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TITLE: The relationship of post-traumatic stress disorder with major depressive disorder in the context of reported psychological trauma

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ABSTRACT: Symptoms of post-traumatic stress disorder (PTSD) and major depressive disorder (MDD) are commonly reported after exposure to psychological trauma. Both disorders are heritable and share genetic associations. We explore the genetic overlap between PTSD and four depression-related phenotypes in the UK Biobank: MDD with and without reported trauma; recurrent MDD; and single-episode MDD. We replicate our analysis using summary statistics for PTSD from the Psychiatric Genomics Consortium. We hypothesise that the genetic correlation between PTSD and MDD is greater in trauma-exposed individuals compared to those unexposed. Since trauma exposure is associated with the chronicity of MDD, we also hypothesise that the genetic correlation between PTSD and recurrent MDD is larger than that of PTSD and single-

episode MDD. We do not find evidence that PTSD is more genetically associated with trauma-exposed MDD ( $r_g = 0.64$ ) compared to trauma-unexposed MDD ( $r_g = 0.64$ ). PTSD consistently shows a high genetic correlation with recurrent MDD ( $r_g = 0.74 - 0.78$ ), although this is not significantly higher than the other genetic correlations with PTSD measured in our analysis. Overall, we report medium to high genetic correlations between PTSD and the depression-related phenotypes regardless of trauma exposure.

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