**Supplementary Materials**

**S1. Protective Factors Scale Items**

**S2. Combat Stress Scale Items**

**S3. Supplementary Figures and Tables for Main Analyses**

**S4. Supplementary Figures for Additional Analyses**

**S5. Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium**

**S1. Protective Factors Scale Items**

**S1A. Trait resilience**

*People differ a lot in how well they handle stress. How would you rate your ability to handle stress in each of the following ways? (Poor; Fair; Good; Very good; Excellent)*

1. Keep calm and think of the right thing to do in a crisis
2. Manage stress.
3. Try new approaches if old ones don’t work
4. Get along with people when you have to
5. Keep your sense of humor in tense situations

Reference: Campbell-Sills L, Kessler RC, Ursano RJ, Sun X, Taylor CT, Heeringa SG, Nock MK, Sampson NA, Jain S, Stein MB (2018). Predictive validity and correlates of self-assessed resilience among U.S. Army soldiers. *Depression and Anxiety* 35, 122–131.

**S1B. Unit cohesion**

*How much do you agree or disagree with each of these statements? (Strongly disagree; Disagree; Neither agree nor disagree; Agree; Strongly agree)*

1. I can rely on members of my unit for help if I need it
2. I can open up and talk to my first line leaders if I need help
3. I respect the Non-Commissioned Officers in my unit
4. I respect the Officers in my unit
5. My leaders take a personal interest in the well-being of all the soldiers in my unit
6. Others in my unit respect the work that I do on my job
7. My morale is high.

Reference: N/A (unpublished)

**S2. Combat Stress Scale Items**

*How many times did you have each of the following experiences during your deployment?*

(Original response categories: Never; 1 time; 2-4 times; 5-9 times; 10+ times)

1. Go on combat patrols or have other dangerous duty (e.g., route clearance, clearing buildings, disarming civilians, working in areas that had IEDs) *(Coded yes if: 10+)*
2. Fire rounds at the enemy or take enemy fire (either direct or indirect fire) *(Coded yes if: 10+)*
3. Get wounded *(Coded yes if: 1+)*
4. Have a close call (that is, equipment shot off body, IED exploded near you) *(Coded yes if: 2+)*
5. Have member(s) of your unit who were seriously wounded or killed? *(Coded yes if: 5+)*
6. Have responsibility for the death of an enemy combatant? *(Coded yes if: 1+)*
7. Have responsibility for the death of a non-combatant? *(Coded yes if: 1+)*
8. Have responsibility for the death of U.S. or ally personnel? *(Coded yes if: 1+)*
9. Save the life of a soldier or civilian? *(Coded yes if: 1+)*
10. See homes or villages that had been destroyed or people begging for food? *(Coded yes if: 1+)*
11. Get exposed to the sights, sounds, or smells of severely wounded or dying people, see dead bodies, or witness violence in the local population? *(Coded yes if: 5+)*
12. You were seriously physically assaulted (e.g., in combat, mugged)? *(Coded yes if: 1+)*
13. You were sexually assaulted or raped? *(Coded yes if: 1+)*
14. You were bullied or hazed by one or more members of your unit? *(Coded yes if: 1+)*
15. You got into a fight either with someone in the military or with a civilian? *(Coded yes if: 1+)*

Reference: Stein MB, Kessler RC, Heeringa SG, Jain S, Campbell-Sills L, Colpe LJ, Fullerton CS, Nock MK, Sampson NA, Schoenbaum M, Sun X, Thomas ML, Ursano RJ, On behalf of the Army STARRS collaborators (2015). Prospective Longitudinal Evaluation of the Effect of Deployment-Acquired Traumatic Brain Injury on Posttraumatic Stress and Related Disorders: Results From the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). *American Journal of Psychiatry* 172, 1101–1111.

