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Prevalence of self-reported subthreshold phenotypes of major mental disorders and their association with functional impairment, treatment and full-threshold syndromes in a community-residing cohort of young adults

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Abstract

Aim: Subthreshold syndromes (STS) frequently precede the onset of full-threshold syndromes (FTS) of the corresponding mental disorder (homotypic continuity). This study examines whether subthreshold conditions are comorbid and whether there is heterotypic continuity also between STS and FTS.

Methods: Data were extracted from the Brisbane "19Up" cohort study of twins and siblings (N = 1838; 56% female) on individuals who (i) completed self-report ratings of depression-like (DLE), hypomanic-like (HMLE) and psychotic-like experiences (PLE) and (ii) were assessed for mood and psychotic FTS using the Composite International Diagnostic Interview (CIDI). Associations between STS and FTS were estimated using adjusted prevalence ratios (APR) and 95% confidence intervals (CI).

Results: STS are prevalent, with 22% reporting DLE, 14% HMLE and 5% PLE; 7% reported >1 STS, with PLE most likely to demonstrate comorbidity. Individuals with DLE were likely to meet CIDI criteria for depression (APR: 3.71, 95% CI: 2.83, 4.89), hypo/mania (APR: 3.62, 95% CI: 2.21, 5.94) and psychotic disorders (APR: 1.74, 95% CI 1.08, 2.83). Individuals with HMLE were likely to meet CIDI criteria for depression (APR: 2.29, 95% CI: 1.58, 3.31) and hypo/mania (APR: 2.51, 95% CI: 1.29, 4.91); those with PLE were likely to meet criteria for hypo/mania (APR: 5.8, 95% CI: 1.90, 17.70) and psychotic disorders (APR: 17.27, 95% CI: 7.54, 39.65).

Conclusions: The findings suggest that STS are common among young adults and show heterotypic as well as homotypic continuity with FTS and support the need for more trans-diagnostic research on the evolution of major mental disorders.

KEYWORDS

heterotypic, homotypic, subthreshold, trans-diagnostic, youth cohort

1 | INTRODUCTION

Recent decades have seen the emergence of two research themes with important implications for clinical practice in youth mental health settings. First, comorbidities are common in individuals in the peak age range for onset of major mental disorders (about 15-27 years) (eg, Costello, Copeland, & Angold, 2011) to the extent that the co-occurrence of full-threshold episodes of mood and psychotic

disorders is the rule rather than the exception (Hickie, Scott, & Hermens, 2019; Krueger & Markon, 2006). Second, research indicates that subthreshold conditions frequently precede the onset of the corresponding threshold mental disorders (referred to as homotypic continuity). For example, attenuated psychotic symptoms are associated with an increased likelihood of the onset of a psychotic disorder meeting recognized diagnostic criteria (eg, Dominguez, Wichers, Lieb, Wittchen, & van Os, 2011). It is clear also that heterotypic continuity (ie, one diagnosis in childhood and adolescence predicting the later presence of a different diagnosis) is common (eg, Kim-Cohen et al., 2003; Lahey, Zald, Hakes, Krueger, & Rathouz, 2014). Less is known about any heterotypic associations between subthreshold syndromes (STS) and full-threshold syndromes (FTS).

Research publications on subthreshold manifestations of major psychiatric syndromes demonstrate that these are common in community and clinical settings (eg, Kessler & Walters, 1998). However, studies vary in the terminology employed to describe STS including: "subthreshold or NOS conditions", "spectrum disorders", "clinical high risk presentations", "micro-phenotypes", "extended community phenotypes", stage 1b conditions, etc. (eg, Hickie et al., 2019; McGorry, 2010; van Os & Reininghaus, 2016). Likewise, they employ various tools to measure these conditions such as self-report and symptom rating scales, structured clinical schedules, or composite measures of symptoms and risk factors (eg, Bechdolf et al., 2014; Nelson, Fusar-Poli, & Yung, 2012). Despite the range of instruments employed, the shared assumption is that symptoms of depression-like, hypomanic-like and psychotic-like experiences are quantitatively rather than qualitatively different from severe and persistent presentations of major mental disorders that meets traditional diagnostic criteria (McGorry, Hickie, Yung, Pantelis, & Jackson, 2006; van Os, 2013). Further, although symptom frequency or severity may be subthreshold for a given diagnosis, it is suggested that some of these presentations demonstrate a similar need for care as the corresponding full-syndromal disorders (eg, Cross, Scott, Hermens, & Hickie, 2018).

