP sample.	18 years or over: Diagnoses based on DSM-IV criteria (SCID) for axis I; Under age 18: KSAD-S to establish the diagnosis of a psychotic disorder Symptoms: PANSS	Included participants who had completed evaluation of estimated premorbid IQ, functional and clinical assessments both at baseline and at two-year follow-up N= 36 with more than 1 year of follow up were included in the analysis. Attrition rate of 18.2% starting with 44 enrolled patients and 8 dropped out before completing one year of follow-up.
17	Paillère-Martinot et al. (2000)	To prospectively examine the predictive value of early clinical characteristics for long-term diagnostic outcome and functioning in adolescents first episode or recent-onset psychotic episodes (within the past 3 years).	Initial diagnosis according to DSM-III-R criteria Symptoms: SANS, SAPS, MADRS, Mania Rating Scale, Depressive Retardation Rating Scale (ERD)	The reasons for dropout are variably reported, including refusal to participate, insufficient follow-up time, and one patient no longer meeting the inclusion criteria (ill-defined diagnosis). The authors note a significant difference in the rate of initial diagnoses between the study group and the dropout group. Half of the dropouts had an initial diagnosis of schizophreniform disorder. This suggests a potential bias in the final sample.
18	Pina-Camacho et al. (2022)	To determine whether the cortical thickness, volume and surface area abnormalities present at first-episode psychosis evolve over the first two years of the illness, and, if so, whether age at FEP onset modulates the observed change trajectories. To describe the clinical characteristics of a biologically driven FEP cluster that shows the most pronounced age-related longitudinal cortical changes.	18 years or over: diagnosis based on DSM-IV criteria (SCID); under 18 years: K-SADS - present and Lifetime version Symptoms: CGI, MADRS, YMRS, PANSS	Only included participants with complete data at both baseline and follow-up

19	Pruessner et al. (2019)	To investigate gender differences in childhood trauma and whether the experience of trauma is differentially associated with symptomatic and functional outcome in male and female patients at psychosis onset and 12 and 24 months thereafter.	Diagnoses for affective and non-affective psychosis based on DSM-IV (SCID IV) criteria Symptoms: BPRS	Complete data on symptom severity and functioning over all three assessment points were available for 120 patients (85 men, 35 women). For symptom data they mention: 202 patients (138 men, 64 women) at baseline, 173 patients (119 men, 54 women) at 12 months, 134 patients (95 men, 39 women) at 24 months.
20	Pruessner et al. (2021)	To identify predictors of long-term functioning outcomes in young people with severe and/or complex mental health problems.	Diagnoses for affective and non-affective psychosis based on DSM-IV (SCID IV) criteria Symptoms: SAPS, SANS, CDS, BPRS ARMS status was established based on BPRS scores, the CASH, GAF and CAARMS. From 1999 the BPRS and CASH was replaced by the CAARMS.	Of the 210 patients with CTQ data, complete data on PSR were available for 144 patients (68.6%) over 12 months, and for 101 patients (48.1%) over 24 months. Data on NSR were available for 134 patients (63.8%) over 12 months, and for 89 patients (42.4%) over 24 months.
21	Reniers et al. (2017)	To investigate the association between baseline grey and white matter density and longer-term functional outcome after identification as ARMS for psychosis	Symptoms: BPRS for positive symptoms, SANS Current diagnoses (psychoses and SUD) according to DSM-IV criteria and past psychiatric diagnoses were determined through all clinical file information	Data are from participants with both baseline MRI and follow-up functional outcome data (n = 109) (did not report N of initial cohort)
22	Schimmelmann et al. (2007)	To identify differences between early-onset and adult-onset psychosis in terms of pre-treatment characteristics, baseline presentation, and treatment outcomes.	Symptoms: CGI-Severity of Illness Scale Current diagnoses (psychoses and SUD) according to DSM-IV criteria and past psychiatric diagnoses were determined through all clinical file information	After exclusions due to non-psychotic diagnoses, medical conditions, or missing data on age at onset, 636 patients were included in the analysis. This sample represents an epidemiological cohort because EPPIC had a mandate to treat all patients with FEP in their catchment area.
23	Schimmelmann et al. (2008)	To determine whether DUP had an effect on patients with first episode psychosis presented for treatment, and whether it impacted on their recovery over an 18-month treatment period.	Symptoms: CGI-Severity of Illness Scale Diagnosis of a “prodromal syndrome,” as defined by the SIPS	After exclusions due to non-psychotic diagnoses, medical conditions, or missing data on duration of untreated psychosis, data on 636 patients were analysed. This sample represents an epidemiological cohort because EPPIC had a mandate to treat all patients with FEP in their catchment area.
24	Schlosser et al. (2012)	To examine trajectories of clinical symptoms and social/role functioning in ARMS youth who did not develop psychosis over 2 years compared to ARMS youth who converted, and identify factors associated with conversion and remission rates.	Symptoms: SOPS positive & negative symptoms, SIPS dysphoric mood item for mood and anxiety symptoms	While the program is scheduled for 18 months, 23.3% of the patients were lost to follow-up due to service disengagement. Data available for 84/125 ARMS participants (67%) with at least one follow-up clinical evaluation. Independent sample t-tests and/or chi-square tests found no significant baseline differences between those with and without usable data for the survival analyses.

Note. BPRS = Brief Psychiatric Rating Scale; CAARMS = Comprehensive Assessment of At-Risk Mental States; CASH = Comprehensive Assessment of Symptoms and History; CDS = Calgary Depression Scale; CDSS = Calgary Depression Scale for Schizophrenia; CGI = Clinical Global Impression; CGI-BP = Clinical Global Impression – Bipolar; CGI-S = Clinical Global Impression – Severity; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th edition; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, 5th edition; EIS = Early Intervention Service; ERIRaos = Early Recognition Inventory Retrospective Assessment of Symptoms; FEP = First Episode Psychosis; GAF = Global Assessment of Functioning; HoNOS = Health of the Nation

Outcome Scales; HRSD = Hamilton Rating Scale for Depression; ID = Study ID; ICD-10 = International Classification of Diseases, 10th edition; K-SADS = Schedule for Affective Disorders and Schizophrenia for School-Age Children; MADRS = Montgomery-Åsberg Depression Rating Scale; NEURAPRO = Neuroprotection and Early Psychosis; PANSS = Positive and Negative Syndrome Scale; PUFA = Polyunsaturated Fatty Acid; RCT = Randomized Controlled Trial; SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms; SCID = Structured Clinical Interview for DSM; SIPS = Structured Interview for Prodromal Syndromes; SOPS = Scale of Prodromal Symptoms; ARMS = Ultra-High Risk; YMRS = Young Mania Rating Scale.

Appendix E. MMAT Quality Assessment of Systematic Review Studies

Table E1.

MMAT Quality Assessment of Included Studies (N = 24).

Author(s)	MMAT Criteria					Rating (0-5)
	1. Representative sample of target population	2. Appropriate measurements for the outcome and intervention (or exposure)	3. Complete outcome data	4. Confounders accounted for in the design and analysis	5. Intervention administered (or exposure occurred) as intended	
1. Abdel-Baki et al. (2017)	Y	Y	Y	N	Y	4
2. Alameda et al. (2015)	Y	Y	N	Y	Y	4
3. Alameda et al. (2017)	Y	Y	CT	Y	Y	4
4. Amminger et al. (2020)	Y	Y	N	Y	N	3
5. Berger et al. (2020)	CT	Y	N	Y	N	3
6. Burgher et al. (2023)	CT	Y	N	N	Y	2
7. Cocchi et al. (2008)	Y	Y	N	N	Y	3
8. Conus et al. (2017)	Y	Y	CT	N	Y	4
9. Cotton et al. (2009)	Y	Y	CT	Y	Y	4
10. Fraguas et al. (2014)	Y	Y	N	Y	Y	4
11. Hall et al. (2019)	Y	Y	N	Y	Y	4
12. Iorfino et al. (2018)	CT	Y	Y	Y	Y	4
13. Iorfino et al. (2022)	Y	Y	Y	Y	Y	5
14. Lambert et al. (2010)	Y	Y	CT	N	Y	3
15. Lévesque et al. (2020)	Y	Y	Y	N	CT	3
16. Molina-García et al. (2021)	CT	Y	Y	Y	Y	4
17. Paillère-Martinot et al. (2000)	CT	Y	Y	Y	Y	4

18. Pina-Camacho et al. (2022)	CT	Y	CT	Y	CT	2
19. Pruessner et al. (2019)	CT	Y	CT	Y	Y	3
20. Pruessner et al. (2021)	CT	Y	CT	N	Y	2
21. Reniers et al. (2017)	CT	Y	Y	Y	CT	3
22. Schimmelmann et al. (2007)	Y	Y	CT	Y	Y	4
23. Schimmelmann et al. (2008)	Y	Y	CT	Y	CT	3
24. Schlosser et al. (2012)	Y	Y	N	Y	Y	4

Note: All studies received a "Yes" response the two screening questions and were categorised as quantitative non-randomised studies.

Further Details on MMAT Quality Assessment

All studies employed validated scales and standardised tools to assess key variables, enhancing the reliability and validity of findings. Seventeen out of 24 studies (70.8%) appropriately accounted for confounders in their statistical analyses, strengthening the internal validity of the findings. Many of these studies used regression models, mixed-effects models, and other statistical adjustments to reduce the impact of confounding variables such as socioeconomic status, treatment adherence, symptom severity, and comorbidities. However, seven studies (29.2%) did not adequately adjust for confounders in their analysis of functional outcomes, limiting the reliability of their conclusions (Abdel-Baki et al., 2017; Burgher et al., 2023; Cocchi et al., 2008; Conus et al., 2017; Lambert et al., 2010; Lévesque et al., 2020; Pruessner et al., 2021).

A significant proportion of studies failed to report completeness of functional outcome data or had incomplete data, raising concerns about missing data bias. Specifically, 17 out of 24 studies (70.8%) lacked complete functional outcome data (Alameda et al., 2015; Alameda et al., 2017; Amminger et al., 2020; Berger et al., 2020; Burgher et al., 2023; Cocchi et al., 2008; Conus et al., 2017; Cotton et al., 2009; Fraguas et al., 2014; Hall et al., 2019; Lambert et al., 2010; Pina-Camacho et al., 2022; Pruessner et al., 2019; Pruessner et al., 2021; Schimmelmann et al., 2007; Schimmelmann et al., 2008; Schlosser et al., 2012).

Only three out of 24 studies (12.5%) met the $\leq 20\%$ dropout threshold, indicating robust follow-up and lower risk of attrition bias (Abdel-Baki et al., 2017; Lévesque et al., 2020; Paillère-Martinot et al., 2000). In contrast, 9 studies (37.5%) had dropout rates exceeding 30%, making their long-term findings on functioning outcomes more vulnerable to attrition bias (Alameda et al., 2015; Amminger et al., 2020; Berger et al., 2020; Burgher et al., 2023; Fraguas et al., 2014; Hall et al., 2019; Pruessner et al., 2021; Schlosser et al., 2012).

Handling of missing data was inconsistent across studies. While some studies employed strategies such as Last Observation Carried Forward (LOCF) (Hall et al., 2019; Pruessner et al., 2021), others did not specify how missing data were addressed, limiting transparency and reproducibility (Alameda et al., 2017; Berger et al., 2020; Burgher et al., 2023; Pina-Camacho et al., 2022; Schlosser et al., 2012).

A substantial number of studies (11 out of 24, 45.8%) applied a priori selection criteria that required participants to have complete data at more than one time point to be included in the analyses. This approach aimed to ensure data consistency for longitudinal assessments but may have introduced selection bias, as participants who remained engaged in follow-ups were overrepresented, while those with incomplete data were excluded.

Several studies explicitly required baseline and at least one subsequent follow-up assessment. Amminger et al. (2020) included only participants with fatty acid data at two time points, while Conus et al. (2017) restricted inclusion to individuals with existing medication adherence data. Similarly, Fraguas et al. (2014) retained only the 80 participants who completed both baseline and two-year follow-up evaluations, ensuring full longitudinal data but reducing the final sample size.

Other studies set stricter inclusion criteria, requiring multiple follow-up assessments. Berger et al. (2020) only included 106 participants with complete biomarker data from baseline, month 6, and month 12, while Hall et al. (2019) limited their trajectory analyses to participants with at least three assessment data points. Iorfino et al. (2022) followed a similar approach, requiring at least three time points between baseline and 24 months, while Iorfino et al. (2018) included only those with at least two SOFAS data points.

Some studies focused on specific assessment tools or imaging criteria. Schlosser et al. (2012) conducted survival analyses that included all participants with at least one follow-up measurement, ensuring at least partial longitudinal data but reducing the proportion of fully

observed cases (only 67% of the sample had at least one follow-up evaluation). Molina-García et al. (2021) and Pina-Camacho et al. (2022) applied similar restrictions, requiring participants to have both baseline and two-year follow-up evaluations or both baseline and follow-up neuroimaging assessments, respectively. Likewise, Reniers et al. (2016) explicitly required baseline MRI and follow-up functional outcome data, selecting for those with complete imaging data over time.

Appendix F. Detailed Quality Assessment of Included Studies

Table F1.

Detailed Quality Assessment of Included Studies Based on the MMAT Criteria.

Author(s)	1.	2.	3.	4.	5.
1. Abdel-Baki et al. (2017)	The study included almost all incident cases of FEP in two early psychosis intervention services in Montréal. Inclusion/exclusion criteria were well-defined. Representativeness was good though some patients (20.9%) refused participation.	The study used validated scales for symptoms (PANSS), functioning (SOFAS, GAF), symptoms severity (CGI), depression (CDSS), and substance use (AUS, DUS). Medication adherence was assessed using multiple sources (self-report, case managers, files, lab data). These scales are standardised and widely used, suggesting appropriateness.	17% of participants were lost to follow-up at 2 years. The study compares baseline characteristics of lost vs. retained participants. Reasons for loss were reported. Comparisons between lost-to-follow-up and retained participants showed some differences (immigrant status, employment, medication adherence), which could bias results. Authors recognise that these differences suggest that LTF patients might have a better prognosis since they have characteristics known to be associated with better psychiatric and functional outcomes (e.g., fewer schizophrenia spectrum diagnoses, greater proportion in employment).	The study explored differences in baseline clinical and demographic factors between the compared groups. However, the authors do not explicitly state that they controlled for any specific variables when comparing the differences in functional outcomes between SUD groups.	The exposure (SUD persistence vs cessation) was monitored using validated measures. The study clearly describes that no specialized SUD intervention was provided, ensuring that observed effects are natural course outcomes as part of early psychosis care.
2. Alameda et al. (2015)	The study sample consists of all eligible FEP patients treated at the TIPP early psychosis program (Switzerland). Inclusion criteria were well-defined. Limitations: Some participants lost to follow-up (56 out of 225). However, comparison analyses showed no significant differences between those who completed follow-up and those who dropped out.	Exposure (childhood trauma) was assessed using the TIPP Initial Assessment Tool. Potential limitation: SPA was assessed retrospectively but gathered over three years with multiple assessments and collateral information, reducing recall bias. Functioning was assessed using validated clinical scales (GAF, SOFAS). These tools are designed to capture relevant information, suggesting appropriateness.	"No" rating was given as drop-out rate >20%. Follow-up data were available for 169 out of 225 patients (75%) during the 3-year follow-up. Reasons for attrition were given with 37 patients having moved away or transferred to other services and 19 having missing functional outcome data. The study states that baseline characteristics did not differ significantly between those who completed follow-up and those who dropped out. However, no imputation method was mentioned for handling missing data.	The study used regression models and linear mixed effects models to adjust for potential confounders, such as age, sex, SES, history of substance abuse or dependence before age 16, and treatment adherence. These adjustments ensure that the observed effects of SPA on functional outcomes are not solely due to other demographic or clinical variables.	Changes in exposure status were not applicable, as childhood trauma had already occurred before baseline. The study compared pre-existing groups (Early SPA, Late SPA, and Non-SPA) without altering exposure status. The study does not explicitly report whether some participants sought trauma-related therapy. All participants were in the TIPP programme during the study.
3. Alameda et al. (2017)	Participants were recruited for the TIPP early psychosis program (Switzerland) ensuring a representative FEP cohort. Well-defined inclusion criteria. Only 12 out of 221 patients were excluded due to missing trauma exposure data or exposure occurring after psychosis onset.	Exposure (childhood trauma) was assessed through a structured longitudinal patient/caregiver interview, ensuring reliability. Level of functioning was assessed using the GAF, SOFAS. Depressive symptoms were evaluated using the MADRS. Positive and negative symptoms were assessed using the PANSS. These are established scales, suggesting appropriateness.	Although the study clearly states the initial number of participants and the reasons for exclusion, it does not explicitly report attrition rates or the specific number of participants who completed each assessment point (2, 6, 12, 18, 24, 30, and 36 months). No details are provided about missing data handling (e.g., multiple imputation, last observation carried forward). No sensitivity analysis is mentioned to assess the impact of missing data on the findings.	Stratification by age of trauma exposure (early trauma vs. late trauma vs. no trauma) was used to account for developmental differences that might influence outcomes. The study found no significant differences in baseline demographic factors (age, gender, SES) between groups (early trauma vs. late trauma vs. no trauma). Path analysis models were employed to assess the mediating effect of depressive symptoms on functional outcomes, which helps clarify causal pathways. Alternative models with positive and negative symptoms were tested to ensure robustness of the mediation effects.	Exposure (childhood trauma) occurred before study entry, ensuring no bias from changing exposure. The study tracks naturally occurring changes in depression and functioning without introducing an external intervention. Potential Consideration: Unmeasured co-exposures (e.g., therapy, medication changes) may have occurred, but the study does not indicate systematic differences between groups.
4. Amminger et al. (2020)	Authors compared those with and without fatty acid data on baseline demographic and clinical characteristics revealing only minor, nonsignificant differences. ARMS criteria were met for all participants at baseline and were recruited as part of a multi-center RCT.	The intervention was long-chain omega-3 polyunsaturated fatty acid (PUFA) therapy. The n-3 PUFA content of erythrocytes was measured to quantify intake. Clinical outcomes were measured using the CAARMS	"No" rating was given as drop-out rate >20%. Of the 304 RCT participants, 285 (93.8%) had fatty acid data at baseline, and 218 (71.7%) had fatty acid data at baseline and a subsequent time point. Participants with fatty acid data at 2 time points comprised the study sample of this	Analyses involving fatty acid measures were adjusted for baseline levels. Linear regression analyses were applied to investigate associations between n-3 PUFA measures and symptom measures.	Adherence to the study medication (fish oil or placebo) was low in the original RCT. This means that the intervention was not administered as intended for a significant proportion of participants. In addition, participants were permitted to

		criteria and the CGI-I scale. Erythrocyte n-3 PUFA measurement is an objective measure	biomarker analysis. The paper does not report the proportion of participants with complete data for the primary and secondary outcome measures, at 6 or 12 months, or any strategies used to address missing data.		receive other treatments, including selective serotonin reuptake inhibitors (SSRIs) for depression and benzodiazepines for anxiety. The use of these additional treatments could confound the relationship between fatty acid levels and clinical outcomes. Same as Amminger et al. (2020). Low adherence to the omega-3 supplements and the use of additional treatments mean the intended exposure was not achieved
5. Berger et al. (2020)	While the authors describe the inclusion and exclusion criteria for the NEURAPRO trial, they do not explicitly discuss the representativeness of the subsample (n = 106) included in this analysis by comparing those with and without allostatic load data.	The study examines the relationship between allostatic load and clinical outcomes. Symptom scores were measured using the BPRS, SANS, MADRS and YMRS. Functional outcomes were measured using SOFAS and GF-R. These scales are commonly used, suggesting appropriateness.	"No" rating was given as drop-out rate >20%. The paper provides evidence of missing data. For example, the 6-month follow-up had 90 participants out of the initial 106, and the 12-month follow-up had only 74 participants (69.8% of 106). The paper does not provide a detailed account of missing data, or the methods used to address it, which limits the ability to judge the completeness of outcome data fully.	Potential confounding variables were considered as covariates based on hypothesised association with dependent and independent variables, and previous use in the literature. These included age and smoking status as determined from a general health questionnaire administered to participants as well as treatment group.	
6. Burgher et al. (2023)	The paper does not provide enough information to assess the representativeness of the early psychosis and healthy control groups to their respective target populations. This would require further details about the recruitment process, location/setting, and the characteristics of the participants.	The study used fMRI and Multi-Source Interference Task to assess stimulus conflict processing which can be considered appropriate and objective methods for assessing neural correlates of cognitive functions. Reaction time delta is a standard measure of cognitive processing speed and efficiency, making it appropriate for assessing changes in cognitive function. SOFAS was used to measure functioning which is appropriate for its purpose.	"No" rating was given as drop-out rate >20%. At the 12-month follow-up in both case and control group participant dropped from 30 to 19 in each group (36.67% drop-out rate). Analysis only included data from these 38 participants. The paper does not provide details on the reasons for participant dropout or any analyses to assess potential bias related to missing data.	The authors control for age, gender by matching the EP and HC groups at baseline. They also absence/presence of high frequency substance use for both groups and record medication type and dosage for the EP group. The study does not fully address the potential confounding effect of substance use and does not take into consideration other potential confounders that might influence cognitive control and neural activity, such as IQ, education level, illness duration, and specific medication effects.	Exposure: "psychosis" is not varying exposure. The study does not fully address the potential impact of unplanned co-exposures like substance use and medication variations.
7. Cocchi et al. (2008)	Authors offer clear exclusion/inclusion criteria and report referral number, accepted number etc. Fifteen individuals who were offered treatment refused it. Knowing their characteristics and reasons for refusal would offer insights into potential differences between those who participated and those who did not.	GAF was used for global functioning and BPRS to assess general psychopathology, among other validated and widely used measures. All measures were appropriate for the purpose of the study.	"No" rating was given as drop-out rate >20%. The authors mention that only a portion of the enrolled patients had complete data for the 6-month and 1-year follow-up. Complete data for the 6-month and 1-year follow-up was available for 51 out of 72 patients with first-episode psychosis and 50 out of 71 subjects at high risk of psychosis. This represents 70.83% of the first-episode psychosis group and 70.42% of the high-risk group. Understanding the characteristics of those lost to follow-up and the reason for attrition is crucial to assess whether the analysed sample remained representative over time.	No confounders were taken into consideration in the design or analysis	The study describes the components of the Programma 2000 intervention package, including pharmacotherapy, CBT, psychoeducation, skills training, and social support and number of participants offered each intervention (e.g. vast majority of patients in both FEP and ARMS groups received tailored CBT >90%). Compliant with treatment: 92% among FEP and 90% among ARMS, respectively.
8. Conus et al. (2017)	Authors considered all admitted patients to a community EI service. They reported that 82 patients (10%) were transferred to other services, and their files were unavailable. However, the reasons for transfer and the potential differences between these patients and the included sample are not clear. 43 patients (5%) were excluded due to non-psychotic diagnoses at the study endpoint. This exclusion potentially narrows the representativeness to those with confirmed psychotic diagnoses.	The study generally employed appropriate measures. Diagnostic assessments used DSM-IV criteria with good validity and inter-rater reliability, outcome variables such as symptom remission and functional recovery were clearly defined, using CGI scores and scores on MVSI and independent living according to MLCI respectively. Medication adherence was evaluated through file notes and patient contact records.	Based on the study aim, only those with existing files were included. No mention on lost to follow-up. The never received antipsychotic medication (NA) group had a significantly shorter duration in the service compared to the group receiving antipsychotics. This difference in treatment duration could bias the outcome assessment, potentially underestimating the NA group's achievements if they had remained in treatment longer.	Adjusted logistic regression models for the variables that the two groups differed significantly at baseline as appropriate. However, while substance use was assessed and differences between groups were noted, the analyses predicting outcomes in the NA group did not directly control for substance use. For functional recovery logistic regression model were adjusted for time in service and working/studying and independent living status at service entry. Factors such as substance use and illness duration were not addressed in the analyses, limiting the study's ability to isolate the effects of refusing medication.	"Exposure" is the refusal of antipsychotic medication which was measured over time. Treatment variations within the NA group (e.g., different types or intensities of psychosocial interventions) are not detailed.

