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A comparison of conversion rates, clinical profiles and predictors of outcomes in two independent samples of individuals at clinical high risk for psychosis in China

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ABSTRACT

Objective: In a previous epidemiological study, we reported on the ascertainment and outcomes of “clinical high risk” (CHR) individuals at the Shanghai Mental Health Center (SMHC, “2011 cohort”). The current study compares demographic and clinical characteristics, including conversion rates, of this sample with a subsequently recruited, independent CHR sample and with published data from western samples.

Method: A new sample of 100 CHR subjects (“2013 cohort”) was selected based on screening and semi-structured interviews. Both studies used the Structured Interview for Prodromal Syndromes (SIPS) for CHR assessment and conducted a naturalistic two-year follow-up. The two cohorts were compared on conversion rates, demographic and clinical characteristics, psychosis risk symptoms, and risk factors for psychotic conversion.

Results: Ninety one (91%) of the 2013 cohort subjects completed the clinical two-year follow-up and 25 (27.5% of the 91) converted to a psychotic disorder over the follow-up period. A comparison of conversions to full psychosis between the 2013 and the 2011 cohorts showed no significant difference in time to conversion (Pairwise comparison: $\chi^2 = 0.3$, $p = 0.562$). Both cohort studies showed that CHR subjects with more severe clinical symptoms at baseline and decline in functioning were more likely to convert to psychosis.

Conclusions: Conversion rates in this new, independent Chinese sample are similar to those reported in non-Chinese samples and to the 2011 cohort. Future research is needed to examine whether the implementation of early intervention for CHR/prodromal symptoms reduces the risk of psychosis and decreases the conversion rate.

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1. Introduction

Numerous studies (Addington et al., 2011a; Cannon et al., 2008; Lemos-Giraldez et al., 2009; Nelson et al., 2013; Yung et al., 2008) and meta-analyses (Fusar-Poli et al., 2012; Fusar-Poli et al., 2016a; Giuliano et al., 2012) over the past two decades have described clinical

syndromes (Fusar-Poli et al., 2016b; Lo Cascio et al., 2016) that are predictive of later psychotic illness. These are considered to represent a clinical high risk (CHR) or prodromal phase of psychosis (also called ultra high risk/UHR or At Risk Mental State/ARMS). One focus of this research has been to determine the degree of risk these syndromes convey. However, published conversion rates are quite variable across countries and over time and all studies show high false positive rates due to limited specificity of current CHR syndromes. In fact, recent follow-up studies of CHR samples have provided evidence suggestive of a declining conversion rate compared to earlier studies (Hartmann et al., 2016; Nelson et al., 2016; Yung et al., 2007), though reasons for this cohort effect are not clear. As argued by Yung et al. (2007), the decline is possibly due to either greater awareness, the implementation of more effective treatments in those identified as CHR, or dilution during identification (including greater numbers of subjects who are false positives to begin with). It would be helpful to clarify this question by

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² In loving memory of Dr. Larry Seidman.

comparing conversion rates in two sequential, matched cohort samples from the same research and clinical setting, which does not employ a specific treatment program.

Since 2010, a series of clinical investigations of early identification of psychosis were conducted at the Shanghai At Risk for Psychosis Program (“SHARP”) of the Shanghai Mental Health Center (SMHC) (Zhang et al., 2015a; Zhang et al., 2015b; Zhang et al., 2015c; Zhang et al., 2014). The SMHC is the largest outpatient mental health clinic in China and provides medication management and psychotherapy. The Chinese research and clinical team at SHARP has been working closely with a U.S. team led by Dr. Larry Seidman (Beth Israel Deaconess Medical Center, Harvard Medical School). Together, they have implemented a systematic research program focused on the CHR phase of psychosis and its identification in Mainland China. Between 2010 and 2011, the team set up a standard procedure for clinical screening, assessment, diagnostic consensus conferences, and periodic site trainings. Then, from 2011 to 2012, an epidemiological study was carried out to determine the frequency of CHR syndromes in a hospital population of Chinese youths presenting for care (Zhang et al., 2014). We found a 2-year conversion rate of 29.1% (Zhang et al., 2016), comparable to that of specialized help-seeking samples world-wide (29%) (Fusar-Poli et al., 2012). The current study compares features of this 2011 cohort with a subsequent study (2013–2015) supported by an R21 MH093294 Fogarty/NIMH grant, “Broadening the Investigation of Psychosis Prodrome to Different Cultural Groups”. While the SHARP clinicians and researchers have increasing awareness of CHR syndromes and the need for referral in the Shanghai clinical community, guidelines for treatment of CHR have not yet been fully developed or implemented.

