



## Transition and remission in adolescents at ultra-high risk for psychosis

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### ABSTRACT

**Background;** Future success of early intervention initiatives to prevent the onset of psychosis will rely on the validity of methods to predict clinical outcome. Proper identification is particularly essential for young adolescents, as psychotic-like symptoms are often transitory during this period and mislabeling can lead to early stigmatization and unnecessary treatment. This article presents results from a prospective, naturalistic 2-year follow-up study of a cohort of young adolescents putatively at ultra-high risk (UHR) for psychosis.

**Methods;** Seventy-two adolescents between 12 and 18 years were recruited, fulfilling either UHR criteria or the basic symptom-based criterion cognitive disturbances (COGDIS). Incidence of transition as well as the remission rate from UHR status was calculated. Individuals who made a transition (UHR-P) were compared to those who did not (UHR-NP) and to those who remitted (UHR-R) on socio-demographic and clinical characteristics.

**Results;** Fifty-seven UHR individuals completed the 2-year follow-up assessment. The confirmed transition rate was 15.6% and 35.3% still met UHR criteria. The remaining 49.1% had remitted from an initial UHR status. The UHR subgroups did not differ on socio-demographic or clinical variables at baseline.

**Conclusions;** Half of young adolescents meeting UHR criteria continue to experience prodromal or psychotic symptoms after 2 years. However, they are at least three times more likely to have remitted from their UHR status than to have made a transition to psychosis. In addition, baseline characteristics are not indicative of clinical outcome at follow-up. Our results emphasize the need for further improvement and stratification of relative risk factors for psychosis.

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### 1. Introduction

The emergence of early intervention initiatives has rekindled the conviction that therapeutic efforts can make a significant contribution to the prevention of schizophrenia and psychotic disorders. However, successful implementation of treatment requires a high level of accuracy in identifying individuals at risk for developing psychosis to omit negative side effects (McGorry et al., 2009). The introduction of ‘ultra-high risk’ (UHR) and ‘basic symptoms’ criteria (Cornblatt

et al., 2003; Klosterkötter et al., 2001; Yung et al., 2003) has provided international research groups with useful assessment tools to help identify young individuals who are ‘prodromal’ or putatively at risk. UHR criteria refer to a combination of: 1) Attenuated Positive Symptoms (APS); 2) Brief Limited Intermittent Psychotic Symptoms (BLIPS); 3) Trait plus state risk factor (Yung et al., 2003). With the basic symptoms approach self-experienced disturbances are assessed in a range of domains, such as cognition, perception, affect regulation and motor function (Klosterkötter et al., 2001; Schultze-Lutter, 2009). While there is substantial overlap between UHR and basic symptoms criteria, they can also be used in parallel to define a more homogeneous sample of clinically and cognitively impaired individuals (Simon et al., 2006). From here on the term *UHR* will be used in

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reference to studies applying UHR and/or basic symptoms criteria.

UHR criteria have been relatively successful in identifying individuals at incipient risk of a psychotic transition. While the overall estimate of the 1-year transition rate is 36.7% (Ruhmann et al., 2003), individual study sites have reported transition rates as low as 9% (Carr et al., 2000) and as high as 70% (Klosterkötter et al., 2001), with follow-up intervals ranging from 1 to 9.6 years (Cannon et al., 2008). Additionally, recent reports of declining transition rates (15–19%) have been attributed to earlier referral, effective treatment strategies and/or inclusion of a larger proportion of ‘false positives’ (Haroun et al., 2006; Ruhmann et al., 2010; Yung et al., 2008).