9. Cotton et al. (2009)	The study excluded 43 patients who had a non-psychotic diagnosis at discharge and 82 who had their files transferred to other services. This implies a degree of selection bias, although it is a necessary step to ensure that the study is focused on first-episode psychosis. Participants were part of consecutive FEP patients admitted to a service covering a defined catchment area, minimizing selection bias. Minimal leakage into private facilities ensured an epidemiological sample of early psychosis cases. Well-defined inclusion criteria.	The study uses standardised measures and criteria such as the DSM-IV for diagnoses, the DAAS for substance use, the CGI-S for severity of illness, and the GAF for functioning. The use of these established tools ensures that the measurements are appropriate for capturing the variables of interest. There was also good inter-rater reliability.	Based on the study aim, only those with existing files were included. The study began with 786 patients, but 82 patient files were transferred to other services and 43 patients were excluded because they had a non-psychotic diagnosis at discharge. Data was therefore available on 661 patients. This information is clearly stated, but there is no indication of whether there was any systematic difference between these patients compared to those included in the analysis. The study does not specify how many patients completed the full 18-month follow-up.	Stratification by gender allowed for direct gender comparisons (design). Multivariate logistic regression controlled for time in service, baseline GAF, and treatment adherence. The study adjusted for variables that were significantly different in univariate analyses, ensuring that gender comparisons were not confounded by baseline differences. The study described baseline demographic and clinical differences (e.g., substance use, psychiatric history, GAF scores) between genders to contextualise findings.	The study did not introduce an intervention but observed natural illness progression in male vs. female FEP patients. Exposure to psychosis-related treatment (EPPIC program) was consistent across groups, ensuring comparability. Potential unmeasured co-exposures (e.g., external therapy, social support) were not accounted for but unlikely to introduce major bias.
10. Fraguas et al. (2014)	The study began with a sample of 110 participants and included only those (N=80) who completed both the baseline and the 2-year follow-up assessments. The study compared the 80 participants who completed the follow-up with the 30 participants who did not and reported that no significant differences were found between these two groups in terms of age, gender, total PANSS score at baseline, C-GAF at baseline, or IQ. The study recruited children/adolescents with FEP from multiple specialized child psychiatry units across Spain, enhancing generalizability. Inclusion/Exclusion criteria were clearly defined.	Authors used recognised instruments for measurement, including the C-GAF scale to assess psychosocial functioning, and the PANSS to measure symptom severity. DUP was measured using a clinical questionnaire to retrospectively monitor the date of onset of positive symptoms, with a threshold of a score of 3 or more on the PANSS. Chlorpromazine equivalents were used to measure antipsychotic dosage. Premorbid adjustment was measured using the Premorbid Adjustment Scale (PAS). IQ was measured using the Wechsler Intelligence Scale for Children or the Wechsler Adult Intelligence Scale.	"No" rating was given as non-completion rate >20%. A total of 80 participants completed the baseline and 2-year follow-up assessments (80/110 patients, which equates to 72.7% complete data). The study does not explicitly state the percentage of participants with complete data for all measures, but a flow chart showing subject eligibility indicates that data for the C-GAF and date of onset were unavailable for 29 participants. The study also notes that 30 patients did not complete the follow up but does not find significant differences in socio-demographic or clinical factors between those who completed the study and those who did not.	The study accounts for several potential confounders in their regression models (baseline C-GAF, PANSS, cumulative antipsychotic dose, PAS score, IQ, diagnosis, manic episode at baseline). Interactions between key variables were tested, ensuring robust findings. The study also performs separate analyses for different diagnostic groups, to account for potential diagnostic-related confounding results	The exposure (DUP) was fixed before study entry and did not change over time. Treatment was delivered consistently across sites, ensuring minimal risk of systematic bias in care. The study does account for cumulative antipsychotic doses as a potential confounder in the analysis, addressing the potential influence of treatment during the follow-up
11. Hall et al. (2019)	The study sample is representative of FEP patients within the Western Psychiatric Institute and Clinic (Pittsburgh), but with limitations. 93% were antipsychotic-naïve, which may not generalise to broader FEP populations with prior medication exposure. The inclusion and exclusion criteria are clear. No significant baseline differences between those included in trajectory analyses and the full sample, but the authors do not explain why a large proportion were excluded or why some participants did not complete follow-ups, raising concerns about selection bias.	Functional recovery was assessed using validated measures (GAF, SAPS, SANS, NEA).	129 patients (35% of baseline sample) had at least 3 follow-up time points and were included in the trajectory analysis. High attrition rate (65%) raises concerns about missing data bias. While the authors did not find any significant differences between the baseline sample and those included in the kml3d analyses, such a large attrition rate may impact the generalizability of the findings. Missing values were imputed using Last Observation Carried Forward (LOCF), but impact on results is unclear.	Multivariate analyses controlled for key confounders, including IQ, SES, premorbid adjustment, executive function, substance use, personality disorder, race/ethnicity, and diagnosis. Cluster analysis inherently accounts for individual variation in predictor-outcome relationships.	The 'exposure' were participants' baseline characteristics. The study aimed to investigate a cohort of minimally treated or antipsychotic-naïve patients with FEP and then assess changes in their functional status over a one-year period, and this was achieved. The researchers did not introduce any interventions, but instead observed the cohort, and measured the changes in functioning at multiple time points. Treatment adherence, medication changes, and engagement with services were not assessed, making it unclear if unplanned co-interventions influenced recovery trajectories.
12. Iorfino et al. (2018)	Clear inclusion/exclusion criteria. The sample included young people registered in a research register and authors state that this sample represents approximately 18% of the research register and it is unclear what proportion of the whole population attending these services this sample represents.	Trajectories of function were identified using growth mixture modelling of SOFAS scores during two-year follow-up. Using SOFAS scores and growth mixture modelling allows for quantitative assessment of functional trajectories over time.	The median number of observations per person was 4 and median follow-up time was 23 months. While the authors acknowledge that the occurrence of 'time last seen' may not align with a complete period of care as some participants may still be engaged in care, they argue that the Group-Based Trajectory Modelling is beneficial as it accounts for the overall trends to provide a clearer picture of change over time.	To explore baseline predictors of functional trajectories were associated with each trajectory group, the authors used step wise logistic regression, which included baseline demographic and clinical characteristics: age, gender, receipt of government benefits, NEET status, mental health diagnosis, medical diagnosis, childhood mental health diagnosis, hospitalised (ever), suicide ideation (ever), suicide planning (ever) and suicide attempts (ever). This means they accounted for multiple relevant confounders.	"Exposure" is the presence of mental health difficulties and seen by the mention youth mental health clinic. This does not change over the study.

13. Iorfino et al. (2022)	Clear inclusion/exclusion criteria. The sample included young people registered in a research register registry of 6743 people with at least three data points between one and 24 months after baseline. Total of 1510 people were included, and authors provide the characteristics of the sample and the 1391 excluded candidates and significant differences in characteristics vs those included.	Trajectories of function were identified using growth mixture modelling of SOFAS scores during two-year follow-up. Using SOFAS scores and growth mixture modelling allows for quantitative assessment of functional trajectories over time.	The study included participants with at least three data points between 1 and 24 months after baseline. While the authors acknowledge that 'time last seen' might not reflect a complete care period for all participants, they employed growth mixture modelling, which accounts for variability in the number of follow-up assessments and individual trajectories. This approach is suitable for handling missing data and analysing longitudinal data with varying follow-up durations.	To explore baseline predictors of functional trajectories were associated with each trajectory group, the authors used step wise logistic regression, which accounted for age, sex, physical illness, NEET status, mental health presentation (depression, anxiety, psychosis, bipolar disorder, psychosis-like and mania-like experiences, circadian disturbance, substance-related disorder), history of any childhood disorder or family history, past psychiatric treatment use (hospitalisation, medication), self-harm and suicidality.	"Exposure" is the presence of mental health difficulties and seen by the mention youth mental health clinic. This does not change over the study.
14. Lambert et al. (2010)	The study uses an epidemiological cohort of first-episode psychosis patients treated at EPPIC. The EPPIC has a mandate to treat all patients aged 15 to 29 years with FEP in their catchment area, and the study sample is "as close to epidemiological representativeness as possible". The study acknowledges that 82 patients were excluded because their files were not available, and 56 patients were excluded because of a nonpsychotic diagnosis, missing adherence data, or early end of treatment in the first 6 weeks. However, the study notes that "The excluded 56 patients did not differ in any demographic or clinical variables" meaning this is unlikely to introduce any bias.	The study uses a range of validated tools and scales such as the Royal Park Multi-Diagnostic Instrument for Psychosis, the Drug and Alcohol Assessment Schedule, the DUP scale, the CGI-S scale, the GAF, the Modified Vocational Status Index, and the Modified Location Code Index. These tools are appropriate for measuring the variables of interest. Medication adherence was assessed using inpatient and outpatient file notes.	This sample was derived from a larger cohort of 786 patients, with some exclusions due to file unavailability due to being transferred or discharged to other services, a non-psychotic diagnosis at the end of the study, missing or non-assessable adherence ratings, ended treatment early within the first 6 weeks after entry, related to transfer to other services and not service disengagement. The study used the data of 605 patients. 56 (8.4%) were excluded because of missing or nonassessable adherence ratings. The excluded patients did not differ from the included patients on clinical or demographic variables. There is no 'loss to follow-up' in the traditional research sense. Once the patient was in the service, their data was potentially available for inclusion in the study. The study does not specify how many patients completed the full 18-month follow-up.	Although the study uses logistic regression models to predict medication refusal and nonadherence, controlling for potential confounders, it did not adjust for potential confounders in analyses that explored differences in GAF outcomes and employment status at discharge.	The study does account for the <i>occurrence</i> of medication exposure as a variable and considers factors that may affect it.
15. Lévesque et al. (2020)	Clear inclusion/exclusion criteria. All consecutive FEP admissions to an Early Psychosis Intervention Service considered. The authors compared the baseline characteristics of participants lost to follow-up with those who remained in the study and found no significant differences, suggesting that attrition did not significantly bias the sample.	The study used validated scales such as PANSS, CDS, QLS, and SOFAS to evaluate symptoms and functioning. It also collected data on substance use, childhood trauma, and service utilisation.	Attrition rate 19.8% and reasons for lost to follow-up were reported.	The authors compared homeless and housed groups on these variables at baseline using various statistical tests (chi-square, t-tests, Wilcoxon, Mann-Whitney tests). Although the groups differed on a lot of baseline characteristics, there was no adjustment during outcome analysis when analysing the relationship between homelessness and the 2-year outcomes.	The "exposure" was homelessness which was captured satisfactorily. Information on homelessness after the first year of follow-up is lacking.
16. Molina-García et al. (2021)	While the study describes inclusion and exclusion criteria, specifying that they only included those who had completed evaluation of estimated premorbid IQ, as well as functional and clinical assessments both at baseline and at two-year follow-up, it lacks detailed information on the recruitment process and how participants were selected within the larger CAFEPS and PEPs studies. This approach suggests a convenience sampling strategy. This makes it difficult to conclusively determine if the sample is truly representative of the broader population of individuals experiencing a FEP. However, they compared those who were and were not included in the study.	The study used established measures such as the Vocabulary subtest of the Wechsler Intelligence Tests to estimate premorbid IQ, PANSS for clinical symptoms, and GAF/c-GAF for general functioning. These measurements are justified and appropriate for answering the research questions. The reliability of the PANSS scale administration was also evaluated	The study authors included only participants who had complete data for estimated premorbid IQ, and functional and clinical assessments at both baseline and the two-year follow-up.	Authors divided the sample into four subgroups based on premorbid IQ and age of onset to account for the inherent influence of these factors. They compared the subgroups on socioeconomic status and duration of untreated psychosis, finding no significant differences. They used ANCOVA to explore the potential confounding effects of antipsychotic medication, although the details of these analyses are not fully reported. They employed hierarchical multiple regression to predict functioning at two years, controlling for age of onset, premorbid IQ, diagnosis, and PANSS subscale scores with the latter two being included as potential confounders since it was significantly associated with GAF/c-GAF at initial bivariate analysis - however it is unclear what other variables were tested.	The primary exposures, premorbid IQ and age of onset, are static and did not change during the study. The authors attempt to statistically control for antipsychotic medication, a key time-varying confounder, but it is unclear how effectively this was done or whether other time-varying confounders were considered.

17. Paillère-Martinot et al. (2000)	Target population: Adolescents with psychotic episodes experiencing diagnostic uncertainty between schizophrenia spectrum and affective disorders. Sample: Consecutive admissions to two locked wards in a teaching hospital in Paris. Clear inclusion/exclusion: "psychotic episode" was defined by the presence of positive symptoms. Patients with definite diagnoses of schizophrenia or affective disorders were excluded, increasing potential recruitment bias. The study does not provide details on the characteristics of the broader population of adolescents admitted with psychosis to allow for a comparison with the study sample.	The study used DSM-III-R diagnoses and standardised scales like the SANS, SAPS, Mania Rating Scale, and MADRS to assess symptoms. Psychosocial adjustment was assessed using the GAF. These measurements are generally appropriate for the research questions	Attrition rate of 18.2%: 8 out of 44 initially enrolled patients dropped out before completing one year of follow-up. Reasons for dropout: The reasons for dropout are variably reported, including refusal to participate, insufficient follow-up time, and one patient no longer meeting the inclusion criteria (ill-defined diagnosis). The authors note a significant difference in the rate of initial diagnoses between the study group and the dropout group. Half of the dropouts had an initial diagnosis of schizophreniform disorder. This suggests a potential bias in the final sample. Authors do not explicitly discuss whether all these participants had complete data for all variables at every assessment point.	The authors used stepwise multiple regression of final GAF scores including five index variables as predictors in the final model (anhedonia, index GAF score, number of hospital admissions, alogia, MADRS score). The study started with a set of "index variables" for the regression but it does not specify exactly which variables were initially included in the model, but it likely encompassed demographic data, baseline symptom scores (and other clinical characteristics assessed at admission). The study acknowledges that medication was not controlled but notes that all patients received antipsychotic drugs.	The study states that patients were treated according to their main symptoms, with all receiving antipsychotic drugs. The prescribed treatments did not differ significantly between final diagnostic groups
18. Pina-Camacho et al. (2022)	Drawn from the FEP imaging study. Researchers recognised the potential for selection bias due to attrition and undertook a comparison between those who completed the study and those who did not stating that there was a higher proportion of low socioeconomic status subjects both in the "completer" FEP and healthy control groups (all $p < 0.05$), without any other differences in demographic/clinical variables, nor in their main global measurements at baseline. Although authors also mention inclusion and exclusion criteria, they do not provide sufficient details about the sampling strategy.	Standard and validated methods were used for both brain imaging (MRI and FreeSurfer) and clinical assessments (CGAS/GAF and PANSS)	It is noted that less than half of the imaging study cross-sectional sample was included in the longitudinal study due to two of the six sites not participating in the longitudinal branch. It is unclear whether all participants contributed to all outcome measures (e.g., clinical assessments) at both time points.	The researchers controlled for several potential confounders in their analyses, including sex, total brain volume, and site. However, other potential confounders, such as premorbid IQ, antipsychotic medication dosage, and illness duration, while considered, were not included in the final models due to their non-significant effects on the main outcomes. Additionally, the authors acknowledge the limitation of not fully accounting for the potential influence of socioeconomic status.	The "exposure" in this context is the occurrence of FEP itself. Knowing that antipsychotic intake was examined, even if not ultimately included in the final models, provides some reassurance that potential co-exposures were considered. However, it is important to note that the source still lacks clarity regarding other potential co-exposures like changes in therapy, life stressors, or substance use.
19. Pruessner et al. (2019)	Patients were recruited from a naturalistic early intervention service (PEPP) in Montreal, with clearly defined inclusion and exclusion criteria. The paper describes inclusion and exclusion criteria for the PEPP program from which participants were drawn, it does not explicitly define the intended target population of the study or whether the participants represent all PEPP participants during the recruitment period or if a subgroup was selected.	The study employs validated and relevant measures for key variables of interest: childhood trauma (CTQ), psychotic symptoms (BPRS), and overall functioning (GAF)	The source mentions some attrition in the sample size over the two-year follow-up period but does not provide specific details on the extent of missing data at each assessment point, explain the reasons for participant dropout (e.g., withdrawal, loss to follow-up) nor describe any strategies used to handle missing data.	The study includes relevant baseline sociodemographic and clinical variables, differing between males and females, as covariates in the analyses. The authors include some potential confounders in their analyses, such as substance abuse and dependence, depression, and mania scores at baseline and gender via stratification. Subsequent multiple linear regression analyses with the CTQ subscales as independent factors entered stepwise were conducted to determine which specific trauma experience(s) best predicted symptomatic and functional outcomes.	While the exposure itself (childhood trauma) remains fixed, other factors emerging during the 2-year follow-up could influence the relationship between childhood trauma and functional outcomes. Authors acknowledge this by controlling for substance abuse/dependence, depression, and mania at baseline. All patients received services from a specialised early intervention program. There was limited information on medication use and specific treatment modalities during the follow-up period.
20. Pruessner et al. (2021)	The paper describes inclusion and exclusion criteria for the PEPP program from which participants were drawn, it does not explicitly define the intended target population of the study or whether the participants represent all PEPP participants during the recruitment period or if a subgroup was selected.	The study uses established and validated measures for key variables: CTQ for assessing childhood trauma, Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS) for measuring positive and negative symptom and GAF for assessing overall functioning.	Complete data on positive symptom remission (PSR) were available for 68.6% of patients over 12 months and only 48.1% over 24 months. Similarly, data on negative symptom remission (NSR) were available for 63.8% over 12 months and 42.4% over 24 months. The study used the last observation carried forward (LOCF) method to handle missing data. The study does not provide specific details on the completeness of data over time for GAF.	Demographic, clinical and medication variables that were significantly different between groups (duration of untreated illness and antipsychotic medication) were entered as covariates in the ANOVAs assessing childhood trauma effects on remission. However, the analysis that explored predictor of functioning outcomes did not consider any confounders.	While the exposure itself (childhood trauma) remains fixed, other factors emerging during the 2-year follow-up could influence the relationship between childhood trauma and functional outcomes (e.g. co-exposures). All patients received services from a specialised early intervention program. There was limited information on medication use and specific treatment modalities during the follow-up period, however this is addressed in question 3.4