What is unclear at present, however, is whether there is a change in conversion rate over time among the Chinese CHR population as reported in other settings around the world. This is a key issue for further investigating the concept of CHR in China. Since 2013, we have recruited and conducted two year follow-ups on 100 CHR subjects using the same raters and same procedures as in our epidemiological study (2011 cohort). We hypothesized that the “dilution” phenomena would not occur in the current Chinese setting given the lack of time and specific psychiatric treatments for this condition in Shanghai. To be specific, we hypothesized that the conversion rate of the new 2013 cohort would not show significant decline compared to the previous 2011 cohort. However, we anticipate clinicians would be more experienced in identifying CHR, thus reducing false positives. We also examined additional risk factors for future conversion in the two cohorts. We hypothesized that the risk factors for conversion would not significantly differ between the two cohorts.

2. Method

2.1. Participants

The 2011 cohort study (Zhang et al., 2014) was approved for epidemiological investigation of CHR by the Research Ethics Committee at the SMHC in 2011. The 2013 cohort for broader investigation of CHR subjects was approved by the Research Ethics Committee at the SMHC and Institutional Review Boards of Florida A&M University and Beth Israel Deaconess Medical Center (BIDMC). These subjects either participated in the 2011–2012 (2011 cohort) or the 2013–2015 (2013 cohort) study. As detailed in previous papers, the 2011 cohort was made up of 117 CHR subjects attending their initial outpatient assessment at SMHC during 2011–2012, identified from a consecutive series of outpatients presenting to SMHC. The 2013 cohort was made up of 100 CHR subjects ascertained from 2013 to 2014. The two cohorts followed the same inclusion and exclusion criteria: (i) age of 15–45 years; (ii) individuals younger than 18 years had to be accompanied by either a parent or legal guardian; (iii) capacity to provide informed consent or assent if under 18; and (iv) must have completed at least six years of primary school education; (v) excluded for severe somatic

diseases, such as pneumonia, cancer or heart failure, mental retardation, or dementia. All CHR subjects were diagnosed in a face-to-face interview with the Structured Interview for Prodromal Symptoms (SIPS) and rated on the Scale of Prodromal Syndromes (SOPS), Chinese version (Zheng et al., 2012). The researchers followed up with the CHR subjects two years after the baseline assessment. Clinical information was also collected from subjects' medical records and community clinicians.

In addition, the two cohorts were recruited with the same procedure. For detailed recruitment information, please refer to Zhang et al. (2014). In short, the 117 CHR subjects included in 2011-cohort were recruited from both clinic-wide questionnaire screening ($n = 89$) and clinician referrals ($n = 28$). The 89 CHR subjects were identified by a screening method (The Prodromal Questionnaire –Brief version: PQ-B) (Loewy et al., 2011). Patients received same-day SIPS/SOPS interview if they met the following criteria: (i) A total score of 3 or higher on the PQ-B; (ii) A PQ-B distress score of 6 or higher, and/or (iii) one or more first-degree relatives with affective or non-affective psychosis. As to the 2013-cohort, the 100 CHR subjects were recruited with the same procedure as the 2011 cohort, from both clinic-wide PQ-B screening ($n = 55$) and clinician referrals ($n = 45$). It should be noted that more of the 2013 subjects were ascertained and recruited through clinician referral.

