DOI:
10.1016/j.schres.2017.06.015

Document Version
Peer reviewed version

WHY TRANSITION RISK TO PSYCHOSIS IS NOT DECLINING AT THE OASIS ULTRA HIGH RISK SERVICE: THE HIDDEN ROLE OF STABLE PRETEST RISK ENRICHMENT

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Word count:

Abstract: 249

Text: 3093

Tables: 4

Figures: 1

Endnote reference file: Neuroprevent.enl

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ABSTRACT

Background

The reason for declining risk to psychosis across individuals assessed and meeting Ultra High Risk (UHR) criteria is still unclear. No studies have investigated the potential substantial role of the underlying risk enrichment across all the individuals undergoing a UHR assessment.

Methods

Cohort study including all non-psychotic subjects who were assessed on suspicion of psychosis risk by the OASIS UHR service in the period 2001 to 2015. Posttest (after UHR assessment) and pretest risk (before UHR assessment) of psychosis were stratified and compared across three time periods (2001-2005, 2006-2010, 2011-2015) with Cox analysis and modulating factors were investigated.

Results

The posttest risk of psychosis at the OASIS service has increased from the initial pilot years of the service (2001-2005) and then stabilised and not declined over the following decade (2006-2010 and 2011-2015). This was paralleled by a similar course of pretest risk for psychosis. Stability of pretest risk for psychosis over the past decade was associated with a lack of change in ethnicity and to counterweighting changes in the type of referral sources over different time periods.

Conclusions

The time course of transition risk to psychosis in UHR services is strictly associated with the time course of pretest risk enrichment. If the latter remains stable over time, as for the OASIS service, no declining transition risk is observed over the most recent years. Pretest risk enrichment is determined by recruitment and sampling strategies. This study confirms the need to control these factors in the UHR field.

1. INTRODUCTION

The prevention of psychosis has become clinically feasible due to the introduction of the Ultra High Risk (UHR hereafter) construct (Fusar-Poli et al., 2015a) to reliably identify young individuals who are at heightened risk for the development of psychotic disorders (Fusar-Poli and Schultze-Lutter, 2016) -mostly schizophrenia spectrum disorders (Fusar-Poli et al., 2013a)- over the following few years (Kempton et al., 2015). Conversely, there is no evidence that individuals meeting UHR criteria are at increased risk of developing new and incidental non-psychotic disorders compared to individuals assessed for a UHR state but not meeting criteria (Fusar-Poli et al., 2016c; Webb et al., 2015). The meta-analytical prognostic accuracy of the UHR designation is considered good (AUC at 38 months = 0.9) (Fusar-Poli et al., 2015a) and comparable to other preventative approaches in medicine (Fusar Poli et al., 2014). However, declining transition risks from a UHR state to psychosis over recent years has put the field into question. The two-year risk of transition to psychosis from an initial UHR state has shifted from an early 30% (Fusar-Poli et al., 2012) to the current 20% (see Table 4 in (Fusar-Poli et al., 2016a)). Declining transition risk is concerning because it can undermine the clinical significance of preventative detection (Fusar-Poli, 2017c) and treatment, yielding negative findings (Fusar-Poli, 2017b). Understanding the reason for declining transition risk is of paramount relevance to overcome these limitations. Earlier studies had suggested that declining transition risk in UHR samples may be due to the fact that treatments were more effective (treatment effect). However, with the largest randomized controlled trials in UHR individuals yielding negative findings (Fusar-Poli, 2017b), there is no strong evidence indicating that the recommended preventative treatments are effective in preventing psychosis (Morrison et al., 2012). In fact, recent studies concluded that treatment effect (Nelson

et al., 2016) cannot fully account for the observed decline in the transition risks. Another line of research has suggested that the declining transition risk may be due to a dilution effect (Hartmann et al., 2016) i.e. finding more false-positives despite individuals meeting the initial UHR criteria (dilution effect) (Yung et al., 2007). The dilution effect was only partially explained by different clinical characteristics of the UHR samples at intake over time periods (Hartmann et al., 2016). While these studies have been entirely focused on transition risk in individuals who meet the UHR criteria (posttest risk), no studies have investigated whether the dilution effect is secondary to a change in the level of risk enrichment of the entire pool of individuals undergoing a UHR assessment (pretest risk, for explanatory details see (Fusar-Poli and Schultze-Lutter, 2016)). The strong association between pretest risk enrichment and observed transition risk in UHR samples is an established finding and has been confirmed in all UHR samples worldwide (Fusar-Poli et al., 2016d; Fusar-Poli et al., 2016f). Since the prognostic accuracy of the UHR criteria depends on the pretest risk of the sample to which they are being applied (Fusar-Poli, 2017a), it is possible that changes of transition risk over time may parallel changes in the underlying pretest risk of the samples undergoing UHR assessment. Furthermore, the changes in pretest risk enrichment of individuals undergoing a UHR assessment are in turn modulated by outreach campaigns of clinical services, recruitment strategies (Fusar-Poli et al., 2016f) and referral pathways (Fusar-Poli et al., 2016d).