Research on comorbid full-threshold diagnoses is well-established; however, studies focused specifically on STS have only begun to be published in recent decades. To date, this research has primarily focused on whether a specific STS increases the likelihood of being diagnosed with the corresponding mental disorder (which can be described as homotypic transition). In such studies, subthreshold conditions that do not evolve to the corresponding mental disorder are usually described as failing to demonstrate transition (Addington et al., 2018; Lin et al., 2015). Furthermore, it is frequently implied that lack of homotypic progression to the full syndrome under investigation can be categorized as a good outcome (Addington et al., 2018; Lin et al., 2015). However, this line of reasoning may underestimate the morbidity associated with subthreshold conditions, and critically, it does not consider those STS that evolve into a condition that meet diagnostic criteria for a different mental disorder (ie, heterotypic transition) (McGorry, Hartmann, Spooner, & Nelson, 2018).

There are few studies that simultaneously assess more than one STS for major mental disorders in the same population or that report the pattern and prevalence of co-occurring STS (eg, Iorfino et al., 2019). Furthermore, little is known about the impact of the presence of greater than or equal to 1 STS on day-to-day functioning, seeking or being offered mental health care and treatment, or being diagnosed with greater than or equal to 1 FTS. To address some of these gaps, the present study used data extracted from the database of a large-scale community-based longitudinal prospective research program focused on twins and non-twin siblings in Australia. This article focuses specifically on a subset of participants who (i) undertook self-report ratings of STS and (ii) participated in a Composite International Diagnostic Interview (CIDI; Kessler et al., 2004) during the peak age range for onset of adult-pattern mood and psychotic disorders. The extracted data were used to investigate the following questions:

1. Regarding characteristics and patterns of STS-
   a. what is the prevalence of depression-like (DLE), hypomanic-like (HMLE) and psychotic-like experiences (PLE) and what are the patterns of comorbidities among DLE, HMLE and PLE?
   b. and is the number of self-reported STS associated with functional impairment, help-seeking or mental health treatment?
2. Regarding the inter-relationships between STS and FTS
   a. does the presence of greater than or equal to 1 STS increase the likelihood that an individual will meet criteria for a FTS?
   b. do STS show homotypic or heterotypic continuity with FTS, that is, are the STS associated with the corresponding FTS or with a different CIDI diagnoses?

2 | METHODS

Given limitations of space, we can only provide a brief overview of the full methodology of the Brisbane Longitudinal Twin Study (BLTS). Detailed descriptions of the protocol and assessments undertaken at baseline and at each wave of the follow-up are provided elsewhere (eg, for the "19UP study" see Couvy-Duchesne et al., 2018) and/or are highlighted in Supporting Information 1 and 2 (eg, STROBE checklist) or are available from the authors.

Ethical approval was obtained from the Human Research Ethics Committee at the Queensland Institute of Medical Research (QIMR) for all (BLTS) research projects (reference numbers: EC00278 and P1212).

To briefly summarize, the BLTS is a community-based study of twins and their non-twin siblings aged greater than or equal to 12, and participants were recruited continuously between 1992 and 2015 and have been interviewed in waves every three or so years. Written informed consent was obtained from potential participants (if aged ≥18) or a parent (if aged <18 years). Individuals were excluded if parental report indicated a history of head injuries, neurological or pre-existing psychiatric conditions, substance misuse and/or taking medications with significant central nervous system effects. Follow-up assessments were coordinated to ensure interviews began with older cohort members and moved toward younger members. Individuals who miss one follow-up can be interviewed at the next wave. Follow-ups (waves) have increased the assessments of mental health

(see XX), with those undertaken between 2009 and 2016 including assessments of STS and CIDI.

