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Research paper

Polygenic risk for suicide attempt is associated with lifetime suicide attempt in US soldiers independent of parental risk

Murray B. Stein [a,b,c,*], Sonia Jain [c], Santiago Papini [d], Laura Campbell-Sills [a], Karmel W. Choi [f], Brian Martis [a,b], Xiaoying Sun [c], Feng He [c], Erin B. Ware [e], James A. Naifeh [i], Pablo A. Aliaga [i], Tian Ge [f], for International Suicide Genetics Consortium[1], for MVP Suicide Exemplar Workgroup[1], for VA Million Veteran Program[1], for Suicide Working Group of the Psychiatric Genomics Consortium[1], Jordan W. Smoller [f], Joel Gelernter [g], Ronald C. Kessler [h], Robert J. Ursano [i]

[a] Department of Psychiatry, University of California, San Diego, La Jolla, CA, USA
[b] VA San Diego Healthcare System, San Diego, CA, USA
[c] Herbert Wertheim School of Public Health and Human Longevity Science, University of California, San Diego, La Jolla, CA, USA
[d] Department of Psychology, University of Hawai'i at Mānoa, Honolulu, HI, USA
[e] Institute for Social Research, University of Michigan, Ann Arbor, MI, USA
[f] Psychiatric and Neurodevelopmental Genetics Unit, Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA
[g] Departments of Psychiatry, Genetics, and Neuroscience, Yale University School of Medicine, New Haven, CT, USA
[h] Department of Health Care Policy, Harvard Medical School, Boston, MA, USA
[i] Center for the Study of Traumatic Stress, Department of Psychiatry, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

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ABSTRACT

Background: Suicide is a leading cause of death worldwide. Whereas some studies have suggested that a direct measure of common genetic liability for suicide attempts (SA), captured by a polygenic risk score for SA (SA-PRS), explains risk independent of parental history, further confirmation would be useful. Even more unsettled is the extent to which SA-PRS is associated with lifetime non-suicidal self-injury (NSSI).

Methods: We used summary statistics from the largest available GWAS study of SA to generate SA-PRS for two non-overlapping cohorts of soldiers of European ancestry. These were tested in multivariable models that included parental major depressive disorder (MDD) and parental SA.

Results: In the first cohort, 417 (6.3 %) of 6573 soldiers reported lifetime SA and 1195 (18.2 %) reported lifetime NSSI. In a multivariable model that included parental history of MDD and parental history of SA, SA-PRS remained significantly associated with lifetime SA [aOR = 1.26, 95%CI:1.13–1.39, $p < 0.001$] per standardized unit SA-PRS]. In the second cohort, 204 (4.2 %) of 4900 soldiers reported lifetime SA, and 299 (6.1 %) reported lifetime NSSI. In a multivariable model that included parental history of MDD and parental history of SA, SA-PRS remained significantly associated with lifetime SA [aOR = 1.20, 95%CI:1.04–1.38, $p = 0.014$]. A combined analysis of both cohorts yielded similar results. In neither cohort or in the combined analysis was SA-PRS significantly associated with NSSI.

Conclusions: PRS for SA conveys information about likelihood of lifetime SA (but not NSSI, demonstrating specificity), independent of self-reported parental history of MDD and parental history of SA.

Limitations: At present, the magnitude of effects is small and would not be immediately useful for clinical decision-making or risk-stratified prevention initiatives, but this may be expected to improve with further iterations. Also critical will be the extension of these findings to more diverse populations.

* Correspondence to: M. B. Stein, Department of Psychiatry and School of Public Health, University of California San Diego, 9500 Gilman Drive, La Jolla, CA, USA.
E-mail address: mstein@health.ucsd.edu (M.B. Stein).

[1] Names and affiliations of collaborators from these consortia and workgroups are included in Acknowledgments.

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1. Introduction

Suicide is a serious global societal and public health problem (Lovero et al., 2023). In the United States in 2021, suicide was the ninth leading cause of death, and the second leading cause of death for individuals between the ages of 10–14 and 25–34 (Center for Disease Control CDC, 2023). Additionally, concern about suicide has raised alarms in the US military, where from 2014 to 2019, the suicide death rate for the Active Component increased from 20.4 to 25.9 suicides per 100,000 Service members (Department of Defense, 2020). Despite a great deal of research into risk factors (Holliday et al., 2020) and substantial investments in suicide prevention (Stein et al., 2019; Curley et al., 2020), it remains uncertain why suicidality has trended higher. These observations have called for the development of better predictive models that can help target those individuals at highest risk (Kessler et al., 2020).

An emerging body of research has extended the search for suicide risk factors to include genetic risk. Twin studies had initially set the stage for expecting to find specific genetic risk factors, providing heritability estimates of 30–55 % (Tidemalm et al., 2011). It is now clear that suicidal behaviors are genetically complex – as are most neuropsychiatric traits (Wendt et al., 2020) – and the evidence suggests that many common variants, each of small effect, contribute to risk (with the possibility that rare variants confer greater risk) (Sokolowski and Wasserman, 2020).

Epidemiological studies have shown that risk factors for various aspects of self-harm (i.e., ideation, attempts, and deaths) overlap only partially (Nock et al., 2013; Naifeh et al., 2020). This awareness has carried over to the genetic epidemiological study of self-harm where, increasingly, studies are each centered on one stage or type of self-harm (e.g., suicide ideation; suicide attempts; violent suicide attempts; suicide deaths).

Early genetic studies of suicidality, including our own genome-wide association study (GWAS) of suicide attempts in US Army soldiers (Stein et al., 2017), were underpowered (Mirkovic et al., 2016). More recent GWAS of suicide attempts, which have achieved much larger sample sizes thanks to data-sharing within and across consortia, have emphasized a genetic correlation between major depressive disorder (MDD) and SA (Mullins et al., 2019; Levey et al., 2019; Mullins et al., 2022). Similar conclusions were reached from a GWAS of death by suicide, which found a polygenic association with MDD (and several other behavioral traits phenotypically linked with suicide deaths) (Docherty et al., 2020). Our work has shown a polygenic association between MDD and SA in U.S. Army soldiers (Stein et al., 2021), consistent with findings that polygenic risk for MDD was associated with SA in adults across 4 clinical samples (Fanelli et al., 2022) and with suicidal behaviors in preadolescent youths (Joo et al., 2022).

Given the recent completion of the largest available GWAS meta-analysis of SA (Docherty et al., 2023), we asked two questions: (Lovero et al., 2023) whether polygenic risk of SA, per se, is predictive of lifetime SA in two independent cohorts of US Army soldiers, over and above the robust risks associated with parental history of SA (or suicide death) (Wang et al., 2022) and parental history of MDD; and (Center for Disease Control CDC, 2023) whether polygenic risk of SA is predictive of lifetime non-suicidal self-injury (NSSI), which has epidemiological similarities and differences from SA. The first question has been addressed in recent studies showing an independent association of polygenic risk for SA on suicidal thoughts and behaviors in children (Lee et al., 2022) and suicide attempts in adolescents (Barzilay et al., 2022), but we believe this to be the first replication of these findings in an adult sample. The second question has been addressed in a report from the Collaborative Study on the Genetics of Alcoholism (COGA) where it was shown that NSSI was less strongly genetically related to SA than were other forms of suicidal thoughts and behaviors (Colbert et al., 2023). To the best of our knowledge, that finding has yet to be replicated.

In the present study, we used data from two non-overlapping cohorts evaluated in the Army Study to Assess Risk and Resilience in Servicemembers (STARRS) (Naifeh et al., 2019) to answer these questions.

2. Methods

2.1. Subjects

Data come from two components of Army STARRS: the *New Soldier Study (*NSS*)* and the *Pre/Post Deployment Study (*PPDS*)*. Detailed information about the design and conduct of STARRS is available in a separate report (Ursano et al., 2014). Soldiers from the respective studies described below are nonoverlapping as confirmed by genetic analysis.