2.2. Measures

2.2.1. SIPS/SOPS

The SIPS/SOPS (Miller et al., 2003) includes four domains of symptoms: positive (P), negative (N), disorganized (D) and general (G). It is a well-validated semi-structured diagnostic interview that assesses and identifies CHR syndromes, specifically Brief Intermittent Psychotic Symptom syndrome (BIPS), Attenuated Positive Symptom Syndrome (APSS), and/or Genetic Risk and Deterioration Syndrome (GRDS). The APSS criteria require that subjects receive a rating level of “3 (moderate),” “4 (moderately severe),” or “5 (severe but not psychotic)” on the positive symptoms scale of the SOPS (symptoms were rated based on a 7-point severity scale, from 0 to 6) and that at least one symptom worsened over the past year. The BIPS criteria require that subjects receive a rating of “6,” which suggests a diagnosis of “severe and psychotic”. Also, specific criteria for sufficient frequency and duration of symptoms must be met. In addition, GRDS is defined as having a genetic risk (one or more first-degree relative with an affective or non-affective psychotic disorder or meeting the DSM-IV schizotypal personality disorder criteria) accompanied by a drop of 30% or greater in the Global Assessment of Functioning (GAF) score in the past 12 months. Our team translated the Chinese version of the SIPS/SOPS (led by the first author) and tested the validity and reliability, which showed good inter-rater reliability ($r = 0.96$, $p < 0.01$ on the SOPS score) (Zheng et al., 2012). The Cronbach's α for all SOPS items was 0.71, and the total SOPS score correlated significantly with the Chinese PANSS total score ($r = 0.63$, $p < 0.01$) (Zhang et al., 2014).

2.2.2. Follow-up outcome measures

There were 10- and 24-month follow-up assessments for each cohort. Subjects were seen by the same clinicians who completed interviews at baseline. The major outcome measure of the two cohort studies was conversion to psychosis. Conversion was operationalized as the criteria of POPS (Presence of Psychotic Symptoms in SIPS/SOPS) (McGlashan et al., 2010). Subjects had to demonstrate at least one psychotic level symptom (rated a ‘6’) on at least one of the five P(Positive) symptoms (P1, unusual thought content; P2, suspiciousness; P3, grandiosity; P4, perceptual abnormalities; and P5, disorganized communication), with either sufficient frequency and duration or at a level that was disorganizing or dangerous (Addington et al., 2015).

2.2.3. Procedures

After an intake evaluation and a short screening questionnaire, potential CHR subjects were invited by either study clinicians or nurses

Table 1
Demographic and clinical variables, comparison between 2011 and 2013-cohort CHR sample.

Variables	2011-Baseline CHR sample	2013-Baseline CHR sample	2011 VS. 2013	
			t/χ^2	<i>p</i> value
Demographic information (at baseline)				
Cases (<i>n</i>)	117	100	–	–
Age (years), [Mean (SD)] [range]	24.7 (7.6) [15–45]	21.0 (5.4) [15–37]	4.17	<0.001
Male [n(%)]	56 (47.9%)	43 (43.0%)	0.51	0.473
Education (years), [Mean (SD)]	12.7 (3.0)	11.3 (2.9)	3.55	<0.001
Marriage: single [n(%)]	89 (76.1%)	85 (85.0%)	2.71	0.100
Birthplace (Shanghai), [n(%)]	57 (48.7%)	40 (40.0%)	1.66	0.198
Clinical information (at baseline) ^a				
Suspected psychosis, [n(%)]	43 (36.8%)	48 (48.0%)	2.80	0.094
Suspected mood/anxiety disorder, [n(%)]	57 (48.7%)	18 (18.0%)	22.50	<0.001
Others, [n(%)]	17 (14.5%)	34 (34.0%)	11.37	0.001
Anti-psychotic medication prescription, [n(%)]	58 (49.6)	69 (69.0%)	8.38	0.004

^a Clinical diagnosis was collected from outpatients' medical records, which were created by their attending doctors according to the Chinese mental health diagnostic manual. Here, "suspected" indicates a nonconclusive diagnosis. As an example, when a clinician gives the diagnosis of "suspected schizophrenia" or "state of suspiciousness," we classify them into the "Suspected Psychosis" group.

for baseline SIPS interview. Those fulfilling criteria of CHR were assessed approximately one and two years thereafter. Clinical records, diagnosis, and prescriptions were collected at each time point. If a face-to-face interview was not possible at follow-up (e.g., hospitalized at a local hospital), the diagnoses of those who either converted to a psychotic disorder or had other non-psychotic disorders were obtained by at least two senior research psychiatrists via phone interview. Information offered by subjects' family members and confirmed by their clinical and medical records were also used for those who declined to talk to the interviewers.

Table 2
Baseline SIPS/SOPS variables, comparison between 2011 and 2013-cohorts of CHR sample.

