Transdiagnostic dimensions of psychopathology at first episode psychosis: findings from the multinational EU-GEI study

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Abstract

Background. The value of the nosological distinction between non-affective and affective psychosis has frequently been challenged. We aimed to investigate the transdiagnostic dimensional structure and associated characteristics of psychopathology at First Episode Psychosis (FEP). Regardless of diagnostic categories, we expected that positive symptoms occurred more frequently in ethnic minority groups and in more densely populated environments.
and that negative symptoms were associated with indices of neurodevelopmental impairment.

**Method.** This study included 2182 FEP individuals recruited across six countries, as part of the European network of national schizophrenia networks studying Gene–Environment Interactions (EU-GEI) study. Symptom ratings were analysed using multidimensional item response modelling in Mplus to estimate five theory-based models of psychosis. We used multiple regression models to examine demographic and context factors associated with symptom dimensions.

**Results.** A bifactor model, composed of one general factor and five specific dimensions of positive, negative, disorganization, manic and depressive symptoms, best-represented associations among ratings of psychotic symptoms. Positive symptoms were more common in ethnic minority groups. Urbanicity was associated with a higher score on the general factor. Men presented with more negative and less depressive symptoms than women. Early age-at-first-contact with psychiatric services was associated with higher scores on negative, disorganized, and manic symptom dimensions.

**Conclusions.** Our results suggest that the bifactor model of psychopathology holds across diagnostic categories of non-affective and affective psychosis at FEP, and demographic and context determinants map onto general and specific symptom dimensions. These findings have implications for tailoring symptom-specific treatments and inform research into the mood-psychosis spectrum.

**Introduction**

Current nosology classifies the observed manifestations of psychosis into two main categories of non-affective (e.g. schizophrenia, schizoaffective disorder) and affective psychosis (e.g. bipolar and major depressive disorders with psychotic features) (World Health Organization, 1992; American Psychiatric Association, 2013). However, the scientific accessibility of discrete ‘natural disease entities’ in psychiatry has been questioned since Kraepelin’s original distinction between dementia praecox and manic-depressive psychosis (Kraepelin, 1899; Murray et al., 2004; Craddock and Owen, 2005; Hoff, 2017). On this basis, it has been proposed, and is now widely accepted, that the categorical classification system alone is too reductionist to explain the complexity of psychotic phenomena (Van Os et al., 1999; Linscott and van Os, 2010). Various evidence-based perspectives might support a scheme incorporating symptom dimensions in psychotic disorders, as a possible approach to address the following limitations of categorical distinctions.

First, the dichotomous model of non-affective and affective psychosis does not fit the cases presenting with both prominent mood and psychotic symptoms. This is testified by the notion of a third category of schizoaffective disorder (Kasanin, 1933), which nevertheless implies further nosological challenges (Abrams et al., 2008).

In addition, if criteria-based classification systems could identify genuine disorders within the psychosis spectrum, the diagnostic overlap would be relevant to only a few patients. On the contrary, there is a large comorbidity index between schizophrenia, schizoaffective, bipolar, and major depressive disorders (Laursen et al., 2009; Upthegrove et al., 2017). Similarly, the 10-year outcomes of the Aetiology and Ethnicity in Schizophrenia and Other Psychoses (ÆSOP-10) study showed that diagnoses within psychosis other than schizophrenia at baseline tend to be unstable over time (Heslin et al., 2015).

Also, the dichotomous model is neither consistent with family studies showing familial co-aggregation of non-affective and affective psychosis (Cardno et al., 2002; Lichtenstein et al., 2009; Chou et al., 2017) nor with the accumulated evidence from genome-wide association studies that genetic risk is in part shared among schizophrenia, bipolar disorder, and major depressive disorder (International Schizophrenia Consortium et al., 2009; Demjaha et al., 2011; Cardno and Owen, 2014; O’Donovan and Owen, 2016; Power et al., 2017).

Last, several studies show the efficacy of agents which impact on dopamine signalling in the treatment of both non-affective and affective symptoms. For example, antipsychotics antagonise D2-receptor functioning and are used in bipolar disorder and schizophrenia (Post, 1999; Taylor et al., 2015), and clozapine is prescribed for both treatment-resistant bipolar disorder and schizophrenia (Li et al., 2015; Goodwin et al., 2016; Howes et al., 2016). These findings suggest that dopamine dysregulation may contribute to both positive and manic symptoms, as supported by recent positron emission tomographic findings (Jauhar et al., 2017).