2.1 | Current study sample

Data management is co-ordinated by QIMR Berghofer Institute in Brisbane in conjunction with the Brain and Mind Centre (BMC) at The University of Sydney. De-identified data were extracted from the BLTS dataset only for individuals who had completed a self-report rating of greater than or equal to 1 STS between 2009 and 2016 *and* participated in a CIDI assessment at the 19Up follow-up. The extracted sample did not differ on clinical or demographic characteristics from the original sample (Couvy-Duchesne et al., 2018). Further details are provided in the STROBE and Appendix 2.

2.2 | Assessments

2.2.1 | Demographics

2.2.2 | Subthreshold syndromes

Items rated by the STS are shown in Appendix 2. We extracted data on three STS (HMLE, DLE, PLE) and noted the earliest age at onset. This was defined as the age reported by the participant (they could report an age before follow-up or could be the age at STS completion). These self-rated STS all closely resemble criteria used for identifying individuals who meet "at risk" criteria for mood or psychotic syndromes (eg, Bechdolf et al., 2014; Lewinsohn, Shankman, Gau, & Klein, 2004; Yung et al., 2009). The test-retest reliability of STS ratings is good (inter-class correlations = 0.8) (Scott et al., 2017), and when ratings of the same items are completed by a researcher the inter-rater reliability (weighted kappas) is about 0.75 for each STS (Carpenter, Iorfino, Cross, & Hickie, 2019).

2.2.3 | Social functioning and mental health treatment

A priori, we selected three items available in an established survey (Burns, Davenport, Durkin, Luscombe, & Hickie, 2010). The data recorded perceived level of functional impairment associated with self-reported mental health problems, help-seeking and/or recommendations for treatment of a mental health problem.

2.2.4 | Full-threshold syndromes

For this study, we focus only on the three FTS corresponding to the self-rated STS. Data were extracted on CIDI assessments of the presence/absence and age at onset of full threshold depressive, hypo/manic and/or psychotic syndromes (see Appendix 2).

2.3 | Statistical analyses

Analyses were undertaken using SAS and R programme software (further details available from the authors).

Descriptive statistics applied to sample and subsample characteristics included percentages, means and standard deviations (SD) and medians and interquartile ranges (IQR). Chi-square tests were used for analyses of associations between STS and functioning or treatment (individuals with missing data were excluded from these analyses). If age at onset of the first STS or first CIDI diagnosis was not recorded, we imputed the age using the sample median for each condition. Handling of other missing data is reported in the text or legends for the tables and figures.

We estimated adjusted prevalence ratios (APR) as this is a recommended approach for cross-sectional epidemiological data

TABLE 1 Key characteristics of the study cohort

	N = 1838
Characteristic	**Mean ± SD**
Current age in years	26.4 ± 4.2
	Number (%)
Sex	
Female	1056 (57%)
Male	782 (43%)
Highest level of education[a]	
Junior (secondary school or lower)	30 (2%)
Senior (secondary school)	297 (16%)
Diploma or first degree	1277 (60%)
Postgraduate qualification	232 (13%)
Employment status[a]	
Full-time employment (≥30 hr/week)	1108 (60%)
Part-time employment (<30 hr/week)	232 (13%)
Student	282 (15%)
Unemployed/absent from work[b]	104 (6%)
Home duties	96 (5%)
Marital status	
Single	1026 (56%)
Currently married/with partner	782 (42.5%)
Separated/divorced/widowed	30 (1.5%)
Zygosity[c]	
Monozygotic twins: females/males	331 (18%)/246 (13%)
Dizygotic twins: same sex/both sexes	345 (19%)/346 (19%)
Non-twin siblings	569 (31%)

Note: % reported to the nearest whole number.
[a]Item information missing for two persons;
[b]Absent from work includes, for example, the absence due to sick leave, current disability and so on.
[c]Item information missing for one individual; also, we report odd numbers (eg, 331 monozygotic females) when one co-twin participated in the study, but their co-twin did not.