Cohort 1: New Soldier Study (NSS). The NSS was carried out among new soldiers at the start of their basic training at three Army Installations between April 2011 and November 2012. Of 39,784 NSS respondents who completed the Self-Administered Questionnaire (SAQ), 33,088 (83.2 %) provided blood samples. Funding constraints led us to genotype a subset of respondents that would be optimally informative for the aims of STARRS: All cases of reported lifetime SA and PTSD were genotyped, as were a set of controls stratum-matched on sex, service type (Regular Army vs. Guard/Reserve), and childhood adversity quartile. The NSS analyses described herein include 6573 soldiers of European ancestry with available survey and genotype data (see below).

Cohort 2: Pre/Post Deployment Study (PPDS). The PPDS collected baseline data (also using a version of the SAQ) from US Army soldiers in three Brigade Combat Teams during the first quarter of 2012, within approximately six weeks of their upcoming deployment to Afghanistan. A total of 9949 Soldiers were present for duty in the three Brigade Combat Teams; 9488 (95.3 %) consented to participate in the survey with 8558 (86.0 %) providing complete baseline survey responses and consent to link their survey responses to their administrative records. The PPDS analyses described herein include 4900 soldiers of European ancestry with available survey and genotype data (see below).

2.2. Measures

The SAQ surveyed socio-demographic characteristics, lifetime and past-30-day mental disorders, and an array of potential risk and resilience factors.

Suicide Attempt and Non-Suicidal Self-Injury Assessment. Suicidal behaviors were assessed using an adaptation of the Columbia Suicidal Severity Rating Scale (Posner et al., 2011). Pertinent to the data presented here, all respondents were asked if they had a history of SA (*"Did you ever make a suicide attempt [i.e., purposefully hurt yourself with at least some intention to die]?"*). All respondents were also asked if they had a history of non-suicidal self-injury (NSSI) (*"Did you ever do something to hurt yourself on purpose, but without wanting to die [*e.g.*, cutting yourself, hitting yourself, or burning yourself]?"*).

This information was available at baseline for NSS and PPDS, and at approximately 6- and 9-months post index deployment for PPDS. It was also available at later dates for those NSS and PPDS soldiers who subsequently took part in a 6- to 8-year follow-up survey referred to as STARRS-LS (STARRS Longitudinal Study), for which data collection began 12 September 2016 and is ongoing; data included here are for assessments obtained through 10 April 2018. The STARRS-LS survey was conducted using a mixed-mode design, with participants given the option of completing the interview as a self-administered survey on the web, or with an interviewer over the telephone. This self-report information on suicidality was complemented by access to Army health records where SA(s) were recorded if medical attention was sought. For the analyses presented here, cases are soldiers with a lifetime history of SA (from either self-report [non-fatal attempts] or Army health records [fatal or non-fatal attempts]) and controls are those individuals with no lifetime history of SA.

Parental History of Major Depressive Disorder. The Army STARRS surveys queried parental history of MDD separately for the

respondent's biological mother and father. The survey item (*"Did any of them ever have times lasting two weeks or longer when they were so depressed they couldn't concentrate, felt worthless, or felt their life was not worth living?"*) was derived from the Family History Screen (Weissman et al., 2000). An affirmative response for either (or both) parent(s) was considered as YES for parental MDD.

Parental History of Suicide Attempt or Death. The Army STARRS surveys queried parental history of SA (or suicide death) asking whether, during the respondent's childhood, "A parent attempted suicide", or "A parent committed suicide". An affirmative response to either (for one or both parents) was coded as YES for parental SA.

2.3. Genetic data collection and procedures

Samples were genotyped using either the Illumina OmniExpress + Exome array with additional custom content or the Ilumina PsychChip. Quality control (QC) of genotype data used standard protocols as described elsewhere (Stein et al., 2016). Relatedness testing was carried out with PLINK v1.90 (Chang et al., 2015) and, for pairs of subjects with π of >0.2, one member of each relative pair was removed at random.

Genotype imputation was performed with a 2-step pre-phasing/imputation approach with a multi-ancestry reference panel from 1000 Genomes Project (August 2012 phase 1 integrated release; 2186 phased haplotypes with 40,318,245 variants). We removed SNPs that were not present in the 1000 Genomes Project reference panel, had non-matching alleles to 1000 Genome Project reference, or with ambiguous, unresolvable alleles (AT/GC SNPs with minor allele frequency [MAF] > 0.1). A total of 664,457 SNPs for the Illumina OmniExpress array and 360,704 for the Illumina PsychChip entered the imputation. We performed the following QC procedures to obtain the genotype data for population assignment and principal components analysis (PCA). We retained autosomal SNPs with missing rate < 0.05; samples with individual-wise missing rate < 0.02; SNPs with missing rate < 0.02; and SNPs with missing rate difference between cases and controls <0.02. After QC, we merged our study samples with HapMap3 samples. We retained SNPs with MAF $\geq$ 0.01 and performed LD pruning at $R^2 > 0.02$. Finally, we excluded SNPs in MHC region (Chr 6:25-35 Mb) and Chr 8 inversion (Chr 8:7-13 Mb). Population (ancestry) assignment was conducted using standard methods (see (Stein et al., 2017) for details).

Polygenic Risk Scores (PRS) computation. PRS for the SA phenotype were computed using PRS-CS-auto, a method that uses a Bayesian regression framework and places a continuous shrinkage prior on the effects sizes of SNPs in the discovery GWAS summary statistics (Ge et al., 2019). PLINK 2.0 (Chang et al., 2015) was used to weight all SNPs by their effect sizes calculated using PRS-CS-auto and sum all SNPs into PRS for each individual in the target cohort. PRS analyses were conducted only in the European ancestry subsamples because of the unavailability of reference GWAS data for other populations (Choi et al., 2020; Peterson et al., 2019). Summary statistics from the International Suicide Genetics Consortium-Million Veteran Program (ISGHC-MVP) meta-analysis (doi.org/10.1101/2022.07.03.22277199) (Docherty et al., 2023) with Army STARRS data withheld (N = 35,116 cases, 768,755 controls) were used as the discovery GWAS; 1000 Genomes European was used as the LD reference panel. PRS were standardized within each study (NSS and PPDS) for the analysis.

2.4. Statistical analysis

Multivariable logistic regression models were performed to assess the association of SA-PRS, parental history of MDD, and parental history of SA with lifetime SA and NSSI, controlling for the top 10 ancestral principal components, age, batch (for NSS, which had been genotyped in two batches) and sex. Additional models included personal history of MDD (lifetime and past-30-day). Adjusted odds ratios (aOR) were reported with 95 % confidence intervals. Nagelkerke's pseudo-R-square was reported for models. Likelihood ratio test (LRT) was used to examine whether adding the SA-PRS improved model prediction. All analyses were conducted in R version 3.6.1.

3. Results

3.1. Findings in New Soldier Study (NSS)

The NSS sample consisted of 417 lifetime SA cases (6.3 %) and 6156 controls with no history of lifetime SA; and 1195 lifetime NSSI cases (18.2 %) and 5378 controls with no history of lifetime NSSI. The sample was 15 % female. Mean age of the sample was 20.8 (SD 3.3) years; median = 20 years, interquartile range: 19–22 years. 1086 (17.0 % of) soldiers had a lifetime history of MDD and 532 (8.4 %) had a past-30-day history of MDD. 2107 (32.1 %) soldiers reported a parental history of MDD and 553 (8.4 %) reported a parental history of SA (Table 1, top).