Two recent studies on clinical remission in UHR individuals (Simon and Umbricht, 2010; Velthorst et al., 2010) showed that a 50–75% of UHR individuals between 12 and 40 years of age remit from their initial UHR status within 1 to 3 years post-inclusion. The authors concluded that symptoms may be transitory for a majority of UHR individuals which increases the chance of social stigma by mislabeling. This may particularly hold for individuals in the young adolescent phase, when prodromal and psychotic-like experiences are most likely to occur for the first time (Häfner, 1995; Häfner and Maurer, 2006). Prevalence of prodromal symptoms in typically developing adolescents can be relatively high (30%) (Meng et al., 2009) and show high levels of discontinuation (van Os et al., 2009; Escher et al., 2002; Simon et al., 2009). Because peak age of onset for psychotic disorders is estimated around the late teens/early twenties (Kessler et al., 2007), and early onset psychosis may represent more severe variants of the disorder (Amminger et al., 2006; Hollis, 2000), it is of critical importance to test the predictive validity of UHR criteria in adolescent cohorts (Borgmann-Winter et al., 2006).

The present report is an exploratory investigation of the clinical outcome of an adolescent UHR cohort from the Dutch Prediction of Psychosis Study (DUPS), a naturalistic longitudinal study (Sprong et al., 2008). Rates for transition and remission are discussed and baseline characteristics are compared for individuals with different clinical outcomes. It was hypothesized that a considerable amount of UHR adolescents would no longer meet UHR criteria at the 2-year follow-up assessment. Additionally, it was expected that clinical status at follow-up would be independent of any differences in socio-demographic and clinical characteristics at baseline.

## 2. Methods

### 2.1. Participants

All data were collected at the Child and Adolescent Psychiatry Department of the University Medical Center Utrecht. Participants were between 12 and 18 years of age at the time of recruitment and were included after informed consent was given. Individuals younger than 16 years of age signed for assent, while their parents signed for consent. Individuals aged 16 years or older provided informed consent themselves.

Participants were help-seeking adolescents referred by general practitioners or other psychiatric clinics, of which 72

individuals met UHR inclusion criteria. Inclusion criteria were adopted from the European Prediction of Psychosis Study (EPOS), a prospective multicenter study (Klosterkötter et al., 2005). Participants had to fulfil at least one of the following criteria: 1) attenuated positive symptoms (APS), 2) brief, limited, or intermittent psychotic symptoms (BLIPS), 3) genetic risk for psychosis, combined with a deterioration in overall level of social, occupational/school, and psychological functioning in the past year (GRD) and 4) two or more of a selection of nine basic symptoms used to assess mild cognitive disturbances (COGDIS). The COGDIS items have the highest predictive validity of all basic symptoms and have previously been associated with a transition rate to psychosis of 46.3% at 24 months (Schultze-Lutter et al., 2007). The first three inclusion criteria were assessed with the Structured Interview for Prodromal Syndromes (SIPS) and the accompanying Scale of Prodromal Symptoms (SOPS) (McGlashan et al., 2001; Miller et al., 1999). The fourth inclusion criterion was assessed with the Bonn Scale for the Assessment of Basic Symptoms-Prediction List (BSABS-P) (Schultze-Lutter and Klosterkötter, 2002).

Exclusion criteria consisted of a past or present psychotic episode lasting >1 week, traumatic brain injury or any known neurological disorder; verbal intellectual functioning (VIQ) <75. Drug abuse and alcohol abuse were additional exclusion criteria, although UHR subjects were permitted a history of drug use if symptoms had also been present in the absence of drugs. Alcohol and drug use was assessed with sections J and L of the composite international diagnostic interview (CIDI) (World Health Organization, 1993). Frequent use of cannabis was defined as  $\geq 1$  consumption per week.

Follow-up assessments were conducted 9, 18 and 24 months post-baseline to determine presence of a psychotic transition. A psychotic syndrome was operationalized as the presence of positive symptoms that are seriously disorganizing, i.e. a score of 6 on any of the items of the SIPS-Positive Symptoms subscales for a period of more than 7 days (Cannon et al., 2008; Ruhmann et al., 2010). Chart reviews were used to retrospectively confirm psychotic transition by clinical consensus (HvE, PS) and psychotic subjects were subsequently diagnosed according to *DSM-IV* guidelines (American Psychiatric Association, 1994).