21. Reniers et al. (2017)	Participants were ARMS individuals recruited from the PACE clinic (Melbourne), making the sample representative of help-seeking ARMS populations. While the study clearly defines the target population and inclusion/exclusion criteria, the exclusion of participants without both baseline and follow-up data introduces a potential selection bias. They also do not explicitly discuss the characteristics of those who were excluded, nor do they explore whether the included participants differ from the excluded participants in any way, which is a limitation.	The study employs well-established and validated measures for assessing functional outcomes, such as the SOFAS and GAF. The 'exposure' in this study is the baseline grey and white matter density, measured using MRI, and the study uses standard MRI acquisition protocols and voxel-based morphometry for processing.	109 ARMS participants with both baseline MRI and follow-up functional data. The study only included participants with complete follow-up data, avoiding missing data within the analysed sample. Retention rates and attrition data are not reported, making it unclear if a significant proportion of the original sample was lost over time. However, data on the GAF was available for 108 participants at both baseline and follow-up.	The researchers used multiple regressions, with gender, age, field strength of the scanner, length of the follow-up period, and transition status specified as nuisance variables. Analyses were adjusted for baseline symptom severity (SANS, BPRS psychotic subscale), reducing potential confounding. This approach accounted for potential confounding effects of these variables on the association between baseline grey and white matter density and functional outcome	The study examines a fixed past exposure (baseline brain structure), so exposure itself remained stable. However, long follow-up duration (2.4 - 12.9 years) raises concerns about uncontrolled treatment exposures (e.g., therapy, medication, lifestyle changes), which were not systematically tracked. The study explicitly states that limited information was available regarding participants' treatment during follow-up, making it unclear whether unplanned co-exposures influenced functional outcomes.
22. Schimmelmann et al. (2007)	This constitutes an epidemiological cohort, which is designed to be representative of all cases within the catchment area. The study also notes that excluded patients did not differ significantly from the included participants regarding age, gender, and diagnostic distribution. The study describes some of the inclusion and exclusion criteria. The representativeness is also strengthened by the fact that it is a "first contact with treatment"	Outcomes were assessed using validated clinical measures: GAF (functioning), CGI-S (severity), and DSM-IV diagnoses. Data were extracted using a structured file audit method with high inter-rater reliability. Limitations: Some measures (e.g., full Premorbid Adjustment Scale) were too complex to reliably extract from files.	The study does address how they arrived at their final sample, through reporting exclusions, and comparing those excluded from the study with those who were included in terms of age, gender, and diagnostic distribution. The study acknowledges that there were some missing data points (not report retention rates during follow-up), which are mentioned in the analyses, but states that almost all the participants contributed to almost all measures. The study explicitly states that the initially excluded 82 patients were similar to the included patients in terms of age, gender and diagnostic distribution. Employment/occupation outcome data at discharge has missing data in 88 cases (13.8%). Authors do not explicitly state that all included participants have complete data on GAF at follow-up.	The researchers used ANCOVA and regression analyses to control for several potential confounders, including premorbid functioning, social adjustment, gender, and diagnostic group. This suggests a good understanding of the need to control for confounders to avoid misinterpreting the results and strengthen the validity of the findings. The analysis that examined GAF as an outcome controlled for time in treatment and the respective baseline scores.	The exposure, age at onset of psychosis, was a fixed characteristic. All participants received standardized treatment at EPPIC following Australian Guidelines for Early Psychosis, minimizing inconsistencies in care. However, the study did not systematically track treatment details such as medication adherence, raising the possibility of unplanned co-exposures influencing outcomes. While the study acknowledges potential differences in diagnostic distribution (e.g., higher schizophrenia rates in early-onset psychosis), it did not explicitly adjust for treatment variability in the analyses.
23. Schimmelmann et al. (2008)	The study used a population-based cohort of 786 patients with FEP admitted to an EI programme with a mandate to treat all patients aged 15-29 in their catchment area, making the sample as close to epidemiologically representative as possible. Only a small number of patients were excluded because they were sent to other services (82 files, 10%), did not have a psychotic disorder (59 patients, 8.4%) or had missing data for DUP (9 patients). The excluded patients did not differ significantly from the included sample in available demographic characteristics and diagnostic distribution.	Outcomes were assessed using validated clinical measures (PANSS, GAF, CGI, DSM-IV diagnoses). Follow-up assessments were conducted systematically over 4 years, ensuring longitudinal validity. The study used a structured file review process using a standardised questionnaire, the "Early Psychosis File Questionnaire," which was completed by trained clinicians	The study reports that while the EPPIC program was scheduled for 18 months, 23.3% of the patients were lost to follow up due to service disengagement. The study does not specifically state whether the outcome data is complete for the remaining 76.7%. The researchers also report that the rate of disengagement from the study was not different across DUP groups. Missing data on employment/occupation at discharge in 88 cases (13.8%). Authors do not explicitly state that all included participants have complete data on GAF at follow-up.	The study acknowledges that premorbid functioning is a potential confounder and controls for this using the GAF scale and social adjustment scores in the analysis. The study also controls for other relevant confounders such as time in treatment, age of onset, non-adherence with medication, persistent substance use, and respective baseline variables in ANCOVA and logistic regression analyses. They also note that they analysed the data for both the total FEP sample and for FEP excluding Bipolar I disorder because of the significant differences in baseline diagnoses across the DUP groups.	The DUP was not measured as a fixed value at the start of the study but was allowed to be revised by clinicians throughout the 18-month study period. This means that the 'exposure' was not consistent over time. The process of revision was not standardised, and the reasons for changing DUP values were not recorded. This lack of standardisation and the potential for bias due to clinician knowledge of patient status, means that the exposure, DUP, may have not been used as intended
24. Schlosser et al. (2012)	Clear inclusion/exclusion criteria. Reasons for dropout or provide details on the proportion not reported. The mix of recruitment locations suggests that the study aimed to capture a range of individuals at risk, some of whom were already engaged with mental health services, and some who were not, who presented through community pathways.	Outcomes were assessed using validated clinical measures for key variables of interest: the SOPS for symptom assessment and the GFS for social and role functioning.	"No" rating was given as attrition rate >20%. Authors state a 33% attrition rate, but they do not specify details on the proportion of missing data for specific outcome measures. But they checked for "attrition" bias by exploring baseline differences between those with and without usable data for the survival analyses.	The researchers used covariates in their analysis to account for confounders related to functioning outcomes. They included age, gender, medication status, and time-varying symptom scores as covariates in their models	The 'exposure' (conversion to psychosis) is the primary outcome being investigated, and changes in this 'exposure' status constitute the central research focus.

Appendix G. Code and Outputs of Power Calculations

Figure G1

Code and outputs of power calculations for multinomial logistic regressions with sample size of $N = 270$, using the *pwr* in R.

```
1 library(pwr)
2
3
4 num_categories = 3
5 num_covariates = 16
6 sample_size = 270
7 alpha = 0.05
8
9 power1 = pwr.f2.test(u = num_categories * (num_covariates + 1),
10 v = sample_size - num_categories * (num_covariates + 1) - 1,
11 f2 = 0.02,
12 sig.level = alpha, power = NULL)
13
14 power2 = pwr.f2.test(u = num_categories * (num_covariates + 1),
15 v = sample_size - num_categories * (num_covariates + 1) - 1,
16 f2 = 0.15,
17 sig.level = alpha, power = NULL)
18
19 power3 = pwr.f2.test(u = num_categories * (num_covariates + 1),
20 v = sample_size - num_categories * (num_covariates + 1) - 1,
21 f2 = 0.35,
22 sig.level = alpha, power = NULL)
```

2:1 (Top Level) ↓

Console Terminal Background Jobs

R 4.3.2 · ~/

```
· power1
Multiple regression power calculation
      u = 51
      v = 218
      f2 = 0.02
sig.level = 0.05
power = 0.1219953

· power2
Multiple regression power calculation
      u = 51
      v = 218
      f2 = 0.15
sig.level = 0.05
power = 0.8725022

· power3
Multiple regression power calculation
      u = 51
      v = 218
      f2 = 0.35
sig.level = 0.05
power = 0.9998599
```

Note. Three calculations were conducted to identify power given small, medium, and large effects. One dependent variable with four categories and 15 predictor variables were considered in all calculations.

Appendix H. Participant Information Sheet for the PRODIGY Trial

PRODIGY Randomised Controlled Trial Participant Information Sheet (Version 3.0 29/09/2015):



[insert site-specific logos]

PRODIGY: Prevention of long term social disability amongst young people with emerging psychological difficulties: a definitive randomised controlled trial of Social Recovery Cognitive Behavioural Therapy.

This project is funded by the National Institute for Health Research Health Technology Assessment Programme (project number 10/104/51).

Participant Information Sheet

You have been given this information sheet because you are being invited to take part in a research project. It is up to you to decide whether or not you want to take part. Before you decide, it is important that you know about the project. This information sheet will tell you about why the project is being done and what will happen if you decide to take part. Please take as much time as you need to read and understand this information: you can talk about it with other people if you want. If there is anything you don't understand you can speak to a member of the PRODIGY team. You will find the team's contact details at the end of this information sheet.

Why is the project being done?

Some young people who experience psychological difficulties sometimes find it hard to carry on living the life they want to live: they might have problems going to school or college, finding a job or taking part in social activities. "Social recovery" is a term used to describe when someone is living the life they want to despite having experienced psychological difficulties. We think that people might make a better social recovery if they work with a therapist using a technique called Social Recovery Cognitive Behavioural Therapy (SRCBT for short). This research project is being done to see whether working with a therapist in this way can help people to make a better social recovery.

Why have I been invited to take part?

We are inviting young people receiving support from youth services in East Anglia, Manchester and Sussex who are experiencing psychological difficulties and not spending much time doing structured activities to take part in the project. Structured activities include things like work, education, childcare, housework, sport and leisure activities. If you are interested in taking part in the project we will ask you some questions about how you are spending your time at the moment to help us decide whether this project is right for you.

Do I have to take part?

No, it is up to you to decide whether or not you want to take part. If you do decide to take part you will be given this information sheet to keep and will also be asked to sign a consent form. Even if you

decide to take part, you can change your mind at any time without having to give a reason. If you decide not to take part, or to stop taking part, this will not affect the standard of care you receive.

What is the therapy being tested?

The therapy being tested, Social Recovery Cognitive Behavioural Therapy (SRCBT), is a new talking therapy which aims to help individuals spend more time doing activities which are meaningful for them. During the therapy, the therapist works with a young person to identify activities they would like to do. The therapist and young person will then work together to try to understand anything that is making it difficult for them to do these activities and to overcome these difficulties. The therapy aims to help the young person to understand what they are experiencing and feeling, cope with it differently, and feel less worried when they do new things. The therapy sessions will be approximately weekly for up to 9 months. Some of the sessions will involve talking and others will involve going out and trying new things. Sessions usually last for about an hour. Sessions are flexible and the timing and location of meetings will be decided between the young person and therapist.

Why is the study called a 'randomised controlled trial'?

SRCBT is a relatively new therapy so we don't know whether or not it is helpful yet. To help us find out, we want to compare SRCBT, together with the care you would usually get from your team, with usual care alone. In order to do this, we will put people into two groups: one group will receive the SRCBT and the other group will not. The group that does not receive SRCBT is called the 'control' group and is very important as it allows comparisons to be made. This is why this type of trial is called 'controlled'. A computer will decide which of the two groups participants are in. The computer will make sure that each group has the same number of males and females and that the groups have an equal spread of ages and level of social difficulties. The computer will not have any other information about individuals so the decision about which group people go into will be random. This is what is meant by 'randomised'. The two groups will be the same size so participants have a 50/50 chance of receiving SRCBT in addition to usual care.

What will happen if I decide to take part?

If you decide to take part, you will meet with a PRODIGY research assistant, at a time and place to suit you, to complete an assessment. The research assistant will be independent from your usual care team (if you have one). In the assessment, the research assistant will ask you to complete four questionnaires with them about your current difficulties and social situation. The research assistant will then ask you to complete ten more questionnaires. The assessment will take about two hours to complete in total. This will be spread over two or more sessions, whichever is more convenient and comfortable for you. You can invite a friend, relative or worker to be with you during the assessment if you like. If you would like, we will write a brief summary of the assessment in the form of a letter addressed to you. We can provide you with copies of the letter to share with your care team if you wish. After the assessment you will be put into either the group which will be offered SRCBT (the therapy group) or the group which will not (the control group). You will be told which of the groups you have been put into by a member of the research team. If you have a current care team, we will also let them know which of the groups you are in.

You will be invited to meet with the research assistant again to repeat the assessment at three further time points: 9 months, 15 months and 24 months on from your first assessment. This means you will be part of the project for up to 2 years.

If you are in the therapy group, in addition to your usual care you will be offered weekly or fortnightly meetings with a therapist for up to nine months. The therapy sessions will be at a time and place that is convenient for you. If you are in the control group you will still receive your usual care but without the additional SRCBT.

If you are at school or college, the research team may ask for your permission to speak with relevant staff members (for example, the school nurse, counsellor or special educational needs coordinator) to help make sure that you are being offered the best possible support. We would also ask school/college staff to let us know if they felt that your participation in the study was having a negative effect on your performance or attendance at school, but we do not anticipate this to be the case.

What are the possible risks of taking part?

If people feel pressurised into undertaking new activities they can sometimes find that certain psychological difficulties get worse or come back. However, the aim of SRCBT is to help people explore new activities they want to do while taking care to minimise the risk of any psychological difficulties.

What are the possible benefits of taking part?

We hope that the therapy will help those people who are offered it but we can't guarantee this. The information we find out from this research may help us to provide people with better help in the future. You will receive £20 at each research assessment as a thank you for giving up your time.

What happens when the research stops?

When the research project finishes, all participants will receive standard care from their usual team.

What happens if something goes wrong?

If you are harmed by taking part in a research project there are no special compensation arrangements. If you are harmed by someone's negligence you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of the study, the normal National Health Service complaints mechanisms will be available to you.

Will my taking part in this project be kept confidential?

All information collected as part of this research including consent forms, questionnaires, typed up notes of interviews and recording of interviews will be kept in a locked filing cabinet and secure computer systems on University or NHS sites. Data will be transferred between sites securely to ensure no-one outside the research team is able to access it. Any information from or about you will have your name, address and any other identifying features removed so that you cannot be recognised from it. This means that your anonymity will be preserved at all times during and after the study time period. All data will be destroyed 10 years after the study has been completed in line with NHS research policy.

If you are in the therapy group, we may audio record some of the sessions you have with your therapist with your permission. This is because we want to check that the therapy is being carried out in the way that we expect. All recordings will be stored securely and anyone listening to the tapes will sign a declaration of confidentiality.

If you consent to participate in the study we will inform your GP and the team responsible for your care that you are taking part in the research project. If we believe that there is any risk to your safety

or the safety of anyone else, we will have to pass this information on to your GP and current care team.

With your permission, we may also share other information you give us during your assessments with your GP or current care team (or both) of the information you share with us during the assessments, for example, information about your mental health and social situation. The study team and individuals from authorities responsible for making sure the research is done properly may look at relevant sections of your medical records.

Where and how long will records be stored?

Data will be stored in locked cabinets and secure computer systems on NHS or university premises. The data will be kept for 10 years after the completion of the study and then destroyed. Audio recordings of sessions will be stored electronically on secure computer systems and destroyed 10 years after completion of the study.

What will happen to the results of the research?

The results of the study will be written up for publication in health professional journals and will be presented at conferences in the UK and abroad. When we report the results of the research we may quote some of your words, however your anonymity will be preserved at all times. If you would like to be kept informed of any publications resulting from the study, please let the research team know.

Who is organising and paying for the research?

The research is being paid for by the National Institute of Health Research (NIHR) Health Technology Assessment Programme and sponsored by Sussex Partnership NHS Foundation Trust. The research is being carried out by researchers from Sussex Partnership NHS Foundation Trust, Norfolk and Suffolk NHS Foundation Trust, Greater Manchester West Mental Health NHS Foundation Trust, University of Sussex, University of East Anglia and The University of Manchester.

Who has approved the research?

Research projects like this one can't go ahead without being approved by an NHS Research Ethics Committee. The Ethics Committee checks that the risks associated with the study have been reduced to a minimum and balanced against potential benefits. They also check you have been given enough information to make an informed choice about whether or not to take part. This study has been considered and approved by the Preston Research Ethics Committee (15/NW/0590).

Where can I get more information?

For general information about taking part in research you can contact your local NHS trusts' research and development department:

[contact details]

If you need further information about this specific project, please contact a member of the PRODIGY team. You can contact the team at any time using the following email address:

[contact details]

If you would prefer to contact the team by phone, the names and telephone numbers of some PRODIGY team members are given below. They can be reached during office hours, Monday to Friday.

[contact details]

If you would like to speak to someone independent of the PRODIGY team, for more information or if something goes wrong, you can speak to your local PALS (Patient Advice and Liaison Service).

[contact details]

Thank you for reading this!

Thank you for taking the time to read this information sheet. If you decide to take part in the project you will be given a copy of this sheet, together with a copy of your consent form, to keep.

Appendix I. Participant Consent Form for the PRODIGY Trial

PRODIGY Participant Randomised Controlled Trial Consent Form (Version 3.0
29/09/2015)

[insert site-specific logos here]

The PRODIGY Trial

PRODIGY Team [contact details]

CONSENT FORM

PRODIGY: Prevention of long term social disability amongst young people with emerging psychological difficulties: a definitive randomised controlled trial of Social Recovery Cognitive Behavioural Therapy.

This project is funded by the National Institute for Health Research Health Technology Assessment Programme (project number 10/104/51)

Name of Researcher:

NOTE: Items which are optional (you do not have to agree to them) are labelled optional. All other items are mandatory (*), which means you cannot participate unless you agree to these items.

**Please
initial
box**

- 1.* I confirm that I have read and understand the information sheet dated 29/09/2015 (Version 3) for the above study and have had the opportunity to have my questions answered.
- 2.* I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- 3.* I understand that the researchers and staff overseeing the study may want to look at my case notes and I am happy for them to do this.

4. * I give consent to the PRODIGY team informing my care team/consultant psychiatrist and GP that I am taking part in the study.

5. * I understand that anonymised data may be transferred outside of the trust by a secure method in order to be analysed by the research team.

6. * I understand that relevant sections of my medical notes and data collected from the study may be looked at by regulatory authorities or by persons from the Trust where it is relevant to my taking part in this research. I give permission for these individuals to have access to this information.

7. * I agree to take part in the study of the new talking therapy Social Recovery Cognitive Behavioural Therapy (SRCBT).

8. **OPTIONAL:** I give my consent to the PRODIGY team to share assessment information regarding my current problems and social circumstances with my care team/consultant psychiatrist and GP.

9. **OPTIONAL:** I give my consent for tape recordings of assessment and treatment sessions to be made. I understand that this is for the purposes of training and supervision only, that any person hearing the tape will keep the information confidential, and that recordings will be stored under locked conditions.

10. **OPTIONAL:** I give permission for a copy of this consent form to be kept confidentially and securely by the Norwich Clinical Trials Unit (coordinating centre)

11. **OPTIONAL:** For participants in education ONLY:

12. I am happy for you to inform relevant staff members at my school or college that I am taking part and to discuss the support I receive and school performance if relevant.

Name of Participant

Date

Signature

Researcher

Date

Signature

Appendix J. Ethics Approval Letter



University of East Anglia
Norwich Research Park
Norwich, NR4 7TJ

Email: ethicsmonitor@uea.ac.uk
Web: www.uea.ac.uk

Study title: Exploring social recovery for help-seeking young people with severe and complex mental health difficulties: a secondary data analysis of the PRODIGY trial data

Application ID: ETH2324-0183

Dear Kat,

Your application was considered on 5th October 2023 by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee).

The decision is: **approved**.

You are therefore able to start your project subject to any other necessary approvals being given.

If your study involves NHS staff and facilities, you will require Health Research Authority (HRA) governance approval before you can start this project (even though you did not require NHS-REC ethics approval). Please consult the HRA webpage about the application required, which is submitted through the [IRAS](#) system.

This approval will expire on **26th September 2025**.

Please note that your project is granted ethics approval only for the length of time identified above. Any extension to a project must obtain ethics approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) before continuing.

It is a requirement of this ethics approval that you should report any adverse events which occur during your project to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) as soon as possible. An adverse event is one which was not anticipated in the research design, and which could potentially cause risk or harm to the participants or the researcher, or which reveals potential risks in the treatment under evaluation. For research involving animals, it may be the unintended death of an animal after trapping or carrying out a procedure.

Any amendments to your submitted project in terms of design, sample, data collection, focus etc. should be notified to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) in advance to ensure ethical compliance. If the amendments are substantial a new application may be required.

Approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) should not be taken as evidence that your study is compliant with the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018. If you need guidance on how to make your study UK GDPR compliant, please contact the UEA Data Protection Officer (dataprotection@uea.ac.uk).

Please can you send your report once your project is completed to the FMH S-REC (fmh.ethics@uea.ac.uk).

I would like to wish you every success with your project.

On behalf of the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee)

Yours sincerely,

Dr Paul Linsley

Appendix K. PRODIGY Trial List of Measures

Table K1.

The PRODIGY Measures, the Intended Measured Constructs, the Data Collection Time

Points and the Method of Collection (based on Fowler et al., 2021).