**S3. Supplementary Figures for Main Analyses**

**Table S3A. Number of SNPs included in polygenic risk scoring**

|  |  |
| --- | --- |
| **pT** | **Number† of SNPs**  |
| 0.00000005 | 13 |
| 0.00001 | 110 |
| 0.001 | 2,640 |
| 0.01 | 18,450 |
| 0.05 | 76,550 |
| 0.10 | 140,700 |
| 0.50 | 548,000 |
| 1.0 | 859,500 |
| **†**Approximate; each individual’s score was weighted by number of SNPs included |

**Table S3B. Adjusted logistic model of polygenic risk and incident MDD**

|  |  |  |
| --- | --- | --- |
| **Variable** | **aOR (95%CI)** | **p-value** |
| Polygenic risk: low (reference) | - | - |
| Polygenic risk: intermediate | 1.38 (1.03-1.88) | .04 |
| Polygenic risk: high | 1.58 (1.12-2.25) | .01 |
| Age | 1.00 (0.98-1.02) | .71 |
| Sex (male) | .57 (0.37-0.92) | .02 |
| aOR=adjusted odds ratio. 95% CI=95% confidence interval. Top three principal components were included to adjust for population stratification, all with non-significant effects (not shown). Nagelkerke’s pseudo-R2 above and beyond covariates-only model = *0.4%* |

**Table S3C. Adjusted logistic models of unit cohesion, polygenic risk, and incident MDD**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Model 1** |  | **Model 2 (interaction)** |
| **Variable** | **aOR (95%CI)** | **p-value** | **aOR (95%CI)** | **p-value** |
| Unit cohesion | 0.67 (0.60-0.74) | 5.8x10-15 | 0.63 (0.49-0.81) | .0003 |
| Polygenic risk: low (reference) | - | - | - | - |
| Polygenic risk: intermediate | 1.36 (1.01-1.86) | .05 | 1.36 (1.0-1.89) | .06 |
| Polygenic risk: high | 1.55 (1.09-2.21) | .02 | 1.63 (1.13-2.36) | .009 |
| Age | 1.00 (0.98-1.02) | .71 | 1.00 (0.98-1.02) | .72 |
| Sex (male) | 0.62 (0.40-1.02) | .05 | 0.62 (0.39-1.01) | .05 |
| Unit cohesion\*polygenic risk (int) | - | - | 1.02 (0.77-1.35) | .88 |
| Unit cohesion\*polygenic risk (high) | - | - | 1.19 (0.86-1.66) | .29 |

aOR=adjusted odds ratio. 95% CI=95% confidence interval. Top three principal components were included to adjust for population stratification, all with non-significant effects (not shown). Statistics for the effects of unit cohesion on incident MDD within each polygenic risk group are reported in the main text. Nagelkerke’s pseudo-R2 for Model 1 and Model 2 above and beyond covariates-only model = *5.7%* and *5.8%*, respectively.

**Table S3D. Adjusted logistic models of unit cohesion, (continuous) polygenic risk, and incident MDD**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Model 1** |  | **Model 2 (interaction)** |
| **Variable** | **aOR (95%CI)** | **p-value** | **aOR (95%CI)** | **p-value** |
| Unit cohesion | 0.67 (0.60-0.74) | 3.5x10-15 | 0.66 (0.60-0.74) | 2.6x10-15 |
| Polygenic risk score | 1.13 (1.02-1.27) | 0.02 | 1.15 (1.03-1.29) | 0.01 |
| Age | 1.00 (0.98-1.02) | .72 | 1.00 (0.98-1.02) | .73 |
| Sex (male) | 0.63 (0.40-1.02) | .05 | 0.63 (0.40-1.02) | .05 |
| Unit cohesion\*polygenic risk score | - | - | 1.05 (0.95-1.16) | .36 |

aOR=adjusted odds ratio. 95% CI=95% confidence interval. Top three principal components were included to adjust for population stratification, all with non-significant effects. Examining polygenic risk as a continuous variable did not change the pattern of substantive findings, i.e., main effects of unit cohesion and polygenic risk, with no interaction effect.