especially for tests that consider the degree of similarity (identical/non-identical twins/non-twin siblings) or familial clustering within the sample (Santos et al., 2008). Adjusted prevalence ratios are useful indices for quantifying the strength of association between the proportion of individuals with a given condition and the proportion exposed (Greenland, 1987). We estimated the APR using logistic modelling with random effects, with 95% confidence intervals (CI) estimated using the delta method (which produces an approximated SE for prevalence ratio) (Petersen & Deddens, 2008). For the main analyses, we also indicate any confounding by current age or sex (reference value: male sex = 1).

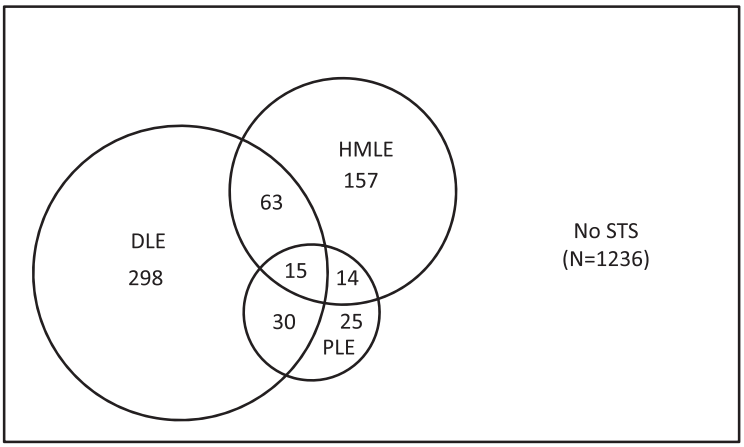
3 | RESULTS

As shown in Table 1 (and Table S1), the sample comprised 1838 participants (female = 1056; 56%) with a mean current age of 26.4 years (median age at "19Up" wave was about 20 years).

3.1 | Patterns of STS

As shown in Figure 1 (and its legend), 33% (N = 612) of individuals self-reported greater than or equal to 1 STS, with 26% (N = 480) meeting criteria for one STS and 7% (N = 122) for two or more STS. About 22% (N = 406) of the sample met criteria for DLE, 14% (N = 249) for HMLE and 5% (N = 84) for PLE. The median age at onset for the first reported STS was about 16 years (IQR: 13-18).

As detailed in the legend of Figure 1, APR analyses reveal that PLE was the most comorbid STS (APR for one comorbidity: 4.06, 95% CI: 2.51, 6.55; APR for two comorbidities: 7.42, 95% CI: 4.19, 13.15), whereas the APR are similar for STS co-occurring with DLE or HMLE (APR >1.7 for one co-morbid STS; APR >2.5 for two co-morbid STS). There was an increased likelihood that PLE would co-occur with another STS in males (APR: 1.93, 95% CI: 1.24, 2.97) and that DLE would co-occur with another STS in females (APR: 0.72, 95% CI: 0.60, 0.87). Age and twin status were not associated with the likelihood of co-occurrence of any STS.



HMLE: Hypomanic-Like Experiences; DLE: Depression-Like Experiences; PLE: Psychotic-Like Experiences; STS subthreshold syndromes

FIGURE 1 Diagrammatic representation of rates of self-reported STS in 1838 cohort members. HMLE: hypomanic-like experiences; DLE: depression-like experiences; PLE: psychotic-like experiences; STS: subthreshold syndromes. Legend: Comorbidity between self-reported STS

Legend for Figure 1: Comorbidity between self-reported sub-threshold syndromes (STS)

Dependent variable	Adjusted Prevalence Ratios (95% Confidence Intervals)			
	1 Other STS[a]	2 Other STS[a]	Sex[b]	Age
DLE	1.75 (1.44 – 2.12)	2.59 (1.84 – 3.64)	0.72 (0.60 – 0.87)	0.89 (0.75 – 1.06)
HMLE	1.71 (1.33 – 2.20)	2.74 (1.79 – 4.19)	1.18 (0.93 – 1.50)	0.86 (0.68 – 1.08)
PLE	4.06 (2.51 – 6.55)	7.42 (4.19 – 13.15)	1.93 (1.24 – 2.97)	1.01 (0.66 – 1.55)