In this study, we first hypothesized that the changes in posttest transition risk over time would be determined by changes in pretest risk over time. To test this hypothesis, we stratified the course of posttest and pretest transition risk over the same fifteen-year referral period in the entire pool of individuals who were

undergoing an UHR assessment at the Outreach and Support in South London (OASIS) UHR service (Fusar-Poli et al., 2013b), and addressed the relationship between pretest and posttest risk of psychosis. Our second aim was to investigate potential sociodemographic and referral pathway factors (Fusar-Poli et al., 2016d) that may account for any changes in pretest psychosis risk enrichment over different time periods.

2. METHODS

2.1. Sample

We included all non-psychotic subjects who were assessed on suspicion of psychosis risk by the OASIS UHR service (Fusar-Poli et al., 2013b). All subjects referred to the OASIS in the period 2001 to 2015 were initially considered eligible. We then excluded those who were referred but never assessed by the team, and those who were already psychotic at baseline. The remaining sample was therefore composed of all non-psychotic subjects undergoing a Comprehensive Assessment of At Risk Mental State (CAARMS)-based UHR assessment (Yung et al., 2006) at the OASIS. Details of the clinical care received at the OASIS service have been described elsewhere (Fusar-Poli et al., 2015b).

2.2. Procedure

This was a clinical register-based cohort study. Measures of interest were automatically extracted with the use of the Clinical Record Interactive Search (CRIS) tool (Stewart et al., 2009). CRIS is a case register system that provides anonymized information from electronic clinical records, which are documented by professionals involved in each patient's clinical care relating to mental health care services across South London and the Maudsley (SLaM). SLaM is a National Health Service (NHS)

mental health trust that provides secondary mental health care to a population of roughly 1.3 million residents of four London boroughs, namely, Lambeth, Southwark, Lewisham and Croydon. The OASIS team is part of SLaM, which has a near-monopoly in terms of secondary mental healthcare provision to its local catchment area. Also, it is a legal requirement for SLaM healthcare professionals to keep these records up to date (Stewart et al., 2009). Because the CRIS model draws directly from these electronic health records, it provides valuable 'real-world' and 'real-time' information on routine mental health care (Perera et al., 2016). Ethical approval for the study was granted by the Oxfordshire Research Ethics Committee C (reference 08/H0606/71+5) (Stewart et al., 2009).

2.3. Study measures

The primary measure of interest for the current study was the pretest and posttest risk of developing psychosis, stratified across referral period. Pretest risk of psychosis was measured across the entire pool of individuals who were undergoing UHR assessment at the OASIS (for explanatory details see (Fusar-Poli and Schultze-Lutter, 2016)). Posttest risk of psychosis was measured within those individuals who met the UHR criteria post-assessment (for explanatory details see (Fusar-Poli and Schultze-Lutter, 2016)). Psychosis onset was defined by the presence of ICD-10 (WHO, 1990) diagnosis of psychotic disorders in the CRIS electronic clinical records. Time to diagnosis of a psychotic disorder was measured from the date of first referral to OASIS, censored at February 1, 2016, and was truncated at a maximum of 5-year follow-up to mitigate the potential differences in follow-up time across the referral periods. The referral period was categorized into three 5-year groups (2001-2005, 2006-2010, 2010-2015). The first group, 2001-2005 corresponded to the early setup

period of the OASIS (for details see (Fusar-Poli et al., 2013b)). In addition, secondary measures included ethnicity and source of referral as previously defined (Fusar-Poli et al., 2016d).

2.4. Statistical analysis

Sociodemographic characteristics of the sample were described with means and standard deviations for continuous variables and absolute and relative frequencies for categorical variables. The impact of referral period on posttest risk of psychosis and pretest risk of psychosis (first aim) was investigated using Cox proportional hazards models, which evaluated the effects of referral period on psychosis onset and time to transition, after checking for proportional hazards assumption (Grambsch and Therneau, 1994). The relationship between pretest and posttest risk of psychosis onset (first aim) was formally investigated with a regression of the individualized 5-year posttest risk estimates, on the 5-year pretest risk estimates. The association of ethnicity and source of referral with the referral period (second aim) was investigated and contingency tables reported the standardized adjusted residuals, with an alpha corrected at 0.001 to account for multiple comparisons (which corresponded to a value of ± 2.58 for the adjusted standardized residuals). All analyses were conducted in STATA 13 (STATA Corp., TX, USA).