**Table S3E. Adjusted logistic models of trait resilience, polygenic risk, and incident MDD**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Model 1** |  | **Model 2 (interaction)** |
| **Variable** | **aOR (95%CI)** | **p-value** | **aOR (95%CI)** | **p-value** |
| Trait resilience | 0.86 (0.78-0.96) | .005 | 0.80 (0.62-1.04) | .09 |
| Polygenic risk: low (reference) | - | - | - | - |
| Polygenic risk: intermediate | 1.34 (1.02-1.86) | .04 | 1.39 (1.03-1.89) | .04 |
| Polygenic risk: high | 1.57 (1.11-2.23) | .01 | 1.57 (1.10-2.24) | .01 |
| Age | 1.00 (0.98-1.02) | .72 | 1.00 (0.98-1.02) | .73 |
| Sex (male) | 0.61 (0.39-1.02) | .04 | 0.61 (0.39-0.99) | .04 |
| Trait resilience\*polygenic risk (int) | - | - | 1.13 (0.84-1.50) | .37 |
| Trait resilience\*polygenic risk (high) | - | - | 1.00 (0.72-1.40) | .74 |

aOR=adjusted odds ratio. 95% CI=95% confidence interval. Top three principal components were included to adjust for population stratification, all with non-significant effects. Statistics for the effects of trait resilience on incident MDD within each polygenic risk group are reported in the main text. Nagelkerke’s pseudo-R2 for Model 1 and Model 2 above and beyond covariates-only model = *0.9%* and *1.0%*, respectively.

**Table S3F. Adjusted logistic models of trait resilience, (continuous) polygenic risk, and incident MDD**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Model 1** |  | **Model 2 (interaction)** |
| **Variable** | **aOR (95%CI)** | **p-value** | **aOR (95%CI)** | **p-value** |
| Trait resilience | 0.86 (0.77-0.95) | .004 | 0.86 (0.77-0.95) | .004 |
| Polygenic risk score | 1.14 (1.03-1.27) | .02 | 1.14 (1.03-1.27) | 0.01 |
| Age | 1.00 (0.98-1.02) | .73 | 1.00 (0.98-1.02) | .73 |
| Sex (male) | 0.61 (0.39-0.99) | .04 | 0.61 (0.39-0.99) | .04 |
| Trait resilience\*polygenic risk score | - | - | 1.02 (0.92-1.12) | .74 |

aOR=adjusted odds ratio. 95% CI=95% confidence interval. Top three principal components were included to adjust for population stratification, all with non-significant effects. Examining polygenic risk as a continuous variable did not change the pattern of substantive findings, i.e., main effects of trait resilience and polygenic risk, with no interaction effect.

**Table S3G. Adjusted logistic models of unit cohesion, polygenic risk, combat stress exposure, and incident MDD**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Model 1** |  | **Model 2 (interactions)** |
| **Variable** | **aOR (95%CI)** | **p-value** | **aOR (95%CI)** | **p-value** |
| Unit cohesion | 0.67 (0.60-0.74) | 9.0x10-15 | 0.63 (0.49-8.00) | .0003 |
| Polygenic risk: low (reference) | - | - | - | - |
| Polygenic risk: intermediate | 1.36 (1.01-1.86) | .05 | 1.31 (0.90-1.70) | .10 |
| Polygenic risk: high | 1.54 (1.08-2.20) | .02 | 1.61 (1.08-2.25) | .01 |
| Age | 1.00 (0.98-1.02) | 0.75 | 1.00 (0.99-1.02) | .68 |
| Sex (male) | 0.54 (0.34-0.88) | 0.01 | 0.54 (0.34-0.86) | .01 |
| Combat stress exposure | 1.34 (1.21-1.50) | 9.0x10-8 | 1.12 (0.93-1.60) | .42 |
| Cohesion\*combat stress | - | - | 1.00 (0.78-1.22) | .98 |
| Polygenic (int)\*cohesion | - | - | 1.04 (0.81-1.42) | .81 |
| Polygenic (high)\*cohesion  | - | - | 1.20 (0.89-1.69) | .28 |
| Polygenic (int)\*combat stress | - | - | 1.32 (0.96-1.76) | .08 |
| Polygenic (high)\* combat stress  | - | - | 1.10 (0.76-1.52) | .98 |
| Polygenic (int)\*cohesion\*combat | - | - | 1.01 (0.76-1.27) | .96 |
| Polygenic (high)\*cohesion\*combat | - | - | 1.06 (0.77-1.37) | .71 |