Taken together, the above evidence challenges the binary categorization of non-affective and affective psychosis, enhancing research into non-categorical approaches. Pioneering studies using factor analysis examined associations among non-affective symptoms in schizophrenia and showed that these symptoms segregated in three groups (Liddle, 1987); however, these groups could not accommodate the whole symptom diversity in schizophrenia (Kay and Sevy, 1990). Thus, psychopathology models including also depressive and manic factors were proposed and replicated in schizophrenia (Lindenmayer et al., 1994; Salokangas, 1997; Wickham et al., 2001; Wallwork et al., 2012). This type of structure was likewise confirmed in psychotic disorders (Salokangas, 2003; Dikeos et al., 2006; Demjaha et al., 2009), and in a sample of bipolar patients (Lindenmayer et al., 2008). Hence, its validity across the spectrum of non-affective and affective psychosis has been consistently supported.

Recent findings suggest a more fundamental general, trans-diagnostic dimension encompassing non-affective and affective symptoms, in addition to five specific symptom dimensions (Reininghaus et al., 2013; Reininghaus et al., 2016; Shevlin et al., 2017). This conceptualization statistically reflects a bifactor model, with one general factor representing shared variance among all symptoms, and a set of specific factors where the remainder of the variance is shared among subsets of symptoms (Reise et al., 2007). This is the first study set to investigate, in an incidence sample of First Episode Psychosis (FEP) patients: (1) whether the general psychosis dimension holds across
diagnostic categories of non-affective psychosis (i.e. schizophrenia, schizoaffective disorder) and affective psychosis (i.e. bipolar and major depressive disorder with psychotic features); (2) whether formation of specific symptom dimensions is justified in addition to a general psychosis dimension; and (3) the association of demographic characteristics (i.e. age, gender, ethnicity), social context (i.e. urbanicity), and clinical factors (i.e. diagnosis) with general and specific psychosis dimensions.

The hypotheses underlying the third aim, based on the existing literature, were:

(a) Positive symptoms would be more common in ethnic minority groups and in people living in more densely populated environments (van Os et al., 2001, Janssen et al., 2003).
(b) Negative symptoms would be associated with indices suggestive of neurodevelopment impairment in psychosis (Limosin, 2014; Patel et al., 2015), such as being a man or having an early age at onset.

Methods
Sample design and procedures

Individuals suffering from their FEP were recruited between 2010 and 2015 as part of the large European network of national schizophrenia networks studying Gene–Environment Interactions (EU-GEI) study (http://www.eu-gei.eu). Specifically, FEP individuals were recruited as part of the ‘Functional Enviromics’ work package, which consisted of an incidence and a case-sibling-control study conducted across six countries with the aim to investigate clinical, genetic, and environmental interaction in the development of psychotic disorders.

The study had 17 catchment areas, including urban and less urban populations: Southeast London, Cambridgeshire and Peterborough (England); central Amsterdam, Gouda and Voorhout (the Netherlands); part of the Veneto region, Bologna municipality, city of Palermo (Italy); 20th arrondissement of Paris, Val-de-Marne, Puy-de-Dôme (France); Madrid (Vallecas), Barcelona, Valencia, Oviedo, Santiago, Cuenca (Spain); and Ribeirão Preto (Brazil).

Participants

We screened all subjects who were referred to mental healthcare services with a suspicion of psychosis. The ascertainment period of cases ranged from 12 months in London to 48 months in Val-de-Marne and Bologna, with a median of 25 months. In each site, a psychiatrist experienced in epidemiology research oversaw the local team, which was centrally trained to minimize non-differential recruitment bias in the different healthcare systems. Written consent was obtained from the subjects who agreed to take part of the case-sibling-control study. For incidence-only cases, local research ethics committees approved the extraction to take part of the case-sibling-control study. For incidence-only cases, local research ethics committees approved the extraction to take part of the case-sibling-control study.

Excluding previous analyses of OPCRIT data in individuals with enduring psychosis (Reininghaus et al., 2016), we estimated five alternative item-response models (online Supplementary Fig. S1): (a) a unidimensional model with one unique general factor (model A), which is consistent with the pre-Kraepelinian unitary concept of psychosis (Berrios and Beer, 1994); (b) a multidimensional model with five uncorrelated specific factors of positive, negative, disorganization, manic, and depressive symptoms (model B); (c) a multidimensional model with five correlated specific factors (model C), which, together with model B, is consistent with the pentagonal psychosis model (van Os and Kapur, 1996); (d) a bifactor model with one general latent factor along with five uncorrelated specific factors (model D) (Reininghaus et al., 2016); and (e) a hierarchical model with five first-order specific factors and one general second-order factor (model E), which, as model D, is consistent with the notion of a transdiagnostic spectrum of non-affective and affective psychosis (Craddock and Owen, 2005; Reininghaus et al., 2016). Some previous

Data on age, gender, and ethnicity was collected using a modified version of the Medical Research Council Sociodemographic Schedule (Mallett, 1997). Ethnicity was defined as self-reported. Country of heritage, birth or ethnicity was used as a proxy for ethnicity in people of a North African background. The OPerational CRITeria (OPCRIT) system (McGuinnes et al., 1991; Williams et al., 1996) was used by centrally trained investigators, whose reliability was assessed throughout the study (κ = 0.7). The OPCRIT system allows: (1) assess the pre-morbid history and current mental state; and (2) establish the diagnosis of psychotic disorders based on algorithms for several diagnostic classification systems. It consists of a checklist which can be filled using different sources, e.g. case records or clinical interviews. Fifty-nine items relate to the mental state examination. We used diagnoses based on Research Diagnostic Criteria (RDC) (Spitzer et al., 1978), since this classification system provides a better representation of schizoaffective disorder, which is a common presentation in clinical practice. OPCRIT RDC-based diagnoses have a good-to-excellent agreement with best-estimate consensus diagnostic systems (Craddock et al., 1996). In each catchment area, population density was computed as a number of inhabitants per square kilometre, based on official population estimates.

Statistical analysis

Psychopathology items were dichotomized as 0 ‘absent’ or 1 ‘present’. In order to ensure sufficient covariance coverage for item response modelling, we used the items with a valid frequency of ‘present’ ≥10% in our sample, which included individuals with ≤20 missing values in the psychopathology rating. OPCRIT data used in the analysis contained missing values, which we assumed to be missing at random, allowing for the maximum likelihood estimator to provide unbiased estimates. We performed multidimensional item response modelling in Mplus, version 7.4 (Muthén and Muthén, 2012) to estimate unidimensional, multidimensional, bifactor, and second-order models of psychosis.

Extending previous analyses of OPCRIT data in individuals with enduring psychosis (Reininghaus et al., 2016), we estimated five alternative item-response models (online Supplementary Fig. S1): (a) a unidimensional model with one unique general factor (model A), which is consistent with the pre-Kraepelinian unitary concept of psychosis (Berrios and Beer, 1994); (b) a multidimensional model with five uncorrelated specific factors of positive, negative, disorganization, manic, and depressive symptoms (model B); (c) a multidimensional model with five correlated specific factors (model C), which, together with model B, is consistent with the pentagonal psychosis model (van Os and Kapur, 2009); (d) a bifactor model with one general latent factor along with five uncorrelated specific factors (model D) (Reininghaus et al., 2016); and (e) a hierarchical model with five first-order specific factors and one general second-order factor (model E), which, as model D, is consistent with the notion of a transdiagnostic spectrum of non-affective and affective psychosis (Craddock and Owen, 2005; Reininghaus et al., 2016). Some previous
OPCRIT exploratory analysis showed a combined negative/disorganization dimension (Serretti et al., 2001; Fanous et al., 2005). We did not have a strong theoretical rationale for testing such a structure in a confirmatory analysis. By contrast, we considered specific negative symptoms as a clinically observable marker of neurodevelopmental impairment in psychosis (Limosin, 2014).

The five models were compared using Log-Likelihood (LL), Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and Sample-size Adjusted BIC (SABIC) as model fit statistics. For the model showing the best fit, we calculated reliability and strength indices, such as McDonald’s omega (ω), omega hierarchical (ωH), and index H. Coefficient ω is an estimate of the proportion of common variance accounted by general and specific symptom dimensions. Coefficient ωH is an estimate of the proportion of reliable variance accounted by the general dimension, treating variability in scores due to specific dimensions as measurement error (Rodriguez et al., 2016b). Ω formula can be extended to each specific factor, i.e., treating variability in scores due to the general factor as a measurement error, to compute omega hierarchical for subscales. Based on omega and omega hierarchical coefficients, which can vary from 0 to 1, we computed the ratios of ω/ωH, namely the relative omega, as the amount of reliable variance explained in the observed scores attributable to (1) the general factor independently from the specific symptom dimensions, and (2) each specific symptom dimension independently from the general factor. To estimate the extent to which symptom dimensions were represented by their own set of OPCRIT items and their replicability across studies, we computed the construct reliability index H (Hancock and Mueller, 2001). The index H ranges from 0 to 1, with values closer to 1 indicating better reliability and replicability (Rodriguez et al., 2016a). Quantitative scores for all symptom dimensions were calculated using the ‘FSCORES’ function in Mplus.

Further, we examined the diagnostic classification accuracy based on general and specific symptom dimension scores using multinomial receiver operating characteristic (ROC) analysis in STATA 14 (StataCorp, 2015). In addition, we performed a sensitivity analysis, examining subjects with item ratings based on face-to-face interview and based on clinical records separately.

We used multiple linear regression to examine the association between factor scores of general and/or specific psychosis dimensions as the outcome variable and demographic variables, including gender, age-at-first-contact with psychiatric services, ethnicity, and diagnosis as covariates. Country and assessment method were treated as a priori confounders.