Variables	2011-baseline CHR sample	2013-baseline CHR sample	2011 VS. 2013	
			t/χ^2	<i>p</i> value
Attenuated positive symptom syndrome, [n(%)]	92 (78.6%)	98 (98.0%)	18.56	<0.001
Genetic risk and deterioration syndrome, [n(%)]	27 (23.1%)	9 (9.0%)	7.72	0.005
Brief intermittent psychotic syndrome, [n(%)]	4 (3.4%)	3 (3.0%)	0	1 ^a
Duration of untreated prodromal symptoms, [Mean (SD)]	4.0 (3.3)	4.2 (3.7)	0.29	0.774
Current GAF, [Mean (SD)]	58.8 (6.4)	53.5 (7.5)	5.675	<0.001
Change in GAF ^b , [Mean (SD)]	21.6 (7.5)	25.0 (8.5)	–3.196	0.002
Family history of psychosis				
(None), [n(%)]	82 (70.1%)	88 (88.0%)	10.20	0.001
(Low-risk ^c), [n(%)]	14 (12.0%)	8 (8.0%)	0.93	0.34
(High-risk ^d), [n(%)]	21 (17.9%)	4 (4.0%)	10.29	0.001
Schizotypal personality disorder, [n (%)]	8 (6.8%)	4 (4.0%)	0.831	0.362
Symptoms rating (SOPS)				
Positive symptoms, [Mean (SD)]	7.1 (4.5)	8.9 (3.2)	–3.405	0.001
P1 > 2, Unusual thought content, [n(%)]	54 (46.2%)	63 (63.0%)	6.158	0.013
P2 > 2, Suspiciousness, [n(%)]	54 (46.2%)	75 (75.0%)	18.610	<0.001
P3 > 2, Grandiose ideas, [n(%)]	2 (1.7%)	2 (2.0%)	0	1 ^a
P4 > 2, Perceptual abnormalities, [n(%)]	45 (38.5%)	58 (58.0%)	8.254	0.004
P5 > 2, Disorganized communication, [n(%)]	7 (6.0%)	6 (6.0%)	0	1
Negative symptoms, [Mean (SD)]	9.4 (5.1)	14.3 (5.4)	–6.964	<0.001
Disorganized symptoms, [Mean (SD)]	3.4 (2.3)	6.2 (3.0)	–7.665	<0.001
General symptoms, [Mean (SD)]	8.1 (3.4)	9.5 (2.8)	–3.142	0.002
Total score, [Mean (SD)]	28.0 (10.2)	38.9 (9.6)	–8.017	<0.001

^a Pearson chi-square with Yates's continuity correction.

^b Change in GAF: Highest GAF score in the past year minus current GAF.

^c Low-risk family history: having no family members with mental disorders or a first-degree relative with non-psychotic disorders.

^d High-risk family history: having at least one first-degree relative with psychosis.

2.3. Statistical analyses

The present study compared the two cohorts in 3 ways: 1) the differences in conversion rates, 2) baseline demographic and clinical characteristics, and 3) SOPS symptoms between the two CHR cohorts, which were evaluated by independent samples *t*-tests and chi-square tests. Comparing the risks of conversion, subjects were classified according to whether they converted or remitted during the 2-year follow-up. Kaplan–Meyer survival analyses were used separately by cohort, and survival curves were compared using the log-rank test and Cox regression and logistic regression. Possible predictors including age, sex, education, marital status, diagnostic impression (clinical diagnosis, antipsychotic medication prescription), SIPS items (positive symptoms P1–5, P1–5 > 2), DUPrS (duration of untreated prodromal symptoms, the period between the onset of the first attenuated psychotic symptom and the commencement of professional help at psychiatric services), Schizotypal Personality Disorder (SPD), and GAF drop, were selected for Cox and logistic regression analyses with the method of forward stepwise (Conditional LR). The factors that predicted conversion in Cox or logistic regression for either cohort are summarized and presented in a schematic diagram (Fig. 2).

3. Results

3.1. Demographics and clinical characteristics at baseline

The demographic and clinical information of the 2011 and 2013 CHR samples at baseline can be found in Table 1. The comparison between 2011 and 2013 cohorts did not reveal significant differences in proportions of sex, marriage status nor being native to Shanghai. However, significant differences were observed in age, years of education, clinical diagnostic impression, and antipsychotics prescription. Specifically, the CHRs in 2013 cohort were younger, with fewer years of education, and more on antipsychotic medication.

Table 3
Cox regression for predicting the conversion to psychosis.

