**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Reference: N/A (unpublished)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.

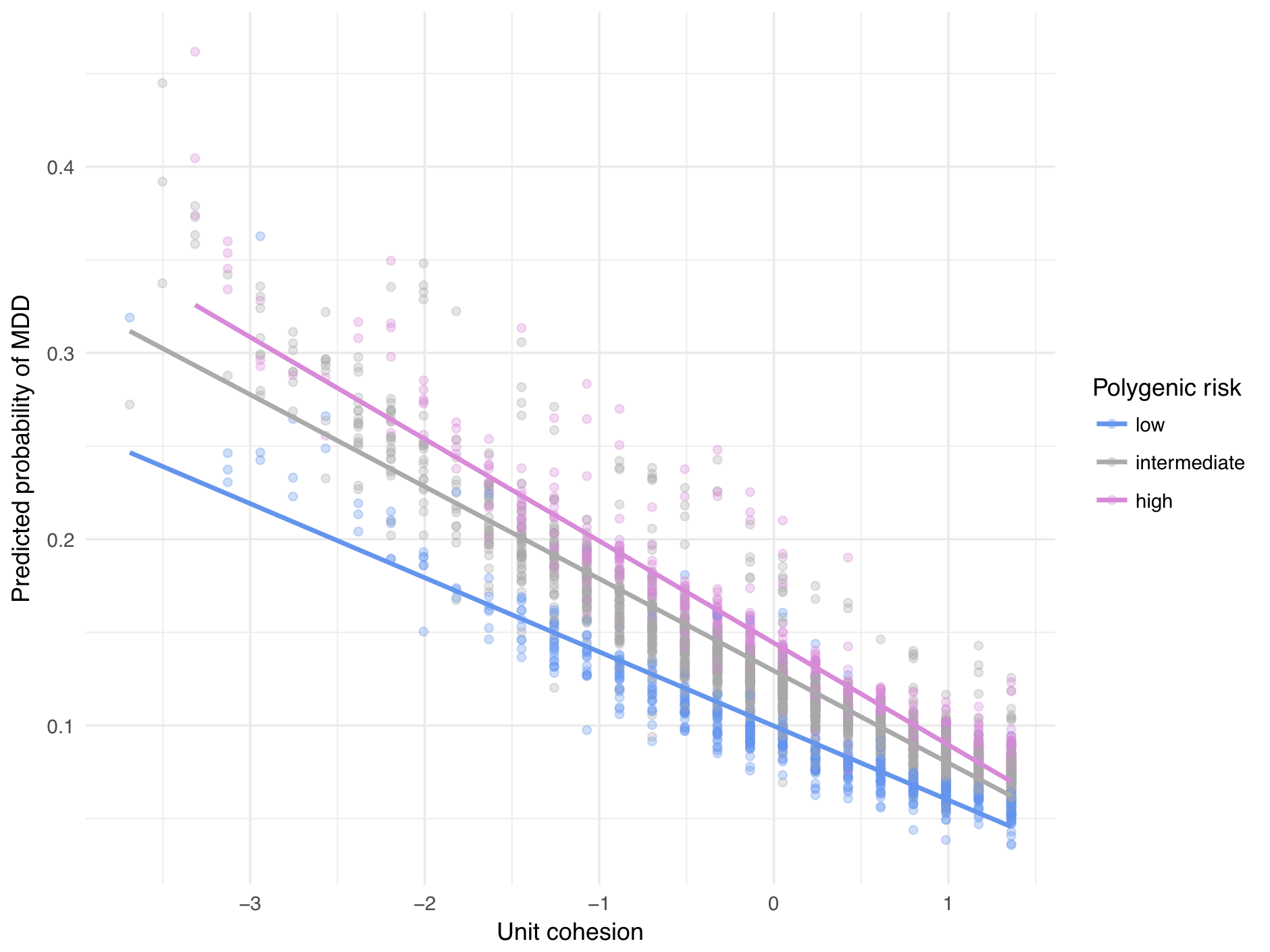


**Figure S3B. Distribution of MDD PRS.** This PRS was divided into low (quintile 1), intermediate (quintiles 2-4), and high (quintile 5) polygenic risk groups.



**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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