Online supplementary data for:

**Outcomes of non-transitioned cases in a sample at ultra-high risk for psychosis**

## Demographic information for the entire cohort and subsamples

Demographics for the entire cohort and subsamples are presented in Supplementary Table S1. Baseline data was comparable across subsamples, except for the notable difference of fewer participants meeting brief limited intermittent psychotic symptoms intake group in more recent subsamples.

*Supplementary Table S1.* Demographic data for the entire cohort and subsamples

| | **Entire cohort** | | **1993-2000** | | **2001-2003** | | **2004-2006** | |
|---|---|---|---|---|---|---|---|---|
| | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* |
| Length of follow-up | 6.89 | 3.14 | 10.61 | 1.65 | 5.73 | 0.85 | 3.72 | 0.59 |
| Age at baseline | 18.64 | 3.28 | 19.29 | 3.55 | 18.40 | 3.24 | 18.10 | 2.87 |
| Verbal IQ | 97.96 | 13.70 | 97.54 | 12.49 | 98.51 | 12.61 | 97.65 | 16.00 |
| Performance IQ | 101.25 | 14.31 | 100.76 | 16.77 | 103.63 | 11.81 | 98.80 | 14.64 |
| Full-scale IQ | 99.58 | 13.45 | 98.45 | 13.75 | 101.55 | 12.58 | 98.43 | 14.10 |
| GAF | 60.00 | 10.84 | 65.56 | 12.23 | 57.65 | 8.61 | 56.49 | 9.00 |
| BPRS psychotic subscale | 9.30 | 2.82 | 7.95 | 2.54 | 10.08 | 2.74 | 10.05 | 2.65 |
| BPRS affective subscale | 13.64 | 3.59 | 13.11 | 4.04 | 14.01 | 3.20 | 13.86 | 3.43 |
| SANS total | 18.80 | 12.51 | 16.59 | 12.50 | 22.55 | 12.00 | 17.17 | 12.27 |
| CAARMS disorders of thought content | 1.78 | 0.98 | 1.81 | 1.15 | 1.92 | 0.90 | 1.58 | 0.86 |
| CAARMS perceptual abnormalities | 2.26 | 1.35 | 2.05 | 1.59 | 2.29 | 1.27 | 2.45 | 1.13 |
| CAARMS conceptual disorganisation | 1.57 | 1.08 | 2.12 | 1.04 | 1.47 | 0.95 | 1.07 | 1.00 |
| | *N* | *%* | *N* | *%* | *N* | *%* | *N* | *%* |
| Female gender | 125 | 55.3 | 36 | 43.9 | 43 | 55.8 | 46 | 68.7 |
| Attenuated psychotic symptoms criteria | 176 | 77.9 | 55 | 67.1 | 60 | 77.9 | 61 | 91.0 |
| Brief limited intermittent psychotic symptoms criteria | 23 | 10.2 | 15 | 18.3 | 6 | 7.8 | 2 | 3.0 |
| Vulnerability criteria | 58 | 25.7 | 27 | 32.9 | 19 | 24.7 | 12 | 17.9 |

*Abbreviations:* GAF, Global Assessment of Functioning; BPRS, Brief Psychiatric Rating Scale; SANS, Scale for the Assessment of Negative Symptoms; CAARMS, Comprehensive Assessment of the At-risk Mental State.

**Predictors of the incident disorder and remission for each subsample**

Baseline symptomatology, functioning, IQ, age, gender and length of the follow-up period were candidate predictors of incident (compared to never having the disorder) or persistence/recurrence (compared to remission) of mood, anxiety or substance use disorders, or of any disorder. There were no consistent predictors of non-psychotic disorders when each subsample was investigated separately. Here we present univariate analyses only because of small sample sizes. Mann-Whitney tests were used to test continuous variables and chi-square (continuity corrected statistic) for binary ones. We report all results with a p-value <0.05, but none of these survived correction for multiple comparisons.