For our group analyses the UHR group was subdivided into individuals with subsequent psychotic transition (UHR-P), individuals with sustained UHR status at 24 months (UHR-NP) and those who had remitted from their UHR-status at 24 months (UHR-R). This study was not a treatment trial and did not involve a clinical intervention. When applicable, treatment as usual was continued between follow-up assessments.

### 2.2. Data analysis

All statistical analyses were performed with the Statistical Package for Social Science (SPSS 15.0) for Windows. Baseline data were examined using descriptive statistics. A Kaplan-Meier Survival Analysis was performed to assess rate of transition. For group comparisons (UHR-R vs UHR-NP vs UHR-P) of socio-demographic and clinical variables all data were checked for homogeneity and normality. In order to compare our results with a previous study (Simon and Umbricht, 2010), we also analyzed the results for the UHR-R

group compared to the combined UHR-NP and UHR-P group. ANOVA,  $\chi^2$  and Kruskal–Wallis tests were then used to analyze the data. To take into account statistical correction for multiple comparisons without being overly conservative, alpha-level was set at 0.01, two-tailed. Cox regression analysis was not performed to predict clinical status at 2-year follow-up, because the overall sample size was too small to produce a reliable regression model.

### 3. Results

#### 3.1. Baseline characteristics

Socio-demographic and clinical data for all UHR individuals ( $n = 72$ ) at baseline are provided in Table 1. A majority of individuals (>80%) was still living at home with their families and received formal full-time education at the time of assessment. Atypical antipsychotics were the most frequently prescribed psychotropic medication type ( $n = 18$ ), followed by antidepressants ( $n = 12$ ). 38 individuals met only one UHR criterion, 29 met two UHR criteria and 5 individuals qualified for three inclusion criteria. Most UHR individuals fulfilled the criterion for APS (90.3%), and then COGDIS (54.2%), BLIPS (5.6%) and GRD (4.2%).

#### 3.2. Attrition

After 1 year ten of the original 72 UHR individuals (13.9%) had withdrawn their consent for further participation. At 18 months one additional individual had discontinued par-

ticipation and four more did not complete the final assessment. This resulted in a cumulative attrition rate of 20.8% for a 2-year follow-up period. All individuals lost to attrition met the APS criterion at baseline and 8 individuals fulfilled at least one other criterion (2 BLIPS, 1 GRD, 7 COGDIS). Reasons for discontinuation were generally related to time-consuming aspects of the assessments. Eleven individuals (or parents) gave their consent for a semi-structured telephone interview at 2-year follow-up. None of these individuals had experienced a psychotic episode. One individual, whose consent was not obtained, had ceased to participate after being admitted to our hospital with psychotic complaints, after which he was found psychotic. Three individuals could no longer be contacted and consequently no additional information was available for them.

At baseline UHR individuals lost to attrition and UHR individuals who completed 2-year follow-up did not differ in age ( $t = -0.312$ ,  $p = 0.757$ ), sex ( $\chi^2 = 0.010$ ,  $p = 0.921$ ), cannabis use ( $\chi^2 = 0.593$ ,  $p = 0.743$ ), medication use ( $\chi^2 = 0.101$ ,  $p = 0.751$ ) or any of the clinical scales (range  $p$ -values: 0.229–0.994).

#### 3.3. Transition

Of the 57 UHR individuals that completed the 2-year follow-up assessment, 8 individuals had experienced a psychotic episode. One additional individual, although unable to complete the full-term follow-up, was found psychotic during an earlier assessment and was added to subsequent analyses ( $n = 58$ ). Using a Kaplan–Meier survival analysis (see Fig. 1), the cumulative 2-year transition rate was 15.6% ( $SE = 4.8\%$ ). When information of UHR individuals lost to attrition was also considered, the corrected transition rate was 13.0% ( $SE = 4.15\%$ ). Characteristics for individuals with a psychotic episode are provided in Table 2. Mean age at transition was 16.9 years ( $SD = 2.8$ ) and mean number of days to transition from baseline was 315.7 days ( $SD = 170.7$ ). Two of eight individuals with a psychotic episode no longer fulfilled UHR criteria at the 2-year follow-up other than having experienced a previous psychotic episode.

