Changing polygenic penetrance on depression among adults in the United Kingdom

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Abstract

Depression is one of the most common mental health disorders. The frequency of depression occurrence ranges from 8% to 12% in different countries (Flint and Kendler, 2014). The severity of depression varies from mild symptoms to major depression. All of these factors contribute to growing research covering different aspects of depression. There are various causes of depression and social scientists refer to many different factors, including historical exposures. Depression is also heritable and there is an interdisciplinary field investigating how various environmental aspects interplay with genes.

Depression can be triggered by socio-economic factors, such as educational attainment (Lee, 2011), job loss (Drydakis, 2015; Paul and Moser, 2009), and recessions (Frasquilho et al., 2015; Jahoda, 1988). More broadly, the prevalence of depression is believed to have a historical trend and to occur more frequently among recent birth cohorts (Marcus and Olfson, 2010; Bell, 2014). Observed increases in depression occurrence could be due to various factors, including environmental and lifestyle changes, policy contexts, and economic downturns. Genetic influences on depression may also affect individual responses to contextual components (for example, by shaping stress-internalisation processes). The latter would lead to variation in the genetic penetrance on depression across birth cohorts. As previously suggested, estimates of the percentage of variation in social outcomes explained by genetic and environmental differences are likely to be context specific, varying systematically across different social conditions, policy environments, or subgroups of the population (Boardman et al., 2011). These notions have yielded a growing field of research wherein birth cohorts are potential modifiers of genetic influences.

This paper identifies changes in the polygenic penetrance on depression within the UK during the 20th century. The research investigates whether the polygenic prediction of depression varies by birth cohorts in the UK or, in other words, whether we observe gene-by-cohort interactions for this mental health trait. I

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also aim to answer the question of whether historical contexts (such as economic recessions) contribute to gene-by-cohort variations.

In a conventional demographic classification for the UK, there are six birth cohorts. Two cohorts are devoted to people exposed to the two World Wars: a WWI cohort born between 1916 and 1930; and a WWII cohort with birth years in 1931–1945. A demographic cohort of those born in 1946–1964 is distinguished as Boomers to reflect the period of the Baby Boom. After that, there is a Generation X cohort (people born in 1965–1980) followed by Millennials or Generation Y (those born between 1981 and 1995). People born at the very end of the century are referred to as Generation Z.

The focus on gene-by-cohort interactions has the potential to shed a light on how historical contexts shape polygenic prediction across different generations. The insight for social science, in particular, is whether the rise in the prevalence of depression at certain historical points in the 20th century is driven by those with a higher polygenic risk of depression; alternatively, prevalence could be independent of genetic risks. Within the literature, there is a notable gap in studies covering the UK context. Consequently, this paper contributes to existing knowledge by providing a gene-cohort interaction analysis of depression in the UK.

I use data from the Understanding Society genetic sample which is a national sample of UK adults. Gene-by-birth-cohort interactions are examined using multilevel Poisson models. The choice of model is initially determined by the nature of UKHLS data, which contains multiple observations over time. The strategy permits consideration for the correlation of repeated measurements (Hox et al., 2017; Raudenbush and Bryk, 2002). This correlation is particularly important for the depressive symptoms data. Due to the count-based and skewed nature of the depressive symptoms scores, I employ a Poisson family of regression models. This type of model is an appropriate tool for taking the complexity of skewed data into account (Wooldridge, 2010).

I find evidence that an increase in depressive symptoms occurred among people born in the second half of 20th century. Age-comparable analysis indicates that the increase is especially profound for Baby Boomers. However, I do not find support for the proposition of increased genetic penetrance on depressive symptoms across all cohorts. I find evidence of increased depression prevalence in two birth cohorts, as well as significant gene-cohort moderation patterns for one of the cohorts (Baby Boomers) and suggestive moderation for the Generation X cohort. These findings are robust towards mortality selection, and marginal in the range of age-comparable robustness checks. These findings further contribute to the notion that the cohort of Baby Boomers is different from others: they achieved higher educational attainments, experienced more marital disruptions and changes in

family structures that constitute their distinctive life histories (Dennis and Migliaccio, 1997) and results in greater polygenic penetrance of depression. I also find that the polygenic prediction of depressive symptoms weakens across all birth cohorts during periods of recession – except for Baby Boomers. Thus, historical times have the potential to shape polygenic predictions within populations and across generations differently. Moreover, my findings on recessions also indicate that not only cohort-specific historical exposures can potentially shape genetic penetrance, but also historical exposures experienced by everyone have differentiating trends.

References

Bell, A. (2014). Life-course and cohort trajectories of mental health in the uk, 1991–2008 – a multilevel age–period–cohort analysis. *Social Science and Medicine*, 120:21 – 30. doi: `https://doi.org/10.1001/archgenpsychiatry.2010.151`.

Boardman, J. D., Blalock, C. L., Pampel, F. C., Hatemi, P. K., Heath, A. C., and Eaves, L. J. (2011). Population composition, public policy, and the genetics of smoking. *Demography*, 48(4):1517–1533.

Dennis, H. and Migliaccio, J. (1997). Redefining retirement: The baby boomer challenge. *Generations: Journal of the American Society on Aging*, 21(2):45–50.

Drydakis, N. (2015). The effect of unemployment on self-reported health and mental health in greece from 2008 to 2013: A longitudinal study before and during the financial crisis. *Social Science and Medicine*, 128:43 – 51. doi: `https://doi.org/10.1016/j.socscimed.2014.12.025`.

Flint, J. and Kendler, K. S. (2014). The genetics of major depression. *Neuron*, 81(3):484–503. doi: `https://doi.org/10.1016/j.neuron.2014.01.027`.

Frasquilho, D., Matos, M. G., Salonna, F., Guerreiro, D., Storti, C. C., Gaspar, T., and Caldas-de Almeida, J. M. (2015). Mental health outcomes in times of economic recession: a systematic literature review. *BMC public health*, 16(1):115.

Hox, J. J., Moerbeek, M., and Van de Schoot, R. (2017). *Multilevel analysis: Techniques and applications*. Routledge.

Jahoda, M. (1988). Economic recession and mental health: Some conceptual issues. *Journal of social Issues*, 44(4):13–23.

Lee, J. (2011). Pathways from education to depression. *Journal of cross-cultural gerontology*, 26(2):121–135.

Marcus, S. C. and Olfson, M. (2010). National Trends in the Treatment for Depression From 1998 to 2007. *JAMA Psychiatry*, 67(12):1265–1273. doi: `https://doi.org/10.1001/archgenpsychiatry.2010.151`.

Paul, K. I. and Moser, K. (2009). Unemployment impairs mental health: Meta-analyses. *Journal of Vocational Behavior*, 74(3):264 – 282. doi: `https://doi.org/10.1016/j.jvb.2009.01.001`.

Raudenbush, S. W. and Bryk, A. S. (2002). *Hierarchical linear models: Applications and data analysis methods*, volume 1. Sage.

Wooldridge, J. M. (2010). *Econometric analysis of cross section and panel data*. MIT press.