Supplementary Table S1

*Results of logistic regression models for the associations between polygenic scores, stressful life events and clinically relevant depressive symptoms (dichotomous variable)*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Polygenic Score Pdiscovery Thresholds | | | | | | | | | | | | | | |
|  |  | p < .10 | | | p < .20 | | | p < .30 | | | p < .40 | | | p < .50 | | |
| Model | Var/Stat | β | SE | p | β | SE | p | β | SE | p | β | SE | p | β | SE | p |
| Main Effects:  PG only | PG | .09 | .02 | .0001 | .14 | .03 | <.0001 | .17 | .04 | <.0001 | .21 | .05 | <.0001 | .23 | .06 | <.0001 |
| rr | .0075 | | | .0086 | | | .0091 | | | .0095 | | | .0095 | | |
|  |  |  | | |  | | |  | | |  | | |  | | |
| Main Effects:  PG and SLEs | PG | .09 | .02 | .0001 | .14 | .03 | <.0001 | .17 | .04 | <.0001 | .21 | .05 | <.0001 | .23 | .06 | <.0001 |
| SLEs | .79 | .08 | <.0001 | .79 | .08 | <.0001 | .79 | .08 | <.0001 | .79 | .08 | <.0001 | .79 | .08 | <.0001 |
| r2 | .0182 | | | .0193 | | | .0197 | | | .0201 | | | .0201 | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Interaction | pg score | -.03 | .09 | .7553 | -.06 | .13 | .6589 | -.03 | .16 | .8365 | -.02 | .18 | .9079 | -.04 | .21 | .8379 |
| SLE | 1.06 | .45 | .0180 | 1.15 | .39 | .0031 | 1.14 | .40 | .0043 | 1.11 | .43 | .0093 | 1.12 | .43 | .0085 |
| PG\*SLEs | -.04 | .06 | .5207 | -.04 | .08 | .6761 | -.05 | .11 | .6656 | -.06 | .13 | .6525 | -.05 | .14 | .7220 |
| r2 | .0183 | | | .0193 | | | .0197 | | | .0201 | | | .0201 | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | p < .60 | | | p < .70 | | | p < .80 | | | p < .90 | | | p < 1.0 | | |
|  |  | β | SE | p | β | SE | p | β | SE | p | β | SE | p | β | SE | p |
| Main effects:  PG only | PG | .26 | .06 | <.0001 | .28 | .07 | <.0001 | .30 | .07 | <.0001 | .32 | .08 | <.0001 | .33 | .08 | <.0001 |
| rr | .0096 | | | .0095 | | | .0095 | | | .0094 | | | .0095 | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Main effects:  pg score and SLEs | PG | .26 | .06 | <.0001 | .28 | .07 | <.0001 | .30 | .07 | <.0001 | .31 | .08 | <.0001 | .33 | .08 | <.0001 |
| SLEs | .79 | .08 | <.0001 | .79 | .08 | <.0001 | .78 | .08 | <.0001 | .79 | .08 | <.0001 | .79 | .08 | <.0001 |
| r2 | .0203 | | | .0201 | | | .0201 | | | .0201 | | | .0201 | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Interaction | PG | -.05 | .23 | .8203 | -.05 | .25 | .8508 | -.05 | .27 | .8431 | -.06 | .29 | .8380 | .06 | .30 | .8404 |
| SLEs | 1.13 | .43 | .0087 | 1.12 | .44 | .0104 | 1.13 | .44 | .0109 | 1.13 | .44 | .0097 | 1.13 | .44 | .0097 |
| PG\*SLEs | -.05 | .16 | .7729 | -.06 | .17 | .7451 | -.06 | .19 | .7570 | -.06 | .20 | .7556 | -.07 | .20 | .7488 |
| r2 | .0203 | | | .0201 | | | .0201 | | | .0201 | | | .0201 | | |

*Note.*pg = polygenic score, var = variable, stat = statistic*.* All models adjusted for age (centered), education, gender and the first 3 principal components (centered). Interaction models adjusted for all polygenic score X covariate and SLE X covariate interaction terms.