aOR=adjusted odds ratio. 95% CI=95% confidence interval. Top three principal components were included to adjust for population stratification, all with non-significant effects. Statistics for the effects of unit cohesion on incident MDD within each level of combat stress exposure are reported in the main text. Nagelkerke’s pseudo-R2 for Model 1 and Model 2 above and beyond covariates-only model = *7.4%* and *7.8%,* respectively.

**Figure S3A. PRS effects on incident MDD across p-value thresholds. \*** refers to p <.05, GWS refers to p-value threshold < 5x10e-8. The most predictive p-value threshold (pT) was 0.01, with remaining thresholds suggesting that relevant SNPs for incident MDD in this sample were largely in the upper range of GWAS results.



**Figure S3B. Distribution of MDD PRS.** This PRS was divided into low (quintile 1), intermediate (quintiles 2-4), and high (quintile 5) polygenic risk groups.



**S4. Supplementary Figure for Additional Analyses**

**Figure S4A. Predicted probabilities of incident MDD, plotted against unit cohesion scores and grouped by polygenic risk.** This plot further visualizes reported results from the manuscript. As unit cohesion scores increase in the sample, the model-predicted probability of incident MDD—based on a logistic model with unit cohesion, polygenic risk, and covariates**—**appears to decrease. Grouping these data points according to polygenic risk also suggests that individuals with higher polygenic risk generally have higher predicted probabilities of incident MDD. Given the original model results, no statistical interaction should be interpreted from this plot—only main effects of unit cohesion and polygenic risk.

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**S5. Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium**