In a multivariable model that included age, sex, 10 ancestral PCs, and batch, the SA-PRS was significantly associated with lifetime history of SA (adjusted odds ratio (aOR) = 1.27 [95 % CI: 1.15–1.41] per SD increase in SA-PRS). SA-PRS continued to be significantly associated with lifetime SA (aOR = 1.26 [95 % CI: 1.13–1.39]) in a multivariable model that included all of the aforementioned predictors and added parental history of MDD (aOR = 1.57 [95 % CI: 1.26–1.96]) and parental history of SA (aOR = 1.48 [95 % CI: 1.09–2.02]). (Table 2, top). This model explained significantly more of the variance in the lifetime SA outcome than a model that did not include SA-PRS (pseudo-R-square = 4.5 % vs 3.7 %, LRT p = 0.0002).

In a multivariable model that included age, sex, 10 ancestral PCs, and batch, the SA-PRS was not significantly associated with lifetime history of NSSI (aOR = 1.01 [95 % CI: 0.94–1.07]). Neither was SA-PRS significantly associated with lifetime history of NSSI (aOR = 0.99 [95 % CI: 0.93–1.06]) in a multivariable model that included all of the aforementioned predictors and added parental history of MDD (aOR = 1.67 [95 % CI: 1.45–1.92]) and parental history of SA (aOR = 1.25 [95 % CI: 1.00–1.55]). (Table 2, bottom).

3.2. Replication in Pre-Post Deployment Study (PPDS)

The PPDS sample consisted of 204 lifetime SA cases (4.2 %) and 4696 controls with no history of lifetime SA; and 299 lifetime NSSI cases (6.1 %) and 4601 controls with no history of lifetime NSSI. The sample was 4 % female, reflecting the overwhelming male majority deployed to combat at the time of the survey. Mean age was 25.9 (SD 5.9) years; median = 24 years, interquartile range: 21–29 years. 551 (11.2 % of) soldiers had a lifetime history of MDD and 310 (6.3 %) had a pst-30-day history of MDD. 958 (19.6 % of) soldiers reported a parental history of MDD and 218 (4.5 %) reported a parental history of suicide attempt or death (Table 1, bottom).

In a multivariable model that included age, sex, and 10 ancestral PCs,

Table 1
Personal (Lifetime) and parental histories of soldiers in each study.

	Yes	No
New Soldier Study		
Lifetime Suicide Attempt	417 (6.3 %)	6156 (93.7 %)
Lifetime Non-Suicidal Self-Injury	1195 (18.2 %)	5378 (81.8 %)
Lifetime MDD	1086 (17.0 %)	5288 (83.0 %)
Past-30-Day MDD	532 (8.4 %)	5842 (91.7 %)
Parental History of Major Depression	2107 (32.1 %)	4466 (67.9 %)
Parental History of Suicide Attempt or Death	553 (8.4 %)	6020 (91.6 %)
Pre-Post Deployment Study		
Lifetime Suicide Attempt	204 (4.2 %)	4696 (95.8 %)
Lifetime Non-Suicidal Self-Injury	299 (6.1 %)	4601 (93.9 %)
Lifetime MDD	551 (11.2 %)	4349 (88.8 %)
Past-30-Day MDD	310 (6.3 %)	4590 (93.7 %)
Parental History of Major Depression	958 (19.6 %)	3942 (80.5 %)
Parental History of Suicide Attempt or Death	218 (4.5 %)	4682 (95.6 %)

Table 2
Multivariable model for lifetime suicide attempt and lifetime non-suicidal self-injury in New Soldier Study (NSS)*

	Adjusted Odds Ratio (aOR)	aOR 95 % CI	*p*-value
Lifetime Suicide Attempt (SA)			
Parental Major Depression	1.57	1.26–1.96	<0.001
Parental Suicide Attempt or Death	1.48	1.09–2.02	0.0134
Suicide Attempt Polygenic Risk Score (SA-PRS)	1.26	1.13–1.39	< 0.001
Lifetime Non-Suicidal Self-Injury (NSSI)			
Parental Major Depression	1.67	1.45–1.92	<0.001
Parental Suicide Attempt or Death	1.25	1.003–1.55	0.047
Suicide Attempt Polygenic Risk Score (SA-PRS)	0.99	0.93–1.06	0.841

* Models also include the following covariates (not shown in tables): age (years), sex, batch, and 10 principal components of ancestry.

the SA-PRS was significantly associated with lifetime history of SA (aOR = 1.22 [95 % CI: 1.06–1.41] per SD increase in SA-PRS). SA-PRS continued to be significantly associated with lifetime SA (aOR = 1.20 [95 % CI: 1.04–1.38]) in a multivariable model that included all of the aforementioned predictors and added parental history of MDD (aOR = 1.89 [95 % CI: 1.36–2.61]) and parental history of SA (aOR = 1.53 [95 % CI: 0.90–2.59]) (Table 3, top). This model explained significantly more of the variance in the lifetime SA outcome than a model that did not include SA-PRS (pseudo-R-square = 3.6 % vs 3.2 %, LRT $p = 0.014$).

In a multivariable model that included age, sex, and 10 ancestral PCs, the SA-PRS was not significantly associated with lifetime history of NSSI (aOR = 1.09 [95 % CI: 0.97–1.23]). Neither was SA-PRS significantly associated with lifetime history of NSSI (aOR = 1.06 [95 % CI: 0.94–1.20]) in a multivariable model that included all of the aforementioned predictors and added parental history of MDD (aOR = 2.69 [95 % CI: 2.07–3.50]) and parental history of SA (aOR = 1.15 [95 % CI: 0.72–1.81]). (Table 3, bottom).

3.3. Combined sample

In the combined sample consisting of soldiers from both cohorts (N = 11,473) a multivariable model that included age, sex, cohort, 10 ancestral PCs, parental history of MDD, and parental history of SA, SA-PRS was significantly associated with lifetime history of SA (aOR = 1.23 [95 % CI: 1.13–1.34] per SD increase in SA-PRS). This model explained significantly more (15.6 %; $p < 0.000001$) of the variance in the lifetime SA outcome than a model that did not include SA-PRS. In a multivariable model that included all of the aforementioned predictors in addition to the soldier's lifetime history of MDD (positive in 1637 [14.52 %] of soldiers) and past-30-day history of MDD (positive in 842 [7.47 %] of soldiers) the association of SA-PRS with lifetime SA was largely unchanged (aOR = 1.21 [95 % CI: 1.11–1.32]).

In none of the above models was SA-PRS significantly associated with lifetime NSSI.

Table 3
Multivariable model for lifetime suicide attempt and lifetime non-suicidal self-injury in Pre-Post Deployment Study (PPDS)*.

	Adjusted Odds Ratio (aOR)	aOR 95 % CI	p-value
Lifetime Suicide Attempt (SA)			
Parental Major Depression	1.89	1.36–2.61	<0.001
Parental Suicide Attempt or Death	1.53	0.90–2.59	0.113
Suicide Attempt Polygenic Risk Score (SA-PRS)	1.20	1.04–1.04	0.014
Lifetime Non-Suicidal Self-Injury (NSSI)			
Parental Major Depression	2.69	2.07–3.50	< 0.001
Parental Suicide Attempt or Death	1.15	0.72–1.81	0.563
Suicide Attempt Polygenic Risk Score (SA-PRS)	1.06	0.94–1.20	0.336

* Models also include the following covariates (not shown in tables): age (years), sex, and 10 principal components of ancestry.

4. Discussion

Among the numerous potential applications of polygenic risk scores (PRS) is their use to stratify individuals based on their predicted risk for a range of mental and physical health outcomes (Polygenic Risk Score Task Force of the International Common Disease A, 2021; Wray et al., 2021; Murray et al., 2020). A suicidality PRS has been shown to be associated with suicidal thoughts and behaviors in a recent study of US military veterans, providing proof-of-concept for their usefulness in this regard (Nichter et al., 2023). Previous studies have shown that genetic liability for MDD is associated with risk for SA (Mullins et al., 2019; Levey et al., 2019; Mullins et al., 2014; Ruderfer et al., 2020) as well as for suicide death (Docherty et al., 2020).