3. RESULTS

3.1. Sociodemographic and clinical characteristics of the sample

From 2001 to 2015, a total of 1,115 subjects were referred to the OASIS clinic for UHR assessment. Among them, 125 subjects did not undergo the UHR assessment and had no contact with the OASIS service. An additional 280 subjects were already psychotic at baseline (the clinical fate of these subjects is described elsewhere (Fusar-

Poli et al., 2016b)). Therefore, a final sample of 710 non-psychotic subjects who underwent UHR assessment was used in the current study (Table 1).

The mean follow-up was 1472 days (median 1181, range 8-5015). The average age of the sample was 23 years and 56% were male. Half of the sample was of white ethnicity. The vast majority were single. Approximately one-third of referrals (34%) came from general practitioners. The Index of Multiple Deprivation (IMD) score was 32% (for details on the IMD see the supplementary material).

3.2. Pretest and posttest risk of psychosis over referral period

There was a significant effect of referral period on the posttest risk for developing psychosis in individuals who met the UHR criteria (X^2=6.19, P=0.0453) (Figure 1 and Table 2). This was due to an increase of posttest risk of psychosis in the 2011-2015 period as compared to the 2001-2005 period. In fact, the study analysis revealed that there were no significant differences between the 2006-2010 and the other two time periods (i.e. 2010-2015 or 2001-2005). There was no effect of the time period on the pretest risk for developing psychosis in individuals undergoing the UHR assessment at the OASIS (X^2=0.79, P=0.673) (Figure 1 and Table 2). However, this was due to the fact that the 2001-2005 group was rather small with infrequent events, yielding a large 95%CI. Figure 1 shows a clear trend for an increased pretest and posttest risk across the three referral periods. In fact, regression of the individualized 5-year pretest risk estimates of psychosis onset on the 5-year posttest risk estimates of psychosis onset was highly significant (F=2010, df=708, P>0.001, adjusted R^2=0.74) and confirmed that pretest risk explained 74% of the variance in the posttest risk

(β=2.368, 95%CI 2.264-2.471, P<0.001, constant = -0.365, 95%CI -0.402 to -0.328, P<0.001).

3.3. Predictors of pretest risk enrichment and referral period

The study analysis revealed that there was no association between ethnicity and referral period (Table 3). This indicated that there were no significant changes over time in ethnicity composition of individuals who were referred to the OASIS for UHR assessment. However, there were significant changes in the source of referrals over the time period. According to the study findings, there was a higher proportion of referrals from physical health services during the 2001-2005 period and a lower proportion during the 2006-2010 period. The 2006-2010 period was also associated with a higher proportion of self-referrals and referrals from early intervention services. Conversely, the 2011-2015 period was associated with a lower proportion of self-referrals and referrals from early intervention services.

4. DISCUSSION

To our best knowledge, this is the first study to test the hypothesis that the time course of posttest transition risk in UHR samples is determined by the underlying time course of pretest risk enrichment of individuals undergoing UHR assessment. Contrary to our expectations, the posttest risk of psychosis in individuals meeting the UHR criteria at the OASIS service has increased since the first pilot years (2001-2005) and remained stable over the following decade (2006-2010 and 2011-2016). In line with our hypothesis, non-declining transition risk was due to a stable underlying pretest risk for psychosis, which did not change over the same years. Further in line with our hypothesis, the pretest risk enrichment accounted for the vast majority (74%)

of the observed posttest risk. Stability of pretest risk for psychosis over the 2006-2016 years was likely due to the lack of changes in ethnicity of individuals referred to the OASIS over time and to counterweighting changes in the type of referral sources over different time periods.

Our first hypothesis that the changes in posttest transition risk over time would be determined by the underlying time-course of the pretest risk was confirmed. Surprisingly, we found no evidence that risk of psychosis at the OASIS service was declining over the recent years. On the contrary, there was some evidence for an increase in risk over time. However, this was uniquely due to an increase of risk in the later period (2011-2016) as compared to the early years (2001-2005). As previously indicated, these early years corresponded to the setup pilot period of the OASIS service. This period was characterized by initiation of outreach campaigns and a small number of referrals, most of which were likely not appropriate, resulting in a high proportion of false positives. Although this period of time could not represent the standard clinical routine of a UHR service, it confirms once more that the early inefficient recruitment strategies and outreach led to a negligible transition risk. Once the OASIS service was fully established (i.e. after 2005) no significant differences in the posttest transition risks (2006-2010 vs 2011-2015) were further observed. Therefore, our findings indicate that within individuals meeting the UHR criteria at the OASIS, the transition risk has remained stable over the past decade (2006-2016). Although such a finding was unexpected, it still allowed elucidating our hypothesis. Indeed, as shown in Figure 1, the time-course of posttest risk was paralleled by the time-course of pretest risk, which was unchanged across the three time periods. To further elucidate the temporal relationship, we conducted a regression analysis