Naomi R Wray 1, 2

Stephan Ripke 3, 4, 5

Manuel Mattheisen 6, 7, 8, 9

Maciej Trzaskowski 1

Enda M Byrne 1

Abdel Abdellaoui 10

Mark J Adams 11

Esben Agerbo 9, 12, 13

Tracy M Air 14

Till F M Andlauer 15, 16

Silviu-Alin Bacanu 17

Marie Bækvad-Hansen 9, 18

Aartjan T F Beekman 19

Tim B Bigdeli 17, 20

Elisabeth B Binder 15, 21

Douglas H R Blackwood 11

Julien Bryois 22

Henriette N Buttenschøn 8, 9, 23

Jonas Bybjerg-Grauholm 9, 18

Na Cai 24, 25

Enrique Castelao 26

Jane Hvarregaard Christensen 7, 8, 9

Toni-Kim Clarke 11

Jonathan R I Coleman 27

Lucía Colodro-Conde 28

Baptiste Couvy-Duchesne 2, 29

Nick Craddock 30

Gregory E Crawford 31, 32

Gail Davies 33

Ian J Deary 33

Franziska Degenhardt 34, 35

Eske M Derks 28

Nese Direk 36, 37

Conor V Dolan 10

Erin C Dunn 38, 39, 40

Thalia C Eley 27

Valentina Escott-Price 41

Farnush Farhadi Hassan Kiadeh 42

Hilary K Finucane 43, 44

Jerome C Foo 45

Andreas J Forstner 34, 35, 46, 47

Josef Frank 45

Héléna A Gaspar 27

Michael Gill 48

Fernando S Goes 49

Scott D Gordon 28

Jakob Grove 7, 8, 9, 50

Lynsey S Hall 11, 51

Christine Søholm Hansen 9, 18

Thomas F Hansen 52, 53, 54

Stefan Herms 34, 35, 47

Ian B Hickie 55

Per Hoffmann 34, 35, 47

Georg Homuth 56

Carsten Horn 57

Jouke-Jan Hottenga 10

David M Hougaard 9, 18

Marcus Ising 58

Rick Jansen 19

Ian Jones 59

Lisa A Jones 60

Eric Jorgenson 61

James A Knowles 62

Isaac S Kohane 63, 64, 65

Julia Kraft 4

Warren W. Kretzschmar 66

Jesper Krogh 67

Zoltán Kutalik 68, 69

Yihan Li 66

Penelope A Lind 28

Donald J MacIntyre 70, 71

Dean F MacKinnon 49

Robert M Maier 2

Wolfgang Maier 72

Jonathan Marchini 73

Hamdi Mbarek 10

Patrick McGrath 74

Peter McGuffin 27

Sarah E Medland 28

Divya Mehta 2, 75

Christel M Middeldorp 10, 76, 77

Evelin Mihailov 78

Yuri Milaneschi 19

Lili Milani 78

Francis M Mondimore 49

Grant W Montgomery 1

Sara Mostafavi 79, 80

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Michel G Nivard 10

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Paul F O'Reilly 27

Hogni Oskarsson 84

Michael J Owen 59

Jodie N Painter 28

Carsten Bøcker Pedersen 9, 12, 13

Marianne Giørtz Pedersen 9, 12, 13

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Erik Pettersson 22

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Giorgio Pistis 26

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Jianxin Shi 94

Stanley I Shyn 95

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Grant C B Sinnamon 97

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Hreinn Stefansson 99

Stacy Steinberg 99

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Jana Strohmaier 45

Katherine E Tansey 100

Henning Teismann 101

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Wesley Thompson 9, 53, 103, 104

Pippa A Thomson 105

Thorgeir E Thorgeirsson 99

Matthew Traylor 106

Jens Treutlein 45

Vassily Trubetskoy 4

André G Uitterlinden 107

Daniel Umbricht 108

Sandra Van der Auwera 109

Albert M van Hemert 110

Alexander Viktorin 22

Peter M Visscher 1, 2

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Shantel Marie Weinsheimer 9, 53

Jürgen Wellmann 101

Gonneke Willemsen 10

Stephanie H Witt 45

Yang Wu 1

Hualin S Xi 112

Jian Yang 2, 113

Futao Zhang 1

Volker Arolt 114

Bernhard T Baune 115

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Preben Bo Mortensen 8, 9, 12, 13

Bertram Müller-Myhsok 15, 16, 129

Merete Nordentoft 9, 130

Markus M Nöthen 34, 35

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Sara A Paciga 131

Nancy L Pedersen 22

Brenda WJH Penninx 19

Roy H Perlis 38, 132

David J Porteous 105

James B Potash 133

Martin Preisig 26

Marcella Rietschel 45

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Jordan W Smoller 38, 39, 40

Kari Stefansson 99, 137

Henning Tiemeier 36, 138, 139

Rudolf Uher 140

Henry Völzke 102

Myrna M Weissman 74, 141

Thomas Werge 9, 53, 142

Cathryn M Lewis 27, 143

Douglas F Levinson 144

Gerome Breen 27, 145

Anders D Børglum 7, 8, 9

Patrick F Sullivan 22, 146, 147,

1, Institute for Molecular Bioscience, The University of Queensland, Brisbane, QLD, AU

2, Queensland Brain Institute, The University of Queensland, Brisbane, QLD, AU

3, Analytic and Translational Genetics Unit, Massachusetts General Hospital, Boston, MA, US

4, Department of Psychiatry and Psychotherapy, Universitätsmedizin Berlin Campus Charité Mitte, Berlin, DE

5, Medical and Population Genetics, Broad Institute, Cambridge, MA, US

6, Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, SE

7, Department of Biomedicine, Aarhus University, Aarhus, DK

8, iSEQ, Centre for Integrative Sequencing, Aarhus University, Aarhus, DK

9, iPSYCH, The Lundbeck Foundation Initiative for Integrative Psychiatric Research,, DK

10, Dept of Biological Psychology & EMGO+ Institute for Health and Care Research, Vrije Universiteit Amsterdam, Amsterdam, NL