In this study of two non-overlapping cohorts of United States Army soldiers, and in the combined sample, we found polygenic risk for suicide attempt (SA-PRS) was associated with lifetime risk of suicide attempt (SA) as determined from a combination of self-report and Army medical records. We were able to show that SA-PRS added to the predictive utility of two readily obtainable self-report parameters of SA risk, parental history of MDD and parental history of SA (Andlauer et al., 2021). The findings were largely unchanged by the addition of personal lifetime and past-30-day history of MDD. These findings, which we believe to be the first in adults, are consistent with those emanating from two recent studies of children and adolescents, respectively (Lee et al., 2022; Barzilay et al., 2022).

Importantly, we found no association between SA-PRS and NSSI, supporting the notion that NSSI and SA have different underlying predispositions. These findings are consistent with recent observations from COGA, where an NSSI PRS was relatively weakly genetically correlated with other PRS for suicidal thoughts and behaviors (including SA), and where a PRS for SA had relatively little predictive value for NSS (compared to other forms of suicidal thoughts and behaviors) (Colbert et al., 2023). Our results further strengthen the argument that not all types of suicidal thoughts and behaviors share the same underlying genetic etiology, and that NSSI is a good example of one such outlier.

Strengths of the study are the relatively large sample sizes, the use of the largest available GWAS on SA for computation of the PRS, the systematic ascertainment of SA through surveys and access to health records, and the ability to test for replication of findings across two cohorts. In this regard, it is of particular interest that the adjusted odds ratio (aOR) for SA-PRS predicting lifetime SA was very similar (aOR ~ 1.2) in both cohorts (and in the combined sample). A weakness is the possibility of incomplete ascertainment (e.g., if soldiers who left the Army were not part of STARRS-LS, and they attempted suicide after leaving the Army, they would be misclassified as controls), which would have biased findings toward the null. An additional weakness stems from the reliance on participant's reporting of parental history of SA and depression, which may be inaccurate. Another potential weakness is that reports of SA by self-report and health record-reporting were not infrequently discordant, leaving open the possibility that additional reporting biases may have been operating. We chose to include either indication of SA for the outcome, to maximize sensitivity, considering that some SAs would only be ascertainable by self-report if medical attention was not sought. An additional potential shortcoming is that soldiers' reporting of parental history may be inaccurate.

Another possible limitation is the distinction in methods used to ascertain lifetime history of non-suicidal self-injury (NSSI) and SA. For the former, we relied exclusively on self-report whereas for the latter we used a combination of self-report or medical records. This approach may

have resulted in some misclassification for either outcome but is of even greater concern when relying solely on medical records (Randall et al., 2017).

This study was not designed to test if SA-PRS would predict *new-onset* SA among soldiers who did not report SA at baseline; the number of new-onset cases was insufficient to provide adequate statistical power for that analysis. Nevertheless, it will be crucial to demonstrate, in future prospective studies, whether SA- (or other) PRS offer predictive value in this regard. Lastly, our analyses focused solely on individuals of European ancestry (Peterson et al., 2019), given the known limitations of extending PRS from European to other ancestral groups. New approaches hold promise as a solution to this limitation (Marnetto et al., 2020; Hujoel et al., 2022; Ruan et al., 2022) and could be applied to this and other samples in the future.

Twin and other genetically informative studies suggest that SA is moderately (17 %) heritable (Fu et al., 2002), and that parental mental illness explains almost half of the genetic transmission of SA (Kendler et al., 2020). Studies of familial transmission of suicidal behavior have shown that in addition to parents, other first- and second-degree relatives contribute to familial risk, and it is likely that our SA-PRS is detecting some of this risk (Brent et al., 2015). The largest GWAS of SA to date has found a SNP-based heritability of approximately 6 % (Docherty et al., 2023). As genomic studies of suicide attempts increase in size and power, we expect that PRS for SA will incrementally improve in their predictive utility over and above other sociodemographic and life (and combat) stress measures that frequently enter into SA predictive models (Kessler et al., 2020). Recent GWAS findings related to suicidal thoughts and behaviors (Mirza et al., 2022; Kimbrel et al., 2022; Kimbrel et al., 2023) are also anticipated to result in PRS that can help with prediction of other important suicide-related traits beyond suicide attempts.

Much work needs to be done to demonstrate the clinical utility of PRS outside of the military setting. Given the magnitude of variance predicted by the current PRS, these are highly unlikely to be of clinical utility. Importantly, prospective longitudinal study designs are needed to determine if PRS can contribute to the prediction of new (or recurrent) suicide attempts. Given the fact that 50–60 % of people do not disclose their suicidal ideation and behavior to others (Hallford et al., 2023), PRS for SA may have a role to play in identifying those non-disclosing individuals at-risk for SA. Any applications of PRS for this purpose will need to tread carefully, balancing the ethical issues of an individual's rights to privacy with medicine's aims of preserving life (Docherty et al., 2021).

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CRediT authorship contribution statement

Murray B. Stein: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **Sonia Jain:** Formal analysis, Methodology, Supervision. **Santiago Papini:** Formal analysis, Investigation, Methodology. **Laura Campbell-Sills:** Conceptualization, Investigation, Writing – review & editing. **Karmel W. Choi:** Conceptualization, Data curation, Investigation, Methodology, Writing – review & editing. **Brian Martis:** Investigation, Writing – review & editing. **Xiaoying Sun:** Data curation, Formal analysis. **Feng He:** Data curation, Formal analysis. **Erin B. Ware:** Investigation, Methodology, Writing – review & editing. **James A. Naifeh:** Methodology, Writing – review & editing. **Pablo A. Aliaga:** Data curation. **Tian Ge:** Conceptualization, Methodology, Writing – review & editing. **Jordan W. Smoller:** Investigation, Methodology, Writing – original draft. **Joel Gelernter:** Formal analysis, Investigation, Methodology, Writing – review & editing. **Ronald C. Kessler:** Conceptualization, Investigation, Methodology, Writing – original draft. **Robert J. Ursano:** Funding acquisition, Investigation, Writing – original draft.

Declaration of competing interest

Dr. Kessler has in the past three years received support for his epidemiological studies from Sanofi Aventis; and was a consultant for Datastat, Inc., Sage Pharmaceuticals, and Takeda. Dr. Stein has in the past three years been a paid consultant for Aptinyx, BigHealth, Biogen, Bionomics, Boehringer-Ingelheim, Cerevel Therapeutics, EmpowerPharm, Engrail Therapeutics, Genentech/Roche, GW Pharma, Janssen, Jazz Pharmaceuticals, Otsuka, Oxeia Biopharmaceuticals, PureTech Health, and Sage Therapeutics. Dr. Smoller is a member of the Scientific Advisory Board of Sensorium Therapeutics (with equity), and has received grant support from Biogen, Inc., is PI of a collaborative study of the genetics of depression and bipolar disorder sponsored by 23andMe for which 23andMe provides analysis time as in-kind support but no payments. The remaining authors have no disclosures.