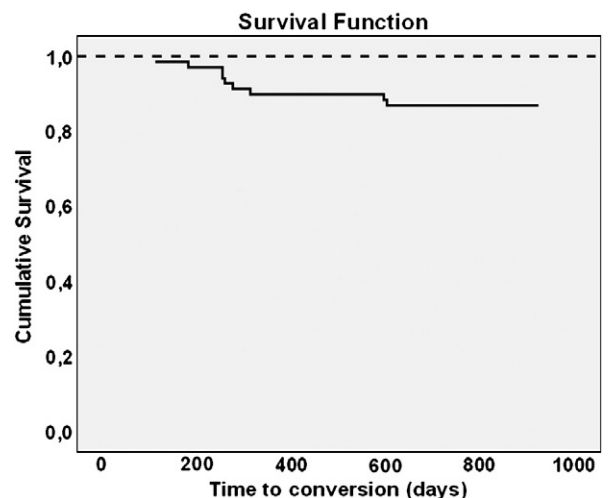
**Table 1**

Baseline characteristics of ultra-high risk individuals ( $n = 72$ ).

Age (mean $\pm$ SD)	15.3 $\pm$ 1.9
Sex (male/female)	44/28
1st/2nd degree relative with psychosis (%)	12 (16.7)
Cannabis use (%)	
Never used	57 (79.2)
Last (regular) use >1 month ago	10 (13.9)
Regular use <1 month ago	5 (7.9)
Psychotropic medication (%)	
Not medicated	41 (56.9)
Medicated	31 (43.1)
Living situation (%)	
With family/friends	64 (88.9)
In group home	8 (11.1)
School/work situation (%)	
Full-time education	60 (83.3)
Part-time work and/or education	3 (4.2)
Unemployed/not in school	9 (12.5)
Earliest onset of symptoms (%)	
<10 years	38 (52.8)
10–15 years	28 (38.9)
>15 years	6 (8.3)
SIPS/SOPS-subcales (mean $\pm$ SD)	
Positive symptoms <sup>a</sup>	8.9 $\pm$ 4.0
Negative symptoms	6.7 $\pm$ 5.0
Disorganized symptoms <sup>a</sup>	4.9 $\pm$ 3.9
General symptoms	6.7 $\pm$ 4.3
BSABS-subcales <sup>b</sup> (mean $\pm$ SD)	
Cognitive disturbances	13.4 $\pm$ 8.5
Perceptual disturbances	7.9 $\pm$ 7.1
Motor disturbances	1.4 $\pm$ 2.2
Current GAF-score (mean $\pm$ SD)	59.6 $\pm$ 13.0

<sup>a</sup> Data missing for 1 individual.

<sup>b</sup> Data missing for 2 individuals.



**Fig. 1.** Two-year survival function of adolescent UHR individuals ( $n = 58$ ).

**Table 2**

Characteristics of individuals with a psychotic transition within the 2-year follow-up period.

Gender	Age at baseline	Age at onset	Days to onset	Inclusion criteria at baseline	DSM IV Diagnosis
Female <sup>a</sup>	13.2	14.3	110	APS	295.10 Schizophrenia, disorganised
Male	15.8	16.3	181	APS, COGDIS	295.30 Schizophrenia, paranoid
Male	12.5	13.2	253	APS, BLIPS, COGDIS	295.90 Schizophrenia, undifferentiated
Male	18.0	18.7	254	APS, COGDIS	295.30 Schizophrenia, paranoid
Male	17.0	17.7	258	APS, COGDIS	296.04 Bipolar I disorder, psychotic features
Male	14.8	15.5	275	APS, COGDIS	298.90 Psychosis NOS
Male	13.9	14.7	313	APS	295.30 Schizophrenia, paranoid
Male <sup>b</sup>	19.1	20.7	595	APS, GRD, COGDIS	295.70 Schizo-affective disorder
Male <sup>b</sup>	19.1	20.8	602	APS, COGDIS	295.30 Schizophrenia, paranoid

<sup>a</sup> COGDIS assessment was not available at baseline.<sup>b</sup> Recruited before the age of 19.