*1993-2000:* Persistent/recurrent anxiety disorder was associated with lower full-scale IQ ($p$=0.03; $M$=89.63, $SD$=10.65, $N$=8) compared to remitted anxiety disorder ($M$=102.40, $SD$=10.68, $N$=10). Incident substance use disorder was significantly associated with a shorter follow-up period ($p$=0.04; $M$=9.23, $SD$=1.28, $N$=7) than never having a substance use disorder ($M$=10.29, $SD$=1.26, $N$=25). The incidence of any non-psychotic disorder was associated with lower GAF scores ($p$=0.003; $M$=61.83, $SD$=11.95, $N$=24) compared to those who never had any non-psychotic disorder ($M$=79.00, $SD$=7.42, $N$=5). Participants who entered PACE with brief limited intermittent psychotic symptoms were less likely to have persistence/recurrence of any disorder ($p$=0.04, 40%). No baseline variables significantly predicted the incidence of mood or anxiety disorder, or the persistence/recurrence of mood or substance use disorder.

*2001-2003:* Incident mood disorder was associated with better performance IQ ($p$=0.1; $M$=116.33, $SD$=7.64, $N$=3) than never having the disorder ($M$=96.18, $SD$=10.60, $N$=11). Participants with persistent/recurrent disorder had higher BPRS affective scores ($p$=0.007; $M$=14.73, $SD$=3.70, $N$=40) than those who remitted from any disorder ($M$=12.77, $SD$=1.88, $N$=22). Incidence of anxiety, substance or any disorder, and persistence/recurrence of mood, anxiety and substance use disorders were not significantly associated with baseline variables.

*2004-2006:* Incident mood disorder was associated with higher performance IQ ($p$=0.05; $M$=114.50, $SD$=7.94, $N$=4) compared to participants who never had a mood disorder ($M$=97.38, $SD$=12.72, $N$=8). A shorter follow-up period was associated with persistent/recurrent mood disorder ($p$=0.01; $M$=3.55, $SD$=0.57, $N$=28) compared to remitted mood disorder ($M$=4.01, $SD$=0.57, $N$=23). Incident anxiety disorder was significantly associated with higher disorders of thought content on the CAARMS ($p$=0.02; $M$=2.08, $SD$=0.79, $N$=12) at baseline compared to never having an anxiety disorder ($M$=1.30, $SD$=0.87, $N$=27), while persistent/recurrent anxiety disorder was significantly

associated with higher verbal IQ ($p$=0.03; $M$=104.40, $SD$=15.74, $N$=10) compared to remitted anxiety disorder ($M$=91.55, $SD$=14.25, $N$=11). The incidence of any disorder was associated with higher performance IQ ($p$=0.03; $M$=103.22, $SD$=14.32, $N$=18) and higher affective scores on the BPRS ($p$=0.04, $M$=13.75, $SD$=3.65, $N$=24) compared to participants who never had any disorder (performance IQ: $M$=93.33, $SD$=8.66, $N$=6; BPRS affective: $M$=10.50, $SD$=2.59, $N$=6). The persistence/recurrence of any disorder was associated with a shorter follow-up period ($p$=0.01; $M$=3.57, $SD$=0.57, $N$=30) than remitted disorder ($M$=4.09, $SD$=0.61, $N$=16). The course of substance use disorders was not associated with any baseline variables.

**Exploratory analyses of neurocognitive performance at baseline as a predictor of the course of non-psychotic disorders**

Exploratory data analyses were conducted to investigate whether neurocognitive variables predicted the course of mood, anxiety and substance use disorders, or the course of any non-psychotic disorder.

*Methodology:*

Neurocognitive assessment at baseline varied according to the period during which participants were recruited. Neurocognitive tasks are listed in Supplementary Table S2, which includes the number of participants in each subsample who completed the task. Given the small group sizes, data was analysed using Mann-Whitney tests. We analysed data for the whole cohort only. P-values <0.05 are reported below.