between the two and confirmed that pretest risk enrichment accounts for 74% of the observed posttest risk. This is in line with the previous meta-analysis, which did not include the current sample, indicating that the UHR assessment is very good in ruling out psychosis but only modest in ruling in psychosis (Fusar-Poli et al., 2015a). These psychometric properties of the UHR assessment are indexed by a small meta-analytical positive likelihood ratio (see for explanatory details (Fusar-Poli and Schultze-Lutter, 2016)) of 1.82 (Fusar-Poli et al., 2015a). These findings confirm that the ultimate prognostic accuracy of the UHR criteria is dependent on the sample to which they are applied, and in particular, to its pretest risk. For example, meeting UHR criteria at the OASIS during the pilot years (2001-2005) that were characterised by inefficient recruitment strategies and low risk enrichment, was associated with a reduced transition risk compared to the other time periods. These findings, in concurrence with previous studies, show that the dilution of pretest risk may result in diluted posttest risk (Fusar-Poli et al., 2016e) (see also table 2 in the study (Fusar-Poli et al., 2015a) for more examples).

Our second aim was to investigate the reason for stable pretest risk enrichment over time at the OASIS service. We capitalized on previous work by our group indicating that the type of recruitment strategies used to select samples to undergo the UHR assessment, may modulate pretest risk enrichment (Fusar-Poli et al., 2016f). In a recent meta-analysis (Fusar-Poli et al., 2016f), we confirmed that the type of outreach campaign and the source of referral modulate the pretest risk enrichment in samples undergoing UHR assessment worldwide. Another recent study conducted in the current sample confirmed that pretest risk enrichment in subjects undergoing CHR assessment is dependent on the adopted recruitment strategies, and therefore, on the

referral source (Fusar-Poli et al., 2016d). This study found that the subjects that had passed through several adult mental health service filters, such as early intervention for psychosis services or inpatient units show the highest risk enrichment (referrals from child and adolescent mental health services show a reduced pre-test risk), while referrals from outside adult mental health (i.e. self, carer or relatives, schools or colleges, police and criminal justice system, social services) diluted risk enrichment (Fusar-Poli et al., 2016d). We additionally found that sociodemographic factors such as well-known risk factors for psychosis, including ethnicity (Kirkbride et al., 2012), modulate pretest risk enrichment in these samples. When we tested in the current study the association between changes in ethnicity and referral period, we found no substantial differences across the three time periods. Conversely, we found some changes with respect to the referral source. Although the proportion of referrals from physical health services was higher during the 2001-2005 period when compared to the 2011-2015 period, the contribution of this factor to pretest risk enrichment is minimal (see eFigure 5 in (Fusar-Poli et al., 2016d)) and thus unlikely to have produced any change in the observed pretest risk. In contrast, changes in the proportion of referrals from first episode services and from self may substantially increase and dilute the pretest risk of psychosis, respectively (Fusar-Poli et al., 2016d). Interestingly we found that these two changes were counterbalancing each other across the 2006-2010 and 2011-2015 periods, with an increased proportion of self-referrals and referrals from first episode services, during the 2006-2010 period and a decrease in the proportion of the two factors during the 2011-2015 period. It is thus likely that the two changes had exerted opposite and counterweighting effects on the pretest risk enrichment, resulting in an overall stable pretest risk at the OASIS over the past decade. These findings provide additional evidence to support an earlier

original study conducted in UHR samples, which suggested that changes in referral pathways and increasing awareness of UHR symptoms in the general population have resulted in faster referral of young people to specialized mental health services and consequently, dilution of posttest risk of psychosis onset (Wiltink et al., 2013).

This study had some limitations. First, we were unable to control the potential effect of treatments on the observed posttest risk. However, beyond the questionable efficacy of preventative treatments for UHR individuals as discussed above, the treatments provided at the OASIS have been relatively stable (Fusar-Poli et al., 2015b). Second, since all UHR sampling procedures are idiosyncratic and opportunistic (Fusar-Poli et al., 2016f), the current findings clearly reflect the local recruitment policies, and so different UHR research groups should investigate these findings in their local scenario. We expect that the declining transition risk observed in other UHR sites would be similarly explained by changes in the local recruitment strategies, leading to changes in sociodemographic factors or type of referral sources.

5. CONCLUSIONS

The time course of transition risk to psychosis in UHR services is strictly associated with the time course of pretest risk enrichment. If the latter remains stable over time, as for the OASIS service, no declining transition risk is observed over the most recent years. Pretest risk enrichment is determined by recruitment and sampling strategies. This study confirms the need to control these factors in the UHR field.