[a]The phrase 'other STS' indicates the number of comorbidities (in addition to the dependent variable);
[b]Reference value: Male=1.00; for this column (Sex) a value >1.00 indicates a higher prevalence ratio in males
STS: subthreshold syndrome; DLE: Depression-Like Experiences; HMLE: Hypomanic-Like Experiences; PLE: Psychotic-Like Experiences.

3.2 | Social functioning and mental health treatment

As shown in Table 2 (and in Table S2), data were available regarding functional impairment, help-seeking and/or mental health treatment for 1778 participants.

There was an incremental increase in functional impairment according the presence of greater than or equal to 1 STS. Eleven percentage of individuals without any STS (N = 126) reported moderate or severe impairment in functioning compared with 24% (N = 113) of those with one STS, 31% (N = 30) of those with two STS and 57% (N = 8) of those with three STS (chi-square test [df 3] =72.93, P = 0.001). Rates of help-seeking were higher than for functional impairment but showed a similar significant increase according to the presence of 0-3 STS (interestingly, 21% of those without a STS reported seeking help). The proportion of individuals who were offered treatment for a mental health problem increased from 12% in those with no self-reported STS to 71% of those with three STS (chi-square test [df 3] =105.57, P = 0.001).

The APR analyses demonstrated that the presence of a greater number of STS was associated with a higher prevalence of functional impairment (APR 2.79, 95% CI 2.16, 3.63), help-seeking (APR 2.45, 95% CI 1.98, 3.04) and mental health treatment (APR 3.05, 95% CI 2.83, 3.89). Adjusted prevalence ratios showed no association with age or twin status; however, there was an association with female sex for both help-seeking (APR: 0.57, 95% CI: 0.48, 0.71) and treatment (APR: 0.52, 95% CI .39, .68).

TABLE 2 Rates of self-reported functional impairment, help-seeking and mental health treatment according to the number of subthreshold syndromes (STS)

Number of STS	Number of respondents[a] (N = 1778)	Functional impairment[b]	Help-seeking[c]	Treatment[d]
None	1195	126 (11%)	256 (21%)	148 (12%)
1	470	113 (24%)	176 (38%)	132 (28%)
2	97	30 (31%)	51 (53%)	34 (35%)
3	14	8 (57%)	11 (79%)	10 (71%)

Note: NB % are reported to nearest whole number and refer to row totals.
[a]The number of individuals (per row) who responded to greater than or equal to 1 of the three questions (see text for details).
[b]Proportion of individuals who self-reported moderate or severe functional impairment according to number of STS: chi-square test (df 3) = 72.93, P = 0.001.
[c]Proportion of individuals who self-reported seeking help from a doctor or mental health professional according to number of STS: chi-square test (df 3) =87.10, P = 0.001.
[d]Proportion of individuals who self-report that the doctor or mental health professional recommended treatment according to number of STS: chi-square test (df 3) =105.57, P = 0.001.

3.3 | Associations between STS and FTS

About 30% individuals met criteria for one or more CIDI diagnosis (see Table S3 for details of rates of CIDI depression hypo/mania or a psychotic disorder), and the median age at onset of the first recorded FTS was about 20 years (IQR: 18-23). The APR was 6.61 (95% CI 2.32, 34.70) for the occurrence of any CIDI diagnosis in an individual reporting one or more STS. Furthermore, the likelihood of meeting criteria for any CIDI diagnosis increased according to number of STS, with APR of 3.10 (95% CI 2.47, 3.88), 8.95 (95% CI: 5.55, 14.37) and 11.61 (95% CI 3.25, 41.41), respectively, for the presence of one, two, or three STS. The association was increased for female sex (APR: 0.63, 95% CI 0.51, 0.78), but not age or twin status.