*Results:*

Incident mood disorder was associated with better performance on WASI block design ($p$=0.01; $M$=58.75, $SD$=6.99, $N$=8) and WASI matrix reasoning ($p$=0.01; $M$=57.00, $SD$=4.28, $N$=8) compared to participants who never had a mood disorder (block design: $M$=50.50, $SD$=7.42, $N$=20; matrix reasoning: $M$=48.05, $SD$=9.24, $N$=20). Persistent/recurrent anxiety disorder was associated with poorer digit symbol coding ($p$=0.02; $M$=7.88, $SD$=2.10, $N$=8) compared to those with remitted anxiety disorder ($M$=10.38, $SD$=1.41, $N$=8). Incident substance use disorder was associated with lower scores on WAIS-R/WISC-III similarities ($p$=0.03; $M$=8.50, $SD$=1.76, $N$=6) compared to never having a substance use disorder ($M$=10.65, $SD$=2.18, $N$=20). Persistent/recurrent substance use disorder was associated with poorer performance on visual reproduction ($p$=0.01; $M$=65.67, $SD$=33.05, $N$=9) and Trail Making Task A ($p$=0.006; $M$=29.78, $SD$=11.16, $N$=9) and B ($p$=0.02; $M$=92.44, $SD$=58.94, $N$=9) compared to participants with remitted substance use disorder (visual reproduction: $M$=95.40, $SD$=1.34, $N$=5; Trails A: $M$=19.50, $SD$=0.58, $N$=4; Trails B: $M$=44.00,

*SD*=10.68, *N*=4). Neurocognition did not significantly differ between those participants with incident anxiety or substance use disorder compared to never having these disorders, or participants with persistent/recurrent mood disorder compared to remitting mood disorder.

Those who developed any non-psychotic disorder showed better performance on WASI block design ($p$=0.03; *M*=54.85, *SD*=6.83, *N*=40) compared to participants who never had a non-psychotic disorder (*M*=48.40, *SD*=8.66, *N*=10). The persistence/recurrence of any disorder was associated with lower COWAT scores ($p$=0.05; *M*=33.50, *SD*=9.45, *N*=20) and lower scores on digit span ($p$=0.04; *M*=8.77, *SD*=3.02, *N*=26) than participants with remission from all non-psychotic disorders (COWAT: *M*=46.00, *SD*=13.54, *N*=6; digit span: *M*=11.10, *SD*=2.03, *N*=10).

**Comparison of frequency of non-psychotic disorders with data from Australian general population**

The prevalence of non-psychotic disorders over the follow-up period (two to 14 years) was compared to general population data from the Australian 2007 National Survey of Mental Health and Wellbeing (1). This is presented in Supplementary Table S3. This survey presents 12-month prevalence rates for mood, anxiety and substance use disorders by age and gender. We investigated three age groups that correspond to the age range of our cohort at the time of follow-up assessment (16-24 years, 25-34 years and 35-44 years). In the survey, lifetime prevalence is only present for all adults (16-85 years, by gender). Although neither of these rates corresponds perfectly to the length of the follow-up period of the PACE cohort, they provide an indication that young people identified as being ultra-high risk for psychosis do experience elevated rates of mental health problems.

In summary, the data in Supplementary Table S3 indicates that mood disorders in our cohort were five times more common than the 12-month prevalence in the general population, and approximately three times more common than lifetime prevalence. Anxiety disorders in our cohort were twice more common than 12-month population prevalence, and still higher than population lifetime prevalence. Our cohort showed a threefold increase in substance use disorders compared to 12-month prevalence, but this lessened when compared to lifetime prevalence. Having any disorder was approximately two and a half times more common in our cohort compared to 12-month prevalence of similar age groups from the general population. Rates of any disorder were still over 20% higher in our cohort than the lifetime prevalence of any disorder in the general population. The pattern of females showing higher rates of mood and anxiety disorders than males, and the opposite for substance use disorders, was mirrored in the general population.