### 3.4. Group comparisons clinical outcome

Baseline variables did not differ between UHR individuals that no longer fulfilled UHR-criteria after 2 years (UHR-R), UHR individuals that still fulfilled UHR criteria at follow-up (UHR-NP) and UHR individuals that experience a psychotic transition during the follow-up period (UHR-P) (see Table 3). After combining the UHR-NP and UHR-P group the results were similar, except there was a trend showing that fewer UHR-R individuals than UHR-NP+UHR-P were fulfilling the APS inclusion criterion at baseline ( $\chi^2 = 4.275$ ,  $p = 0.039$ ).

### 4. Discussion

Efficient early intervention to help prevent the onset of psychosis requires a valid identification of young at-risk individuals with a negative clinical prognosis. To address this issue the current paper reports on the transition and remission rate in a 2-year follow-up study of help-seeking adolescents at Ultra High Risk (UHR) for psychosis. Our results show that at the end of the follow-up period 15.6% of UHR adolescents had experienced a psychotic transition, 35.3% still fulfilled UHR criteria and 49.1% of UHR individuals had remitted from their original UHR status. Socio-demographic variables

**Table 3**Baseline characteristics of UHR individuals grouped by clinical outcome at 2-year follow-up ( $n = 58$ ).

	UHR-R ( $n = 28$ )	UHR-NP ( $n = 21$ )	UHR-P ( $n = 9$ )	Statistic	$p$
Age (mean $\pm$ SD)	15.2 $\pm$ 2.1	15.1 $\pm$ 2.0	16.0 $\pm$ 2.4	$F = 0.71$	0.495
Sex (male/female)	16/12	12/9	8/1	$\chi^2 = 3.26$	0.196
Relative with psychosis (%)	4 (14.3)	5 (23.8)	1 (11.1)	$\chi^2 = 1.04$	0.594
Cannabis use <1 month (%)	1 (3.6)	3 (14.3)	1 (11.1)	$\chi^2 = 1.83$	0.400
Psychotropic Medication (%) <sup>a</sup>	15 (53.6)	8 (38.1)	3 (33.3)	$\chi^2 = 1.73$	0.421
Antipsychotic	7	6	1	$\chi^2 = 1.07$	0.585
Antidepressant	4	3	2	$\chi^2 = 0.37$	0.833
Psychostimulant	3	1	0	$\chi^2 = 0.96$	0.620
Anxiolytic	1	2	1	$\chi^2 = 1.45$	0.484
Other	2	1	0	$\chi^2 = 0.72$	0.698
Living in institution (%)	3 (10.7)	3 (14.3)	1 (11.1)	$\chi^2 = 0.15$	0.926
Earliest onset of symptoms (%)				$\chi^2 = 4.61$	0.330
<10 years	16 (57.1)	14 (66.7)	4 (44.4)		
10–15 years	11 (39.3)	6 (28.6)	3 (33.3)		
>15 years	1 (3.6)	1 (5.8)	2 (22.2)		
SIPS/SOPS (mean $\pm$ SD)					
Positive symptoms	7.8 $\pm$ 3.6	9.0 $\pm$ 4.6	11.33 $\pm$ 4.1	$H = 5.05$	0.080
Negative symptoms	5.7 $\pm$ 4.6	7.0 $\pm$ 4.8	10.22 $\pm$ 6.5	$H = 4.36$	0.113
Disorganized symptoms	4.6 $\pm$ 2.9	5.0 $\pm$ 4.8	7.1 $\pm$ 4.3	$H = 2.78$	0.249
General symptoms	6.5 $\pm$ 4.9	6.0 $\pm$ 3.5	7.9 $\pm$ 4.9	$H = 1.59$	0.451
BSABS-subcales (mean $\pm$ SD) <sup>b</sup>					
Cognitive disturbances	12.6 $\pm$ 7.1	13.1 $\pm$ 10.4	18.5 $\pm$ 9.0	$H = 3.50$	0.179
Perceptual disturbances	8.4 $\pm$ 8.4	7.2 $\pm$ 5.5	10.6 $\pm$ 8.5	$H = 1.43$	0.488
Motor disturbances	1.3 $\pm$ 1.6	1.7 $\pm$ 2.6	2.4 $\pm$ 1.6	$H = 0.09$	0.955
Current GAF-score (mean $\pm$ SD)	59.6 $\pm$ 15.6	55.0 $\pm$ 15.9	57.0 $\pm$ 15.0	$H = 0.52$	0.773
UHR criteria (%) <sup>b</sup>					
APS	22 (78.6)	20 (95.2)	9 (100.0)	$\chi^2 = 4.60$	0.100
COGDIS	15 (53.6)	11 (52.4)	7 (77.8)	$\chi^2 = 3.35$	0.187
BLIPS	1 (3.6)	1 (5.8)	1 (11.1)	$\chi^2 = 0.80$	0.670
GRD	0 (0.0)	1 (5.8)	1 (11.1)	$\chi^2 = 2.70$	0.260