To examine the individual-level effect of urbanicity on symptom dimension scores, standardized population density values were used as a continuous independent variable, while controlling the analysis for gender, age-at-first-contact, ethnicity, diagnosis, and assessment method. Sensitivity analysis included post-hoc multiple regressions within each country, where population density was dichotomized at its median as a dummy variable for urbanicity.

Results

Sample characteristics

We identified 2774 treated incidence cases of psychosis (Jongsma et al., 2018), of whom 2182 had (complete or missing at random) OPCRIT data available for analysis under the provision of local research ethics committees (Table 1). OPCRIT item ratings were completed based on face-to-face assessment for 51% (n = 1112) and based on clinical records for 49% (n = 1070) of the sample. The sample prevalence of psychotic symptoms is presented in Supplementary Table S1.

Fifty-seven per cent of FEP were men. Subjects were mostly people of a White ethnicity. Other main ethnic groups included Black African and Black Caribbean, North African, Mixed, and Asian. Mean age-at-first-contact with psychiatric services was 32.1 years; this was lower in men (M = 30.1) compared with women (M = 34.7; t = −9.6, p < 0.001). Age-at-first-contact differed across ethnic groups, with individuals of Black ethnicity (M = 29) being younger than individuals of White ethnicity (M = 32.7; F = 7.72, p < 0.001). The most common RDC-based diagnosis was broad or narrow schizophrenia (38.6%), followed by schizoaffective disorders (35%), unspecified non-organic psychotic disorder (16.3%), bipolar disorder (5.9%), and psychotic depression (4.2%).

Symptom dimensions in the EU-GEI sample

The bifactor model was the best fit for the OPCRIT symptom data compared with all other models, as consistently indicated by each of the model fit statistics (Table 2), and explained 54% of the total variance.

Figure 1 shows that, within the bifactor model, general and specific dimensions accounted for 93% of the common variance. Overall, statistical indices derived from the bifactor model suggest that its explained variance was due to individual differences in both general and specific symptom dimensions, which therefore might complement each other in reflecting the psychopathological structure at FEP. This is illustrated by the relative omega coefficients, which, for example, showed that 47% of the reliable variance was due to the general factor when partitioning out the variability in scores due to the specific factors (Fig. 1). High H values were consistently observed for all latent factors, indicating that they were well defined, and that the bifactor model had high reliability and replicability (Fig. 1). Sensitivity analysis showed that the bifactor model was the best fit for the OPCRIT data in both the assessment methods (online Supplementary Tables S2.1 and S2.2).

Symptom dimensions and item factor loadings

Table 3 shows standardized factor loadings for the bifactor model. On the general dimension, a positive factor loading was observed for all OPCRIT items with statistically significant loadings. In addition, the magnitude of factor loadings of items on the general dimension was small, except for some manic/delusional items for which loadings of moderate magnitude were observed. On the specific dimensions, most of the items showed moderate to strong positive loadings. Finally, latent factor scores were strongly and positively associated with simplified weighted OPCRIT sum scores for use in clinical practice (online Supplementary Table S3).

Symptom dimensions and categorical diagnoses

Findings from regression analyses are shown in Table 4 and predicted symptom dimension scores for each RDC-based diagnostic category are reported in Fig. 2. Compared with bipolar disorder, factor scores for the positive dimension were moderately higher in schizophrenia and schizoaffective disorder; factor scores for the negative dimension were moderately higher in schizophrenia,
schizoaffective and psychotic depression; and factor scores for the depressive dimension were markedly higher in psychotic depression and schizoaffective disorder. Bipolar disorder showed the highest factor scores for the manic and the general dimensions. Dimension scores based on ICD diagnostic categories are presented in Supplementary Fig. S2 and Supplementary Table S4.

Finally, ROC analysis showed that classification accuracy into RDC categories based on general and specific symptom dimensions was markedly higher for patients with psychopathology rating based either on face-to-face interview (95% CI 0.54–0.63) or case note review (95% CI 0.56–0.65), compared with a classification by chance (95% CI 0.32–0.41). Moreover, symptom dimensions showed similar diagnostic classification accuracy across countries (online Supplementary Figs S3.1 and S3.2).

Symptom dimensions by gender, age-at-first-contact, and ethnicity

Findings on factor scores by gender, age-at-first-contact, and ethnicity, are shown in Fig. 2 and Table 4. Early age-at-first-contact was associated with higher scores for the general, negative, disorganized, and manic symptom dimensions, and with lower scores for the depressive symptom dimension. Men showed fewer depressive symptoms and more negative symptoms than women, even after adjusting the analysis for several confounders. Table 4 further shows that participants of Black and North African ethnicity presented with higher scores on the positive symptom dimension compared with an individual of White ethnicity. Finally, higher scores for the disorganization dimension and lower scores for the depressive dimension were observed in Black compared with White ethnicity. Noteworthy, the magnitude of the effect was small for all the results.