Table 1. Sociodemographic characteristics of subjects undergoing CHR assessment at the OASIS clinic (n=710)

	N	Mean	SD
Age (years)	710	23.11	5.37
Index of multiple deprivation (IMD)	710	31.96	8.45
	N	Count	%
Gender	710		
Males		399	56.20
Females		311	43.80
Ethnicity	660		
Black		158	23.94
White		329	49.85
Asian		30	4.55
Caribbean		32	4.85
Mixed		35	5.30
Other		76	11.52
Marital status	627		
Married		19	3.03
Divorced or separated		19	3.03
Single		572	91.23
In a relationship		17	2.71
Referral period	710		
2001-2005		40	5.63
2006-2010		251	35.35
2011-2015		419	59.01
Referral source	710		
Self		66	9.30
Carers or relatives		13	1.83
Schools or colleges		6	0.85
Social services or supported accommodation		11	1.55
General medical practitioners		243	34.23
Community mental health services		165	23.24
Child and adolescent mental health services		61	8.59
Early intervention for psychosis services		47	6.62
Accident and Emergency departments		46	6.48
Inpatient mental health services		14	1.97
Police and criminal justice system		7	0.99
Physical health services		31	4.37

Figure 1. Pretest and posttest risk of developing psychosis (at 5 years) at the OASIS service for Ultra High Risk Individuals.

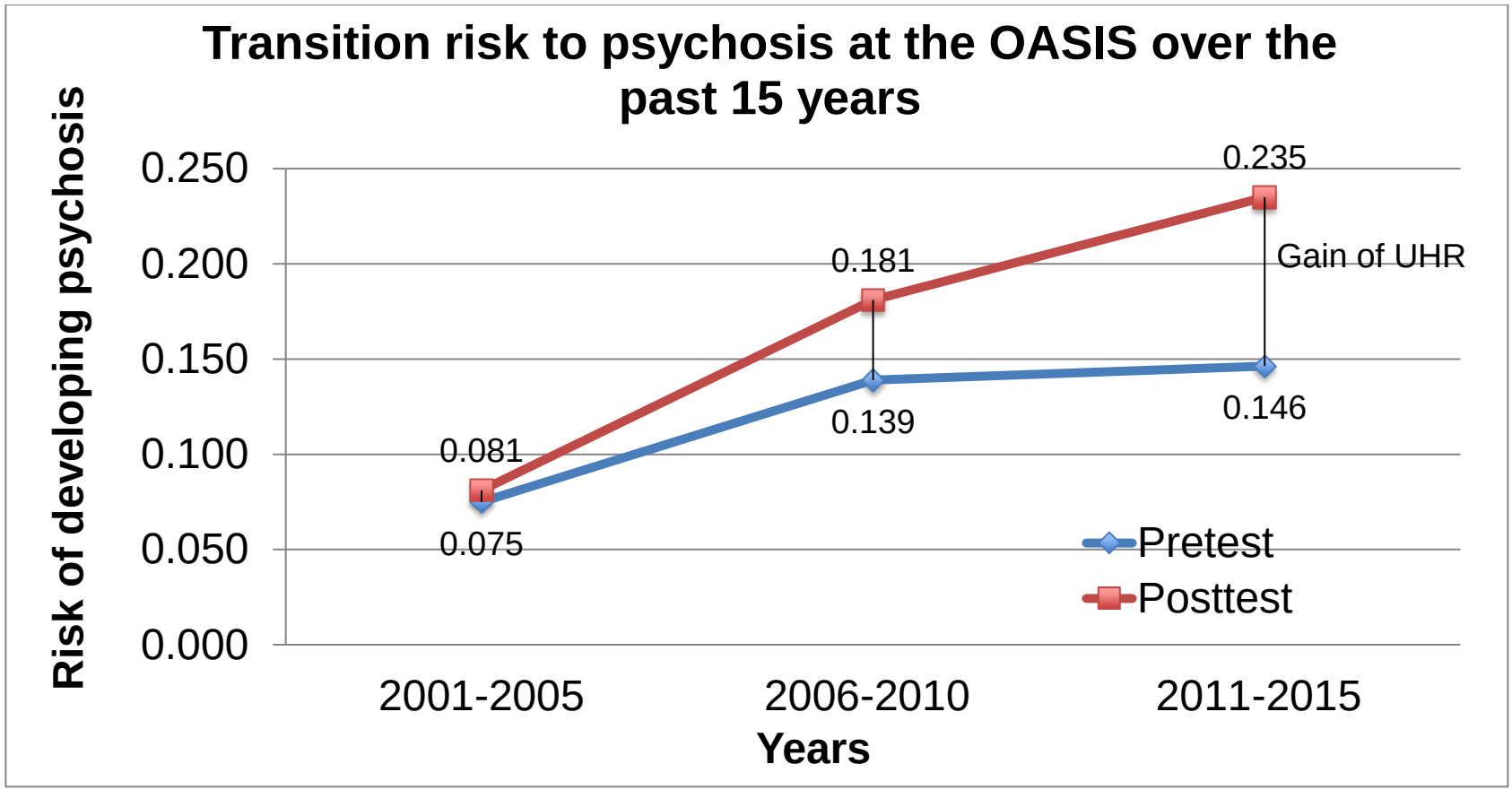

Table 2. Pretest and posttest risk of developing psychosis (at 5 years) at the OASIS service for Ultra High Risk Individuals, stratified for referral period.