Acknowledgments

The Army STARRS Team consists of Co-Principal Investigators: Robert J. Ursano, MD (Uniformed Services University of the Health Sciences) and Murray B. Stein, MD, MPH (University of California San Diego and VA San Diego Healthcare System); Site Principal Investigators: Steven Heeringa, PhD (University of Michigan), James Wagner, PhD (University of Michigan) and Ronald C. Kessler, PhD (Harvard Medical School); Army liaison/consultant: Kenneth Cox, MD, MPH (US Army Public Health Center); and Other team members: Pablo A. Aliaga, MA (Uniformed Services University of the Health Sciences); COL David M. Benedek, MD (Uniformed Services University of the Health Sciences); Laura Campbell-Sills, PhD (University of California San Diego); Carol S. Fullerton, PhD (Uniformed Services University of the Health Sciences); Nancy Gebler, MA (University of Michigan); Robert K. Gifford, PhD (Uniformed Services University of the Health Sciences); Meredith House, BA (University of Michigan); Paul E. Hurwitz, MPH (Uniformed Services University of the Health Sciences); Sonia Jain, PhD (University of California San Diego); Tzu-Cheg Kao, PhD (Uniformed Services University of the Health Sciences); Lisa Lewandowski-Romps, PhD (University of Michigan); Holly Herberman Mash, PhD (Uniformed Services University of the Health Sciences);

James E. McCarroll, PhD, MPH (Uniformed Services University of the Health Sciences); James A. Naifeh, PhD (Uniformed Services University of the Health Sciences); Tsz Hin Hinz Ng, MPH (Uniformed Services University of the Health Sciences); Matthew K. Nock, PhD (Harvard University); Nancy A. Sampson, BA (Harvard Medical School); CDR Patcho Santiago, MD, MPH (Uniformed Services University of the Health Sciences); LTC Gary H. Wynn, MD (Uniformed Services University of the Health Sciences); and Alan M. Zaslavsky, PhD (Harvard Medical School).

International Suicide Genetics Consortium and Suicide Working Group of the Psychiatric Genomics Consortium (*members of both consortia are identical*) consist of:

Anna R Docherty[1,2,3], Niamh Mullins[4,5], Allison E Ashley-Koch[6], Xuejun Qin[6], Jonathan R I Coleman[7,8], Andrey Shabalin[1,2], JooEun Kang[9], Balasz Murnyak[1,2], Frank Wendt[10], Mark Adams[11], Adrian I Campos[12,13], Emily DiBlasi[1,2], Janice M Fullerton[14,15], Henry R Kranzler[16,17], Amanda Bakian[2], Eric T Monson[2], Miguel E Rentería[12,18], Consuelo Walss-Bass[19], Ole A Andreassen[20,21], Cynthia M Bulik[22,23,24], Howard J Edenberg[25,26], Ronald C Kessler[27], J John Mann[28], John I Nurnberger Jr[29,29], Giorgio Pistis[30], Fabian Streit[31], Robert J Ursano[32], Renato Polimonti[10], Michelle Dennis[33], Melanie Garrett[34], Lauren Hair[35], Philip Harvey[36], Elizabeth R Hauser[6,37], Michael A Hauser[6], Jennifer Huffman[38], Daniel Jacobson[39], Jennifer H Lindquist[40], Ravi Madduri[41], Benjamin McMahon[42], David W Oslin[43,44], Jodie Trafton[45], Swapnil Awasthi[46], Andrew W Bergen[47,48], Wade H Berrettini[49], Martin Bohus[50], Harry Brandt[51,52], Xiao Chang[53], Hsi-Chung Chen[54], Wei J Chen[54,55,56], Erik D Christensen[57,58], Steven Crawford[51,52], Scott Crow[59], Philibert Duriez[60,61], Alexis C Edwards[3], Fernando Fernández-Aranda[62], Manfred M Fichter[63,64], Olatunde Olayinka Ayinde[65], Hanga Galfalvy[66], Steven Gallinger[67], Michael Gandal[68], Philip Gorwood[60,61], Yiran Guo[53], Jonathan D Hafferty[11], Hakon Hakonarson[53,69], Katherine A Halmi[70], Akitoyo Hishimoto[71], Sonia Jain[72], Stéphane Jamain[73], Susana Jiménez-Murcia[62], Craig Johnson[74], Allan S Kaplan[75,76,77], Walter H Kaye[78], Pamela K Keel[79], James L Kennedy[75,76,77], Minsoo Kim[68], Kelly L Klump[80], Daniel F Levey[81,82], Dong Li[53], Shih-Cheng Liao[54], Klaus Lieb[83], Lisa Lilenfeld[84], Adriana Lori[85], Pierre J Magistretti[86,87], Christian R Marshall[88], James E Mitchell[89], Richard M Myers[90], Satoshi Okazaki[91], Ikuo Otsuka[66,91], Dalila Pinto[4,5], Abigail Powers[85], Nicolas Ramoz[61], Stephan Ripke[46,92,93], Stefan Roepke[94], Vsevolod Rozanov[95,96], Stephen W Scherer[97,98], Christian Schmahl[50], Marcus Sokolowski[99], Anna Starnawska[100,101,102,103], Michael Strober[104,105], Mei-Hsin Su[56], Laura M Thornton[24], Janet Treasure[106,107], Erin B Ware[108,109], Hunna J Watson[24,110,111], Stephanie H Witt[31], D Blake Woodside[76,77,112,113], Zeynep Yilmaz[24,114,115], Lea Zillich[31], Rolf Adolfsson[116], Ingrid Agartz[117,118,119], Tracy M Air[120], Martin Alda[121,122], Lars Alfredsson[123,124], Adebayo Anjorin[125], Vivek Appadurai[126,127], María Soler Artigas[128,129,130,131], Sandra Van der Auwera[132,133], M Helena Azevedo[134], Nicholas Bass[135], Claiton HD Bau[136,137], Bernhard T Baune[138,139], Frank Bellivier[140,141,142,143], Klaus Berger[144], Joanna M Biernacka[145], Tim B Bigdeli[3,146], Elisabeth B Binder[85,147], Michael Boehnke[148], Marco P Boks[149], Rosa Bosch[128,129,150], David L Braff[151], Richard Bryant[152], Monika Budde[153], Enda M Byrne[13,154], Wiepke Cahn[155], Miguel Casas[128,129,131,150], Enrique Castelao[30], Jorge A Cervilla[156], Boris Chaumette[157,158,159], Sven Cichon[160,161,162,163], Aiden Corvin[164], Nicholas Craddock[165], David Craig[166], Franziska Degenhardt[163], Srdjan Djurovic[167,168], Ayman H Fanous[3,146], Jerome C Foo[169], Andreas J Forstner[160,163,170], Mark Frye[171], Justine M Gatt[14,152], Pablo V Gejman[172,173], Ina Giegling[174], Hans J Grabe[132,133], Melissa J Green[14,176], Eugenio H Grevet[177,178], Maria Grigoroiu-Serbanescu[179], Blanca Gutierrez[180], Jose Guzman-Parra[181], Steven P Hamilton[182], Marian L Hamshere[165], Annette M Hartmann[175]Joanna Hauser[183], Stefanie Heilmann-Heimbach[163], Per Hoffmann[161,162,163], Marcus Ising[184], Ian Jones[165], Lisa A Jones[185], Lina Jonsson[186], René S Kahn[5,187], John R Kelsoe[151,188], Kenneth S Kendler[3], Stefan Kloiber[75,184,189], Karestan C Koenen[92,190,191], Manolis Kogevinas[192], Bettina Konte[175], Marie-Odile Krebs[157,158,159], Mikael Landén[22,193], Jacob Lawrence[194], Marion Leboyer[195,196,197], Phil H Lee[92,93,198], Douglas F Levinson[199], Calwing Liao[200,201], Jolanta Lissowska[202], Susanne Lucae[184], Fermin Mayoral[181], Susan L McElroy[203], Patrick McGrath[204], Peter McGuffin[8], Andrew McQuillin[135], Divya Mehta[205,206], Ingrid Melle[20,207], Yuri Milaneschi[208], Philip B Mitchell[176], Esther Molina[209], Gunnar Morken[210,211], Preben Bo Mortensen[101,114,127,212], Bertram Müller-Myhsok[147,213,214], Caroline Nievergelt[151], Vishwajit Nimgaonkar[215], Markus M Nöthen[163], Michael C O'Donovan[165], Roel A Ophoff[68,216], Michael J Owen[165], Carlos Pato[217,217], Michele T Pato[218], Brenda WJH Penninx[219], Jonathan Pimm[135], James B Potash[220], Robert A Power[8,221,222], Martin Preisig[30], Digby Quested[223], Josep Antoni Ramos-Quiroga[128,129,131,150], Andreas Reif[224], Marta Ribasés[128,129,130,131], Vanesa Richarte[128,129,150], Marcella Rietschel[225], Margarita Rivera[8,226], Andrea Roberts[227], Gloria Roberts[176], Guy A Rouleau[228,229], Diego L Rovaris[230], Dan Rujescu[175], Cristina Sánchez-Mora[128,129,130,131], Alan R Sanders[172,173], Peter R Schofield[14,15], Thomas G Schulze[153,169,231,232,233], Laura J Scott[148], Alessandro Serretti[234], Giuseppe Fanelli[234, 235], Jianxin Shi[236], Stanley I Shyn[237], Lea Sirignano[169], Pamela Sklar[4,5], Olav B Smeland[20,21], Jordan W Smoller[92,191,238], Edmund J S Sonuga-Barke[239], Gianfranco Spalletta[240,241], John S Strauss[75,189], Beata Świątkowska[242], Maciej Trzaskowski[13], Ming T Tsuang[243], Gustavo Turecki[244], Laura Vilar-Ribó[128,131], John B Vincent[245], Henry Völzke[246], James TR Walters[165], Cynthia Shannon Weickert[14,176], Thomas W Weickert[14,176], Myrna M Weissman[247,248], Leanne M Williams[249], Naomi R Wray[13,206], Clement C Zai[92,189,190,250,251,252], Esben Agerbo[114,212,253], Anders D Børglum[100,101,102,103], Gerome Breen[7,8], Ditte Demontis[100,101,102,103], Annette Erlangsen[103,254,255,256], Tõnu Esko[257,258], Joel Gelernter[81,82], Stephen J Glatt[259], David M Hougaard[253,260], Hai-Gwo Hwu[261], Po-Hsiu Kuo[54,56], Cathryn M Lewis[8,262], Qingqin S Li[263], Chih-Min Liu[54], Nicholas G Martin[12], Andrew M McIntosh[11], Sarah E Medland[12], Ole Mors[253,264], Merete Nordentoft[253,265], Catherine M Olsen[266], David Porteous[267], Daniel J Smith[268], Eli A Stahl[4,257,269], Murray B Stein[270], Danuta Wasserman[99], Thomas Werge[126,253,271,272], David C Whiteman[266], Virginia Willour[273], the VA Million Veteran Program (MVP), the MVP Suicide Exemplar Workgroup, Suicide Working Group of the Psychiatric Genomics Consortium, Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium, Bipolar Disorder Working Group of the Psychiatric Genomics Consortium, Schizophrenia Working Group of the Psychiatric Genomics Consortium, Eating Disorder Working Group of the Psychiatric Genomics Consortium, German Borderline Genomics Consortium, Hilary Coon[1,2,274], Jean C Beckham[275,276], Nathan A Kimbrel[275,276], Douglas M Ruderfer[9,277,278].