11, Division of Psychiatry, University of Edinburgh, Edinburgh, GB

12, Centre for Integrated Register-based Research, Aarhus University, Aarhus, DK

13, National Centre for Register-Based Research, Aarhus University, Aarhus, DK

14, Discipline of Psychiatry, University of Adelaide, Adelaide, SA, AU

15, Department of Translational Research in Psychiatry, Max Planck Institute of Psychiatry, Munich, DE

16, Munich Cluster for Systems Neurology (SyNergy), Munich, DE

17, Department of Psychiatry, Virginia Commonwealth University, Richmond, VA, US

18, Center for Neonatal Screening, Department for Congenital Disorders, Statens Serum Institut, Copenhagen, DK

19, Department of Psychiatry, Vrije Universiteit Medical Center and GGZ inGeest, Amsterdam, NL

20, Virginia Institute for Psychiatric and Behavior Genetics, Richmond, VA, US

21, Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, US

22, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, SE

23, Department of Clinical Medicine, Translational Neuropsychiatry Unit, Aarhus University, Aarhus, DK

24, Human Genetics, Wellcome Trust Sanger Institute, Cambridge, GB

25, Statistical genomics and systems genetics, European Bioinformatics Institute (EMBL-EBI), Cambridge, GB

26, Department of Psychiatry, University Hospital of Lausanne, Prilly, Vaud, CH

27, Social Genetic and Developmental Psychiatry Centre, King's College London, London, GB

28, Genetics and Computational Biology, QIMR Berghofer Medical Research Institute, Brisbane, QLD, AU

29, Centre for Advanced Imaging, The University of Queensland, Brisbane, QLD, AU

30, Psychological Medicine, Cardiff University, Cardiff, GB

31, Center for Genomic and Computational Biology, Duke University, Durham, NC, US

32, Department of Pediatrics, Division of Medical Genetics, Duke University, Durham, NC, US

33, Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, GB

34, Institute of Human Genetics, University of Bonn, Bonn, DE

35, Life&Brain Center, Department of Genomics, University of Bonn, Bonn, DE

36, Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NL

37, Psychiatry, Dokuz Eylul University School Of Medicine, Izmir, TR

38, Department of Psychiatry, Massachusetts General Hospital, Boston, MA, US

39, Psychiatric and Neurodevelopmental Genetics Unit (PNGU), Massachusetts General Hospital, Boston, MA, US

40, Stanley Center for Psychiatric Research, Broad Institute, Cambridge, MA, US

41, Neuroscience and Mental Health, Cardiff University, Cardiff, GB

42, Bioinformatics, University of British Columbia, Vancouver, BC, CA

43, Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, US

44, Department of Mathematics, Massachusetts Institute of Technology, Cambridge, MA, US

45, Department of Genetic Epidemiology in Psychiatry, Central Institute of Mental Health,  Medical Faculty Mannheim, Heidelberg University, Mannheim, Baden-Württemberg, DE

46, Department of Psychiatry (UPK), University of Basel, Basel, CH

47, Human Genomics Research Group, Department of Biomedicine, University of Basel, Basel, CH

48, Department of Psychiatry, Trinity College Dublin, Dublin, IE

49, Psychiatry & Behavioral Sciences, Johns Hopkins University, Baltimore, MD, US

50, Bioinformatics Research Centre, Aarhus University, Aarhus, DK

51, Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, GB

52, Danish Headache Centre, Department of Neurology, Rigshospitalet, Glostrup, DK

53, Institute of Biological Psychiatry, Mental Health Center Sct. Hans, Mental Health Services Capital Region of Denmark, Copenhagen, DK

54, iPSYCH, The Lundbeck Foundation Initiative for Psychiatric Research, Copenhagen, DK

55, Brain and Mind Centre, University of Sydney, Sydney, NSW, AU

56, Interfaculty Institute for Genetics and Functional Genomics, Department of Functional Genomics, University Medicine and Ernst Moritz Arndt University Greifswald, Greifswald, Mecklenburg-Vorpommern, DE