Years	5-year transition risk			Cox regression			
	Mean	95% CIs		HR	95% CI		P
2001-2005 Pretest	0.075	0.025	0.215	1.000			
2006-2010 Pretest	0.139	0.102	0.189	1.471	0.523	4.132	0.465
2011-2015 Pretest	0.146	0.102	0.208	1.542	0.546	4.356	0.414
2001-2005 Posttest	0.081	0.027	0.230	1.000			
2006-2010 Posttest	0.181	0.129	0.252	2.471	0.754	8.101	0.135
2011-2015 Posttest (a)	0.235	0.162	0.332	3.471	1.055	11.421	0.041

(a) 2011-2015 vs 2006-2010, HR 1.404, 95%CI 0.8445-2.334, P=0.190

Table 3. Association between ethnicity and referral period

Ethnicity	2001-2005	2006-2010	2011-2015
Black	9	50	99
%	25.71	21.55	25.58
Expected	8.46	56.05	93.49
Adj Residuals	0.22	-1.16	1.023
White	16	121	188
%	45.71	52.16	48.58
Expected	17.39	115.29	192.31
Adj Residuals	-0.48	0.933	-0.69
Mixed	3	8	23
%	8.57	3.45	5.94
Expected	1.82	12.06	20.12
Adj Residuals	0.92	-1.49	1.03
Any other	3	25	47
%	8.57	10.78	12.14
Expected	4.01	26.61	44.38
Adj Residuals	-0.55	-0.412	0.65
Asian	1	13	16
%	2.86	5.6	4.13
Expected	1.61	10.64	17.75
Adj Residuals	-0.5	0.92	-0.67
Caribbean	3	15	14
%	8.57	6.47	3.62
Expected	1.71	11.35	18.94
Adj Residuals	1.04	1.38	-1.82

Adj Residuals: residuals lower than −2.58 or greater than 2.58 indicate that the number of cases in that cell is significantly smaller or larger than expected under the null hypothesis at $p < 0.001$.

Table 4. Association between the source of referral to the OASIS and referral period.

Source of referral		2001-2005	2006-2010	2011-2015
Self		1	38	27
	%	2.5	15.14	6.44
	Expected	3.71	23.32	38.95
	Adj Residuals	-1.52	**3.97**	**-3.14**
Carer or relatives		0	4	9
	%	0	1.59	2.15
	Expected	0.732	4.59	7.67
	Adj Residuals	-0.89	-0.35	0.75
Schools		0	1	5
	%	0	0.4	1.19
	Expected	0.338	2.12	3.54
	Adj Residuals	-0.601	-0.961	1.216
Social services and supported accommodation		1	3	7
	%	2.5	1.2	1.67
	Expected	0.62	3.89	6.49
	Adj Residuals	0.5	-0.57	0.31
General medical practice		13	71	159
	%	32.5	28.29	37.95
	Expected	13.69	85.91	143.4
	Adj Residuals	-0.237	-2.47	2.51
community mental health		7	60	98
	%	17.5	23.9	23.39
	Expected	9.29	58.31	97.37
	Adj Residuals	-0.885	0.31	0.113
child and adolescent		0	20	41
	%	0	7.97	9.79
	Expected	3.44	21.57	35.99
	Adj Residuals	-1.99	-0.44	1.36
early intervention		1	34	12
	%	2.5	13.55	2.86
	Expected	2.65	16.62	27.74
	Adj Residuals	-1.08	**5.49**	**-4.83**
accident and emergency		3	13	30
	%	7.5	5.18	7.16
	Expected	2.59	16.26	27.15
	Adj Residuals	0.27	-1.04	0.89
inpatient mental health		2	2	10
	%	5	0.8	2.39
	Expected	0.789	4.95	8.26
	Adj Residuals	1.42	-1.67	0.95
police and criminal system		0	2	5
	%	0	0.8	1.19
	Expected	0.394	2.475	4.131
	Adj Residuals	-0.65	-0.38	0.67
physical health services		12	3	16
	%	30	1.2	3.82
	Expected	1.75	10.96	18.29
	Adj Residuals	**8.167**	**-3.058**	-0.86

Adj Residuals: residuals lower than −2.58 or greater than 2.58 indicate that the number of cases in that cell is significantly smaller or larger than expected under the null hypothesis at $p < 0.001$.