[1] Huntsman Mental Health Institute, Salt Lake City, UT, USA

[2] University of Utah School of Medicine, Department of Psychiatry, Salt Lake City, UT, USA

[3] Virginia Commonwealth University, Department of Psychiatry, Richmond, VA, USA

[4] Icahn School of Medicine at Mount Sinai, Department of Genetics and Genomic Sciences, New York, NY, USA

[5] Icahn School of Medicine at Mount Sinai, Department of Psychiatry, New York, NY, USA

[6] Duke University Medical Center, Duke Molecular Physiology Institute, Durham, NC, USA

[7] King's College London, National Institute for Health Research (NIHR) Maudsley Biomedical Research Centre at South London and Maudsley NHS Foundation Trust, London, UK

[8] King's College London, Social Genetic and Developmental Psychiatry Centre, London, UK

[9] Vanderbilt University Medical Center, Division of Genetic Medicine, Department of Medicine, Vanderbilt Genetics Institute, Nashville, TN, USA

[10] Yale University School of Medicine, Department of Psychiatry, New Haven, CT, USA

[11] University of Edinburgh, Division of Psychiatry, Edinburgh, UK

[12] QIMR Berghofer Medical Research Institute, Mental Health and Neuroscience Research Program, Brisbane, QLD, Australia

[13] The University of Queensland, Institute for Molecular Bioscience, Brisbane, QLD, Australia
[14] Neuroscience Research Australia, Sydney, NSW, Australia
[15] University of New South Wales, School of Medical Sciences, Sydney, NSW, Australia
[16] University of Pennsylvania Perelman School of Medicine, Department of Psychiatry, Philadelphia, PA, USA
[17] Crescenz VAMC, VISN 4 MIRECC, Philadelphia, PA, USA
[18] The University of Queensland, School of Biomedical Sciences, Faculty of Medicine, Brisbane, QLD, Australia
[19] University of Texas Health Science Center, Department of Psychiatry and Behavioral Sciences, Houston, TX, USA
[20] Oslo University Hospital, Division of Mental Health and Addiction, Oslo, Norway
[21] University of Oslo, NORMENT, Oslo, Norway
[22] Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden
[23] University of North Carolina at Chapel Hill, Department of Nutrition, Chapel Hill, NC, USA
[24] University of North Carolina at Chapel Hill, Department of Psychiatry, Chapel Hill, NC, USA
[25] Indiana University, Department of Medical & Molecular Genetics, Indianapolis, IN, USA
[26] Indiana University School of Medicine, Biochemistry and Molecular Biology, Indianapolis, IN, USA
[27] Harvard Medical School, Department of Health Care Policy, Boston, MA, USA
[28] Columbia University, Departments of Psychiatry and Radiology, New York, NY, USA
[29] Indiana University School of Medicine, Departments of Psychiatry and Medical and Molecular Genetics, Indianapolis, IN, USA
[30] Lausanne University Hospital and University of Lausanne, Department of Psychiatry, Lausanne, Vaud, Switzerland
[31] Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Department of Genetic Epidemiology in Psychiatry, Mannheim, Germany
[32] Uniformed Services University of the Health Sciences, Department of Psychiatry, Bethesda, MD, USA
[33] Duke University Medical Center, Department of Psychiatry and Behavioral Sciences, Durham, NC, USA
[34] Duke University Medical Center, Durham, NC, USA
[35] Durham Veterans Affairs Health Care System, Durham, NC, USA
[36] Miami VA Health Care System, Miami, FL, USA
[37] Durham Veterans Affairs Health Care System, Cooperative Studies Program Epidemiology Center, Durham, NC, USA
[38] Boston VA Health Care System, Boston, MA, USA
[39] Oak Ridge National Laboratory, Oak Ridge, TN, USA
[40] Durham Veterans Affairs Health Care System, VA Health Services Research and Development Center of Innovation to Accelerate Discovery and Practice Transformation, Durham, NC, USA
[41] Argonne National Laboratory, University of Chicago Consortium for Advanced Science and Engineering, Chicago, IL, USA
[42] Los Alamos National Laboratory, Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM, USA
[43] Corporal Michael J. Crescenz VA Medical Center, VISN 4 Mental Illness Research, Education, and Clinical Center, Philadelphia, PA, USA
[44] Perelman School of Medicine, University of Pennsylvania, Department of Psychiatry, Philadelphia, PA, USA
[45] VA Palo Alto Health Care System, VA Program Evaluation and Resource Center, Palo Alto, CA, USA
[46] Charité - Universitätsmedizin Berlin, Department of Psychiatry and Psychotherapy, Berlin, Germany
[47] BioRealm, LLC, Walnut, CA, USA
[48] Oregon Research Institute, Eugene, OR, USA
[49] Perelman School of Medicine at the University of Pennsylvania, Department of Psychiatry, Center for Neurobiology and Behavior, Philadelphia, PA, USA
[50] Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Department of Psychosomatic Medicine and Psychotherapy, Mannheim, Germany
[51] ERCPathlight, Baltimore, MD, USA
[52] University of Maryland St. Joseph Medical Center, Baltimore, MD, USA
[53] Children's Hospital of Philadelphia, Center for Applied Genomics, Philadelphia, PA, USA
[54] National Taiwan University Hospital, Department of Psychiatry, Taipei, Taiwan
[55] National Health Research Institutes, Center for Neuropsychiatric Research, Miaoli County, Taiwan
[56] National Taiwan University, Institute of Epidemiology and Preventive Medicine, College of Public Health, Taipei, Taiwan
[57] Utah Department of Health and Human Services, Utah Office of the Medical Examiner, Taylorsville, UT, USA
[58] University of Utah, Department of Pathology, Salt Lake City, UT, USA
[59] University of Minnesota, Department of Psychiatry, Minneapolis, MN, USA
[60] GHU Paris Psychiatrie et Neurosciences, Hôpital Sainte Anne, Paris, France
[61] Université Paris Cité, Institute of Psychiatry and Neuroscience of Paris (IPNP), INSERM U1266, Paris, France
[62] University Hospital Bellvitge-IDIBELL and CIBEROBN, Department of Psychiatry, Barcelona, Spain
[63] Ludwig-Maximilians-University (LMU), Department of Psychiatry and Psychotherapy, Munich, Germany
[64] Schön Klinik Roseneck affiliated with the Medical Faculty of the University of Munich (LMU), Munich, Germany
[65] Department of Psychiatry, University of Ibadan, Ibadan, Nigeria.
[66] Columbia University, Department of Psychiatry, New York, NY, USA
[67] University of Toronto, Department of Surgery, Faculty of Medicine, Toronto, Canada
[68] University of California, Los Angeles, Department of Psychiatry and Biobehavioral Science, Semel Institute, David Geffen School of Medicine, Los Angeles, CA, USA
[69] University of Pennsylvania, The Perelman School of Medicine, Philadelphia, PA, USA
[70] Weill Cornell Medical College, Department of Psychiatry, New York, NY, USA
[71] Yokohama City University Graduate School of Medicine, Department of Psychiatry, Yokohama, Japan
[72] University of California San Diego, Biostatistics Research Center, Herbert Wertheim School of Public Health and Human Longevity Science, La Jolla, CA, USA
[73] Univ Paris-Est-Créteil, INSERM, IMRB, Translational Neuropsychiatry, Fondation FondaMental, Créteil, France
[74] Eating Recovery Center, Denver, CO, USA
[75] Centre for Addiction and Mental Health, Toronto, ON, Canada
[76] University of Toronto, Department of Psychiatry, Toronto, Canada
[77] University of Toronto, Institute of Medical Science, Toronto, Canada
[78] University of California San Diego, Department of Psychiatry, San Diego, CA, USA
[79] Florida State University, Department of Psychology, Tallahassee, FL, USA
[80] Michigan State University, Department of Psychology, Lansing, MI, USA
[81] Veterans Affairs Connecticut Healthcare Center, Department of Psychiatry, West Haven, CT, USA
[82] Yale University School of Medicine, Division of Human Genetics, Department of Psychiatry, New Haven, CT, USA
[83] University Medical Center, Department of Psychiatry and