Supplementary Table S2

*Results of negative binomial regression models for the associations between polygenic scores, stressful life events and number of depressive symptoms*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Polygenic Score Pdiscovery Thresholds | | | | | | | | | | | | | | | |
|  |  | p < .10 | | | p < .20 | | | p < .30 | | | p < .40 | | | | p < .50 | | |
| Model | Variable | β | SE | p | β | SE | p | β | SE | p | β | SE | | p | β | SE | p |
| Main Effects:  PG only | PG | .04 | .01 | <.0001 | .07 | .01 | <.0001 | .08 | .02 | <.0001 | .09 | .02 | | <.0001 | .11 | .02 | <.0001 |
|  |  |  | | |  | | |  | | |  | | | |  | | |
| Main Effects:  PG and SLEs | PG | .04 | .01 | <.0001 | .06 | .01 | <.0001 | .08 | .02 | <.0001 | .09 | .02 | | <.0001 | .10 | .02 | <.0001 |
| SLEs | .46 | .04 | <.0001 | .46 | .04 | <.0001 | .46 | .04 | <.0001 | .46 | .04 | | <.0001 | .46 | .04 | <.0001 |
|  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |
| Interaction | PG | .002 | .04 | .9518 | -.003 | .05 | .9584 | .006 | .06 | .9191 | -.007 | .07 | | .9271 | -.02 | .08 | .8471 |
| SLEs | .71 | .21 | .0006 | .73 | .18 | <.0001 | .73 | .18 | <.0001 | .74 | .20 | | .0002 | .75 | .20 | .0002 |
| PG\*SLEs | -.008 | .03 | .7776 | .0001 | .04 | .9978 | -.01 | .05 | .8375 | -.0003 | .06 | | .9955 | .005 | .07 | .9479 |
|  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |
|  |  | p < .60 | | | p < .70 | | | p < .80 | | | p < .90 | | | | p < 1.0 | | |
|  |  | β | SE | p | β | SE | p | β | SE | p | β | SE | p | | β | SE | p |
| Main effects:  PG only | PG | .12 | .03 | <.0001 | .13 | .03 | <.0001 | .15 | .03 | <.0001 | .15 | .03 | <.0001 | | .16 | .03 | <.0001 |
|  |  | .12 | .03 | <.0001 | .13 | .03 | <.0001 | .14 | .03 | <.0001 | .15 | .03 | <.0001 | | .16 | .03 | <.0001 |
| Main effects:  PG and SLEs | PG | .46 | .04 | <.0001 | .46 | .04 | <.0001 | .46 | .04 | <.0001 | .46 | .04 | <.0001 | | .46 | .04 | <.0001 |
| SLEs |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Interaction | PG | -.01 | .09 | .9170 | -.004 | .10 | .9705 | .001 | .11 | .9952 | -.001 | .11 | .9930 | | -.002 | .12 | .9899 |
| SLEs | .75 | .20 | .0002 | .75 | .20 | .0002 | .75 | .21 | .0003 | .75 | .20 | .0002 | | .75 | .20 | .0002 |
| PG\*SLEs | .01 | .08 | .8959 | .01 | .08 | .9053 | .009 | .09 | .9207 | .009 | .09 | .9274 | | .009 | .10 | .9280 |

*Note.*PG = polygenic score*.* All models adjusted for age (centered), education, gender and the first 3 principal components (centered). Interaction models adjusted for all polygenic score X covariate and SLE X covariate interaction terms.

Supplementary Table S3

*Results of logistic regression models for the associations between polygenic scores, stressful life events and clinically relevant depressive symptoms (dichotomous variable) in whites, (N = 7,528)*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Polygenic Score Pdiscovery Thresholds | | | | | | | | | | | | | | | |
|  |  | p < .10 | | | p < .20 | | | p < .30 | | | p < .40 | | | p < .50 | | | |
| Model | Var/Stat | β | SE | p | β | SE | p | β | SE | p | β | SE | p | β | | SE | p |
| Main Effects:  PG only | PG | .08 | .03 | .0010 | .13 | .04 | .0005 | .16 | .05 | .0005 | .19 | .05 | .0004 | .21 | | .06 | .0006 |
| rr | .0038 | | | .0043 | | | .0044 | | | .0045 | | | .0044 | | | |
|  |  |  | | |  | | |  | | |  | | |  | | | |
| Main Effects:  PG and SLEs | PG | .08 | .03 | .0017 | .12 | .04 | .0009 | .15 | .05 | .0010 | .18 | .05 | .0008 | .20 | | .06 | .0011 |
| SLEs | .79 | .09 | <.0001 | .79 | .09 | <.0001 | .79 | .09 | <.0001 | .79 | .09 | <.0001 | .79 | | .09 | <.0001 |
| r2 | .0137 | | | .0143 | | | .0143 | | | .0144 | | | .0144 | | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |
| Interaction | PG | -.13 | .11 | .2355 | -.27 | .16 | .0935 | -.34 | .20 | .0845 | -.35 | .23 | .1324 | -.43 | | .27 | .1081 |
| SLEs | .75 | .53 | .1521 | .92 | .46 | .0475 | .92 | .47 | .0536 | .94 | .51 | .0619 | .97 | | .51 | .0560 |
| PG\*SLEs | -.04 | .06 | .5354 | -.008 | .09 | .9311 | -.002 | .12 | .9856 | .01 | .14 | .9302 | .03 | | .16 | .8477 |
| r2 | .0137 | | | .0143 | | | .0143 | | | .0144 | | | .0144 | | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |
|  |  | p < .60 | | | p < .70 | | | p < .80 | | | p < .90 | | | p < 1.0 | | | |
|  |  | β | SE | p | β | SE | p | β | SE | p | β | SE | p | β | | SE | p |
| Main effects  PG only | PG | .24 | .07 | .0004 | .27 | .08 | .0003 | .30 | .08 | .0002 | .31 | .09 | .0002 | .33 | | .09 | .0002 |
| rr | .0047 | | | .0047 | | | .0049 | | | .0049 | | | .0049 | | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |
| Main effects  PG and SLEs | PG | .23 | .07 | .0008 | .26 | .08 | .0006 | .28 | .08 | .0005 | .30 | .09 | .0005 | .31 | | .09 | .0004 |
| SLEs | .79 | .09 | <.0001 | .79 | .09 | <.0001 | .79 | .09 | <.0001 | .79 | .09 | <.0001 | .79 | | .09 | <.0001 |
| r2 | .0146 | | | .0147 | | | .0148 | | | .0148 | | | .0148 | | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |
| Interaction | PG | -.46 | .29 | .1205 | -.47 | .32 | .1402 | -.50 | .34 | .1470 | -.53 | .36 | .1433 | -.55 | | .38 | .1411 |
| SLEs | .97 | .51 | .0588 | .96 | .52 | .0643 | .97 | .52 | .0649 | .97 | .52 | .0618 | .97 | | .52 | .0620 |
| PG\*SLEs | .03 | .18 | .8527 | .03 | .19 | .8841 | .03 | .21 | .8762 | .03 | .22 | .8747 | .03 | | .23 | .8799 |
| r2 | .0146 | | | .0147 | | | .0148 | | | .0148 | | | .0148 | | | |