2011-Cohort	Risk ratio	95%CI	χ^2	P	2013-Cohort	Risk ratio	95%CI	χ^2	P
Drop in GAF	1.123	1.050–1.201	11.417	0.001	Drop in GAF	1.080	1.021–1.142	7.213	0.007
Diagnostic impression	0.061	0.013–0.289	12.374	<0.001	Diagnostic impression	0.216	0.051–0.920	4.294	0.038
DUPrS	1.142	1.030–1.265	6.413	0.011					

3.2. SIPS/SOPS characteristics at baseline

Baseline SIPS/SOPS data are shown in Table 2. Overall, the rates of APSS ($p < 0.001$) were higher and the rates of GRDS ($p = 0.005$) and family history of psychosis ($p = 0.002$) were lower in the 2013 cohort of CHR subjects, in comparison with the 2011 cohort. The decline in current GAF and change in GAF scores were greater in the 2013 cohort compared to the 2011 cohort. Also, the intensity of SOPS symptoms of the 2013 cohort sample was higher than those of the 2011 cohort.

3.3. Follow-up and attrition

In the 2013 cohort, among the 100 CHR subjects, five dropped out before ten months and four others dropped out during the two year follow-up window. Of the 91 CHR subjects who completed the 2-year follow-up (Mean = 25.2, SD = 2.0, Range [20–29 months]), 25 (27.5%) converted to full psychosis by the 2-year assessment. This conversion rate is consistent with the 2011 cohort, in which 29.1% converted to full psychosis (25/86 CHR, 31 CHR dropped out within about 2 years). In the 2011 cohort, there was a mean period of 27.4 months (SD = [4.0], Range [20–33 months]) for those who completed the follow-up assessment. For those non-converters in the 2013 cohort, 33 (36.3%) had an Axis I non-psychotic disorder in the follow-up, with 23 mood disorders, five anxiety disorders, four obsessive-compulsive disorders, and one adjustment disorder. One case from the converter group attempted to commit suicide. The results also show that significantly fewer CHR subjects (9/100 vs. 31/117) were lost during the follow-up in the 2013 cohort ($\chi^2 = 11.0, p = 0.001$) than those in the 2011 cohort.

3.4. Predictors of conversion

Cox regression analyses revealed the variables that remained in Cox models were comparable between the two cohorts (see Table 3). Fig. 1 shows no significant difference in time to conversion (Pairwise comparison: $\chi^2 = 0.3, p = 0.562$) between the 2011 and 2013 cohorts.

3.5. Summary for potential predictors

We investigated the factors that may predict increased risk of conversion to full psychosis by using forward stepwise logistic or Cox regression analysis to test the predictive values among the two cohorts. For the 2011 cohort (as shown on the left side of Fig. 2), the factors such as change in GAF, diagnosis and prescription, DUPrS were identified by Cox regression, while P symptoms and age were identified by Kaplan–Meyer survival analysis. The detailed statistics can be found in our previous work (Zhang et al., 2014; Zhang et al., 2016). The risk factors identified in the 2013 cohort were summarized on the right side of Fig. 2, in which the factors of change in GAF and prescription were identified by Cox regression (also see Table 3), while others such as educational level, P1, D symptoms were identified by logistic regression.

4. Discussion

Results from this study demonstrate that the conversion rate to full psychosis among Chinese youth who present for treatment and meet CHR criteria is consistent across two independent studies over three years and is consistent with rates shown elsewhere (Fusar-Poli et al.,

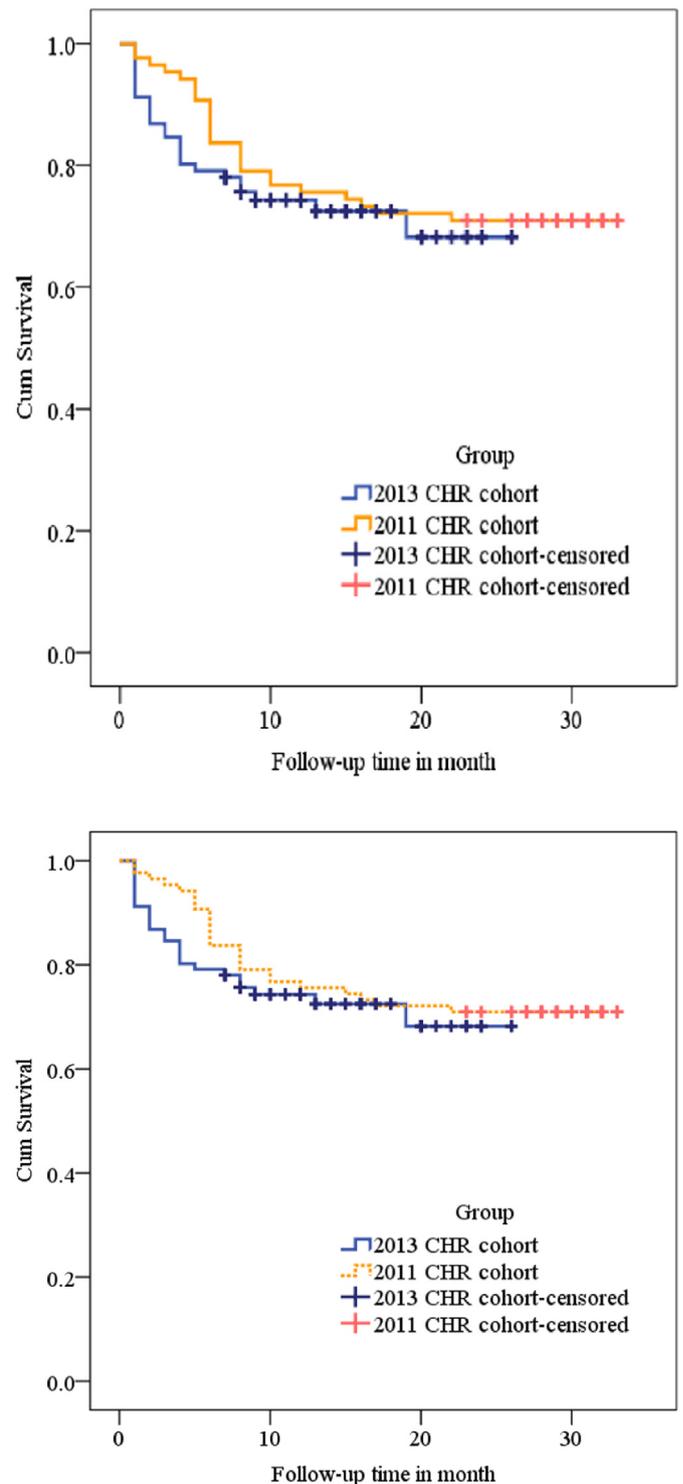


Fig. 1. Kaplan–Meyer survival curves for conversions to psychosis between 2011-cohort and 2013-cohort. Note: Converters classified with certainty and non-converters were “censored”.

2012). As far as we know, this was the first study to compare the 2-year conversion rates between two sequential Chinese CHR cohorts with virtually identical methods (setting, procedures, measurements, and raters). This stability of conversion rates over time is inconsistent with published evidence for a “dilution” effect, or decline in conversion rates in CHR samples over time (Hartmann et al., 2016; Wiltink et al., 2015; Yung et al., 2007). Three possibilities may account for this inconsistency. First, the current studies have a shorter time interval between two cohorts compared with the studies conducted in other settings (Yung et al., 2007). ‘Dilution’ over longer periods of time may reflect increasing awareness of CHR symptoms and syndromes among the general clinical community leading to increasing referrals as prevention efforts have received increasing attention and focus. This early intervention focus is only now beginning in China. Thus, the “dilution” effect may take much longer to be obvious and only occur after extensive implementations of early CHR identification efforts in a very high density population center such as Shanghai.

Secondly, no specific treatment strategies were implemented in either of these SMHC cohorts. Rather, both SHARP studies at SMHC were conducted in a naturalistic way. It is possible that the declining conversion rates in CHR research elsewhere in the world reflect the increasing likelihood that those who meet CHR criteria will be identified and treated in the community or by the research groups who assess them, as reflected in clinical trials that have reduced the transition rate (Addington et al., 2011b; Ising et al., 2016; McGorry et al., 2006; Woodberry et al., 2016). Such treatment-related change in outcomes would not be expected to be manifest in the current results. From this point of view, our results highlight the importance of targeted interventions for CHR populations as valuable for risk reduction. Third, previous studies (Hartmann et al., 2016; Wiltink et al., 2015) comparing conversion rates among heterogeneous CHR samples did so across studies and were limited by varying procedures, sample sources, and concurrent treatment methods. The distinguishing factor in our study is that the two Shanghai cohorts were collected by the same research team,

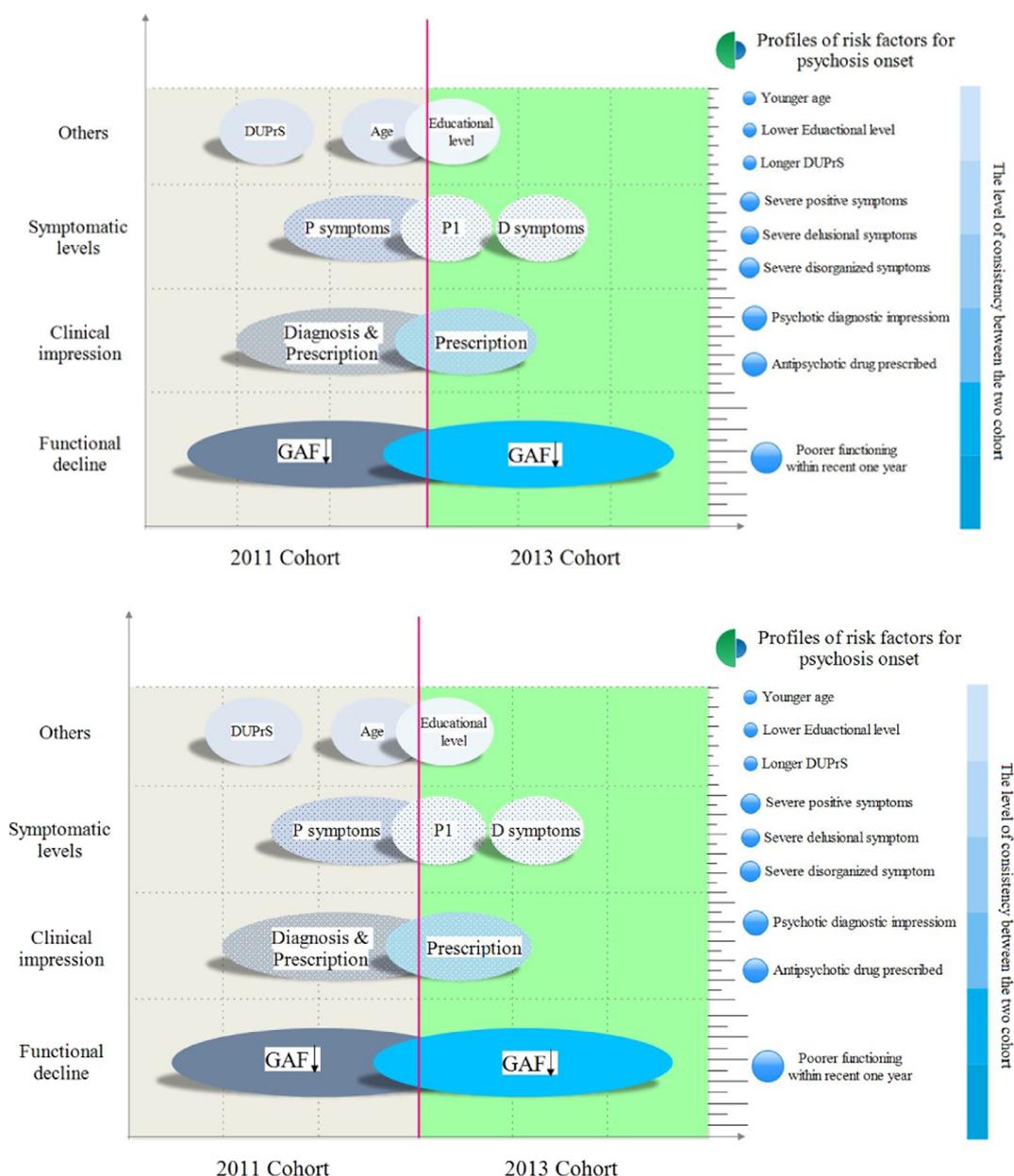


Fig. 2. Summarized profile of risk factors for psychosis onset from CHR sample in the 2011- and 2013-cohorts. Note: P symptoms: positive symptoms; P1: unusual thought content/delusional symptom; D symptoms: disorganized symptoms. The overlap between the ovals represents the consistency of identified predictive factors between the two cohorts.

following similar procedures, and had no specific treatment during the follow-ups. It should be noted that that more CHR cases were prescribed with antipsychotics in the 2013 cohort compared to the 2011 cohort. This may potentially have an impact on the conversion rates. However, it remains unknown whether the antipsychotics play a positive or negative role on the conversion outcome.

