Title

Polygenic, sociodemographic, and clinical associations with five-year prognostic outcomes in patients with major depressive disorder in a hospital setting: a Danish nationwide study

Authors

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Abstract

Background. Major depressive disorder (MDD) has a highly heterogeneous clinical course. The disorder is heritable, and research shows that treatment response and likelihood of recurrence also have a genetic basis. There is growing interest whether prognosis can be predicted from baseline characteristics.

Methods. Using nationally representative data from iPSYCH, 13,244 patients (71% female, mean age at first hospital contact of 19 years) admitted to a Danish psychiatric hospital for MDD (ICD-10 codes F32–F33) were followed up for five years. Follow-up began six months after discharge from their first episode of MDD in a hospital. We categorized patients based on prognostic outcomes during this period: readmission for another MDD episode, readmission for another psychiatric disorder, use of antidepressants, or no further medical treatment for MDD. Risk factors were tested for associations with five-year outcomes, with "no further medical treatment" as the reference. Multinomial logistic regression models incorporated all risk factors. Covariates included genetic principal components, genotyping batch, and calendar year of diagnosis. We used a Bonferroni-adjusted alpha to account for multiple testing (0.05/16=0.003).

Results. The strongest predictor was prior antidepressant use: receiving antidepressants afterwards (odds ratio [OR]=2.39, 95% confidence intervals [CIs]=2.38-2.49), readmission for another disorder (OR=2.05, CIs=2.04-2.07), readmission for MDD (OR=2.34, CIs=2.33-2.35). Compared to those with mild MDD at their first hospital episode, those with moderate MDD had an increased risk of receiving antidepressants (OR=1.44, CIs=1.43-1.45) and of readmission for MDD (OR=1.47, CIs=1.45-1.48). Similarly, those with severe MDD at their first contact had an increased risk of receiving antidepressants (OR=1.48, CIs=1.46-1.50) and of readmission for MDD (OR = 1.84, CIs = 1.82-1.86). In terms of genetic risk factors, having a higher polygenic score for MDD was associated with readmission for MDD (OR=1.12 per unit increase, CIs=1.11-1.3) and readmission for another psychiatric disorder (OR=1.11, CIs=1.10-1.12), while having a parental history of MDD was associated only with readmission for MDD (OR=1.29, CIs=1.28-1.31).

Conclusion. Currently, sociodemographic and clinical risk factors are more robust predictors of clinical outcomes in hospital-treated MDD patients. Nonetheless, having a higher MDD polygenic score was associated with being readmitted to hospital. This supports research showing that inherited genetic risk influences MDD's clinical course.