## Suicide in individuals at Ultra-High Risk (UHR) of psychosis: a 2-year longitudinal study.

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**Background -** Suicide risk is high in first episode schizophrenia. However, little data are available in young individuals at Ultra-High Risk (UHR) of psychosis. Assessing suicidal ideation in this clinical sample is important because suicide risk has been shown to be high at the onset of a first episode psychosis (FEP) (Pompili et al., 2011). Indeed, about 5% of new onset or first admission patients with schizophrenia die committing suicide (Palmer et al., 2005). Moreover, 2-11% of schizophrenic patients make a suicide attempt in the first year of intervention (Addington et al., 2004). Thus, the early detection of FEP and UHR mental states, aimed even only at encouraging adherence to therapy, may also reduce suicide risk (Preti et al., 2009).

**Aim** – Aim of the study was: (1) to assess prevalence and incidence rates of suicide attempts, suicidal ideation, and completed suicide in UHR individuals compared with First Episode Psychosis (FEP) and non-FEP/UHR help-seeking peers at baseline and over a 24-month follow-up time, and (2) to explore any association of suicidal ideation with other psychopathological parameters at baseline.

**Materials and Methods** – 273 young people (13–35 years) were evaluated with the Comprehensive Assessment of At-Risk Mental States (CAARMS), the Beck Depression Inventory – II Edition (BDI), and the World Health Organization Quality Of Life scale – Brief version (WHOQOL-BREF). The BDI item 9 cut-off score of  $\geq$  1 dichotomized the presence/absence of suicidal ideation. In the current research, we defined suicide attempts as potentially injurious, self-inflicted behavior without a fatal outcome for which there was (implicit or explicit) evidence of intent to die (Silverman et al., 2007). Acts of deliberate self-harm or intoxication with alcohol or drugs, but where there was no clear intention to die, were not considered as suicide attempts. According to Silverman et al. (2007), the term "completed suicide" was used to denote when there was a self-inflicted death with (explicit or implicit) evidence of intent to die.

**Results** - At the initial assessment, UHR group had more severe levels of suicidal ideation on the BDI-II item 9 than FEP and nonUHR/FEP, as well as significantly higher percentages of subjects who were above BDI-II item 9 cut-off (table 1). Notably, no difference in BDI-II item 9 scores and percentages was found between FEP and UHR- samples. Within the total sample, 24 individuals (8.8%) had at least one previous attempted suicide before enrollment, with a significantly greater percentage in the UHR sample (n = 10; 14.5%) than in FEP patients (n = 7; 5.7%) (table 1). Although suicide attempt lifetime prevalence was also slightly higher in the UHR sample than in non-UHR/FEP individuals (n = 7; 8.6%), the difference was not significant ( $\chi_2 = 0.699$ ; p = 0.403). Finally, we found an equal proportion of lifetime attempted suicide between FEP and non-UHR/FEP subjects ( $\chi^2 = 0.267$ ; p = 0.605). After 1 year of follow-up, 10 (4.6%) of the residual 217 participants showed a new suicide attempt, with equal proportions in the three groups (table 1). Specifically, although 1-year suicide attempt incidence rate was higher in UHR people (n = 4/51; 7.8%) than in FEP (n = 5/96; 5.2%) and non-UHR/FEP (n = 1/70; 1.4%) subjects, the differences were not significant ( $\chi_2 = 0.40$ , p = 0.719, and  $\chi_2 = 1.66$ , p = 0.161, respectively). Moreover, 3 (1.4%) of the 127 subjects who completed the 1-year follow-up period, died by suicide. Although they were all in the FEP sample, no significant difference in terms of 1-year incidence rates of completed suicide were found among the three groups. Within the 111 subjects who completed the 2 years of follow-up, 7 (6.3%) suicide attempts were found: i.e. 5 (5/30; 16.7%) in the UHR group and 2 (2/55; 3.6%) in the FEP one. Specifically, only two of these 7 attempted suicides were new attempts occurring between the first and second year of treatment (one in the FEP sample and one in the UHR one). No attempted suicide was found in non-UHR/FEP help-seekers who completed the 2-year follow-up period (0/70; 0.0%). However, differences in 2-year incidence rates of suicide attempts achieved significant level only in UHR individuals in comparison with non-UHR/FEP subjects (table 1). Moreover, a further death by suicide was reported in FEP patients, for a completed suicide cumulative incidence of 1.5% (n = 4/273) within the total sample and 3.3% (n = 4/122) in the FEP sample. Although this finding was greater than those observed in UHR (n = 0/70; 0.0%) and non-UHR/FEP (0/81; 0.0%) samples, these differences were not significant ( $\chi_2 = 1.01$ , p = 0.298; and  $\chi_2 = 1.28$ ; p = 0.152, respectively). Within the total UHR sample, BDI-II item 9 score showed significant positive correlation with CAARMS "Anhedonia", "General psychopathology", "Suicidality/Self-Harm", and "Subjective impairment tolerance to normal stress" subscores, as well as with BDI-II total score and "Cognitive" and "Somatic-Affective" factor subscores (table 2). With regards to the longitudinal stability of BDI-II item 9 score within the total UHR+ group, while no significant difference was found between levels of suicidal ideation at baseline and after 12 months of follow-up ( $0.75 \pm 0.70 \text{ vs } 0.57 \pm 0.89$ ; Z = -1.35; p = 0.132), a statistically significant decrease in BDI-II item 9 scores after 2-year follow-up period was observed (0.75  $\pm$  0.70 vs 0.29  $\pm$  0.60; Z = -2.44; p = 0.031) (see supplementary materials [table S2]). Finally, using a for block selection method (with socio-demographic and psychopathological features as independent variables and dichotomized BDI-II item 9 scores as dependent variable) within the total UHR+ group, only two explanatory parameters (i.e. years of education and BDI-II total score) joined in the logistic regression model with a significant power (table 4; see also supplementary materials [table S3]). Specifically, education (in years) had a negative regression coefficient, while BDI-II total score showed a positive one. The percentage of correct dichotomized ascription using this model for predicting suicidal ideation in UHR+ individuals was 74.6%.