UHR-R = UHR-remitted; UHR-NP = UHR-no psychosis; UHR-P = UHR-psychosis.

<sup>a</sup> Individuals using >1 type of medication are counted as 1 medicated individual.<sup>b</sup> Data unavailable for 1 UHR-P individual.

and clinical scales at baseline did not discriminate between UHR individuals with different clinical outcomes as defined by UHR criteria.

Our results are in line with recent reports of declining transition rates (Haroun et al., 2006; Ruhrmann et al., 2010; Simon and Umbricht, 2010; Yung et al., 2008) and high remission rates (Simon and Umbricht, 2010; Velthorst et al., 2010) in UHR cohort studies. Importantly, participants were relatively young in our study and therefore the majority had not yet reached peak age for psychosis at the time of the follow-up assessment. Consequently the transition rate is expected to rise as our cohort is followed-up further into young adulthood and may eventually approximate previous reports of transition rates >30% (Olsen and Rosenbaum, 2006). Nevertheless, part of the rationale of using UHR criteria is the assumption that they are indicative of a proximal onset of psychosis (Yung et al., 2008; Cornblatt et al., 2003) illustrated by an estimated 1-year transition rate of 36.7% (Ruhrmann et al., 2003) and a subsequent decline in transition rate as follow-up continues (Cannon et al., 2008). As such, the outcome of our study suggests that early detection of UHR symptoms may identify a higher number of individuals that will never reach a clinical threshold for psychosis. Several possible explanations for a high ratio of these 'false positives' have previously been proposed, such as potential beneficial effects of early treatment or misidentification due to a lack of symptom specificity (Yung et al., 2007). Alternatively, our high remission rate may partially reflect the transitory nature of psychotic-like symptoms (Simon et al., 2009; Nelson and Yung, 2009). A recent review and meta-analysis of population rates of subclinical psychotic experiences indicated that approximately 75–90% of these experiences are transitory and disappear over time (van Os et al., 2009).

As is commonly reported in UHR studies, a majority of our study cohort (90.3%) qualified for the APS criterion at baseline. Only few individuals met criteria for BLIPS ( $n = 4$ ) or GRD ( $n = 3$ ) and all of these individuals also fulfilled the APS criterion, preventing the use of subgroup-analysis based on inclusion criteria. It has been suggested that the addition of a psychosis risk syndrome in the upcoming DSM-5 should be based on a modified version of the APS criterion (Woods et al., 2010). Although most of our UHR individuals fulfilled this criterion, our sample size was too small to differentiate between those with a positive (UHR-R) and negative (UHR-NP and/or UHR-P) clinical outcome. The COGDIS criterion of the basic symptoms approach, designed to detect self-experienced disturbances in the early course of the psychosis prodrome (Klosterkötter et al., 2001), did not have additional discriminative value for transition to psychosis or remission of UHR status, as was also found in a clinical follow-up study by Velthorst et al. (2009). Additionally, five of the six individuals that exclusively met the COGDIS criterion at baseline had remitted from UHR status at follow-up. Therefore, the idea that basic symptoms precede the onset of APS cannot be supported by the outcome of this study. However, previous reports have shown evidence that inclusion based on basic symptoms can increase the sensitivity of prediction models (Ruhrmann et al., 2010; Schultze-Lutter et al., 2010), and is highly predictive of psychosis in the long run (Klosterkötter et al., 2001).