PRODIGY Trial measure	Construct measured	Data collection time points	Collection method
TUS (Short, 2006; adapted by Hodgekins, French, et al., 2015)	Social functioning as time spent in structured activities	screening, 9, 15, 24 months	Interview
CAARMS [34]	Severity of psychotic-like experiences, presence of psychosis history	screening, 9, 15, 24 months	Interview
GAF [26]	Socio-occupational functioning including impact of mental health symptoms	screening, 9, 15, 24 months	Researcher-rated
SCID [35]	Meeting diagnostic criteria for any mood disorders rated since last assessment point and meeting current month diagnostic criteria for up to two anxiety, somatoform or eating disorders for which diagnostic criteria were met at baseline.	baseline, 9, 15, 24 months	Interview
SSI [94]	Psychotic experiences, specifically anomalous experiences, paranoia and social anxiety.	baseline, 9, 15, 24 months	Self-report
SIAS [36]	Levels of social anxiety	baseline, 9, 15, 24 months	Self-report
BDI-II [37]	Levels of depressive symptom severity	baseline, 9, 15, 24 months	Self-report
SANS [38]	Presence and severity of negative symptoms	baseline, 9, 15, 24 months	Self-report
AAQ-II [95]	Levels of psychological flexibility	baseline, 9, 15, 24 months	Self-report
MLQ [96]	Presence of, and levels of search for, meaning in life	baseline, 9, 15, 24 months	Self-report
THS [97]	Dispositional hope	baseline, 9, 15, 24 months	Self-report
BCSS (Fowler et al., 2006)	Negative and positive schematic beliefs about the self and others	baseline, 9, 15, 24 months	Self-report

BHS [99].	Levels of three aspects of hopelessness, namely feelings about the future, loss of motivation, and expectations	baseline, 9, 15, 24 months	Self-report
COWAT [42]	Verbal fluency	baseline, 15 months	Researcher-rated
LM-I (Wechsler, 1997)	Verbal episodic memory	baseline, 15 months	Researcher-rated
AUDIT [39]	Screening for alcohol use disorders	baseline, 9, 15, 24 months	Self-report
DUDIT [40]	Screening for drug use disorders	baseline, 9, 15, 24 months	Self-report
HSRUQ [100]	NHS and personal social service use	baseline, 9, 15, 24 months	Self-report
EQ-5D [101]	Health-related quality of life respectively	baseline, 9, 15, 24 months	Self-report

Note. TUS, Time Use Survey; CAARMS, Comprehensive Assessment of At Risk Mental States; GAD, Global Assessment of Functioning; SCID, Structured Clinical Interview for DSM-IV Disorders; SSI, Schizotypal Symptoms Inventory ; SIAS, Social Interaction Anxiety Scale; BDI-II, Beck Depression Inventory-II total score; SANS, Scale for the Assessment of Negative Symptoms; AAQ-II, Acceptance and Avoidance Questionnaire II; MLQ, Meaning in Life Questionnaire; THS, Trait Hope Scale; BCSS, Brief Core Schema Scales; BHS, Beck Hopelessness Scale; COWAT, Controlled Oral Word Association Test; LM-I, Logical Memory I, AUDIT, Alcohol Use Disorders Identification Test; DUDIT, Drug Use Disorders Identification Test, HSRUQ, Health Service Resource Use Questionnaire HSRUQ ; EQ-5D, EuroQol-5D.

^a screening: once eligibility had been confirmed in the screening assessment, a date (baseline) was arranged with the participant to complete the remaining assessments. Once remaining assessments were completed, treatment allocation was performed.

Appendix L. Demographics Questionnaire

Demographic Information

1) *Date of Birth:* _____

2) *Gender:* _____

3) *Which ethnic group do you feel you belong to?*

White	A. British	
	B. Irish	
	C. Any other White background	

Mixed	D. White and Black Caribbean	
	E. White and Black African	
	F. White and Asian	
	G. Any other mixed background	

Asian or Asian British	H. Indian	
	J. Pakistani	
	K. Bangladeshi	
	L. Any other Asian background	

Black or Black British	M. Caribbean	
	N. African	
	P. Any other Black background	

Other Ethnic Groups	R. Chinese	
	S. Any other Ethnic groups	

4) *What is your marital status?*

- Single
 Partner
 Married/Civil partnership
 Separated
 Widowed
 Divorced

5) *What is your employment status?*

- Unemployed
 Employed (Paid Work)
 Employed (Voluntary Work)
 Student
 Homemaker

6) *What is your religion (if any)?* _____

7) *What is your country of birth?* _____

8) *What is your residency status?*

- British Citizen
 Other (please give details): _____

9) *What is your sexual orientation?*

- Heterosexual/Straight
 Homosexual/Gay
 Bisexual
 Other
 Unsure

10) *What type of accommodation do you live in?*

- Owner occupied
 Rented (Private Landlord)
 Rented (Local Authority/Housing Association)
 Accommodation with support

Appendix M. Time Use Survey Interview (Short, 2006; adapted by Hodgekins, French,
et al., 2015)

TIME USE INTERVIEW

EMPLOYMENT

1. Did you do any paid work in the last month, either as an employee or self-employed?

YES → ASK DETAILS

NO → GO TO QU 3

Details

2. How many hours a week do you usually work in your main job? Include any overtime.
How many hours have you worked in the last month?

Details

3. Over the last month have you been away from your main job?

YES → ASK DETAILS

NO → GO TO QU 4

Details

4. Have you ever had a paid job?

YES → ASK DETAILS

NO → GO TO 'EDUCATION AND TRAINING' SECTION

Details (What was the job? When left job, etc)

EDUCATION AND TRAINING

1. Are you studying for any formal qualifications at the moment?

YES → ASK DETAILS

NO → GO TO QU 2

Details (e.g. what, where, full/part time, hours in the last month)

2. In the last month, have you been on any taught courses or undertaken learning of any of the following sorts:

Taught courses meant to lead to qualifications (even if you did not obtain them)	
Taught courses designed to help you develop skills that you might use in a job	
Courses or instruction or tuition in driving, in playing a musical instrument, in an art or craft, in a sport or in any practical skill	

Evening classes (e.g. art/craft, languages, cookery)	
Learning which involved working on your own from a package of materials provided	

IF YES TO ANY OF THE ABOVE → ASK DETAILS

IF NONE OF THE ABOVE → GO TO 'VOLUNTARY WORK' SECTION

Details (e.g. what, where, full/part time, hours in the last month)

3. On how many occasions in the last month did you spend time studying at home outside of teaching sessions? How many hours?

Details (e.g. what, where, full/part time, hours in the last month)

VOLUNTARY WORK

Have you done any voluntary work through a group or on behalf of an organisation at any time during the last month? Have you done any unpaid work for anybody else e.g. running errands for elderly relatives?

- YES** → ASK DETAILS
NO → GO TO 'LEISURE ACTIVITIES'

<p><i>Details of voluntary work</i></p> <p><i>How many times in the past month?</i></p>
--

LEISURE AND SPORT ACTIVITIES

1. I am now going to ask some questions about things that some people do in their spare time. For each activity that I mention could you please tell me whether or not you have done this in the last month, AND how often?

ACTIVITY	NUMBER OF TIMES	AMOUNT OF TIME
Been to cinema		
Been to an event as a spectator (e.g. sports event, theatre, live music performance)		
Been to a museum, art gallery or heritage site		
Been to a library		
Been out to eat or drink at a café, restaurant, pub or wine bar		

Been to a shopping centre, or mall, apart from regular shopping for food and household items		
Been to some other place of entertainment (e.g. dance, club, bingo, casino)		
Been on any other outdoor trips (including going to places of natural beauty, picnics, going for a drive or going to the beach)		
Been involved in any community based activities (e.g. Scouts, going to church)		

2. I am now going to ask about sports activities. Could you please tell me whether or not you took part in any of these sports in the last month AND how often?

ACTIVITY	NUMBER OF TIMES	AMOUNT OF TIME
Swimming		
Cycling		
Gym/weight training		
Exercise classes (e.g. aerobics, martial arts)		
Team sports (e.g. rugby, football, cricket, hockey, netball)		
Racquet sports (e.g. tennis, badminton, squash)		
Jogging, cross country, road running		
Walking or hiking for 2 miles or more (recreationally)		
Climbing/mountaineering		
Fishing		
Golf		
Horse riding		
Pub games (e.g. snooker, pool, darts)		

3. How much time do you spend socialising? How many occasions in the last month have you seen friends or family, either visiting them or receiving visitors? How much time did you tend to spend socialising on each occasion on average?

DIRECT SOCIALISING (incl. those living with where for purposes of socialising)

INDIRECT SOCIALISING (phone/text/social media/skype/forums/socialising through online gaming)

CHILD CARE

1. Are you responsible for the care of any children?

YES → ASK 2

NO → GO TO 'HOUSEWORK AND CHORES'

2. How many children do you have? How old are they? Are you their primary carer?

--

3. How much time do you spend doing things with your children?

Physical care (e.g. feeding, dressing, washing)	
Supervision (inside and outside)	

Teaching children (e.g. helping with homework)	
Reading, playing and talking with children	
Accompanying child (e.g. to school, doctor, friend's house, etc)	

HOUSEWORK AND CHORES

How many people do you live with? Who is mainly responsible for the housework?

--

How much time do you spend doing housework and chores per week?

Food management and preparation	
Cleaning, dusting, vacuuming, washing dishes	
Food shopping	
Washing	
Gardening	
DIY and repairs	

TIME USE INTERVIEW SCORE SHEET

EMPLOYMENT

- Is paid work in the last month present or absent?

Present = 'YES' response to Question 1

Absent = 'NO' response to Question 1

- Type of work/job title (Question 1)

- Hours per week in paid employment over the last month

NB. This should be calculated by adding all hours spent in employment (from Questions 1 and 2) and multiplying by 12 then dividing by 52 to get a weekly average.

- Have they been away from main job?

Present = 'YES' response to Question 3

Absent = 'NO' response to Question 3

- Reason for being away from job, e.g. Maternity leave.

- Has paid work ever been present?

Present = 'YES' response to Question 4

Absent = 'NO' response to Question 4

If yes:

Number of weeks since last worked
(Response to Question 4)

What was the last paid job? (Question 4)

EDUCATION

- Current education present or absent?

Present = any 'YES' response to Questions 1 and 2

Absent = 'NO' responses to Questions 1 and 2

Hours per week in education over the last month

NB. This should be calculated by adding all hours spent in education (from Questions 1, 2 and 3) and multiplying by 12 then dividing by 52 to get a weekly average.

VOLUNTARY WORK

- Is voluntary work present or absent?

Present = 'YES' response to Question 1

Absent = 'NO' response to Question 1

- Hours per week spent in voluntary work over the last month

NB. This should be calculated by multiplying number of times by average length of time and multiply by 12 then dividing by 52 to get a weekly average.

LEISURE ACTIVITIES

- Are leisure activities present or absent?

Present

Absent

- Hours per week spent in leisure activities over the last month

NB. This should be calculated by multiplying number of times by average length of time for each activity. Then sum all of these and multiply by 12 then dividing by 52 to get a weekly average.

- Are sport/physical activities present or absent (taken from Question 2)

Present

Absent

- Hours per week spent in sport/physical activities over the last month

NB. This should be calculated by multiplying number of times by average length of time for each activity. Then sum all of these and multiply by 12 then dividing by 52 to get a weekly average.

- Hours per week over last month spent:

Socialising

Non- direct Socialising (e.g. Social networking)

CHILDCARE

- Childcare

Applicable

Non-Applicable

- How many children? Age of youngest child?

- Primary carer?

Yes

No

- Hours per week spent on childcare

NB. Taken from estimate of average time including items from checklist in estimate

HOUSEWORK AND CHORES

- Hours per week spent on housework and chores

NB. Taken from estimate of average time including items from checklist in estimate

CONSTRUCTIVE ECONOMIC ACTIVITY

- Total hours per week in EMPLOYMENT + EDUCATION + VOLUNTARY WORK + CHILDCARE + HOUSEWORK AND CHORES

STRUCTURED ACTIVITY

- Total hours per week in CONSTRUCTIVE ECONOMIC ACTIVITY + LESUIRE ACTIVITIES + SPORTS/PHYSICAL ACTIVITIES

Appendix N. Social Interaction Anxiety Scale (SIAS; Mattick & Clarke, 1998)

Instructions: For each item, please circle the number to indicate the degree to which you feel the statement is characteristic or true for you. The rating scale is as follows:

- 0 = Not at all characteristic or true of me.
- 1 = Slightly characteristic or true of me.
- 2 = Moderately characteristic or true of me.
- 3 = Very characteristic or true of me.
- 4 = Extremely characteristic or true of me.

CHARACTERISTIC	NOT AT ALL	SLIGHTLY	MODERATELY	VERY	EXTREMELY
1. I get nervous if I have to speak with someone in authority (teacher, boss, etc.).		1	2	3	4
2. I have difficulty making eye contact with others.		1	2	3	4
3. I become tense if I have to talk about myself or my feelings.		1	2	3	4
4. I find it difficult to mix comfortably with the people I work with.		1	2	3	4
5. I find it easy to make friends my own age.		1	2	3	4
6. I tense up if I meet an acquaintance in the street.		1	2	3	4
7. When mixing socially, I am uncomfortable.		1	2	3	4
8. I feel tense if I am alone with just one other person.		1	2	3	4
9. I am at ease meeting people at parties, etc.		1	2	3	4
10. I have difficulty talking with other people.		1	2	3	4
11. I find it easy to think of things to talk about.		1	2	3	4
12. I worry about expressing myself in case I appear awkward.		1	2	3	4
13. I find it difficult to disagree with another's point of view.		1	2	3	4
14. I have difficulty talking to attractive persons of the opposite sex.		1	2	3	4

15. I find myself worrying that I won't know what to say in social situations.		1	2	3	4
16. I am nervous mixing with people I don't know well.		1	2	3	4
17. I feel I'll say something embarrassing when talking.		1	2	3	4
18. When mixing in a group, I find myself worrying I will be ignored.		1	2	3	4
19. I am tense mixing in a group.		1	2	3	4
20. I am unsure whether to greet someone I know only slightly.		1	2	3	4

Appendix O. The Beck Depression Inventory-II (BDI-II, Beck, Steer, & Brown, 1996)

This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the one statement in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite)

<p>1. Sadness</p> <ul style="list-style-type: none"> 0 I do not feel sad. 1 I feel sad. 2 I am sad all the time and I can't snap out of it. 3 I am so sad and unhappy that I can't stand it. <p>2. Pessimism</p> <ul style="list-style-type: none"> 0 I am not discouraged about the future. 1 I feel discouraged about the future. 2 I feel I have nothing to look forward to. 3 I feel the future is hopeless and that things cannot improve. <p>3. Past failure</p> <ul style="list-style-type: none"> 0 I do not feel like a failure. 1 I feel I have failed more than the average person. 2 As I look back on my life, all I can see is a lot of failures. 3 I feel I am a complete failure as a person. <p>4. Loss of Pleasure</p> <ul style="list-style-type: none"> 0 I get as much pleasure as I ever did from the things I enjoy. 1 I don't enjoy things as much I used to. 2 I don't get real satisfaction out of anything anymore. 3 I am dissatisfied or bored with everything. <p>5. Guilty Feelings</p> <ul style="list-style-type: none"> 0 I don't feel particularly guilty. 1 I feel guilty over many things I have done or should have done. 2 I feel quite guilty most of the time. 3 I feel guilty all of the time. 	<p>6. Punishment Feelings</p> <ul style="list-style-type: none"> 0 I don't feel I am being punished. 1 I feel I may be punished. 2 I expect to be punished. 3 I feel I am being punished. <p>7. Self-Dislike</p> <ul style="list-style-type: none"> 0 I feel the same about myself as ever. 1 I have lost confidence in myself. 2 I am disappointed in myself. 3 I hate myself. <p>8. Self-Criticalness</p> <ul style="list-style-type: none"> 0 I don't criticize or blame myself more than usual. 1 I am more critical of myself than I used to be. 2 I criticize myself for all of my faults. 3 I blame myself for everything bad that happens. <p>9. Suicidal Thoughts or Wishes</p> <ul style="list-style-type: none"> 0 I don't have any thoughts of killing myself. 1 I have thoughts of killing myself, but I would not carry them out. 2 I would like to kill myself. 3 I would kill myself if I had the chance. <p>10. Crying</p> <ul style="list-style-type: none"> 0 I don't cry any more than I used to. 1 I cry more now than I used to. 2 I cry over every little thing. 3 I feel like crying, but I can't.
---	---

Subtotal page 1:

<p>11. Agitation</p>	<p>17. Irritability</p> <ul style="list-style-type: none"> 0 I am no more irritable than usual.
-----------------------------	---

- 0 I am no more restless or wound up than usual was.
- 1 I feel more restless or wound up than usual.
- 2 I am so restless or agitated that it's hard to stay still.
- 3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

- 0 I have not lost interest in other people or activities.
- 1 I am less interested in other people or things than before.
- 2 I have lost most of my interest in other people or things.
- 3 It's hard to get interest in anything.

13. Indecisiveness

- 0 I make decisions about as well as ever.
- 1 I find it more difficult to make decisions than usual.
- 2 I have much greater difficulty in making decisions more than I used to.
- 3 I have trouble making decisions.

14. Worthlessness

- 0 I do not feel I am worthless.
- 1 I don't consider myself as worthwhile and useful as I used to.
- 2 I feel more worthless as compared to other people.
- 3 I feel utterly worthless.

15. Loss of Energy

- 0 I have as much energy as ever.
- 1 I have less energy than I used to have.
- 2 I don't have enough energy to do very much.
- 3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

- 0 I have not experienced any change in my sleeping pattern.
- 1 a. I sleep somewhat more than usual.
b. I sleep somewhat less than usual.
- 2 a. I sleep a lot more than usual.
b. I sleep a lot less than usual.
- 3 a. I sleep most of the day.
b. I wake up 1-2 hours early and can't get back to sleep.

- 1 I am more irritable than usual.
- 2 I am much more irritable than usual.
- 3 I am irritable all the time.

18. Changes in Appetite

- 0 I have not experience any change in my appetite.

-
- 1 a. My appetite is somewhat less than usual.
b. My appetite is somewhat greater than usual.

-
- 2 a. My appetite is much less than before.
b. My appetite is much greater than usual.

-
- 3 a. I have no appetite at all.
b. I crave food all the time.

19. Concentration Difficulty

- 0 I can concentrate as well as ever.
- 1 I can't concentrate as well as usual.
- 2 It's hard to keep my mind on anything for very long.
- 3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

- 0 I am no more tired or fatigued than usual.
- 1 I get more tired or fatigued more easily than usual.
- 2 I am too tired or fatigued to do a lot of things I used to do.
- 3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

- 0 I have not noticed any recent change in my interest in sex.
- 1 I am less interested in sex than I used to be.
- 2 I am much less interested in sex now.
- 3 I have lost interest in sex completely.

Subtotal page 2:

TOTAL SCORE:

Appendix P. Controlled Word Association Test (COWAT; Benton & Hamsher, 1976)

Instruction Sheet

Say: "I will say a letter of the alphabet. Then I want you to give me as many words that begin with that letter as quickly as you can over one minute. For example, if I say "b" you might give me "bad, battle, bed..." I do not want you to use words that are proper nouns such as "Boston" or "Bob". Also, do not use the same word with different endings such as "eat" and "eating" and do not use numbers. Any questions? **Begin when I say the letter. The first letter is F. Go ahead.**" Begin timing immediately. Allow one minute for each letter (F, A, S). Say "good" after each one-minute performance. If the participant stops before the end of the minute, encourage him or her to try and think of more words.

Write down all words said (even if repetitions or not within rules, these can be discounted at the end) in the order in which they were produced. If repetitions occur that may be acceptable if an alternative meaning was intended (e.g. "four" and "for", "son" and "sun"), ask what was meant by the word after the one-minute period. Include only acceptable words in total.

F	A	S
Total =	Total =	Total =

What age did you leave school? _____

Did you complete GCSEs? YES NO

Appendix Q. Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001)

AUDIT is a comprehensive 10 question alcohol harm screening tool. It was developed by the World Health Organisation (WHO) and modified for use in the UK and has been used in a variety of health and social care settings.

Questions	Scoring system					Your score
	0	1	2	3	4	
How often do you have a drink containing alcohol?	Never	Monthly or less	2 to 4 times per month	2 to 3 times per week	4 times or more per week	
How many units of alcohol do you drink on a typical day when you are drinking?	0 to 2	3 to 4	5 to 6	7 to 9	10 or more	
How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you failed to do what was normally expected from you because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you needed an alcoholic drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you been unable to remember what happened the night before because you had been drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Have you or somebody else been injured as a result of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested that you cut down?	No		Yes, but not in the last year		Yes, during the last year	

Total AUDIT score	
--------------------------	--

Appendix R. Drug Use Disorders Identification Test (DUDIT; Berman et al., 2005)

Here are a few questions about drugs. Please answer as correctly and honestly as possible by indicating which answer is right for you.

	<input type="checkbox"/> Man	<input type="checkbox"/> Woman	Age	<input style="width: 100%;" type="text"/>		
1. How often do you use drugs other than alcohol? (See list of drugs on back side.)						
	Never	Once a month or less often	2-4 times a month	2-3 times a week	4 times a week or more often	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2. Do you use more than one type of drug on the same occasion?						
	Never	Once a month or less often	2-4 times a month	2-3 times a week	4 times a week or more often	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3. How many times do you take drugs on a typical day when you use drugs?						
	0	1-2	3-4	5-6	7 or more	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. How often are you influenced heavily by drugs?						
	Never	Less often than once a month	Every month	Every week	Daily or almost every day	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5. Over the past year, have you felt that your longing for drugs was so strong that you could not resist it?						
	Never	Less often than once a month	Every month	Every week	Daily or almost every day	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
6. Has it happened, over the past year, that you have not been able to stop taking drugs once you started?						
	Never	Less often than once a month	Every month	Every week	Daily or almost every day	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
7. How often over the past year have you taken drugs and then neglected to do something you should have done?						
	Never	Less often than once a month	Every month	Every week	Daily or almost every day	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8. How often over the past year have you needed to take a drug the morning after heavy drug use the day before?						
	Never	Less often than once a month	Every month	Every week	Daily or almost every day	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
9. How often over the past year have you had guilt feelings or a bad conscience because you used drugs?						
	Never	Less often than once a month	Every month	Every week	Daily or almost every day	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
10. Have you or anyone else been hurt (mentally or physically) because <input type="checkbox"/> you used drugs?						
	No	Yes, but not over the past year		Yes, over the past year		
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
11. Has a relative or a friend, a doctor or a nurse, or anyone else, been worried about your drug use or said to you that you should stop using drugs?						
	No	Yes, but not over the past year		Yes, over the past year		
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

LIST OF DRUGS

(Note! Not alcohol!)

Cannabis	Amphetamines	Cocaine	Opiates	Hallucinogens	Solvents/inhalants	GHB and others
Marijuana	Methamphetamine	Crack	Smoked heroin	Ecstasy	Thinner	GHB
Hash	Phenmetraline	Freebase	Heroin	LSD (Lisergic acid)	Trichlorethylene	Anabolic steroids
Hash oil	Khat	Coca leaves	Opium	Mescaline	Gasoline/petrol	Laughing gas
	Betel nut			Peyote	Gas	(Halothane)
	Ritaline (Methylphenidate)			PCP, angel dust (Phencyclidine)	Solution	Amyl nitrate (Poppers)
				Psilocybin	Glue	Anticholinergic compounds
				DMT (Dimethyltryptamine)		

PILLS – MEDICINES

Pills count as drugs when you take

- more of them or take them more often than the doctor has prescribed for you
- pills because you want to have fun, feel good, get "high", or wonder what sort of effect they have on you
- pills that you have received from a relative or a friend
- pills that you have bought on the "black market" or stolen

SLEEPING PILLS/SEDATIVES

Alprazolam	Glutethimide	Rohypnol
Amobarbital	Halcion	Secobarbital
Apodorm	Heminevrin	Sobril
Apozepam	Iktorivil	Sonata
Aprobarbital	Imovane	Stesolid
Butabarbital	Mephobarbital	Stilnoct
Butalbital	Meprobamate	Talbutal
Chloral hydrate	Methaqualone	Temesta
Diazepam	Methohexital	Thiamyl
Dormicum	Mogadon	Thiopental
Ethchlorovynol	Nitrazepam	Triazolam
Fenemal	Oxascand	Xanor
Flunitrazepam	Pentobarbital	Zopiklon
Fluscand	Phenobarbital	

PAINKILLERS

Actiq	Durogesic	OxyNorm
Cocclilana-Etyfin	Fentanyl	Panocod
Citodon	Ketodur	Panocod forte
Citodon forte	Ketogan	Paraflex comp
Dexodon	Kodein	Somadril
Depolan	Maxidon	Spasmoden
Dexofen	Metadon	Subutex
Dilaudid	Morfin	Temgesic
Distalgesic	Nobligan	Tiparol
Dolcontin	Norflex	Tradolan
Doleron	Norgesic	Tramadul
Dolotard	Opidol	Treo comp
Doloxene	OxyContin	

Pills do NOT count as drugs if they have been prescribed by a doctor and you take them in the prescribed dosage.

Appendix S. Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1989)

Evanston Northwestern Healthcare Genome-Wide Association Study of Schizophrenia Pablo V. Gejman, M.D.

VERSION 2.0/MGS
OCT 99

U. SCALE FOR THE ASSESSMENT OF NEGATIVE SYMPTOMS (SANS)

80

See SANS Manual for detailed coding definitions (N. Andreasen, 1984).

INTERVIEWER: Ratings are to be based on the last 30 days.

NONE —————> SEVERE UNK

AFFECTIVE FLATTENING OR BLUNTING

1. Unchanging Facial Expression The patient's face appears wooden--changes less than expected as emotional content of discourse changes.	0	1	2	3	4	5	U
2. Decreased Spontaneous Movements The patient shows few or no spontaneous movements, does not shift position, move extremities, etc.	0	1	2	3	4	5	U
3. Paucity of Expressive Gestures The patient does not use hand gestures or body position as an aid in expressing his ideas.	0	1	2	3	4	5	U
4. Poor Eye Contact The patient avoids eye contact or "stares through" interviewer even when speaking.	0	1	2	3	4	5	U
5. Affective Nonresponsivity The patient fails to laugh or smile when prompted.	0	1	2	3	4	5	U
6. Inappropriate Affect The patient's affect is inappropriate or incongruous, not simply flat or blunted.	0	1	2	3	4	5	U
7. Lack of Vocal Inflections The patient fails to show normal vocal emphasis patterns, is often monotonic.	0	1	2	3	4	5	U
8. Global Rating of Affective Flattening This rating should focus on overall severity of symptoms, especially unresponsiveness, inappropriateness and an overall decrease in emotional intensity.	0	1	2	3	4	5	U

ALOGIA

9. Poverty of Speech The patient's replies to questions are restricted in <u>amount</u> , tend to be brief, concrete, unelaborated.	0	1	2	3	4	5	U
10. Poverty of Content of Speech The patient's replies are adequate in amount but tend to be vague, over concrete or over generalized, and convey little in information.	0	1	2	3	4	5	U

SANS CODES

0 = None/Not at All	3 = Moderate	U = Unknown/
1 = Questionable	4 = Marked	Cannot Be Assessed/
2 = Mild	5 = Severe	Not Assessed

U. SANS (Cont'd)

	NONE	—————▶					SEVERE	UNK
11. Blocking The patient indicates, either spontaneously or with prompting, that his train of thought was interrupted.	0	1	2	3	4	5	U	
12. Increased Latency of Response The patient takes a long time to reply to questions, prompting indicates the patient is aware of the question.	0	1	2	3	4	5	U	
13. Global Rating of Alogia The core features of alogia are poverty of speech and poverty of content.	0	1	2	3	4	5	U	

AVOLITION/APATHY

14. Grooming and Hygiene The patient's clothes may be sloppy or soiled, and he may have greasy hair, body odor, etc.	0	1	2	3	4	5	U
15. Inpersistence at Work or School The patient has difficulty seeking or maintaining employment, completing school work, keeping house, etc. If an inpatient, cannot persist at ward activities, such as OT, playing cards, etc.	0	1	2	3	4	5	U
16. Physical Anergia The patient tends to be physically inert. He may sit for hours and not initiate spontaneous activity.	0	1	2	3	4	5	U
17. Global Rating of Avolition/Apathy Strong weight may be given to one or two prominent symptoms if particularly striking.	0	1	2	3	4	5	U

ANHEDONIA/ASOCIALITY

18. Recreational Interests and Activities The patient may have few or no interests. Both the quality and quantity of interests should be taken into account.	0	1	2	3	4	5	U
--	---	---	---	---	---	---	---

SANS CODES		
0 = None/Not at All	3 = Moderate	U = Unknown/
1 = Questionable	4 = Marked	Cannot Be Assessed/
2 = Mild	5 = Severe	Not Assessed

U. SANS (Cont'd)

	<u>NONE</u>	—————▶	<u>SEVERE</u>	<u>UNK</u>			
19. Sexual Activity The patient may show decrease in sexual interest and activity, or no enjoyment when active.	0	1	2	3	4	5	U
20. Ability to Feel Intimacy and Closeness The patient may display an inability to form close or intimate relationships, especially with opposite sex and family.	0	1	2	3	4	5	U
21. Relationships with Friends and Peers The patient may have few or no friends and may prefer to spend all his time isolated.	0	1	2	3	4	5	U
22. Global Rating of Anhedonia/Asociality This rating should reflect overall severity, taking into account the patient's age, family status, etc.	0	1	2	3	4	5	U

ATTENTION

23. Social Inattentiveness The patient appears uninvolved or unengaged. He may seem "spacey".	0	1	2	3	4	5	U
24. Inattentiveness During Mental Status Testing Refer to tests of "serial 7s" (at least five subtractions) and spelling "world" backwards.	0	1	2	3	4	5	U
25. Global Rating of Attention This rating should assess the patient's overall concentration, both clinically and on tests.	0	1	2	3	4	5	U

SANS CODES		
0 = None/Not at All	3 = Moderate	U = Unknown/
1 = Questionable	4 = Marked	Cannot Be Assessed/
2 = Mild	5 = Severe	Not Assessed

Appendix T. GRoLTS Checklist

Table T1.

GRoLTS-Checklist: Guidelines for Reporting on Latent Trajectory Studies (van de Schoot et al., 2017)

Checklist Item	Reported?
1 Is the metric of time used in the statistical model reported?	Yes
2 Is information presented about the mean and variance of time within a wave?	Data not available
3a. Is the missing data mechanism reported?	Yes
3b. Is a description provided of what variables are related to attrition/missing data?	Yes
3c. Is a description provided of how missing data in the analyses were dealt with?	Yes
4 Is information about the distribution of the observed variables included?	Yes
5 Is the software mentioned?	Yes
6a. Are alternative specifications of within-class heterogeneity considered (e.g., LGCA vs. LGMM) and clearly documented? If not, was sufficient justification provided as to eliminate certain specifications from consideration?	Yes
6b. Are alternative specifications of the between-class differences in variance–covariance matrix structure considered and clearly documented? If not, was sufficient justification provided as to eliminate certain specifications from consideration?	Yes
7 Are alternative shape/functional forms of the trajectories described?	Yes Not applicable
8 If covariates have been used, can analyses still be replicated?	Not applicable
9 Is information reported about the number of random start values and final iterations included?	Yes
10 Are the model comparison (and selection) tools described from a statistical perspective?	Yes
11 Are the total number of fitted models reported, including a one-class solution?	Yes
12 Are the number of cases per class reported for each model (absolute sample size, or proportion)?	Yes
13 If classification of cases in a trajectory is the goal, is entropy reported?	Yes
14a. Is a plot included with the estimated mean trajectories of the final solution?	Yes
14b. Are plots included with the estimated mean trajectories for each model?	Yes
14c. Is a plot included of the combination of estimated means of the final model and the observed individual trajectories split out for each latent class?	Yes
15 Are characteristics of the final class solution numerically described (i.e., means, SD/SE, n, CI, etc.)?	Yes
16 Are the syntax files available (either in the appendix, supplementary materials, or from the authors)?	Yes

Appendix U. Final Mplus Syntax for the Latent Class Growth Analysis

Table U1.

Mplus 8 Syntax for the 3-Class LCGA Quadratic Model.

```
DATA:
  FILE IS "C:/Users/dumsp/Desktop/TUSONLYB_9_15_24.dat";
VARIABLE:
  NAMES = IDLCGA t0_TUS t9_TUS t15_TUS t24_TUS;
  USEVARIABLES = t0_TUS t9_TUS t15_TUS t24_TUS;
  MISSING = ALL (-999);
  CLASSES = c(3);          ! Number of classes
  IDVARIABLE = IDLCGA;
ANALYSIS:
  TYPE = MIXTURE MISSING;
  ALGORITHM = INTEGRATION;
  ESTIMATOR = MLR;        ! Robust SE, handles missing
  STARTS = 500 20;       ! 500 random sets, 20 final
  LRTSTARTS = 100 20 500 20; ! LRT for BLRT
  STITERATIONS = 20;
MODEL:
%OVERALL%
  i s q|
  t0_TUS@0
  t9_TUS@9
  t15_TUS@15
  t24_TUS@24; ! Linear growth model with fixed time scores
  i@0;
  s@0;
  q@0;
OUTPUT:
  TECH1 TECH4 TECH8 TECH11 TECH14; ! Outputs for diagnostics and tests
  SAMPSTAT STANDARDIZED;
PLOT:
  TYPE = PLOT3; ! Plot average trajectories
  SERIES = t0_TUS(0) t9_TUS(9) t15_TUS(15) t24_TUS(24);
SAVEDATA:
  FILE IS "C:/Users/dumsp/Desktop/LCGA_3Class_Q_cor.dat";
  SAVE = cprobabilities;
  FORMAT IS FREE;
```

Appendix V. Missing Values Analysis for All Variables of Interest

A missing value analysis was conducted prior to modelling indicating that data were Missing Completely At Random (MCAR), Little's MCAR test, $\chi^2(310) = 340.24, p = .114$. A total of 172 participants (63.70%) had complete data across all variables of interest, including baseline characteristics and TUS measures across all time points.

Notably, 100 participants were recruited during an internal pilot ($n = 50$, East Anglia; $n = 50$, Manchester), whereas the remaining 170 participants during the main trial extension phase ($n = 57$, Sussex; $n = 59$, East Anglia; $n = 54$, Manchester). The 24-month assessment point was a late addition to the study protocol, at funder's request, during the internal pilot phase, which contributed to the higher level of missing data at this time point.

Missing values analysis indicated that the highest rate of missing cases was 24.1% ($N = 65$) for Time Use Structured Activity at 24 months, followed by 13% ($N = 35$) the Time Use Structured Activity at 15 months and 10.7% ($N = 29$) Time Use Structured Activity at 9 months. Age, gender, ethnicity, Time Use Structured Activity at baseline, ARMS status, AUDIT Total score and trial allocation did not have any missing values. See Table P1 for all missingness rates across all variables used in this study.

Table V1.

Missingness Rates for the Study Variables in the Whole Sample (N=270).

Sample characteristic	Overall missing	
	N	%
TUS 24 months	65	24.1
TUS 15 months	35	13.0
TUS 9 months	29	10.7
SIAS Total	10	3.7
BDI Depression Total	9	3.3
CAARMS Suicidality Summary Composite Score	8	3.0
SANS Individual Item Composite Total	7	2.6
DUDIT Total	3	1.1
CAARMS Symptom Severity Composite Score	3	1.1
Comorbidity Level	1	0.4
Logical Memory 1st Recall Scaled Score	1	0.4

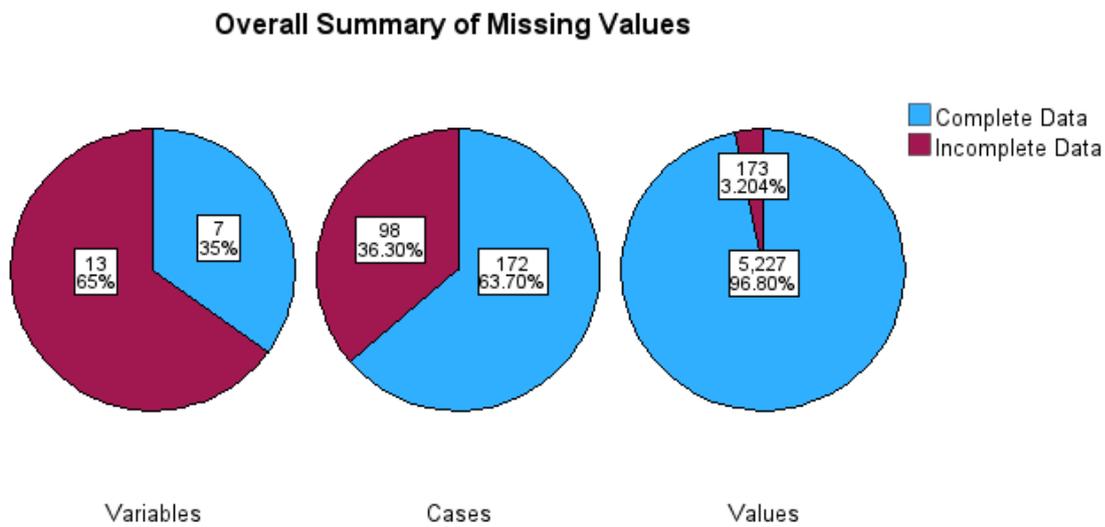
COWAT Total score	1	0.4
NEET status	1	0.4

Note. *N* = Number of participants; TUS = Time Use Survey; SIAS = Social Interaction Anxiety Scale; BDI -II = Beck’s Depression Inventory-II; CAARMS = Comprehensive Assessment of At-Risk Mental States; COWAT = Controlled Oral Word Association Test; DUDIT = Drug Use Disorders Identification Test; NEET = Not in Education, Employment, or Training; SANS = Scale for the Assessment of Negative Symptoms. Percentages indicate the proportion of missing data for each variable.

Figure V1 illustrates the overall summary of missing values in the dataset. Three pie charts display the proportions of complete and incomplete data across variables, cases, and individual values.

Figure V1.

Overall Summary of Missing Values



Note. Pie charts display the proportion of complete and incomplete data across variables, cases, and values. Blue represents complete data, while maroon represents incomplete data. Percentages and counts are displayed for each category.

Appendix W. Latent Class Growth Modelling Sensitivity Analysis for Extreme Cases

In Table W1 below are presented the model indices for the best three model solutions and k-1 solutions without extreme cases.

Table W1.*LCGA Model Indices without Extreme Cases (N = 7).*

Type of method	Classes	AIC	BIC	aBIC	Entropy	VLMR	BLRT	Class sample sizes (Ns)	Min-Max average posterior probabilities
Quadratic	2	7348.271	7387.565	7352.689	.841	-3808.118 ***	-3808.118***	72, 191	.941 - .960
Quadratic	3	7297.294	7350.876	7303.319	.800	-3893.290	-3663.135***	26, 68, 169	.834 - .940
Quadratic	4	7260.688	7328.559	7268.320	.849	-3633.644*	-3633.644***	32, 57, 141, 33	.829 - .948
Cubic	3	7290.678	7354.977	297.908	.801	-3661.833	-3661.833***	68, 30, 165	.810 - .943
Cubic	4	7241.103	7323.263	7250.342	.850	-3627.339*	-3627.339***	12, 61, 28, 162	.828 - .955

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; aBIC = Sample-Size Adjusted Bayesian Information Criterion; VLMR = Vuong-Lo-Mendell-Rubin Likelihood Ratio Test; BLRT = Bootstrap Likelihood Ratio Test. The AIC, BIC, and aBIC are fit indices used to compare model performance, with lower values indicating a better model fit. Entropy represents classification certainty, where values closer to 1 indicate greater accuracy in class assignment. VLMR and BLRT compare a model with k classes to a k-1 class model. A significant p-value ($p < .05$) indicates that the k-class model provides a better fit. Classes refers to the number of latent classes requested in each model. Average posterior probabilities indicate the probability of correct class membership assignment, with values closer to 1 reflecting better classification accuracy.

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$

Figures W1 to W10 show the visual representation of the different model solution for the whole sample and without the extreme cases. X axis represents time in months and Y axis TUS structured activity in hours per week for the estimated trajectory means for each class.

Figure W1.

Two-Class Quadratic Model for the Whole Sample (N = 270).

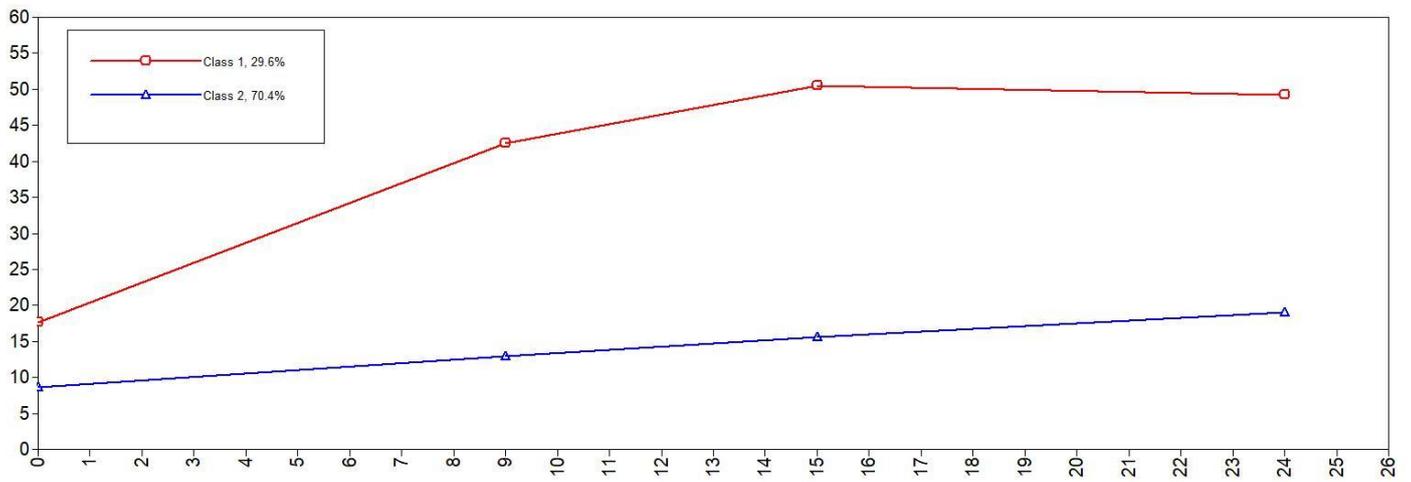


Figure W2.

Two-Class Quadratic Model without Extreme Cases (N = 263).

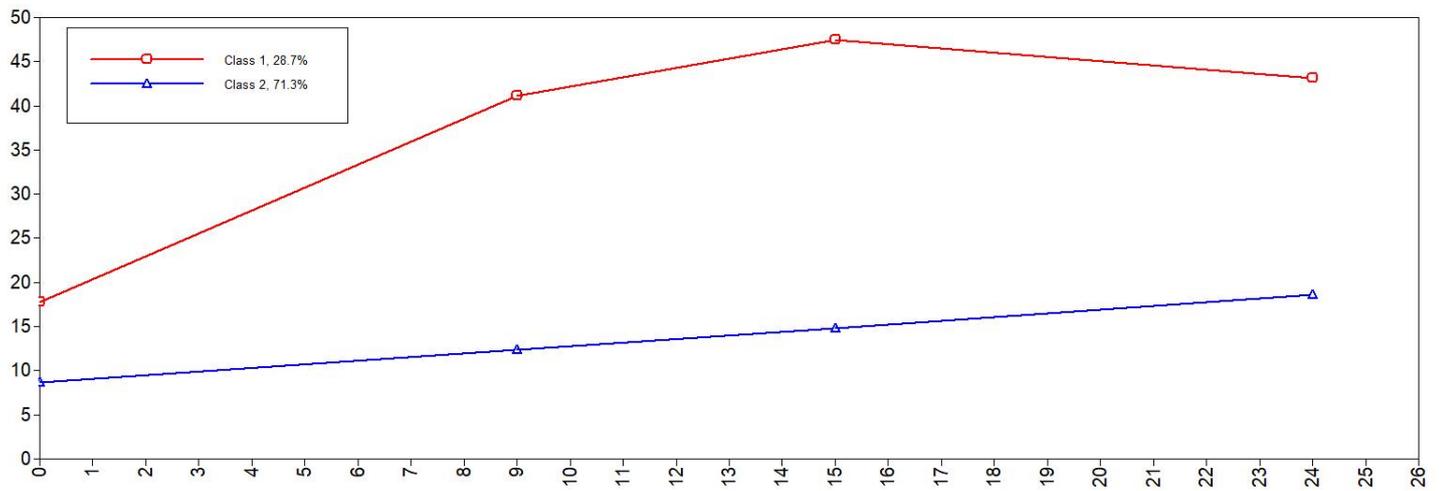


Figure W3.

Three-class Quadratic Model for the Whole Sample (N = 270).

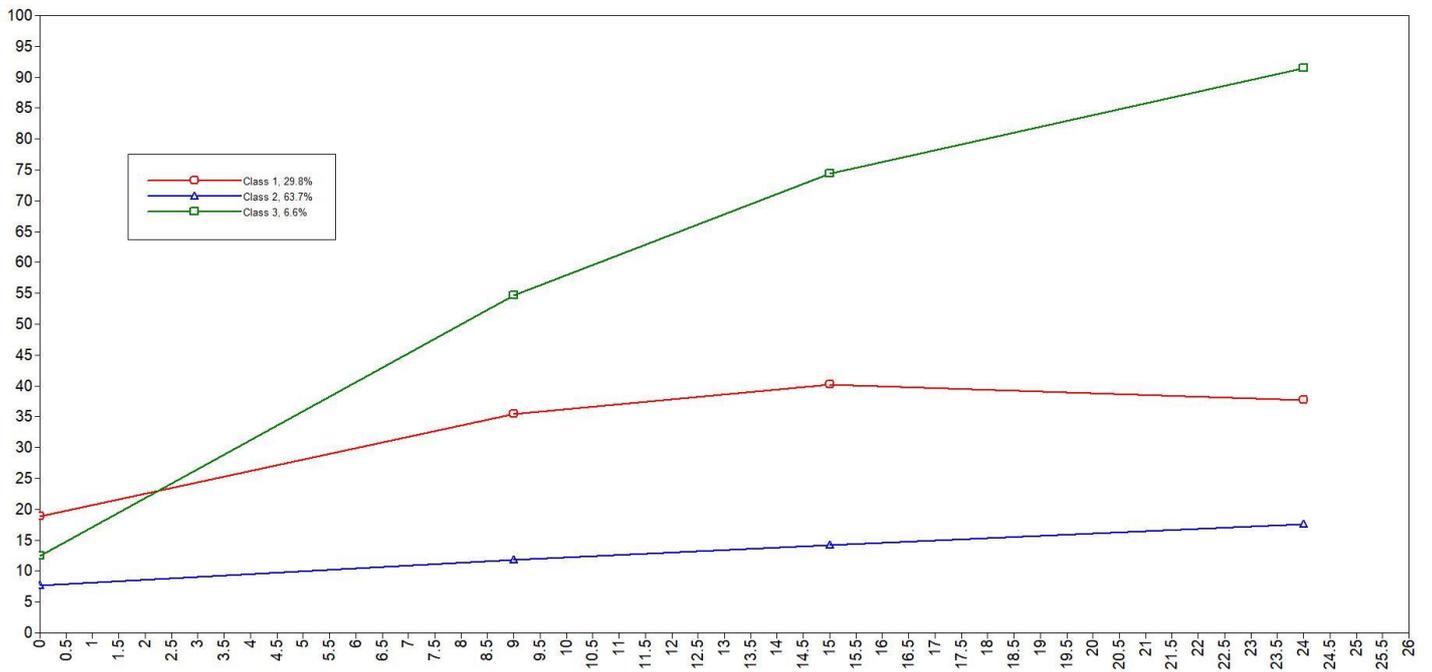


Figure W4.

Three-Class Quadratic Model without Extreme Cases (N = 263).

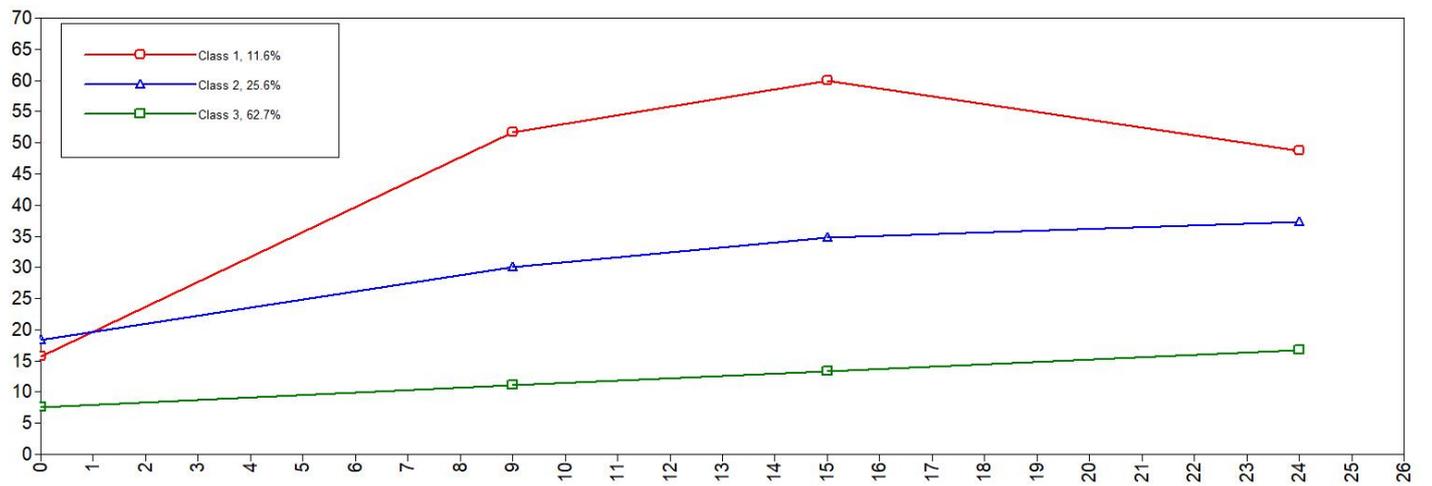


Figure W5.

Four-Class Quadratic Model for the Whole Sample (N = 270).

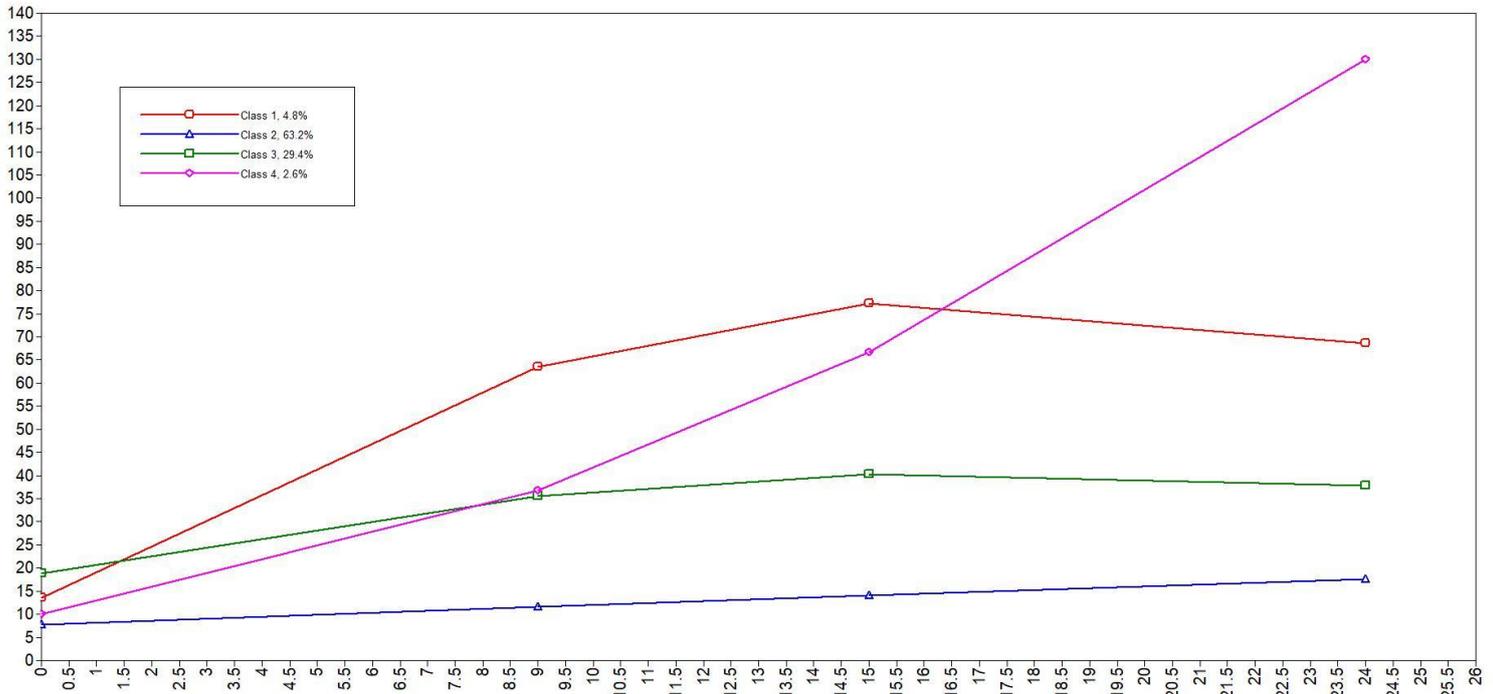


Figure W6.

Four-Class Quadratic Model without Extreme Cases (N = 263).

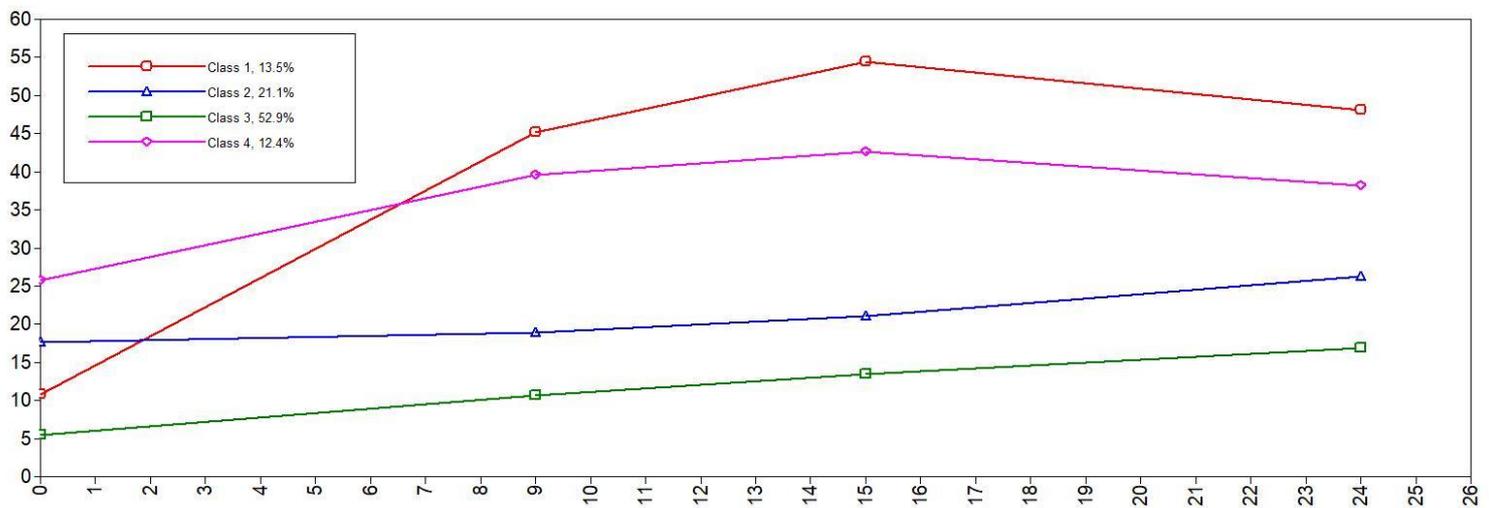


Figure W7.

Three-class Cubic Model for the Whole Sample (N = 270).

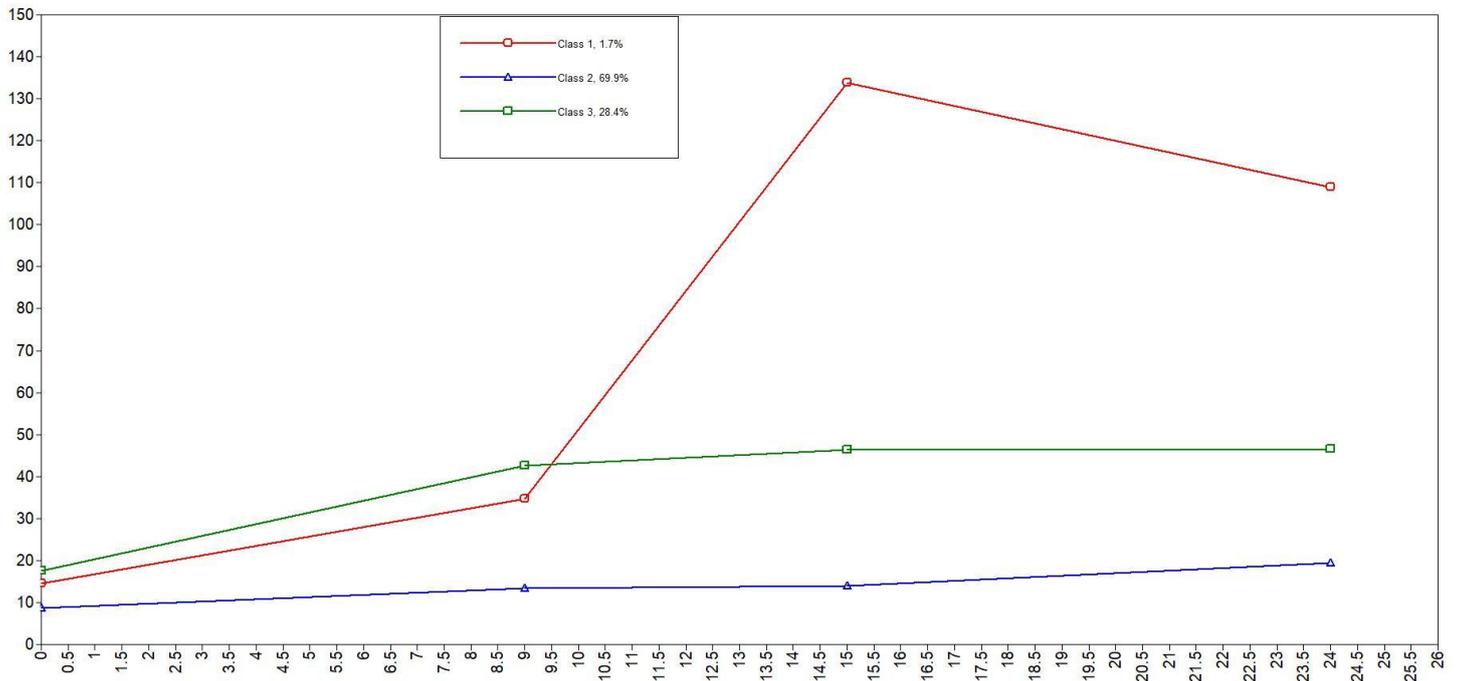


Figure W8.

Three-class Cubic Model without Extreme Xases (N = 263).

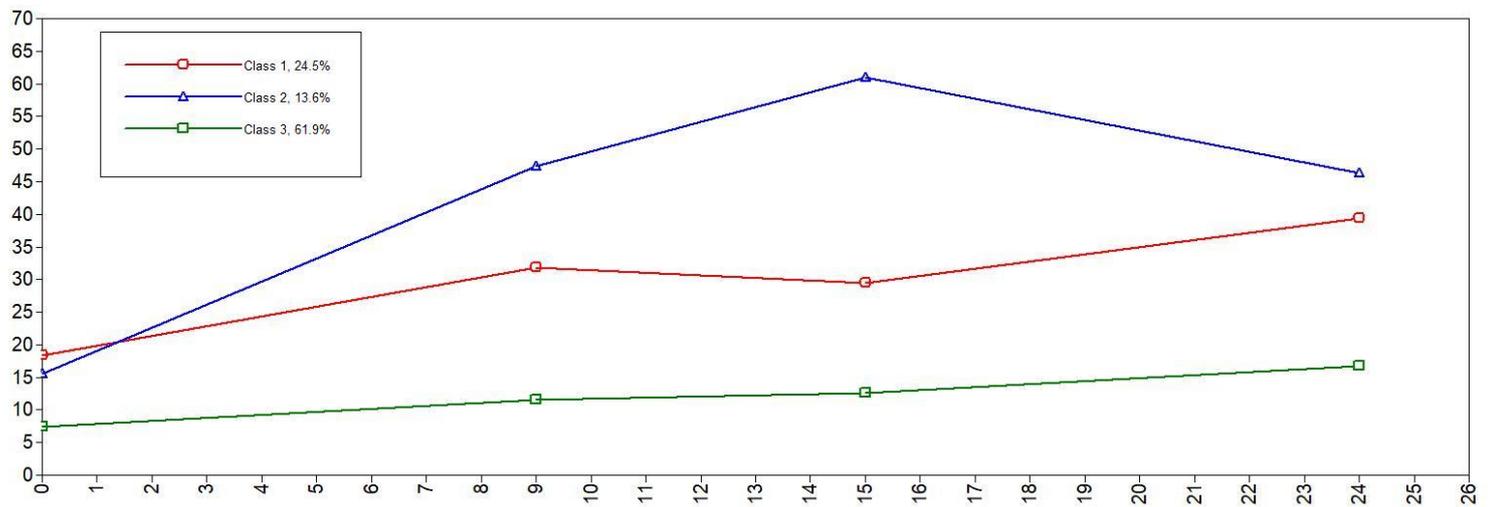


Figure W9.

Four-class Cubic Model for the Whole Sample (N = 270).

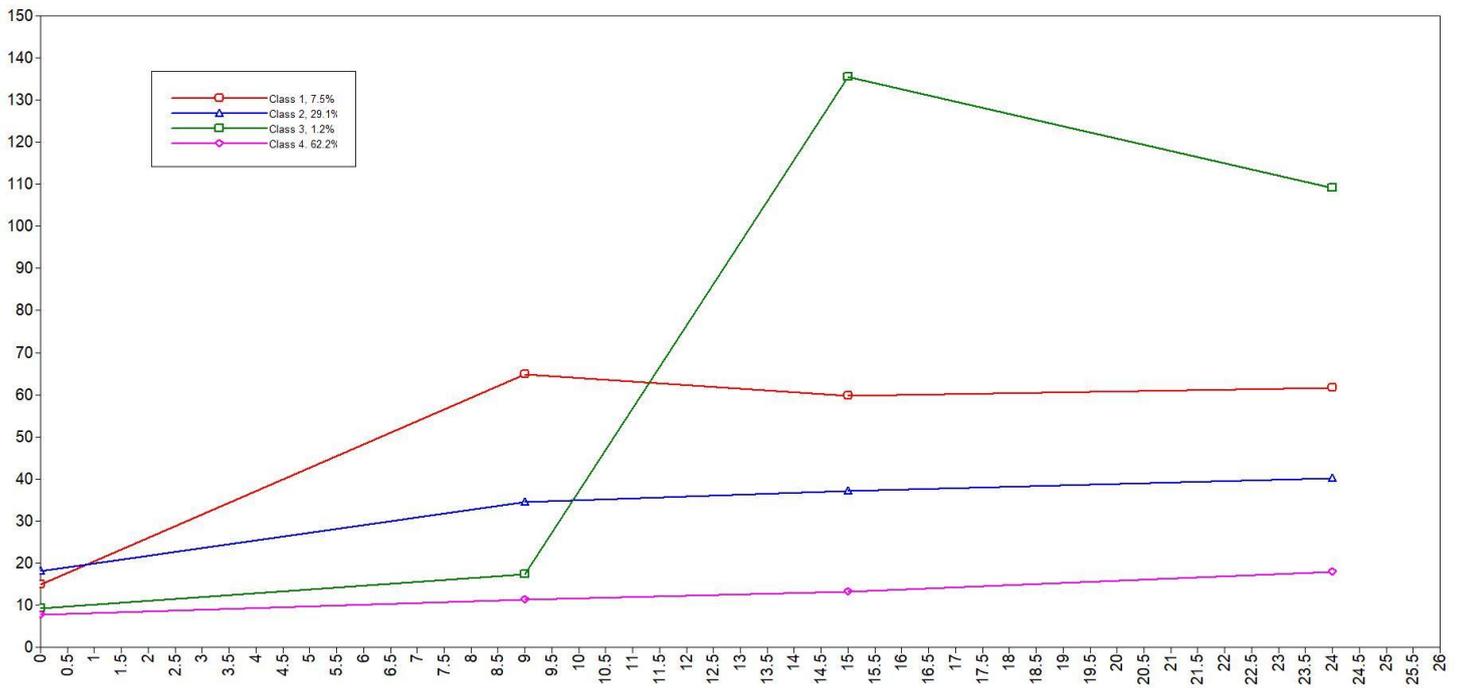
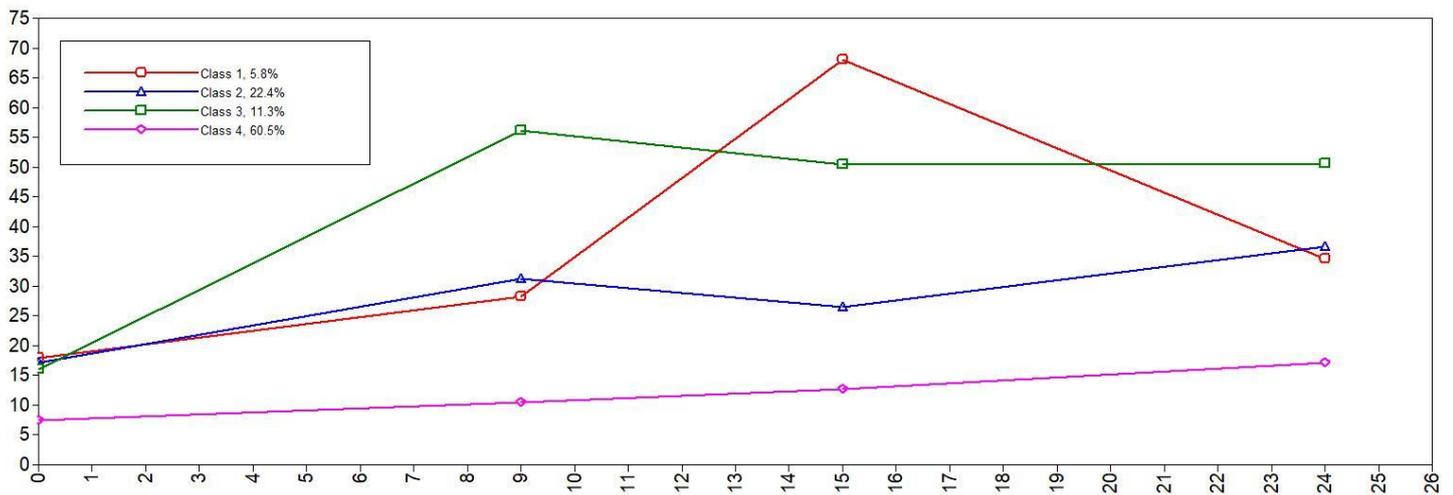


Figure W10.

Four-class Cubic Model without Extreme Cases (N = 263)



Appendix Y. Latent Class Growth Modelling Sensitivity Analysis within Each Trial

Arm

In Table Y1 and Y2 below are presented the model indices for the best three model solutions and k-1 solutions within each trial arm (SRT + ESC and ESC only).

Table Y1.

LCGA Model Indices within the SRT with ESC Trial Arm (N = 138).

Type of method	Classes	AIC	BIC	aBIC	Entropy	VLMR	BLRT	Class sample sizes (Ns)	Min-Max average posterior probabilities
Quadratic	2	4040.344	4072.544	4037.744	.810	-2075.504	-2075.504***	42,96	.910 - .961
Quadratic	3	3980.825	4024.733	3977.278	.870	-2009.172	-2009.172***	5, 42, 91	.929 - .993
Quadratic	4	3966.718	4022.336	3962.227	.896	-1975.412*	-1975.412***	5, 1, 40, 92	.942 - 1.000
Cubic	3	3981.329	4034.019	3977.073	.839	-2008.515	-2008.515***	10, 88, 40	.905 - .989
Cubic	4	3960.423	4027.750	3954.986	.842	-1972.664	-1972.664***	6, 82, 13, 37	.859 - .997

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; aBIC = Sample-Size Adjusted Bayesian Information Criterion; VLMR = Vuong-Lo-Mendell-Rubin Likelihood Ratio Test; BLRT = Bootstrap Likelihood Ratio Test. The AIC, BIC, and aBIC are fit indices used to compare model performance, with lower values indicating a better model fit. Entropy represents classification certainty, where values closer to 1 indicate greater accuracy in class assignment. VLMR and BLRT compare a model with k classes to a k-1 class model. A significant p-value ($p < .05$) indicates that the k-class model provides a better fit. Classes refers to the number of latent classes requested in each model. Average posterior probabilities indicate the probability of correct class membership assignment, with values closer to 1 reflecting better classification accuracy.

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$

Table Y2.

LCGA Model Indices within the ESC Trial Arm (N = 132).

Type of method	Classes	AIC	BIC	aBIC	Entropy	VLMR	BLRT	Class sample sizes (Ns)	Min-Max average posterior probabilities
Quadratic	2	3747.807	3779.517	3744.724	.807	-1919.499	-1919.499 ***	42, 90	.914 - .953
Quadratic	3	3713.741	3756.983	3709.537	.833	-1862.903	-1862.903 ***	8,39,85	.875 - .953
Quadratic	4	3698.580	3753.353	3693.256	.842	-1841.870	-1841.870 ***	5,15,29,83	.834 - .976
Cubic	3	3671.777	3723.667	3666.733	.896	-1862.892 **	-1862.892 ***	2,39,91	.942 - 1.000
Cubic	4	3647.996	3714.300	3641.551	.873	-1817.888	-1817.888 ***	2,10,33,87	.870 - 1.000

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; aBIC = Sample-Size Adjusted Bayesian Information Criterion; VLMR = Vuong-Lo-Mendell-Rubin Likelihood Ratio Test; BLRT = Bootstrap Likelihood Ratio Test. The AIC, BIC, and aBIC are fit indices used to compare model performance, with lower values indicating a better model fit. Entropy represents classification certainty, where values closer to 1 indicate greater accuracy in class assignment. VLMR and BLRT compare a model with k classes to a k-1 class model. A significant p-value ($p < .05$) indicates that the k-class model provides a better fit. Classes refers to the number of latent classes requested in each model. Average posterior probabilities indicate the probability of correct class membership assignment, with values closer to 1 reflecting better classification accuracy.

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$

Figures Y1 to Y10 below show the visual representation of the different model solution for the participant in each trial arm. X axis represents time in months and Y axis TUS structured activity in hours per week for the estimated trajectory means for each class.

Figure Y1.

Two-Class Quadratic Model in the ESC Trial Arm (N = 132).

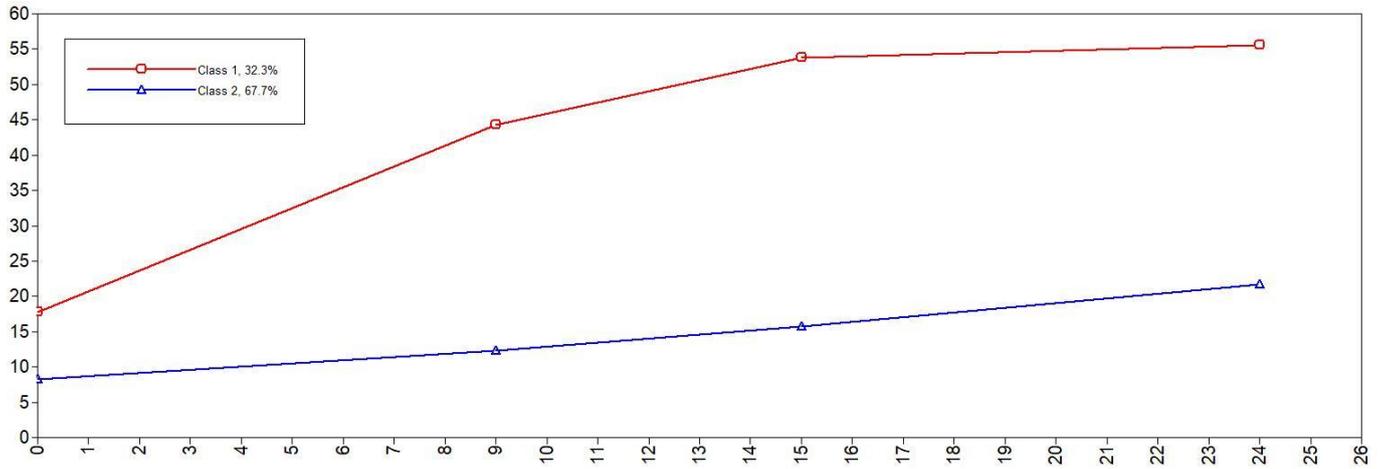


Figure Y2.

Two-Class Quadratic Model in the SRT+ESC Trial Arm (N = 138).

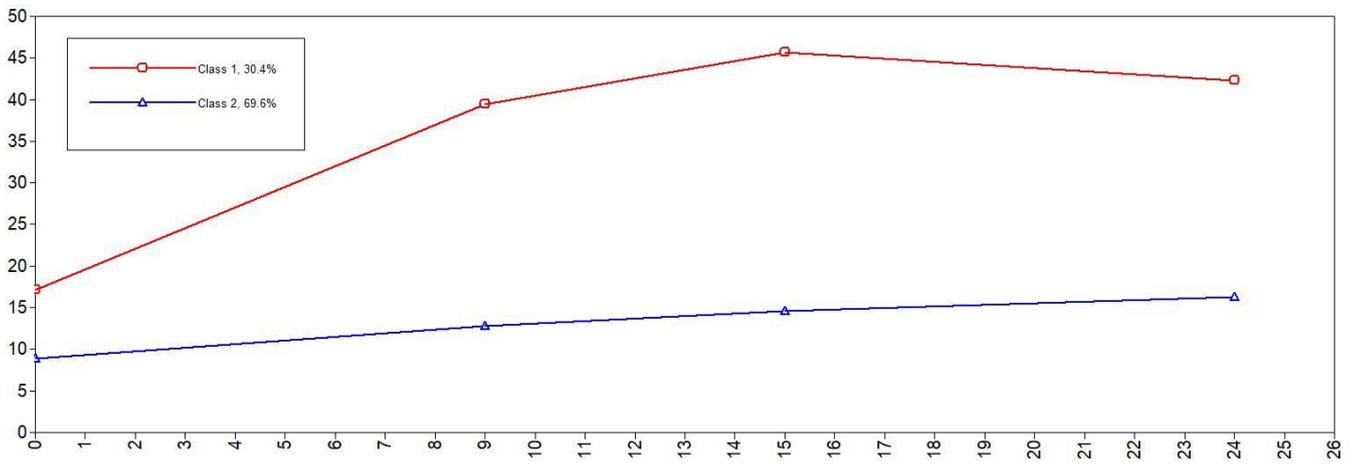


Figure Y3.

Three-class Quadratic Model in the ESC Trial Arm (N = 132).

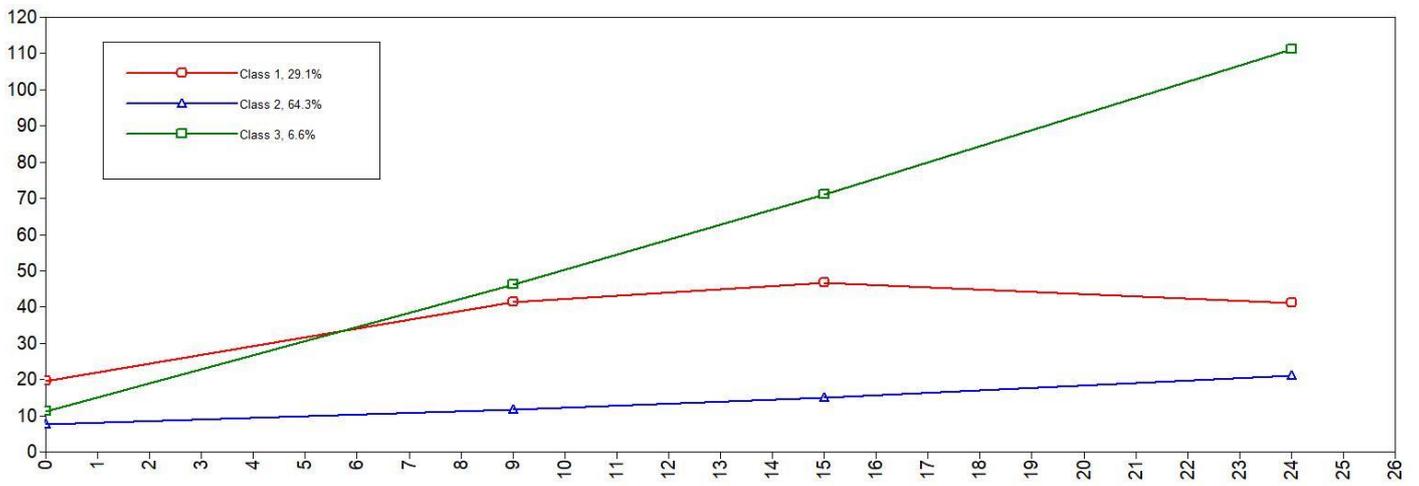


Figure Y4.

Three-class Quadratic Model in the SRT+ ESC Trial Arm (N = 138).

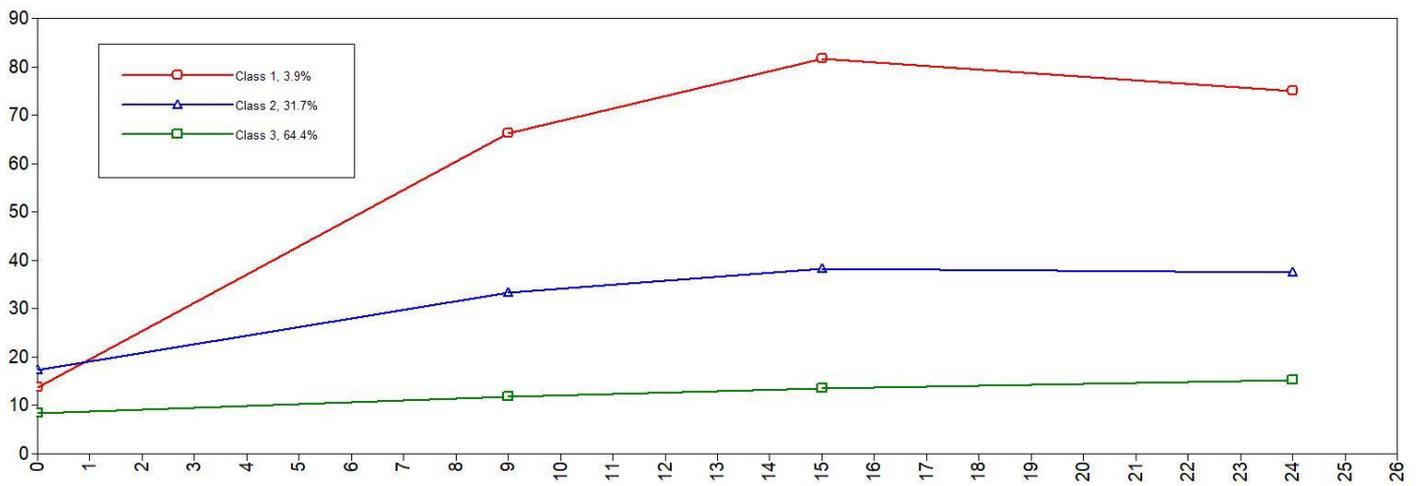


Figure Y5.

Four-class Quadratic Model in the ESC Trial Arm (N = 132).

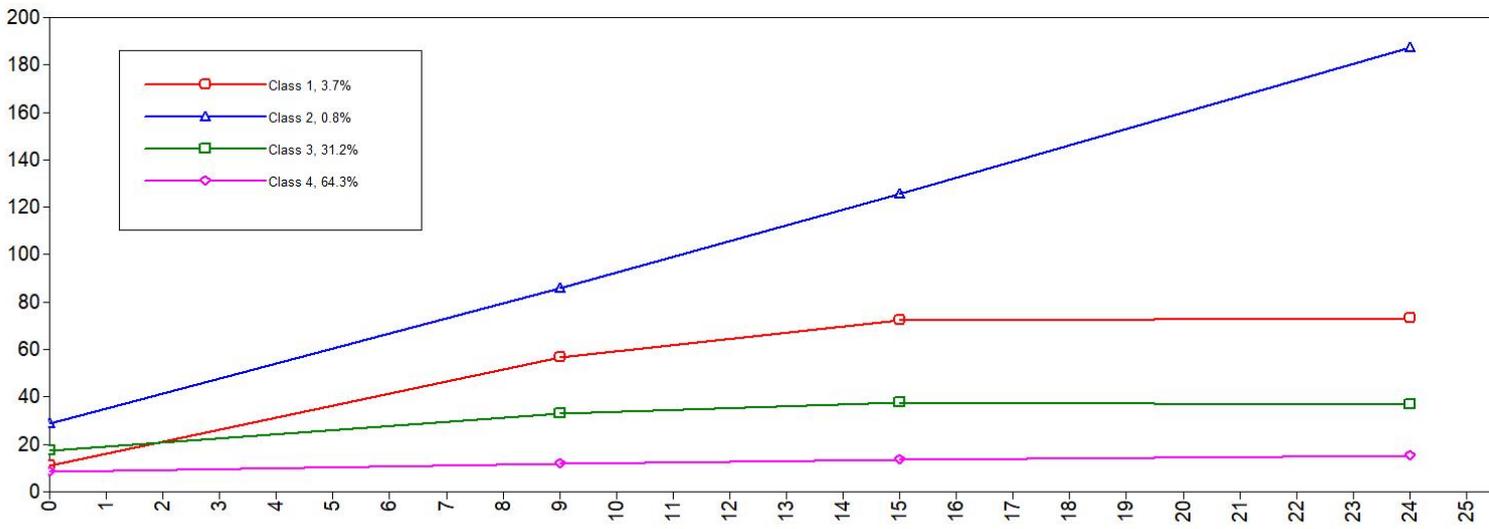


Figure Y6.

Four-class Quadratic Model in the SRT+ESC Trial Arm (N = 138).

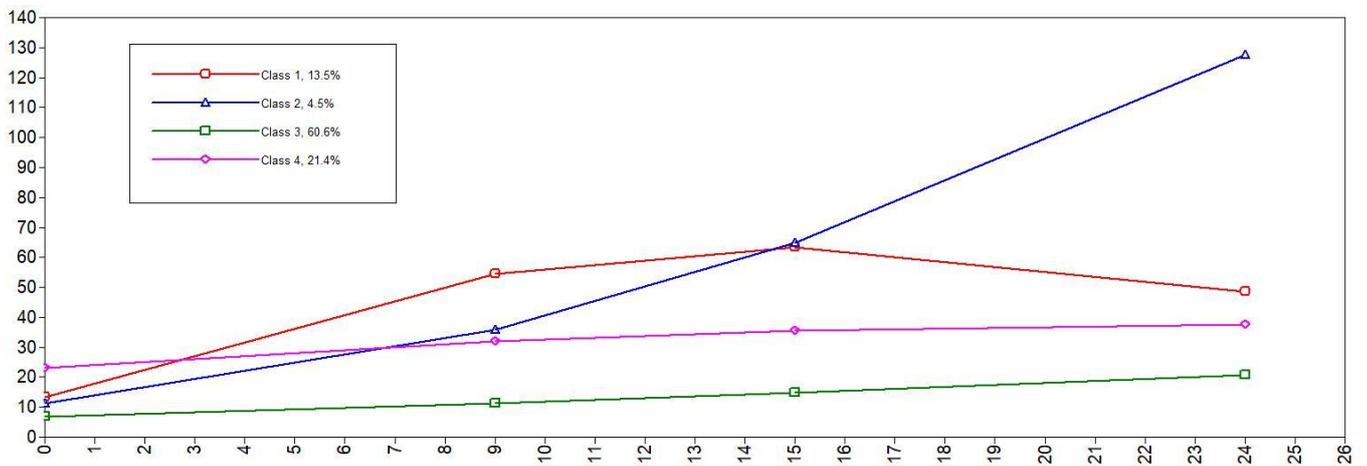


Figure Y7.

Three-class Cubic Model in the ESC Trial Arm (N = 132).

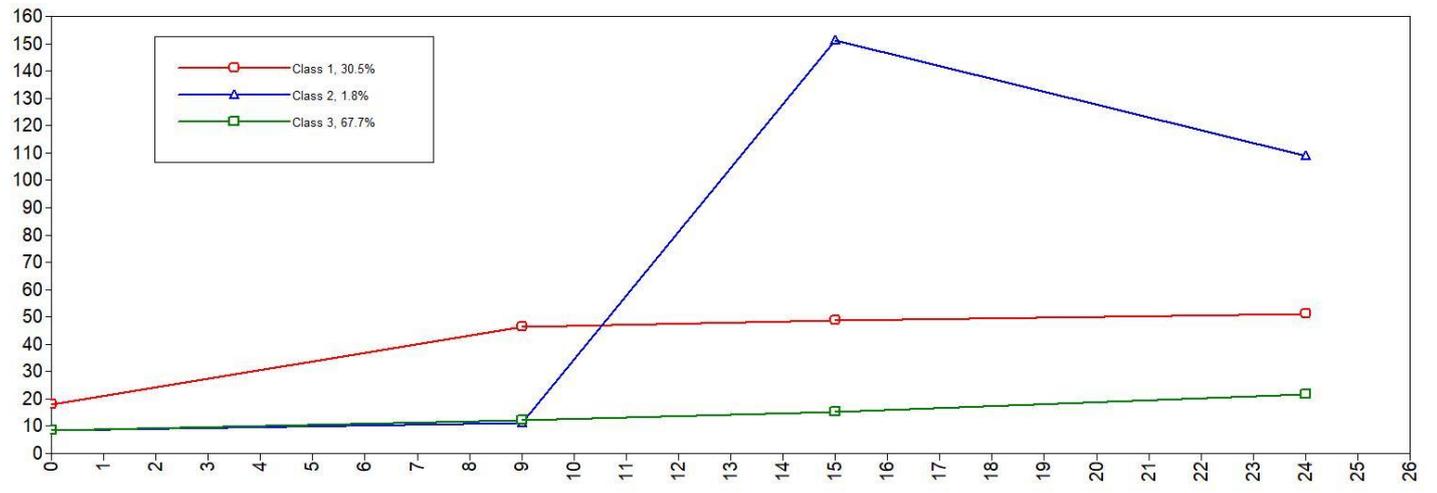


Figure Y8.

Three-class Cubic Model in the SRT+ESC Trial Arm (N = 138).

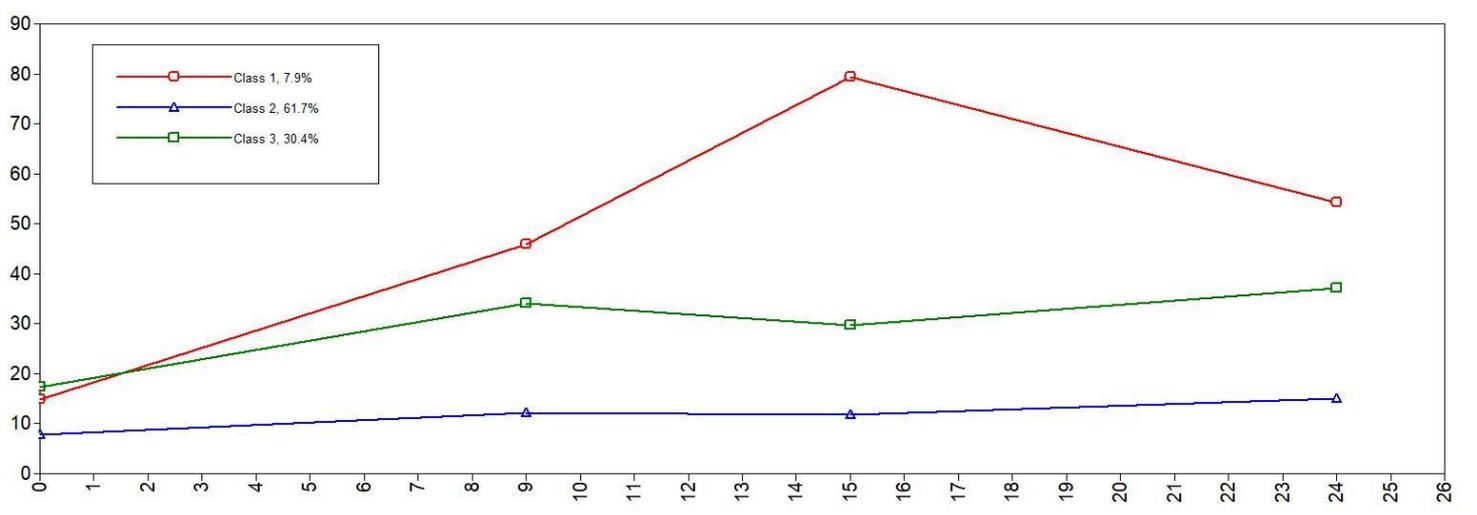


Figure Y9.

Four-class Cubic Model in the ESC Trial Arm (N = 132).

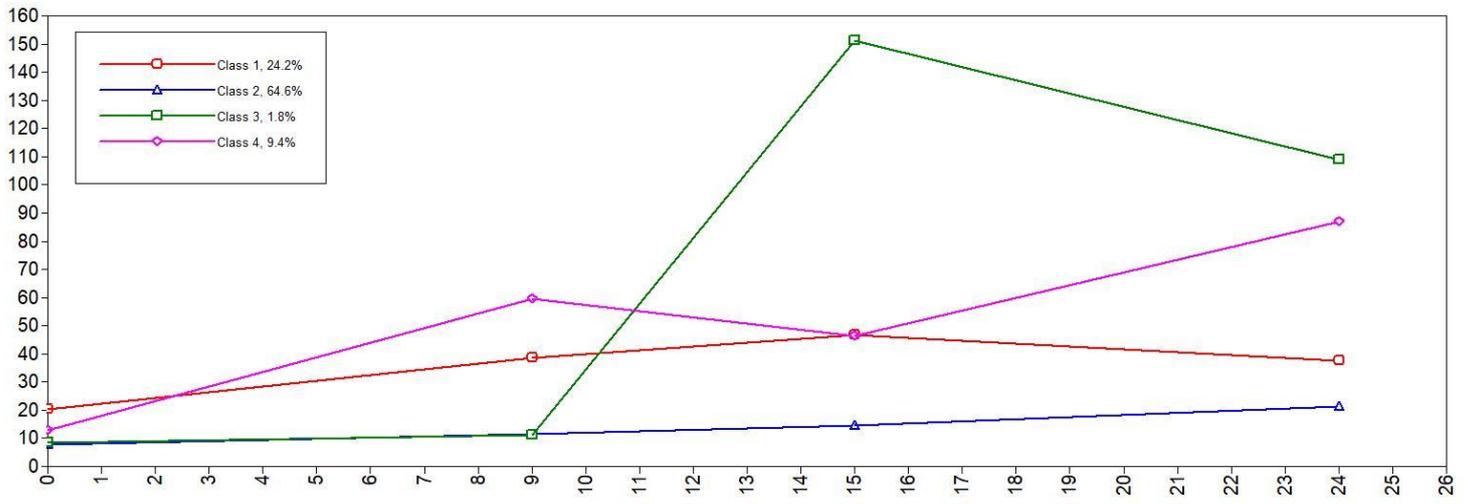
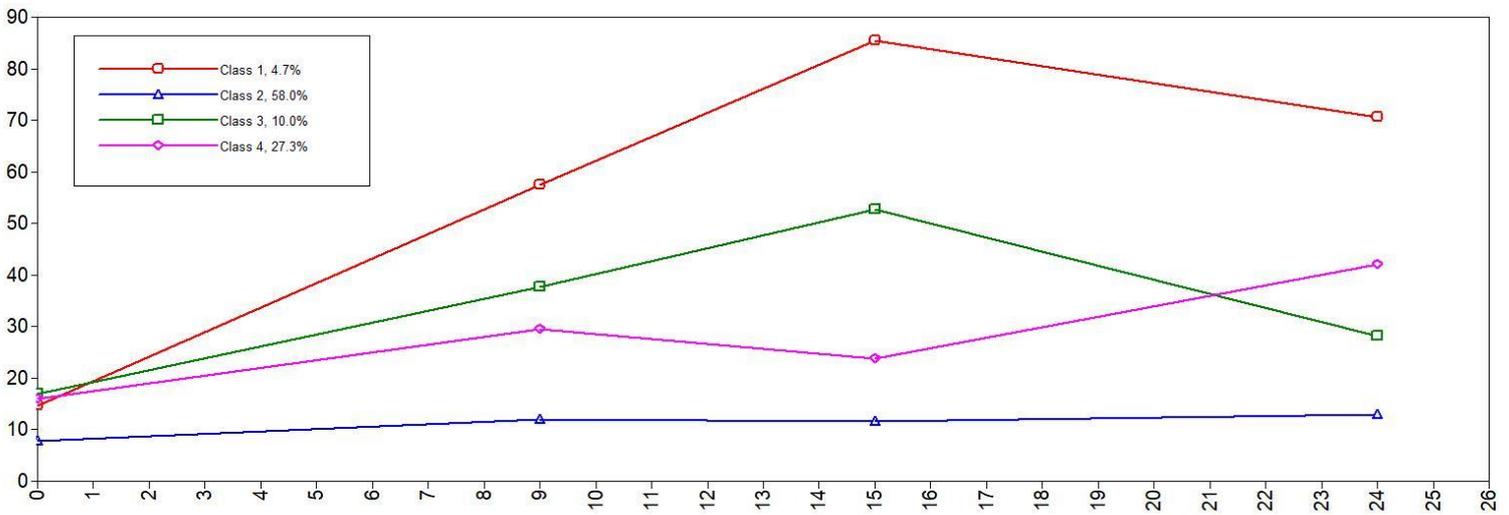


Figure Y10.

Four-class Cubic Model in the SRT+ESC Trial Arm (N = 138).



Appendix Z. LCGA Model Fit Statistics

Table Z1.

Goodness-of-fit statistics of LCGA models for class solutions of functional trajectories examined.

Type of method	Classes	AIC	BIC	aBIC	Entropy	VLMR	BLRT	Class sizes (Ns)	Min-Max average posterior probabilities
Linear	1	8047.295	8068.885	8049.861	-	-	-	-	-
Linear	2	7851.931	7884.317	7855.781	.762	-4017.647 *	-4017.647 ***	187, 83	.885 - .949
Linear	3	7753.954	7797.136	7759.087	.807	-3916.965	-3916.965 ***	169, 82, 19	.881 - .932
Linear	4	7730.086	7784.063	7736.502	.780	-3864.977 *	-3864.977 ***	152, 68, 31, 19	.729 - .907
Linear	5	7709.270	7774.041	7716.969	.812	-3850.043	-3850.043 ***	148, 67, 36, 18, 1	.723 - 1.00
Quadratic	1	8038.964	8064.153	8041.958	-	-	-	-	-
Quadratic	2	7808.581	7848.163	7813.286	.797	-4012.482*	-4012.482 ***	76, 194	.914 - .946
Quadratic	3	7719.448	7773.425	7725.864	.832	-3893.290 *	-3893.290 ***	175, 79, 16	.888 - .943
Quadratic	4	7690.265	7758.635	7698.392	.875	-3844.724 *	-3844.724 ***	173, 80, 10, 7	.890 - .986
Quadratic	5	7672.836	7755.599	7682.674	.818	-3826.132	-3826.132 ***	141, 52, 37, 23, 17	.785- .926
Cubic	1	8040.617	8069.404	8044.039	-	-	-	-	-
Cubic	2	7811.952	7858.732	7817.513	.797	-4012.308 *	-4012.308 ***	193, 77	.909 - .948
Cubic	3	7701.858	7766.630	7709.558	.888	-3892.976	-3892.976 ***	192, 74, 4	.931 - 1.000
Cubic	4	7640.573	7723.336	7650.411	.882	-3832.929	-3832.929 ***	171, 79, 17, 3	.893 - 1.000
Cubic	5	7615.655	7716.410	7627.632	.864	-3797.286	-3797.286	173, 66, 14, 13, 4	.847 - .984

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; aBIC = Sample-Size Adjusted Bayesian Information Criterion; VLMR = Vuong-Lo-Mendell-Rubin Likelihood Ratio Test; BLRT = Bootstrap Likelihood Ratio Test. The AIC, BIC, and aBIC are fit indices used to compare model performance, with lower values indicating a better model fit. Entropy represents classification certainty, where values closer to 1 indicate greater accuracy in class assignment. VLMR and BLRT compare a model with k classes to a k-1 class model. A significant p-value (p < .05) indicates that the k-class model provides a better fit. Classes refers to the number of latent classes requested in each model. Average posterior probabilities indicate the probability of correct class membership assignment, with values closer to 1 reflecting better classification accuracy. Solution in bold indicate the top three best-fitting models.

* p<0.05, **p<0.01, ***p<0.001

**Appendix AA. Additional Baseline Demographic and Clinical Characteristics for the
Three Trajectory Groups**

Table AA1.

Additional Baseline Demographic and Clinical Characteristics for the Three Trajectory Groups.

Sample Characteristic	Class 1 Moderate Improvement (N = 79)	Class 2 Stable Low (N = 175)	Class 3 Increasing Overactive (N = 16)
	<i>M (Min-Max; SD)/ N (Valid %)</i>		
Referral Source			
Self-referral	2 (2.53)	3 (1.71)	0
NHS CAMHS/CHYPS	17 (21.52)	40 (22.86)	1 (6.25)
Council Children/Family	8 (10.13)	33 (18.86)	4 (25.00)
Primary Care/IAPT	12 (15.19)	27 (15.43)	2 (12.50)
Non-NHS Youth service	4 (5.06)	17 (9.71)	0
NHS Adult	7 (8.86)	13 (7.43)	0
Vocational support/YES	9 (11.39)	14 (8.00)	0
Educational institution	12 (15.19)	14 (8.00)	6 (37.50)
NHS EIS/EDT	2 (2.53)	7 (4.00)	1 (6.25)
Housing	2 (2.53)	3 (1.71)	1 (6.25)
Acute	3 (3.80)	1 (0.57)	0
Private/charity therapy	0	2 (1.14)	1 (6.25)
NHS Specialist	1 (1.27)	1 (0.57)	0
Employment status ^a			
Student	25 (31.65)	34 (19.54)	6 (37.50)
Employed (paid)	9 (11.39)	2 (1.15)	0
Employed (voluntary)	4 (5.06)	3 (1.72)	0
NEET	41 (51.90)	135 (77.59)	10 (62.50)
ARMS Status and Category			
Not at risk	34 (43.04)	93 (53.14)	10 (62.50)
Vulnerability group	2 (2.53)	2 (1.14)	0
APS	36 (45.57)	73 (41.71)	6 (37.50)
BLIPS	0	1 (.57)	0
Vulnerability + APS	6 (7.59)	5 (2.86)	0
APS + BLIPS	1 (1.27)	1 (.57)	0
SCID Diagnoses			
MDE	41 (51.90)	83 (47.43)	13 (81.25)
Past MDE	21 (26.58)	50 (28.57)	3 (18.75)

Sample Characteristic	Class 1 Moderate Improvement (N = 79)	Class 2 Stable Low (N = 175)	Class 3 Increasing Overactive (N = 16)
Mania	0	1 (.57)	1 (6.25)
Past Mania	4 (5.06)	3 (1.71)	0
Hypomania	2 (2.53)	4 (2.29)	1 (6.25)
Past Hypomanic Episode	0	2 (1.14)	1 (6.25)
Dysthymia	11 (13.92)	20 (11.43)	0
Bipolar At Risk	15 (18.99)	21 (12)	3 (18.75)
Bipolar Disorder I	4 (5.06)	2 (1.14)	1 (6.25)
Bipolar Disorder II	0	5 (2.86)	0
MDD	60 (75.95)	116 (66.29)	12 (75)
Panic Disorder ^b	5 (6.41)	7 (4)	0
Panic Disorder with Agoraphobia	11 (13.92)	27 (15.43)	5 (31.25)
Agoraphobia	18 (22.78)	34 (19.34)	0
Socia Phobia	32 (40.51)	77 (44)	7 (43.75)
Specific Phobia	3 (3.80)	11 (6.29)	0
OCD	11 (13.92)	10 (5.71)	2 (12.50)
PTSD	9 (11.39)	17 (9.71)	4 (25)
Generalised Anxiety Disorder	22 (27.85)	55 (31.43)	3 (18.75)
Hypochondriasis	1 (1.27)	3 (1.71)	3 (18.75)
Body Dysmorphic Disorder	6 (7.59)	17 (9.71)	1 (6.25)
Anorexia Nervosa	0	2 (1.14)	0
Bulimia Nevrosa	0	1 (.57)	0
Binge Eating Disorder	0	3 (1.71)	0
Anxiety Disorder NOS	2 (2.53)	4 (2.29)	1 (6.25)
Number of SCID diagnoses/episodes ^c			
None	1 (1.28)	2 (1.14)	1 (6.25)
One	9 (11.54)	21 (12.00)	0
Two	18 (23.08)	44 (25.14)	3 (18.75)
Three	20 (25.64)	51 (29.14)	2 (12.50)
Four	21 (26.92)	48 (27.43)	8 (50.00)
Five	8 (10.26)	9 (5.14)	2 (12.50)
Six	1 (1.28)	0	0
GAF	42.56 (20-65; 7.91)	37.67 (20-49; 5.15)	36.75 (31-43; 3.71)
SOFAS	46.33 (15-62; 7.74)	40.69 (16-61;6.64)	42.25 (33-55; 6.45)

Sample Characteristic	Class 1 Moderate Improvement (N = 79)	Class 2 Stable Low (N = 175)	Class 3 Increasing Overactive (N = 16)
Highest GAF in the last 12 months	43.84 (29-100; 14.52)	41.18 (21- 87; 9.29)	41.02 (31-65; 9.36)
Medication Use			
Antipsychotics ^d	9 (11.39)	10 (5.75)	2 (12.50)
Antidepressants	44 (55.70)	101 (57.71)	11 (68.75)
Anxiolytics ^d	8 (10.13)	20 (11.49)	3 (18.75)
Benzodiazepines ^d	3 (3.80)	10 (5.75)	1 (6.3)
Mood stabilisers ^d	2 (2.53)	1 (.57)	0
ADHD medication ^d	5 (6.33)	11 (6.32)	0
Other medication use - anxiolytic/ tranquiliser/ mood stabiliser/ ADHD ^c	16 (20.25)	39 (22.41)	4 (25)

Note. M = Mean; SD = Standard Deviation; Valid % represents the percentage of participants with available data; Acute = Acute mental health services; APS = Attenuated Psychotic Symptoms; ARMS = At-Risk Mental State for Psychosis; BLIPS = Brief Limited Intermittent Psychotic Symptoms; Council Children/Family = Local authority children's or family services; Educational institution = School, college, or university referral; GAF = Global Assessment of Functioning; Housing = Housing support services; MDE = Major Depressive Episode; NEET = Not in Education, Employment, or Training; NHS Adult = National Health Service adult mental health services; NHS CAMHS/CHYPS = National Health Service Child and Adolescent Mental Health Services / Children and Young People's Services; NHS EIS/EDT = National Health Service Early Intervention Service / Early Detection Team; NHS Specialist = National Health Service mental health specialist services; Non-NHS Youth service = Non-National Health Service affiliated youth services; Primary Care/IAPT = Primary Care / Improving Access to Psychological Therapies; Private/charity therapy = Private sector or charitable organization-provided therapy; SCID = Structured Clinical Interview for DSM-IV Axis I Disorders; Self-referral = Self-referral by the individual or their family; SOFAS = Social and Occupational Functioning Assessment Scale; Vocational support/YES = Vocational support services / Youth Employment Services.

Missing data is noted where applicable. Percentages are calculated based on available data. ^a Missing N=1 in Class 2; ^b Missing N = 1 in Class 1; ^c Missing N = 1 in Class 1; ^d Missing N=1 in Class 2

Appendix AB. Multinomial Logistic Regression Assumptions Check

Multicollinearity was assessed using Spearman’s correlations and variance inflation factor (VIF) statistics. No correlations exceeded $r = .70$ (Table V1), and all VIF values were below 2, with tolerance values above 0.1, indicating no multicollinearity concerns [102].

Linearity between continuous predictors and the logit transformation of the dependent variable was assessed visually and with the Box-Tidwell test [103]. Significant interaction terms for verbal fluency (COWAT Total) ($p = .033$) indicated potential nonlinearity. Visual inspection did not confirm these issues and thus, the model was run without transformations.

Table AB1.

Correlation Matrix for the Variables Included as Predictors in the Multinomial Logistic Regression Model Presenting Spearman’s Rho Correlation Coefficients (N = 270).

Variable	1	2	3	4	5	6	7	8
1. Trial Arm Allocation	-	-	-	-	-	-	-	-
	.004							
2. NEET status	<i>N</i> = 269	-	-	-	-	-	-	-
	.03	.27***						
3. Age	<i>N</i> = 270	<i>N</i> = 269	-	-	-	-	-	-
	-.11	-.02	-.21***					
4. Gender	<i>N</i> = 270	<i>N</i> = 269	<i>N</i> = 270	-	-	-	-	-
	.09	.05	-.04	-.003				
5. Ethnicity	<i>N</i> = 270	<i>N</i> = 269	<i>N</i> = 270	<i>N</i> = 270	-	-	-	-
	-.04	.27***	.05	-.02	.09			
6. SANS Avolition/Apathy	<i>N</i> = 270	<i>N</i> = 269	<i>N</i> = 270	<i>N</i> = 270	<i>N</i> = 270	-	-	-
	.08	-.13*	.13*	-.10	.05	-.12		
7. Logical Memory Scaled Total	<i>N</i> = 269	<i>N</i> = 268	<i>N</i> = 269	<i>N</i> = 269	<i>N</i> = 269	<i>N</i> = 262	-	-
	.02	-.16*	.22***	-.14*	-0.04	-.17**	.39***	-
8. COWAT total								

$N = 269$ $N = 268$ $N = 269$ $N = 269$ $N = 269$ $N = 262$ $N = 269$

Note. Values represent Spearman's rho correlation coefficients. Sample sizes (N) are provided for each correlation. NEET = Not in Education, Employment, or Training; SANS = Scale for the Assessment of Negative Symptoms; COWAT = Controlled Oral Word Association Test. Dummy variables were coded as follows: Trial Arm Allocation (1 = Social Recovery Therapy, 0 = Enhanced Standard Treatment); NEET status (1 = NEET, 0 = Non-NEET); Gender (1 = Female, 0 = Male); Ethnicity (1 = White British, 0 = All Others).

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