Symptom dimensions by urbanicity

A moderate positive association was observed for more densely populated environments and the general dimension score. Table 4 further shows a weaker positive association between population density and specific negative, disorganization, and manic symptom dimensions. Post-hoc analysis of symptom dimensions within countries showed that positive symptoms were more common in urban study sites in the UK (i.e. London v. Cambridge), whereas a negative association was observed in Spain (online Supplementary Table S5).

Discussion

Principal findings

This is the first study on general and specific symptom dimensions in an incidence sample of psychosis. First, we found in our FEP sample that manic and delusional symptoms primarily underlie the identified general psychosis factor across diagnostic categories of non-affective and affective psychosis. Second, findings showed that specific dimensions of positive, negative,
disorganized, manic and depressive symptoms are complementary to the general dimension. Third, general and specific symptom dimensions discriminated well between diagnoses of psychotic disorders. Forth, positive symptoms were more common among individuals of Black and North African ethnicity. Fifth, there was some evidence that early age-at-first-contact was associated with higher scores for several dimensions, such as of negative, disorganised and manic symptoms. Sixth, men presented with more negative and less depressive symptoms than women. Finally, higher scores for the general dimension were observed for individuals living in urban neighbourhoods.

Limitations

Before interpreting our findings, we must consider potential limitations. Symptoms were rated with a semi-structured face-to-face interview or from case note review. Still, study investigators underwent a specific and centrally organized training for OPCRIT and demonstrated good inter-rater reliability for individual item ratings; moreover, OPCRIT is a tool specifically designed to allow use with different sources (McGuffin et al., 1991; Cardno et al., 1996; Rucker et al., 2011). However, we found consistently lower symptom ratings using case note review compared with face-to-face interviews. It is possible that clinicians failed to record all symptoms; alternatively, patients presenting with less severe psychopathology had a shorter contact with services, and therefore less chances to be interviewed by researchers. Whether or not differences in ratings are genuine or a surrogate of different sources of item ratings, we treated this potential bias as artificial confounding of our findings and adjusted all analyses for the type of assessment method. On the other hand, the use of an incidence sample allowed the best possible approximation of the true

Table 2. Model fit statistics of unidimensional, multidimensional, bi-factor, and second-order models

<table>
<thead>
<tr>
<th>Sample size: 2182</th>
<th>Full information fit statistics&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LL</td>
</tr>
<tr>
<td>A – Unidimensional Model</td>
<td>−54809</td>
</tr>
<tr>
<td>B – Multidimensional Model (five uncorrelated factors)</td>
<td>−50645</td>
</tr>
<tr>
<td>C – Multidimensional Model (five correlated factors)</td>
<td>−50439</td>
</tr>
<tr>
<td>D – Bifactor Model (one general factor and five specific uncorrelated factors)</td>
<td>−49710</td>
</tr>
<tr>
<td>E – Hierarchical Model (five first-order specific correlated factors and one second-order general factor)</td>
<td>−50608</td>
</tr>
</tbody>
</table>

LL, log-likelihood; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; SABIC Sample-size Adjusted Bayesian Information Criterion.

<sup>a</sup>A difference of 10 in AIC, BIC and SABIC is considered important. Lower values indicate a statistically better model fit.
<table>
<thead>
<tr>
<th>OPCRIT item</th>
<th>Item no.</th>
<th>Factor</th>
<th>Specific factor loading</th>
<th>General factor loading</th>
<th>Communalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persecutory delusions</td>
<td>54</td>
<td>POS</td>
<td>0.36***</td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td>Well organized delusions</td>
<td>55</td>
<td>POS</td>
<td>0.27***</td>
<td>0.34***</td>
<td>0.19</td>
</tr>
<tr>
<td>Delusions of influence</td>
<td>58</td>
<td>POS</td>
<td>0.43***</td>
<td>0.33***</td>
<td>0.29</td>
</tr>
<tr>
<td>Bizarre delusions</td>
<td>59</td>
<td>POS</td>
<td>0.21***</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>Widespread delusions</td>
<td>60</td>
<td>POS</td>
<td>0.42***</td>
<td>0.29***</td>
<td>0.26</td>
</tr>
<tr>
<td>Delusions of passivity</td>
<td>61</td>
<td>POS</td>
<td>0.49***</td>
<td></td>
<td>0.27</td>
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<tr>
<td>Primary delusional perception</td>
<td>62</td>
<td>POS</td>
<td>0.23***</td>
<td>0.51***</td>
<td>0.32</td>
</tr>
<tr>
<td>Other primary delusions</td>
<td>63</td>
<td>POS</td>
<td>0.30***</td>
<td>0.31***</td>
<td>0.19</td>
</tr>
<tr>
<td>Delusions &amp; hallucinations last for 1 week</td>
<td>64</td>
<td>POS</td>
<td>0.81***</td>
<td></td>
<td>0.65</td>
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<tr>
<td>Persecutory/jealous delusions &amp; hallucinations</td>
<td>65</td>
<td>POS</td>
<td>0.66***</td>
<td></td>
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<tr>
<td>Thought insertion</td>
<td>66</td>
<td>POS</td>
<td>0.60***</td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>Thought broadcast</td>
<td>68</td>
<td>POS</td>
<td>0.60***</td>
<td>0.24***</td>
<td>0.41</td>
</tr>
<tr>
<td>Third person auditory hallucinations</td>
<td>73</td>
<td>POS</td>
<td>0.61***</td>
<td></td>
<td>0.37</td>
</tr>
<tr>
<td>Running commentary voices</td>
<td>74</td>
<td>POS</td>
<td>0.62***</td>
<td></td>
<td>0.39</td>
</tr>
<tr>
<td>Abusive/accusatory/persecutory voices</td>
<td>75</td>
<td>POS</td>
<td>0.54***</td>
<td></td>
<td>0.33</td>
</tr>
<tr>
<td>Other (non-affective) auditory hallucinations</td>
<td>76</td>
<td>POS</td>
<td>0.42***</td>
<td></td>
<td>0.19</td>
</tr>
<tr>
<td>Non-affective hallucinations in any modality</td>
<td>77</td>
<td>POS</td>
<td>0.51***</td>
<td></td>
<td>0.26</td>
</tr>
<tr>
<td>Negative formal thought disorder</td>
<td>29</td>
<td>NEG</td>
<td>0.54***</td>
<td></td>
<td>0.30</td>
</tr>
<tr>
<td>Restricted affect</td>
<td>32</td>
<td>NEG</td>
<td>1.00***</td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Blunted affect</td>
<td>33</td>
<td>NEG</td>
<td>0.98***</td>
<td></td>
<td>0.97</td>
</tr>
<tr>
<td>Bizarre behaviour</td>
<td>17</td>
<td>DIS</td>
<td>0.42***</td>
<td>0.21***</td>
<td>0.23</td>
</tr>
<tr>
<td>Speech difficult to understand</td>
<td>26</td>
<td>DIS</td>
<td>0.96***</td>
<td></td>
<td>0.93</td>
</tr>
<tr>
<td>Incoherent</td>
<td>27</td>
<td>DIS</td>
<td>0.62***</td>
<td>0.47***</td>
<td>0.60</td>
</tr>
<tr>
<td>Positive formal thought disorder</td>
<td>28</td>
<td>DIS</td>
<td>0.84***</td>
<td></td>
<td>0.72</td>
</tr>
<tr>
<td>Inappropriate affect</td>
<td>34</td>
<td>DIS</td>
<td>0.23***</td>
<td>0.46***</td>
<td>0.27</td>
</tr>
<tr>
<td>Excessive activity</td>
<td>19</td>
<td>MAN</td>
<td>0.53***</td>
<td>0.73***</td>
<td>0.82</td>
</tr>
<tr>
<td>Reckless activity</td>
<td>20</td>
<td>MAN</td>
<td>0.36***</td>
<td>0.67***</td>
<td>0.58</td>
</tr>
<tr>
<td>Distractibility</td>
<td>21</td>
<td>MAN</td>
<td>0.29***</td>
<td>0.60***</td>
<td>0.45</td>
</tr>
<tr>
<td>Reduced need for sleep</td>
<td>22</td>
<td>MAN</td>
<td>0.55***</td>
<td>0.56***</td>
<td>0.61</td>
</tr>
<tr>
<td>Agitated activity</td>
<td>23</td>
<td>MAN</td>
<td>0.16***</td>
<td>0.76***</td>
<td>0.59</td>
</tr>
<tr>
<td>Pressured speech</td>
<td>30</td>
<td>MAN</td>
<td>0.74***</td>
<td>0.43***</td>
<td>0.73</td>
</tr>
<tr>
<td>Thoughts racing</td>
<td>31</td>
<td>MAN</td>
<td>0.54***</td>
<td>0.49***</td>
<td>0.53</td>
</tr>
<tr>
<td>Elevated mood</td>
<td>35</td>
<td>MAN</td>
<td>0.85***</td>
<td>0.41***</td>
<td>0.89</td>
</tr>
<tr>
<td>Irritable mood</td>
<td>36</td>
<td>MAN</td>
<td>0.12**</td>
<td>0.55***</td>
<td>0.32</td>
</tr>
<tr>
<td>Increased self esteem</td>
<td>56</td>
<td>MAN</td>
<td>0.87***</td>
<td>0.24***</td>
<td>0.81</td>
</tr>
<tr>
<td>Grandiose delusions</td>
<td>57</td>
<td>MAN</td>
<td>0.67***</td>
<td>0.30***</td>
<td>0.54</td>
</tr>
<tr>
<td>Slowed activity</td>
<td>24</td>
<td>DEP</td>
<td>0.55***</td>
<td></td>
<td>0.31</td>
</tr>
<tr>
<td>Loss of energy/tiredness</td>
<td>25</td>
<td>DEP</td>
<td>0.80***</td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td>Dysphoria</td>
<td>37</td>
<td>DEP</td>
<td>0.74***</td>
<td></td>
<td>0.55</td>
</tr>
<tr>
<td>Loss of pleasure</td>
<td>39</td>
<td>DEP</td>
<td>0.87***</td>
<td></td>
<td>0.76</td>
</tr>
<tr>
<td>Poor concentration</td>
<td>41</td>
<td>DEP</td>
<td>0.62***</td>
<td>0.42***</td>
<td>0.56</td>
</tr>
<tr>
<td>Excessive self-reproach</td>
<td>42</td>
<td>DEP</td>
<td>0.60***</td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>43</td>
<td>DEP</td>
<td>0.55***</td>
<td></td>
<td>0.31</td>
</tr>
</tbody>
</table>