*Note.*PG = polygenic score, var = variable, stat = statistic*.* All models adjusted for age (centered), education, gender and the first 3 principal components (centered). Interaction models adjusted for all polygenic score X covariate and SLE X covariate interaction terms. The proportion of white participants who reported experiencing at least 1 SLE (12.4%) was almost identical to that of the full sample (12.5%).

Supplementary Table S4

*Results of negative binomial regression models for the associations between polygenic scores, stressful life events and number of depressive symptoms in whites, (N =7,528)*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Polygenic Score Pdiscovery Thresholds | | | | | | | | | | | | | | |
|  |  | p < .10 | | | p < .20 | | | p < .30 | | | p < .40 | | | p < .50 | | |
| Model | Variable | β | SE | p | β | SE | p | β | SE | p | β | SE | p | β | SE | p |
| Main Effects:  PG only | PG | .04 | .01 | .0013 | .05 | .02 | .0006 | .07 | .02 | .0006 | .08 | .02 | .0008 | .09 | .03 | .0010 |
|  |  |  | | |  | | |  | | |  | | |  | | |
| Main Effects:  PG and SLEs | PG | .03 | .01 | .0020 | .05 | .02 | .0012 | .06 | .02 | .0011 | .07 | .02 | .0018 | .08 | .03 | .0022 |
| SLEs | .48 | .05 | <.0001 | .48 | .05 | <.0001 | .48 | .05 | <.0001 | .48 | .05 | <.0001 | .48 | .05 | <.0001 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Interaction | PG | -.03 | .05 | .5346 | -.06 | .07 | .3558 | -.08 | .08 | .3104 | -.11 | .10 | .2690 | -.13 | .11 | .2146 |
| SLEs | .71 | .24 | .0031 | .74 | .21 | .0005 | .73 | .22 | .0008 | .77 | .23 | .0009 | .78 | .23 | .0009 |
| PG\*SLEs | .001 | .03 | .9753 | .02 | .04 | .6091 | .02 | .06 | .7487 | .04 | .07 | .5529 | .05 | .08 | .5117 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | p < .60 | | | p < .70 | | | p < .80 | | | p < .90 | | | p < 1.0 | | |
|  |  | β | SE | p | β | SE | p | β | SE | p | β | SE | p | β | SE | p |
| Main effects:  PG only | PG | .10 | .03 | .0006 | .12 | .03 | .0004 | .13 | .04 | .0003 | .14 | .04 | .0003 | .14 | .04 | .0002 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Main effects:  PG and SLEs | PG | .10 | .03 | .0013 | .11 | .03 | .0009 | .12 | .03 | .0006 | .13 | .04 | .0006 | .13 | .04 | .0006 |
| SLEs | .48 | .05 | <.0001 | .48 | .05 | <.0001 | .48 | .05 | <.0001 | .48 | .05 | <.0001 | .48 | .05 | <.0001 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Interaction | PG | -.13 | .12 | .2688 | -.14 | .13 | .3043 | -.14 | .14 | .3249 | -.15 | .15 | .3195 | -.16 | .15 | .3120 |
| SLEs | .78 | .24 | .0010 | .79 | .24 | .0010 | .79 | .24 | .0011 | .79 | .24 | .0010 | .79 | .24 | .0010 |
| PG\*SLEs | .06 | .08 | .5020 | .06 | .09 | .5056 | .07 | .10 | .5104 | .07 | .11 | .5109 | .07 | .11 | .5106 |

*Note.*PG = polygenic score*.* All models adjusted for age (centered), education, gender and the first 3 principal components (centered). Interaction models adjusted for all polygenic score X covariate and SLE X covariate interaction terms. The proportion of White participants who reported experiencing at least 1 SLE (12.4%) was almost identical to that of the full sample (12.5%).

Supplementary Figure S1

*Proportion of variance in clinically relevant depressive symptoms explained by polygenic scores at each pdiscovery threshold*