57, Roche Pharmaceutical Research and Early Development, Pharmaceutical Sciences, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd, Basel, CH

58, Max Planck Institute of Psychiatry, Munich, DE

59, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, GB

60, Department of Psychological Medicine, University of Worcester, Worcester, GB

61, Division of Research, Kaiser Permanente Northern California, Oakland, CA, US

62, Psychiatry & The Behavioral Sciences, University of Southern California, Los Angeles, CA, US

63, Department of Biomedical Informatics, Harvard Medical School, Boston, MA, US

64, Department of Medicine, Brigham and Women's Hospital, Boston, MA, US

65, Informatics Program, Boston Children's Hospital, Boston, MA, US

66, Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, GB

67, Department of Endocrinology at Herlev University Hospital, University of Copenhagen, Copenhagen, DK

68, Institute of Social and Preventive Medicine (IUMSP), University Hospital of Lausanne, Lausanne, VD, CH

69, Swiss Institute of Bioinformatics, Lausanne, VD, CH

70, Division of Psychiatry, Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, GB

71, Mental Health, NHS 24, Glasgow, GB

72, Department of Psychiatry and Psychotherapy, University of Bonn, Bonn, DE

73, Statistics, University of Oxford, Oxford, GB

74, Psychiatry, Columbia University College of Physicians and Surgeons, New York, NY, US

75, School of Psychology and Counseling, Queensland University of Technology, Brisbane, QLD, AU

76, Child and Youth Mental Health Service, Children's Health Queensland Hospital and Health Service, South Brisbane, QLD, AU

77, Child Health Research Centre, University of Queensland, Brisbane, QLD, AU

78, Estonian Genome Center, University of Tartu, Tartu, EE

79, Medical Genetics, University of British Columbia, Vancouver, BC, CA

80, Statistics, University of British Columbia, Vancouver, BC, CA

81, DZHK (German Centre for Cardiovascular Research), Partner Site Greifswald, University Medicine, University Medicine Greifswald, Greifswald, Mecklenburg-Vorpommern, DE

82, Institute of Clinical Chemistry and Laboratory Medicine, University Medicine Greifswald, Greifswald, Mecklenburg-Vorpommern, DE

83, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, QLD, AU

84, Humus, Reykjavik, IS

85, Virginia Institute for Psychiatric & Behavioral Genetics, Virginia Commonwealth University, Richmond, VA, US

86, Clinical Genetics, Vrije Universiteit Medical Center, Amsterdam, NL

87, Complex Trait Genetics, Vrije Universiteit Amsterdam, Amsterdam, NL

88, Solid Biosciences, Boston, MA, US

89, Department of Psychiatry, Washington University in Saint Louis School of Medicine, Saint Louis, MO, US

90, Department of Biochemistry and Molecular Biology II, Institute of Neurosciences, Center for Biomedical Research, University of Granada, Granada, ES

91, Department of Psychiatry, University of Groningen, University Medical Center Groningen, Groningen, NL

92, Department of Psychiatry and Psychotherapy, Medical Center of the University of Munich, Campus Innenstadt, Munich, DE

93, Institute of Psychiatric Phenomics and Genomics (IPPG), Medical Center of the University of Munich, Campus Innenstadt, Munich, DE

94, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, US

95, Behavioral Health Services, Kaiser Permanente Washington, Seattle, WA, US

96, Faculty of Medicine, Department of Psychiatry, University of Iceland, Reykjavik, IS

97, School of Medicine and Dentistry, James Cook University, Townsville, QLD, AU

98, Institute of Health and Wellbeing, University of Glasgow, Glasgow, GB

99, deCODE Genetics / Amgen, Reykjavik, IS

100, College of Biomedical and Life Sciences, Cardiff University, Cardiff, GB

101, Institute of Epidemiology and Social Medicine, University of Münster, Münster, Nordrhein-Westfalen, DE

102, Institute for Community Medicine, University Medicine Greifswald, Greifswald, Mecklenburg-Vorpommern, DE

103, Department of Psychiatry, University of California, San Diego, San Diego, CA, US