Younger age at presentation, lower educational level, clinical impression of prodromal psychosis, and more severe SOPS symptomatic levels at baseline were found in the 2013 cohort compared to the 2011 cohort. Interestingly, most of these baseline factors (i.e. younger, poorer functioning, higher total SIPS positive symptom scores, longer DUPrS, and more psychosis-related diagnoses and subsequent prescription of antipsychotics through the clinic) had been reported in the 2011 cohort study (Zhang et al., 2016) to be predictive of psychosis conversion. We speculate that the previous findings have already impacted the sample recruiting process in the later 2013-cohort study, suggesting that Chinese clinicians are attempting to include subjects who are at “real” risk of psychosis. However, we cannot exclude the possibility that subjects with those characteristics may be more likely to meet the CHR criteria. Fewer CHR subjects were lost during follow-up of the 2013 cohort, which might represent the previous experiences of the researchers and an increased ability to communicate and keep in touch with CHR subjects as well as their families that is highly beneficial.

Results in both cohorts showed that CHR subjects with more severe symptoms and decline in functioning at baseline were more likely to transition to psychosis. These findings are largely consistent between the two China cohorts and other CHR studies (Cannon et al., 2008; Fusar-Poli et al., 2012). This has important implications for early identification of CHR individuals in China. Specifically, if Chinese clinicians are aware of those risks of psychosis, they may inquire more about symptomatic levels and functional decline at their first clinical visit. Further, in addition to treatment goals related to a decrease in the severity of symptoms, as is commonly the case in China (perhaps antidepressants or antipsychotics if rapid worsening occurs), results suggest that intervening to protect functioning (such as cognitive training or therapy) should be carefully considered during treatment planning for those CHR individuals.

The decline of CHR conversion rates around the world has raised important questions with regard to possible treatment and/or sample dilution effects across time or cohorts. However, no other studies have tested for changes in conversion rates over time in the absence of early intervention services. The current study compared two cohorts identified in the absence of any specialized early intervention programming. Although sample differences over time were noted, the lack of a dilution effect over a period of intense education suggests that the clinicians in this setting have responded to education and training about early identification with an increase in fairly accurate referrals rather than an increase in referrals but decline in referral accuracy. Future comparison of conversion rates before and after the implementation of specialized treatments will enable a more complete test of the role of treatment, but understanding how to foster accurate referrals over time remains an important priority in early intervention science.

There are limitations to the study. First, the data were collected from help seekers in a mental health service setting. Therefore, those who did not seek help or those who sought help at general hospitals may have different conversion rates and symptom profiles. Second, more studies and various settings should be utilized, along with longer periods of follow-up. Third, a naturalistic study design allowed observation of the subjects' outcome to occur but it did not facilitate active intervention, which may affect how these results compare to those of other studies where people received more care. Fourthly, <30% subjects at follow-up provided exact medication information, therefore, making it impossible to compare the number of subjects receiving a prescription and to compare to other studies of the world. Finally, not all subjects could be followed up or received an interview in the follow-up. Among the missing interviews, none withdrew consent, though. Some reasons that

account for their unwillingness to go through the whole assessment at follow-up might include either improved symptoms or worsening symptoms or other life events. Despite these factors, we found that there has been no decline in the conversion rate among Chinese CHR population during the five year period of these two studies. Future research is needed to determine whether the implementation of early intervention of CHR symptoms would reduce the risk of psychosis and decrease the conversion rate.

Author contributions

H.L. and T.H.Z. conceptualized the study, wrote the first draft of manuscript and conducted the statistical analyses. H.R.C. Y.Y.-W, D.S, L.J.S, and K.W, helped in the design of the study and edited the manuscript. L.H.X. and T.H.Z. interviewed subjects and collected and organized the primary data. Y.Y.T. and X.C.T. managed the literature searches, statistical analyses and edited the manuscript. D.I.-S, K.W., C.B.L., L.J.S. and J.J.W. designed the study and provided supervision in the implementation of the study. All authors have approved the final manuscript.

Competing financial interests

The authors report no biomedical financial interests or potential conflicts of interest.

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