As shown in Table 3, individuals with DLE were greater than three times more likely to meet CIDI criteria for depression (APR: 3.71, 95% CI: 2.83, 4.89) or hypo/mania (APR: 3.62, 95% CI: 2.21, 5.94) and nearly twice as likely to meet criteria for a psychotic disorder than those without a STS (APR: 1.74, 95% CI 1.08, 2.83). Individuals with HMLE were more than twice as likely to meet CIDI criteria for depression (APR: 2.29, 95% CI: 1.58, 3.31) or hypo/mania (APR: 2.51, 95% CI: 1.29, 4.91) as those without a STS. In those with PLE, the APR, respectively, were 5.8 (95% CI 1.90, 17.70) for hypo/mania and 17.27 (7.54, 39.65) for a psychotic disorder.

TABLE 3 Homotypic and heterotypic continuity between self-reported subthreshold syndromes (STS) and full-threshold syndromes (FTS) defined according to CIDI criteria (see text for details)

Dependent variable	Adjusted prevalence ratio[a] (95% confidence intervals)		
CIDI diagnosis	**DLE only**	**HMLE only**	**PLE only**
Depression	**3.72 (2.83-4.89)**	**2.29 (1.58-3.31)**	2.32 (0.98-5.49)
Hypo/mania	**3.62 (2.21-5.94)**	**2.51 (1.29-4.91)**	**5.80 (1.90-17.70)**
Psychotic disorder	**1.74 (1.08-2.83)**	1.13 (0.55-2.31)	**17.29 (7.54-39.65)**

Note: Data in bold type indicate statistically significant associations.
Abbreviations: CIDI: Composite International Diagnostic Interview; HMLE: hypomanic-like experiences; DLE: depression-like experiences; PLE: psychotic-like experiences.

4 | DISCUSSION

Previous publications demonstrate widespread acceptance of four core ideas that informed the hypotheses that drove this study, that is, that: (1) FTS show heterotypic continuity over time, (ii) adult-pattern mood and psychotic disorders frequently co-occur in youth and comorbidities are associated with higher levels of disability, (iii) STS can also be associated with impaired functioning significant need for care (eg, Cross et al., 2018), (iv) STS (variously defined) are robustly associated with the onset of the corresponding FTS. The current study demonstrated that the co-occurrence of greater than or equal to 1 STS increases the likelihood of impairment, help-seeking and mental health treatment in an incremental manner. Furthermore, and most importantly, this study suggests that STS show both homotypic and

heterotypic associations with FTS and that the number of rather than the nature of the self-rated STS may be significantly associated with the likelihood of meeting criteria for a FTS.

The findings are important for three reasons. First, our findings are comparable with youth populations described elsewhere. The 30% prevalence of FTS is similar to other reports (eg, Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Merikangas, He, & Burstein, 2010); our findings for PLE (5%) are analogous to those in several recent large-scale studies (eg, McGrath, Saha, & Al-Hamzawi, 2015); HMLE (14%) shows a similar prevalence to rates reported elsewhere (eg, Tjissen et al (2010); also, rates of DLE (22%) parallel those reported in epidemiological studies of this age group (Klein, Shankman, Lewinsohn, & Seeley, 2009; Lewinsohn et al., 2004). Second, the extent and patterns of the co-occurrence of the STS support calls for researchers to avoid a narrow focus on individual "at-risk" syndromes or STS and/or only assessing associations between one specific STS and the corresponding FTS (Hickie et al., 2019; Quattrone et al., 2018). For example, the APR for hypo/mania demonstrate the relevance of simultaneously assessing HMLE, DLE and PLE. Although findings for the APR for psychotic disorders in those with PLE appear compelling initially, they are undermined by the limitations of the CIDI criteria, the small number of individuals to which they apply and the very wide 95% CI. Third, findings suggest that each STS demonstrates homotypic and heterotypic continuity and offer support for trans-diagnostic research into clinical phenotypes and genotypes, as well as secondary prevention programmes and service planning (Hickie, Scott, & Hermens, 2013; Maier et al., 2015; van Os & Guloksuz, 2017).