104, KG Jebsen Centre for Psychosis Research, Norway Division of Mental Health and Addiction, Oslo University Hospital, Oslo, NO

105, Medical Genetics Section, CGEM, IGMM, University of Edinburgh, Edinburgh, GB

106, Clinical Neurosciences, University of Cambridge, Cambridge, GB

107, Internal Medicine, Erasmus MC, Rotterdam, Zuid-Holland, NL

108, Roche Pharmaceutical Research and Early Development, Neuroscience, Ophthalmology and Rare Diseases Discovery & Translational Medicine Area, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd, Basel, CH

109, Department of Psychiatry and Psychotherapy, University Medicine Greifswald, Greifswald, Mecklenburg-Vorpommern, DE

110, Department of Psychiatry, Leiden University Medical Center, Leiden, NL

111, Virginia Institute for Psychiatric & Behavioral Genetics, Virginia Commonwealth University, Richmond, VA, US

112, Computational Sciences Center of Emphasis, Pfizer Global Research and Development, Cambridge, MA, US

113, Institute for Molecular Bioscience; Queensland Brain Institute, The University of Queensland, Brisbane, QLD, AU

114, Department of Psychiatry, University of Münster, Münster, Nordrhein-Westfalen, DE

115, Department of Psychiatry, Melbourne Medical School, University of Melbourne, Melbourne, AU

116, Institute of Medical Genetics and Pathology, University Hospital Basel, University of Basel, Basel, CH

117, Institute of Neuroscience and Medicine (INM-1), Research Center Juelich, Juelich, DE

118, Amsterdam Public Health Institute, Vrije Universiteit Medical Center, Amsterdam, NL

119, Centre for Integrative Biology, Università degli Studi di Trento, Trento, Trentino-Alto Adige, IT

120, Department of Psychiatry and Psychotherapy, Medical Center, University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, DE

121, Psychiatry, Kaiser Permanente Northern California, San Francisco, CA, US

122, Medical Research Council Human Genetics Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, GB

123, Department of Psychiatry, University of Toronto, Toronto, ON, CA

124, Centre for Addiction and Mental Health, Toronto, ON, CA

125, Division of Psychiatry, University College London, London, GB

126, Neuroscience Therapeutic Area, Janssen Research and Development, LLC, Titusville, NJ, US

127, Institute of Molecular and Cell Biology, University of Tartu, Tartu, EE

128, Psychosis Research Unit, Aarhus University Hospital, Risskov, Aarhus, DK

129, University of Liverpool, Liverpool, GB

130, Mental Health Center Copenhagen, Copenhagen Universtity Hospital, Copenhagen, DK

131, Human Genetics and Computational Biomedicine, Pfizer Global Research and Development, Groton, CT, US

132, Psychiatry, Harvard Medical School, Boston, MA, US

133, Psychiatry, University of Iowa, Iowa City, IA, US

134, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD, US

135, Department of Psychiatry and Psychotherapy, University Medical Center Göttingen, Goettingen, Niedersachsen, DE

136, Human Genetics Branch, NIMH Division of Intramural Research Programs, Bethesda, MD, US

137, Faculty of Medicine, University of Iceland, Reykjavik, IS

138, Child and Adolescent Psychiatry, Erasmus MC, Rotterdam, Zuid-Holland, NL

139, Psychiatry, Erasmus MC, Rotterdam, Zuid-Holland, NL

140, Psychiatry, Dalhousie University, Halifax, NS, CA

141, Division of Epidemiology, New York State Psychiatric Institute, New York, NY, US

142, Department of Clinical Medicine, University of Copenhagen, Copenhagen, DK

143, Department of Medical & Molecular Genetics, King's College London, London, GB

144, Psychiatry & Behavioral Sciences, Stanford University, Stanford, CA, US

145, NIHR Maudsley Biomedical Research Centre, King's College London, London, GB

146, Genetics, University of North Carolina at Chapel Hill, Chapel Hill, NC, US

147, Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill, NC, US