Due to the naturalistic nature of our study we were unable to unambiguously determine any effects of differential (therapeutic) treatment procedures on our results. Although use of psychotropic medication was not associated with a better clinical outcome it may have affected the homogeneity of our study population. A plausible explanation could be that medication was only prescribed to more severely affected individuals, which in turn may have obscured any additional psychotic transitions from occurring. Since our study was not optimally designed to compare intervention strategies, these results need to be interpreted with caution. It should also be emphasized here that, even though UHR-R individuals had remitted from their initial UHR status, they generally continued to report clinical symptoms and problems in social and role functioning, albeit to a lesser extent than individuals who did not remit from a UHR status.

Interpretation of our results is restricted by several further limitations. As with most clinical follow-up studies, there was a considerable attrition rate in our study cohort (20.8%). Although individuals that discontinued participation did not differ from other UHR individuals on baseline characteristics, it is possible that this group consisted mostly of severely affected participants which thereby influenced the outcome of our study. To get a better idea of their clinical progression, these individuals were contacted again at the end of the follow-up period. Except for three participants that could not be retrieved, all individuals were willing to provide information. Based on this information, we concluded that the clinical course was very diverse among these individuals. While some reported little clinical improvement or deterioration, others reported to be completely symptom- and treatment-free. While this does not exclude a potential attrition bias in our results, it is likely that the attrition group is clinically not more or less homogenous than the group of UHR individuals that completed the 2-year follow-up.

Finally, several factors that have been shown to greatly contribute to prediction models of psychosis, such as the GRD criterion (e.g. Cannon et al., 2008; Ruhrmann et al., 2010; Yung et al., 2008) and cannabis use (e.g. Cannon et al., 2008; Van Os and Delespaul, 2005), were relatively absent in our cohort. Consequently statistical power was too limited to exclude any potential influence of these factors in our study. In addition, we were unable to find baseline differences between the small group of UHR individuals who became psychotic ( $n = 9$ ) and those who did not. However, as exemplified by several case reports, Yung et al. (2010a) emphasized that the transition threshold is an arbitrary one in some cases and may not relate to long-term clinical outcome. Therefore, instead of focusing solely on the prediction of psychosis, it may also be prudent to develop a better prognosis of functional outcome in UHR individuals (Nien-dam et al., 2009).

The current study provides evidence that adolescents meeting UHR criteria are at least three times more likely to have remitted from their UHR status after 2 years than to have made a transition to psychosis. Furthermore, clinical and socio-demographic characteristics at initial intake cannot reliably distinguish between individuals with a positive or negative clinical outcome. Our results highlight the need for an improved validation of the risk assessment for psychosis and for subsequent functional outcome in young individuals.

In our opinion these issues need to be addressed before diagnostic classification of a 'prodromal syndrome' may prove to be a useful tool in clinical practice (Yung et al., 2010b; Woods et al., 2009, 2010). Instead, to guide the need for intervention, clinicians may benefit more from a differential stratification of risk severity (Ruhmann et al., 2010), based on validated prediction models in large populations at putative risk.

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#### Contributors

Drs. van Engeland, Schothorst, Sprong and Ziermans conceived the idea and methodology of this study and were all involved in clinical and diagnostic assessments. Drs. Schothorst, Sprong and Dr. Ziermans were involved in subject recruitment. Dr. Ziermans conducted the statistical analyses and wrote the manuscript. All authors contributed to and have approved the final manuscript.

#### Conflict of interest

The authors have no competing financial interests to declare in relation to the current work.

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