Psychotherapy, Mainz, Germany
[84] The Chicago School of Professional Psychology, Washington DC, Department of Clinical Psychology, Washington, DC, USA
[85] Emory University School of Medicine, Department of Psychiatry and Behavioral Sciences, Atlanta, GA, USA
[86] King Abdullah University of Science and Technology, BESE Division, Thuwal, Saudi Arabia
[87] University of Lausanne-University Hospital of Lausanne (UNIL-CHUV), Department of Psychiatry, Lausanne, Switzerland
[88] The Hospital for Sick Children, Department of Paediatric Laboratory Medicine, Toronto, Canada
[89] University of North Dakota School of Medicine and Health Sciences, Department of Psychiatry and Behavioral Science, Fargo, ND, USA
[90] HudsonAlpha Institute for Biotechnology, Huntsville, AL, USA
[91] Kobe University Graduate School of Medicine, Department of Psychiatry, Kobe, Japan
[92] Broad Institute, Stanley Center for Psychiatric Research, Cambridge, MA, USA
[93] Massachusetts General Hospital, Analytical and Translational Genetics Unit, Boston, MA, USA
[94] Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin Institute of Health, Campus Benjamin Franklin, Department of Psychiatry, Berlin, Germany
[95] Saint-Petersburg State University, Department of Psychology, Saint-Petersburg, Russian Federation
[96] V.M. Bekhterev National Medical Research Center for Psychiatry and Neurology, Department of Borderline Disorders and Psychotherapy, Saint-Petersburg, Russian Federation
[97] The Hospital for Sick Children, Department of Genetics and Genomic Biology, Toronto, Canada
[98] University of Toronto, McLaughlin Center, Toronto, Canada
[99] Karolinska Institutet, National Centre for Suicide Research and Prevention of Mental Ill-Health (NASP), LIME, Stockholm, Sweden
[100] Aarhus University, Centre for Genomics and Personalized Medicine, CGPM, Aarhus, Denmark
[101] Aarhus University, Centre for Integrative Sequencing, iSEQ, Aarhus, Denmark
[102] Aarhus University, Department of Biomedicine, Aarhus, Denmark
[103] Aarhus University, The Lundbeck Foundation Initiative for Integrative Psychiatric Research, iPSYCH, Aarhus, Denmark
[104] University of California Los Angeles, David Geffen School of Medicine, Los Angeles, LA, USA
[105] University of California Los Angeles, Department of Psychiatry and Biobehavioral Science, Semel Institute for Neuroscience and Human Behavior, Los Angeles, LA, USA
[106] King's College London, Institute of Psychiatry, Psychology and Neuroscience, Department of Psychological Medicine, London, UK
[107] King's College London and South London and Maudsley National Health Service Foundation Trust, National Institute for Health Research Biomedical Research Centre, London, UK
[108] University of Michigan, Population Studies Center, Institute for Social Research, Ann Arbor, MI, USA
[109] University of Michigan, Survery Research Center, Institute for Social Research, Ann Arbor, MI, USA
[110] Curtin University, School of Psychology, Perth, Western Australia, Australia
[111] The University of Western Australia, Division of Paediatrics, Perth, Western Australia, Australia
[112] University Health Network, Centre for Mental Health, Toronto, Canada
[113] University Health Network, Program for Eating Disorders, Toronto, Canada
[114] Aarhus University, National Centre for Register-Based Research, Aarhus, Denmark
[115] University of North Carolina at Chapel Hill, Department of Genetics, Chapel Hill, NC, USA
[116] Umeå University Medical Faculty, Department of Clinical Sciences, Psychiatry, Umeå, Sweden
[117] Diakonhjemmet Hospital, Department of Psychiatric Research, Oslo, Norway
[118] Karolinska Institutet, Department of Clinical Neuroscience, Centre for Psychiatry Research, Stockholm, Sweden
[119] University of Oslo, NORMENT, Institute of Clinical Medicine, Oslo, Norway
[120] University of Adelaide, Discipline of Psychiatry, Adelaide, SA, Australia
[121] Dalhousie University, Department of Psychiatry, Halifax, NS, Canada
[122] National Institute of Mental Health, Klecany, CZ
[123] Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden
[124] Karolinska Institutet, Inst of Environmental Medicine, Stockholm, Sweden
[125] Berkshire Healthcare NHS Foundation Trust, Psychiatry, Bracknell, UK
[126] Copenhagen University Hospital, Institute of Biological Psychiatry, Copenhagen Mental Health Services, Copenhagen, Denmark
[127] iPSYCH, The Lundbeck Foundation Initiative for Integrative Psychiatric Research, Copenhagen, Denmark
[128] Hospital Universitari Vall d'Hebron, Department of Psychiatry, Barcelona, Spain
[129] Instituto de Salud Carlos III, Biomedical Network Research Centre on Mental Health (CIBERSAM), Madrid, Spain
[130] University of Barcelona, Department of Genetics, Microbiology & Statistics, Barcelona, Spain
[131] Vall d'Hebron Research Institute (VHIR), Universitat Autònoma de Barcelona, Psychiatric Genetics Unit, Group of Psychiatry, Mental Health and Addiction, Barcelona, Spain
[132] University Medicine Greifswald, Department of Psychiatry and Psychotherapy, Greifswald, Mecklenburg-Vorpommern, Germany
[133] German Centre for Neurodegenerative Diseases (DZNE), Partner Site Rostock/Greifswald, Greifswald, Mecklenburg-Vorpommern, Germany
[134] University of Coimbra, Department of Psychiatry, Coimbra, Portugal
[135] University College London, Division of Psychiatry, London, UK
[136] Hospital de Clínicas de Porto Alegre, Laboratory of Developmental Psychiatry, Porto Alegre, RS, Brazil
[137] Universidade Federal do Rio Grande do Sul, Department of Genetics, Porto Alegre, RS, Brazil
[138] University of Melbourne, Department of Psychiatry, Melbourne Medical School, Melbourne, Australia
[139] University of Münster, Department of Psychiatry, Münster, Germany
[140] Assistance Publique - Hôpitaux de Paris, Department of Psychiatry and Addiction Medicine, Paris, France
[141] FondaMental Foundation, Paris Bipolar and TRD Expert Centres, Paris, France
[142] INSERM, UMR-S1144 Team 1: Biomarkers of relapse and therapeutic response in addiction and mood disorders, Paris, France
[143] Université Paris Cité, Psychiatry, Paris, France
[144] University of Münster, Institute of Epidemiology and Social Medicine, Münster, Nordrhein-Westfalen, Germany
[145] Mayo Clinic, Health Sciences Research, Rochester, MN, USA
[146] State University of New York Downstate Medical Center, Department of Psychiatry and Behavioral Sciences, New York, NY, USA
[147] Max Planck Institute of Psychiatry, Department of Translational Research in Psychiatry, Munich, Germany
[148] University of Michigan, Center for Statistical Genetics and Department of Biostatistics, Ann Arbor, MI, USA