							Psychopathological parameters	BDI item 9 (ρ)
							SOFAS	-0.110
Gender (males) Ethnic group (Caucasian) Mother tongue (Italian) Age Education (in years) DUI (in weeks) <b>Suicidal Ideation</b> BDI-II item 9 cut-off ≥ 1 BDI-II item 9 CAARMS item 7.3 cut-off ≥ 2 CAARMS item 7.3 <b>Suicide</b> Previous suicide attempts – lifetime prevalence Suicide attempts – 1 year incidence rate Suicide attempts – 2 year incidence rate Completed suicide - 1 year incidence rate	$156 (57.1\%)$ $236 (86.4\%)$ $245 (89.7\%)$ $21.24 \pm 5.85$ $11.46 \pm 2.39$ $77.83 \pm 56.61$ $113 (41.5\%)$ $0.52 \pm 0.66$ $116 (42.6\%)$ $1.43 \pm 1.71$ $24 (8.8\%)$ $10/217 (4.6\%)$ $7/111 (6.3\%)$ $3/217 (1.4\%)$ $4 (1.5\%)$	$\begin{array}{c} 40 \ (49.4\%) \\ 69 \ (85.2\%) \\ 76 \ (93.8\%) \\ 21.26 \pm 6.44 \\ 11.47 \pm 2.40 \\ 66.39 \pm 54.65 \\ \end{array}$ $\begin{array}{c} 27 \ (33.3\%) \\ 0.40 \pm 0.61 \\ 24 \ (29.6\%) \\ 0.91 \pm 1.46 \\ \end{array}$ $\begin{array}{c} 7 \ (8.6\%) \\ 1/70 \ (1.4\%) \\ 0/26 \ (0.0\%) \\ 0 \ (0.0\%) \end{array}$	$32 (45.7\%)  61 (87.1\%)  62 (88.6\%)  18.54 \pm 4.53  11.19 \pm 2.38  72.95 \pm 47.34  42 (60.0\%)  0.75 \pm 0.70  37 (53.6\%)  1.78 \pm 1.72  10 (14.5\%)  4/51 (7.8\%)  5/30 (16.7\%)  0/51 (0.0\%)  0 (0.0\%)$	$84 (68.9\%) 106 (86.9\%) 107 (87.7\%) 22.78 \pm 5.59 11.61 \pm 2.39 91.56 \pm 63.07 45 (36.9\%) 0.48 \pm 0.63 55 (45.1\%) 1.60 \pm 1.79 7 (5.7\%) 5/96 (5.2\%) 2/55 (3.6\%) 3/96 (3.1\%) 4 (3.3\%)$	12.56 <sup>b</sup> 0.16 2.12 26.45 <sup>a</sup> 1.24 3.91 12.42 <sup>b</sup> 11.57 <sup>b</sup> 9.31 <sup>b</sup> 12.66 <sup>b</sup> 4.20 <sup>c</sup> 2.90 7.86 <sup>c</sup> 3.83 3.98	FEP>UHR[+]=UHR[-] 	CAARMS Positive Symptoms Cognitive change Emotional disturbance Negative Symptoms Anhedonia Behavioral change Motor/physical change General psychopathology Suicidality/self-harm Subjective impaired tolerance to normal stress* <b>DD-II</b> BDI-II total score BDI-II total score BDI-II "Cognitive" subscale BDI-II "Somatic-affective" subscale BDI-II "Somatic-affective" subscale	0.099 0.060 0.194 0.199 0.240c 0.067 0.070 0.279c 0.407b 0.257c 0.507b 0.581a 0.444a -0.269c -0.359a -0.265b -0.298b

**Conclusion** – Suicidal ideation is frequent in UHR subjects, supporting the routine monitoring of suicide risk in people at risk of psychosis. Suicide risk is correlated with severity of depression and anhedonia, and with a poorer quality of life.

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