*Supplementary Table S2.* Neurocognitive test battery

| **Neurocognitive task** | **1993-2000** | **2001-2003** | **2004-2006** |
|---|---|---|---|
| | *N* | *N* | *N* |
| Logical memory I, percentile rank (WMS-R) | 50 | 0 | 0 |
| RAVLT, raw score (total of first 3 trials) | 49 | 0 | 0 |
| Verbal Paired Associates, raw score (WMS-R) | 67 | 0 | 0 |
| Visual reproduction I, percentile rank (WMS-R) | 48 | 0 | 0 |
| Matrix reasoning, t-score (WASI) | 2 | 69 | 54 |
| Picture completion, age scaled score (WAIS-R or WISC-III) | 66 | 0 | 0 |
| Block design, age scaled score (WAIS-R or WISC-III) | 49 | 0 | 0 |
| Block design, t-score (WASI) | 2 | 69 | 54 |
| Information, age scaled score (WAIS-R or WISC-III) | 50 | 0 | 0 |
| Similarities, age scaled score (WAIS-R or WISC-III) | 65 | 0 | 0 |
| Similarities, t-score (WASI) | 2 | 68 | 54 |
| Vocabulary, t-score (WASI) | 2 | 69 | 54 |
| COWAT, total of F,A,S | 49 | 0 | 0 |
| Arithmetic, age scaled score (WAIS-R or WISC-III) | 66 | 0 | 0 |
| Digit span, age scaled score (WAIS-R or WISC-III) | 65 | 0 | 0 |
| Digit symbol coding, age scaled score (WAIS-R or WISC-III) | 57 | 0 | 0 |
| Trail Making Test, total time (A and B) | 49 | 0 | 0 |

*Abbreviations:* WMS-R, Wechsler Memory Scale-Revised (2); WAIS-R, Wechsler Adult Intelligence Scale-Revised (3); WISC-III, Wechsler Intelligence Scale for Children-III (4); WASI, Wechsler Abbreviated Scale of Intelligence (5); RAVLT, Rey Auditory Verbal Learning Test (6); COWAT, Controlled Oral Word Association Test (7).

*Supplementary Table S3.* Comparison of frequency of non-psychotic disorders with data from Australian general population

| | **PACE cohort** | | | **Population data:12-month prevalence (16-24 years)** | | | **Population data:12-month prevalence (25-34 years)** | | | **Population data:12-month prevalence (35-44 years)** | | | **Population data: lifetime (ages 16-85 years)** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | M/F | M | F | M/F | M | F | M/F | M | F | M/F | M | F | M/F |
| Any disorder, % | 60.4 | 74.4 | 68.1 | 22.8 | 30.1 | 26.4 | 22.8 | 26.9 | 24.8 | 20.8 | 25.9 | 23.3 | 48.1 | 43.0 | 45.5 |
| Any mood disorder, % | 41.6 | 54.4 | 48.7 | 4.3 | 8.4 | 6.3 | 7.0 | 8.7 | 7.9 | 8.4 | 8.3 | 8.3 | 12.2 | 17.8 | 15.0 |
| Any anxiety disorder, % | 25.7 | 41.6 | 34.5 | 9.3 | 21.7 | 15.4 | 11.5 | 21.2 | 16.3 | 14.9 | 21.2 | 18.1 | 20.4 | 32.0 | 26.3 |
| Any substance use disorder, % | 30.7 | 28.0 | 29.2 | 15.5 | 9.8 | 12.7 | 11.3 | 3.3 | 7.3 | 6.5 | 2.6 | 4.6 | 35.4 | 14.2 | 24.7 |

*Abbreviations:* M=males, N=females, M/F= persons (males and females).

*Note:* Population data is from the 2007 National Survey of Mental Health and Wellbeing, published by the Australian Bureau of Statistics (1). 12-month prevalence rates are available for three age groups similar to that of the PACE cohort: 16-24 years; 25-34 years; 35-44 years. Lifetime data is only presented in the survey for all adults (16-85 years).

## References


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