[149] UMC Utrecht Brain Center, Psychiatry, Utrecht, Netherlands
[150] Universitat Autònoma de Barcelona, Department of Psychiatry and Legal Medicine, Barcelona, Spain
[151] University of California San Diego, Department of Psychiatry, La Jolla, CA, USA
[152] University of New South Wales, School of Psychology, Sydney, NSW, Australia
[153] University Hospital, LMU Munich, Institute of Psychiatric Phenomics and Genomics (IPPG), Munich, Germany
[154] The University of Queensland, Child Health Research Centre, Brisbane, QLD, Australia
[155] UMC Utrecht Hersencentrum Rudolf Magnus, Department of Psychiatry, Utrecht, Netherlands
[156] University of Granada, Mental Health Unit, Department of Psychiatry, Faculty of Medicine, Granada University Hospital Complex, Granada, Spain
[157] CNRS GDR 3557, Institut de Psychiatrie, Paris, France
[158] GHU Paris Psychiatrie et Neurosciences, Department of Evaluation, Prevention and Therapeutic innovation, Paris, France
[159] Université de Paris, Institute of Psychiatry and Neuroscience of Paris (IPNP), INSERM U1266, Team Pathophysiology of psychiatric diseases, Paris, France
[160] Research Centre Jülich, Institute of Neuroscience and Medicine (INM-1), Jülich, Germany
[161] University Hospital Basel, Institute of Medical Genetics and Pathology, Basel, Switzerland
[162] University of Basel, Department of Biomedicine, Basel, Switzerland
[163] University of Bonn, School of Medicine & University Hospital Bonn, Institute of Human Genetics, Bonn, Germany
[164] Trinity College Dublin, Neuropsychiatric Genetics Research Group, Dept of Psychiatry and Trinity Translational Medicine Institute, Dublin, Ireland
[165] Cardiff University, Medical Research Council Centre for Neuropsychiatric Genetics and Genomics, Division of Psychological Medicine and Clinical Neurosciences, Cardiff, UK
[166] University of Southern California, Department of Translational Genomics, Pasadena, CA, USA
[167] Oslo University Hospital, Department of Medical Genetics, Oslo, Norway
[168] University of Bergen, NORMENT, Department of Clinical Science, Bergen, Norway[169] Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Department of Genetic Epidemiology in Psychiatry, Mannheim, Germany
[170] University of Marburg, Centre for Human Genetics, Marburg, Germany
[171] Mayo Clinic, Department of Psychiatry & Psychology, Rochester, MN, USA
[172] NorthShore University HealthSystem, Department of Psychiatry and Behavioral Sciences, Evanston, IL, USA
[173] University of Chicago, Department of Psychiatry and Behavioral Neuroscience, Chicago, IL, USA
[174] Comprehensive Center for Clinical Neurosciences and Mental Health (C3NMH), Medical University of Vienna, Austria.
[175] Medical University of Vienna, Department of Psychiatry and Psychotherapy, Vienna, Austria.
[176] University of New South Wales, School of Psychiatry, Sydney, NSW, Australia
[177] Hospital de Clínicas de Porto Alegre, ADHD Outpatient Program, Adult Division, Porto Alegre, RS, Brazil
[178] Universidade Federal do Rio Grande do Sul, Department of Psychiatry, Porto Alegre, RS, Brazil
[179] Alexandru Obregia Clinical Psychiatric Hospital, Biometric Psychiatric Genetics Research Unit, Bucharest, Romania
[180] University of Granada, Department of Psychiatry, Faculty of Medicine and Biomedical Research Centre (CIBM), Granada, Spain
[181] University Regional Hospital. Biomedicine Institute (IBIMA), Mental Health Department, Málaga, Spain
[182] Kaiser Permanente Northern California, Psychiatry, San Francisco, CA, USA
[183] Poznan University of Medical Sciences, Psychiatric Genetics, Department of Psychiatry, Poznan, Poland
[184] Max Planck Institute of Psychiatry, Munich, Germany
[185] University of Worcester, Department of Psychological Medicine, Worcester, UK
[186] University of Gothenburg, Department of Psychiatry and Neuroscience, Gothenburg, Sweden
[187] UMC Utrecht Brain Center Rudolf Magnus, Psychiatry, Utrecht, Netherlands
[188] University of California San Diego, Institute for Genomic Medicine, La Jolla, CA, USA
[189] University of Toronto, Department of Psychiatry, Toronto, ON, Canada
[190] Harvard TH Chan School of Public Health, Department of Epidemiology, Boston, MA, USA
[191] Massachusetts General Hospital, Department of Psychiatry, Boston, MA, USA
[192] Center for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
[193] University of Gothenburg, Institute of Neuroscience and Physiology, Gothenburg, Sweden
[194] North East London NHS Foundation Trust, Psychiatry, Ilford, UK
[195] Univ Paris Est Créteil, INSERM, AP-HP, IMRB, Translational Neuropsychiatry, DMU IMPACT, FHU ADAPT, Fondation FondaMental, Créteil, France
[196] INSERM, Paris, France
[197] Université Paris Est, Faculté de Médecine, Créteil, France
[198] Massachusetts General Hospital, Psychiatric and Neurodevelopmental Genetics Unit, Boston, MA, USA
[199] Stanford University, Psychiatry & Behavioral Sciences, Stanford, CA, USA
[200] Broad Institute of MIT and Harvard, Stanley Center for Psychiatric Research, Cambridge, MA, USA
[201] Massachusetts General Hospital, Analytical and Translational Genetics Unit, Cambridge, MA, USA
[202] M. Sklodowska-Curie Cancer Center and Institute of Oncology, Cancer Epidemiology and Prevention, Warsaw, Poland
[203] Lindner Center of HOPE, Research Institute, Mason, OH, USA
[204] Columbia University College of Physicians and Surgeons, Psychiatry, New York, NY, USA
[205] