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Commentary

Response to the commentary by Buoli et al., EURPSY-D-18-00265

Dear Editor,

We read with interest the commentary by Buoli et al. [1], on our study "Long-term validity of the At Risk Mental State (ARMS) for predicting psychotic and non-psychotic mental disorders", which was published in European Psychiatry [2]. In our prospective 6-year cohort study we followed up 710 individuals undergoing an assessment for a suspected Clinical High Risk state for Psychosis (CHR-P)3. We investigated their risk of developing psychotic and non-psychotic mental disorders. We concluded that the CHR-P designation [4] is not associated with an increased risk of developing mental disorders other than psychosis [3], replicating earlier independent findings [5].

Overall, we feel that critical appraisals of published studies such as the commentary by Buoli et al are greatly beneficial to the scientific advancement of knowledge in the field of the CHR-P state [3]. However, we also note some inaccuracies, that are discussed below.

Firstly, Buoli et al note that "cognitive strategies" –which should rather have been referred to as cognitive behavioural therapies- have yielded hopeful results for the prevention of psychosis. This is not completely correct, given that the most recent network meta-analyses found no evidence for superior efficacy of any specific treatments compared to each other to prevent the onset of psychosis [6] or reduce the severity of symptoms [7] in CHR-P individuals.

Secondly, Buoli et al argued that we have classified bipolar disorders with psychotic features as non-psychotic conditions. This is incorrect: as clearly indicated in our eMethods, our category of bipolar disorders included ICD-10 non-psychotic bipolar disorder (F31.x, excluding F31.2 and F31.5) and cyclothymia (F34.0) [3]. In our eMethods we have also provided the specific ICD-10 codes that were used to define the psychotic disorders that were considered as outcome in our prospective cohort analysis [3]. Conversely, Buoli et al presented some retrospective data taken from a sample of patients affected with psychotic and non-psychotic bipolar disorders but did not clarify whether ICD or DSM diagnoses were used nor the specific diagnostic types.

Thirdly, there was some degree of conceptual confusion which was inherited by the retrospective vs prospective approach adopted by Buoli et al. The authors stated that, by retrospectively looking at the medical notes of 235 bipolar patients, about 80% were found to satisfy the CHR-P criteria. This is only highly hypothetical and of limited clinical value because the help-seeking criterion that is implicitly necessary to meet a CHR-P state in the real world [8] is not considered by the retrospective analysis of Buoli et al. [9]. In fact, the prospective detection and recruitment of CHR-P individuals is the most challenging area in the field of psychosis prevention [10–13].

Fourthly, the conclusions by Buoli et al are not particularly innovative. They concluded that the presence of CHR-P criteria is more frequently associated with a future diagnosis of psychotic bipolar disorders; however this is just confirming the core finding of our study [2]. Buoli et al also speculated that bipolar disorders should not be considered a psychotic condition like schizophrenia in the light of "different biomarkers". Unfortunately, no reference to support these putative differential biomarkers is provided, and to our best knowledge, no biomarker to distinguish bipolar disorders vs schizophrenia has been validated to date. Buoli et al also recommended distinguishing affective psychoses within the group of psychotic outcomes that are traditionally measured in the CHR-P field. However, this is already done as part of clinical routine to the point that it has alraedy received some meta-analytical demonstration [14]. Buoli et also incorrectly concluded that it is not currently possible to know the extent to which CHR-P individuals are at risk of developing schizophrenia-spectrum vs affective-spectrum psychotic disorders. However, our previous meta-analysis has clearly demonstrated that the 73% of CHR-P individuals who will develop psychotic disorders will actually develop schizophrenia spectrum disorders [14].

Fifthly, as indicated above, retrospective analyses such as those presented by Buoli et al. are unlike to impact the early detection of individuals at risk of bipolar disorders and their preventive care. Our Early Psychosis: Intervention and Clinical-detection (EPIC) lab has recently developed and validated one of the few psychometric tools which can be used to prospectively identify individuals at risk of developing bipolar disorders [15]: the Semistructured Interview for Bipolar At Risk States (SIBARS [15]). The SIBARS has demonstrated good prognostic accuracy and is being currently validated in different clinical scenarios. We hope that research centers such as that the team led by Buoli et al will further leverage on our initial study to refine and improve it, to advance the scientific knowledge in the field of early bipolar

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disorders and to ultimately benefit the lives of many young patients worldwide.

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