(Continued)
distribution of psychosis symptoms at FEP, which may have reduced potentially inflated presence of positive and negative symptoms in previous studies conducted in hospital settings (Allardycse et al., 2007). Also, OPCRT does not cover some relevant aspects of negative symptoms related to passive social withdrawal, lack of motivation, and difficulties in abstract/symbolic thinking. Consequently, we constructed a narrow negative symptom dimension with three items. Finally, some authors have argued that, in a bifactor model, the general factor may be difficult to interpret and in general may overfit the data (Bonifay et al., 2015). We found some evidence of gender differences in symptom dimension scores. Men showed less depressive symptoms and more negative symptoms compared with women. This finding is consistent with other studies in stable schizoider (Shiasel et al., 1992; Roy et al., 2001; Galderisi et al., 2012), first episode psychotic disorder (Morgan et al., 2008), and the general population (Marc et al., 2003). In our sample, we also showed that early age-at-first-contact was associated with a higher level of general and specific psychopathology. Notably, it has been proposed that gender-related and symptom profiles differences in psychosis may be suggestive of different neurodevelopmental trajectories (Castle and Murray, 1991; Seeman, 1997; Riecher-Rössler and Häfner, 2000).

We further found that symptom dimensions vary in terms of ethnicity. Consistent with a previous report (Kirkbride et al., 2016), we provided evidence that people of Black ethnicity presented at FEP with more positive and disorganized symptoms and fewer depressive symptoms compared with people of White ethnicity. Moreover, in line with another study (Velinger et al., 2007), we found in our sample that the North African group presented at FEP with more positive symptoms compared with people of White ethnicity. It has been debated whether similar findings reflect true differences in symptom presentation or instead result from raters being more likely to overrate symptoms in the context of ethnic-cultural diversity (Mukherjee et al., 1983; Hutchinson et al., 1999; Barrio et al., 2003; Arnold et al., 2004; Vega and Lewis-Fernandez, 2008). Recent studies using standardized procedures for assessing symptomatology blind to ethnicity have suggested that misdiagnosis or rating bias cannot account for differences across ethnic groups (Morgan et al., 2010). However, we must remain cautious in interpreting these results.

We showed that high population density is positively associated with the general and specific disorganized, negative and manic dimensions. In our multinational sample, we were not able to replicate previous findings on the relationship between urbanicity and the positive dimension (Kirkbride et al., 2007). Nevertheless, stratified analysis by country was consistent with the previously reported association between urbanicity and positive symptoms in the UK. The relationship between urbanicity and a higher incidence of psychotic disorders is well-established (Vassos et al., 2012). However, it has been found to show non-linearity (Kirkbride et al., 2017), which implies that the effect of urbanicity may depend on exposure to additional socio-environmental factors associated with urban contexts, for example cannabis use (Kuepper et al., 2011) and childhood adversities (Frissen et al., 2015). Similarly, our findings support the

### Table 3. (Continued.)

<table>
<thead>
<tr>
<th>OPCRT item</th>
<th>Item no.</th>
<th>Factor</th>
<th>Specific factor loading</th>
<th>General factor loading</th>
<th>Communalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial insomnia</td>
<td>44</td>
<td>DEP</td>
<td>0.65***</td>
<td>0.32***</td>
<td>0.53</td>
</tr>
<tr>
<td>Middle insomnia (broken sleep)</td>
<td>45</td>
<td>DEP</td>
<td>0.65***</td>
<td>0.25***</td>
<td>0.48</td>
</tr>
<tr>
<td>Early morning waking</td>
<td>46</td>
<td>DEP</td>
<td>0.56***</td>
<td>0.39***</td>
<td>0.46</td>
</tr>
<tr>
<td>Excessive sleep</td>
<td>47</td>
<td>DEP</td>
<td>0.46***</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>Poor appetite</td>
<td>48</td>
<td>DEP</td>
<td>0.69***</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Weight Loss</td>
<td>49</td>
<td>DEP</td>
<td>0.56***</td>
<td>0.20***</td>
<td>0.35</td>
</tr>
</tbody>
</table>

General, general psychosis factor; specific symptom dimensions: DEP, depression; MAN, mania; DIS, disorganization; NEG, negative; POS, positive. Only loadings ⩾0.2 for the general factor are shown for simplicity. Significance: *** = p < 0.001; ** = p < 0.01.
Table 4 - Symptoms dimension scores by sociodemographic, categorical diagnosis, and social context variables

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>General B (95% CI)</td>
<td>Positive B (95% CI)</td>
<td>Negative B (95% CI)</td>
<td>Disorganization B (95% CI)</td>
<td>Manic B (95% CI)</td>
<td>Depressive B (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.01* (−0.07 to 0.09)</td>
<td>0.03* (−0.06 to 0.11)</td>
<td>0.01* (−0.06 to 0.01)</td>
<td>−0.27*** (−0.21 to −0.23)</td>
<td>−0.09*** (−0.14 to −0.04)</td>
<td>0.00 (−0.01 to 0.02)</td>
<td>0.17** (0.02 to 0.32)</td>
<td>0.17** (0.02 to 0.32)</td>
<td>−0.14*** (−0.19 to −0.09)</td>
<td>0.15*** (0.11 to 0.19)</td>
<td>0.18*** (0.14 to 0.22)</td>
<td>0.09*** (−0.02 to 0.17)</td>
<td>0.1*** (−0.05 to 0.14)</td>
<td>0.3** (−0.07 to 0.14)</td>
</tr>
<tr>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
<td>0.27 (−0.25 to 0.1)</td>
</tr>
</tbody>
</table>

hypothesis that urban environment does not have a dimension-specific effect and may act to confer risk for different psychopathological outcomes in psychosis (van Os et al., 2002). Noteworthy, similar findings have been reported in the general population (van Os et al., 2001), which may require future studies to consider the additive interaction between putative risk factors for psychosis and urbanicity.

**Implications**

In the context of a general effort to move away from DSM and ICD categories (Demjaha et al., 2009; Reininghaus et al., 2016; Kotov et al., 2017; Van Dam et al., 2017; Whalen, 2017; Zachar and Kendler, 2017), we found evidence that supports, and may inform, the use of dimensional measures in the field of psychosis. In our sample, the bifactor model was a valid platform for research into FEP. Nevertheless, the plausibility of our statistically-guided approach depends on the extent to which: (1) symptom dimensions represent coherent environmental and biological factors; and (2) meaningful clinical information or decisions may derive from the latent constructs.

From a research perspective, our findings suggest that the general dimension may reflect a phenotype for the study of general risk factors. For example, urbanicity may impact on the risk and profile of psychosis through the combination of other, more specific socio- or bio-environmental factors. In addition, we showed a substantial variation of sociodemographic determinants at the specific dimension level, which may support an integrated socio-developmental model of psychosis (Morgan et al., 2010).

We may further suggest using the general dimension as a quantitative measure of psychopathology for research into the genetic component shared across psychotic disorders. The evidence is required to establish the extent to which pathophysiology of schizophrenia, bipolar disorder, and psychotic depression share the level of pathways and neuronal cell mechanisms (Forstner et al., 2017). Based on the data presented on specific symptom dimensions, it is intriguing to speculate whether the distribution of psychotic symptoms reflects a gradient of neurodevelopmental impairment or socio-environmental risk (Morgan et al., 2010; Howes and Murray, 2014) resulting in different patterns of functional abnormalities (Murray and Lewis, 1987; Murray et al., 1992; Demjaha et al., 2011; Owen and O’Donovan, 2017).

From a clinical perspective, although each patient presents with a specific pattern of psychopathology and response to treatment at FEP, attention has been traditionally focused on the positive dimension management. Mental health professionals may integrate observations of the whole range of symptoms and signs with a consideration of neurodevelopmental and socio-environmental risk factors. Such an approach should aim to plan and optimize pharmacological and non-pharmacological treatments (Murray et al., 2016), thus focusing further on treatment of negative, disorganized and affective dimensions (Wykes et al., 2011; Giacco et al., 2012; Carbon and Correll, 2014; Pelayo-Teran et al., 2014; Rosenbaum et al., 2014).

We may further suggest promoting mental health professionals to adopt treatment plans guided by dimensions, and increasing their confidence in dimensional classifications. Reconciling contradictory concerns of clinicians and researchers (Kendell and Jablensky, 2003) may represent the first milestone towards a gradual nosology refinement.
Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291718002131

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Conflict of interest. The authors have no conflicts of interest to declare in relation to the work presented in this paper.

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Appendix

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