REFERENCES

Fusar Poli, P., Carpenter, W., Wood, S., McGlashan, T., 2014. Attenuated Psychosis Syndrome: ready for DSM-5.1 ? Annual review of clinical psychology 10(April 2014), in press.

Fusar-Poli, P., 2017a. The Clinical High-Risk State for Psychosis (CHR-P), Version II. Schizophrenia bulletin 43(1), 44-47.

Fusar-Poli, P., 2017b. Negative Psychosis Prevention Trials. JAMA Psychiatry.

Fusar-Poli, P., 2017c. Why ultra high risk criteria for psychosis prediction do not work well outside clinical samples and what to do about it. World Psychiatry 16(2), 212-213.

Fusar-Poli, P., Bechdolf, A., Taylor, M.J., Bonoldi, I., Carpenter, W.T., Yung, A.R., McGuire, P., 2013a. At risk for schizophrenic or affective psychoses? A meta-analysis of DSM/ICD diagnostic outcomes in individuals at high clinical risk. Schizophrenia bulletin 39, 923-932.

Fusar-Poli, P., Bonoldi, I., Yung, A.R., Borgwardt, S., Kempton, M., Barale, F., Caverzasi, E., McGuire, P., 2012. Predicting psychosis: a meta-analysis of transition outcomes in individuals at high clinical risk. Arch Gen Psychiatry 69(3), 1-10.

Fusar-Poli, P., Byrne, M., Badger, S., Valmaggia, L.R., McGuire, P.K., 2013b. Outreach and support in south London (OASIS), 2001-2011: ten years of early diagnosis and treatment for young individuals at high clinical risk for psychosis. Eur Psychiatry 28(5), 315-326.

Fusar-Poli, P., Cappucciati, M., Borgwardt, S., Woods, S., Addington, J., Nelson, B., Nieman, D., Stahl, D., Bonoldi, I., Rutigliano, G., Riecher-Rössler, A., Simon, A., Mizuno, M., Lee, T., Kwon, J., Lam, M., Perez, J., Keri, S., Amminger, G., Metzler, S., Kawohl, W., Rössler, W., Lee, J., Labad, J., Ziermans, T., An, S., Liu, C., Woodberry, K., Braham, A., Corcoran, C., McGorry, P., Yung, A., McGuire, P., 2016a. Heterogeneity of risk for psychosis within subjects at clinical high risk: meta-analytical stratification JAMA Psychiatry 73(2), 113-120.

Fusar-Poli, P., Cappucciati, M., Rutigliano, G., Schultze-Lutter, F., Bonoldi, I., Borgwardt, S., Riecher-Rossler, A., Addington, J., Perkins, D., Woods, S., McGlashan, T., Lee, J., Klosterkötter, J., Yung, A., McGuire, P., 2015a. At risk or not at risk? Meta-analysis of the prognostic accuracy of psychometric interviews for psychosis prediction. World Psychiatry 14(3), 322-332.

Fusar-Poli, P., Diaz-Caneja, C.M., Patel, R., Valmaggia, L., Byrne, M., Garety, P., Shetty, H., Broadbent, M., Stewart, R., McGuire, P., 2016b. Services for people at high risk improve outcomes in patients with first episode psychosis. Acta Psychiatr Scand 133(1), 76-85.

Fusar-Poli, P., Frascarelli, M., Valmaggia, L., Byrne, M., Stahl, D., Rocchetti, M., Codjoe, L., Weinberg, L., Tognin, S., Xenaki, L., McGuire, P., 2015b. Antidepressant, antipsychotic and psychological interventions in subjects at high clinical risk for psychosis: OASIS 6-year naturalistic study. Psychological medicine 45(6), 1327-1339.

Fusar-Poli, P., Rutigliano, G., Stahl, D., Davies, C., De Micheli, A., Ramella-Cravaro, V., Bonoldi, I., McGuire, P., 2016c. Long-Term validity of the at risk mental state (ARMS) for predicting psychotic and non-psychotic mental disorders. European Psychiatry 42, 49-54. .

Fusar-Poli, P., Rutigliano, G., Stahl, D., Schmidt, A., Ramella-Cravaro, V., Shetty, H., McGuire, P., 2016d. Deconstructing pretest risk enrichment to optimize prediction of psychosis in individuals at clinical high risk. JAMA Psychiatry 1(73(2)), 1260-1267.

Fusar-Poli, P., Schultze-Lutter, F., 2016. Predicting the onset of psychosis in patients at clinical high risk: practical guide to probabilistic prognostic reasoning. Evidence-based mental health 19(1), 10-15.

Fusar-Poli, P., Schultze-Lutter, F., Addington, J., 2016e. Intensive community outreach for those at ultra high risk of psychosis: dilution, not solution. The lancet. Psychiatry 3(1), 18.

Fusar-Poli, P., Schultze-Lutter, F., Cappucciati, M., Rutigliano, G., Bonoldi, I., Stahl, D., Borgwardt, S., Riecher-Rossler, A., Addington, J., Perkins, D.O., Woods, S.W., McGlashan, T., Lee, J., Klosterkotter, J., Yung, A.R., McGuire, P., 2016f. The Dark Side of the Moon: Meta-analytical Impact of Recruitment Strategies on Risk Enrichment in the Clinical High Risk State for Psychosis. Schizophrenia bulletin 42(3), 732-743.

Grambsch, P., Therneau, T., 1994. Proportional hazards tests and diagnostics based on weighted residuals. Biometrika 81, 515-526.

Hartmann, J.A., Yuen, H.P., McGorry, P.D., Yung, A.R., Lin, A., Wood, S.J., Lavoie, S., Nelson, B., 2016. Declining transition rates to psychotic disorder in "ultra-high risk" clients: Investigation of a dilution effect. Schizophrenia research 170(1), 130-136.

Kempton, M., Bonoldi, I., Valmaggia, L., McGuire, P., Fusar-Poli, P., 2015. Speed of psychosis progression in people at ultra high clinical risk: a complementary meta-analysis. JAMA Psychiatry 72(6), 622-623.

Kirkbride, J.B., Errazuriz, A., Croudace, T.J., Morgan, C., Jackson, D., Boydell, J., Murray, R.M., Jones, P.B., 2012. Incidence of schizophrenia and other psychoses in England, 1950-2009: a systematic review and meta-analyses. PloS one 7(3), e31660.

Morrison, A.P., French, P., Stewart, S.L., Birchwood, M., Fowler, D., Gumley, A.I., Jones, P.B., Bentall, R.P., Lewis, S.W., Murray, G.K., Patterson, P., Brunet, K., Conroy, J., Parker, S., Reilly, T., Byrne, R., Davies, L.M., Dunn, G., 2012. Early detection and intervention evaluation for people at risk of psychosis: multisite randomised controlled trial. Bmj 344, e2233.

Nelson, B., Yuen, H.P., Lin, A., Wood, S.J., McGorry, P.D., Hartmann, J.A., Yung, A.R., 2016. Further examination of the reducing transition rate in ultra high risk for psychosis samples: The possible role of earlier intervention. Schizophrenia research 174(1-3), 43-49.

Perera, G., Broadbent, M., Callard, F., Chang, C.K., Downs, J., Dutta, R., Fernandes, A., Hayes, R.D., Henderson, M., Jackson, R., Jewell, A., Kadra, G., Little, R., Pritchard, M., Shetty, H., Tulloch, A., Stewart, R., 2016. Cohort profile of the South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLaM BRC) Case Register: current status and recent enhancement of an Electronic Mental Health Record-derived data resource. BMJ open 6(3), e008721.

Stewart, R., Soremekun, M., Perera, G., Broadbent, M., Callard, F., Denis, M., Hotopf, M., Thornicroft, G., Lovestone, S., 2009. The South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLAM BRC) case register: development and descriptive data. BMC psychiatry 9, 51.

Webb, J.R., Addington, J., Perkins, D.O., Bearden, C.E., Cadenhead, K.S., Cannon, T.D., Cornblatt, B.A., Heinssen, R.K., Seidman, L.J., Tarbox, S.I., Tsuang, M.T., Walker, E.F., McGlashan, T.H., Woods, S.W., 2015. Specificity of Incident Diagnostic Outcomes in Patients at Clinical High Risk for Psychosis. Schizophrenia bulletin 41(5), 1066-1075.

WHO, 1990. World Health Organization. International classification of diseases, tenth revision (ICD-10). Geneva: WHO, 1990.

Wiltink, S., Velthorst, E., Nelson, B., McGorry, P.M., Yung, A.R., 2013. Declining transition rates to psychosis: the contribution of potential changes in referral pathways to an ultra-high-risk service. Early intervention in psychiatry 9(3), 200-206.

Yung, A., Yuen, H., Berger, G., Francey, S., Hung, T., Nelson, B., Phillips, L., McGorry, P., 2007 Declining transition rate in ultra high risk (prodromal) services: dilution or reduction of risk? Schizophrenia bulletin 33(3), 673-681.

Yung, A.R., Phillips, L.J., Yuen, H.P., McGorry, P.D., 2006. Comprehensive Assessment of at Risk Mental State., Melbourne.