Although our findings are interesting, they should be considered in the context of the study weaknesses. Limitations include the fact that we focused on individuals who self-rated the presence or absence of selected hypomanic, depressive or psychotic symptoms and about the co-occurrence of these STS over relatively brief time periods, without more nuanced consideration of symptom severity or persistence. Furthermore, even at the data extraction phase, we found that about 25% of the original cohort (about 610 out of 2357 cohort members) failed to meet eligibility criteria for the current study. Although we have no evidence of major differences in the excluded subsample, this issue alongside the reliance on self-ratings of STS mean that we may have over-estimated the prevalence of some STS, whereas under-estimating others (Scott et al., 2017). Also, further research will be required to compare our STS criteria with other measures of at-risk syndromes (which incorporate ratings of symptoms alongside additional factors such as family history of a specified mental disorder, etc.) (eg, Wigman et al., 2012). Although the CIDI assessment is the most widely used instrument in epidemiological studies, it is not ideal for identifying DSM IV diagnoses; for instance, it does not include negative symptoms of psychosis. As such, the criteria we employed to diagnose this FTS require further testing (and may partly account for the high APR for PLE and psychosis) and only allow us to consider a broad-based psychotic presentation, not a more specific disorder. Another potential limitation of the current study is that we did not fully explore the impact of the proximity of individual ratings of STS and of FTS. For example, although the median age at onset of STS preceded FTS, we are aware that missing data or inaccurate self-ratings of STS will impact on the validity of some of our analyses. This may have several impacts, for example, it is conceivable that for some individuals, the STS reflects residual symptoms of a FTS rather than a precursor. Furthermore, we can only infer dis/continuity between STS and FTS, we cannot assume transition from a STS to FTS, or that the symptoms evolve without interruption. Indeed, the current findings (about 50% never reported a STS) and our work on depression suggests that some STS may be transient (Scott et al., 2018). Having noted these issues, the next wave of assessments (25 Up) should capture additional information on illness trajectories and allow further prospective evaluation of associations between STS reported in the 19Up study and new onsets of FTS.

As noted earlier, inclusion of co-twins and non-twin siblings in the study is a strength and a weakness (Martin, Eaves, & Kearsey, 1978). For example, we focused our interpretations of findings on an individual rather than a family level and corrected for relatedness. However, twins are not necessarily a random sample of the general population and the prevalence of FTS; however, also STS may be influenced by biopsychosocial factors that do not affect general populations so overtly. Furthermore, although we considered twinning as a potential confounder of the planned statistical analyses, the current sample size and prevalence rates for each condition mitigated against more detailed analysis of all subgroups relevant to twin status or estimating epigenetic and other effects on the inter-relationships between psychopathologies reported by twin pairs. In the long-term, it is predicted that the sample size will be >2500 and the increased statistical power should enable exploration of heritability of STS and FTS and of factors that increase resilience or protect against transition (Purcell, Jorm, Hickie, et al., 2015). Future waves of the NLTS will assess exploration of STS, family history, symptom-level phenomenology and a range of other comorbidities such as anxiety disorders, alcohol and substance misuse and physical illnesses.

5 | CONCLUSIONS

This study provides significant insights into the prevalence and morbidity of STS in the community and the inter-relationships between sub- and full-threshold mood and psychotic disorders in young adults. The next step is to determine whether the co-occurrence of STS and associated increase in the likelihood of experiencing a FTS arises because of the total symptom burden imposed on the individual or whether the presence of specific symptoms from each STS is the critical component in the evolution of FTS's (eg, sleep-wake cycle perturbations; changes in activity or energy). Also, the study offers support for a trans-diagnostic approach to assessment and more inclusive view of transition.

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DECLARATIONS

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DATA AVAILABILITY STATEMENT

Data are still being collected in the main cohort study and not all data are yet available for release. However, the dataset analysed during the current study is available from the corresponding author on reasonable request (and permission from grant holders and grant givers).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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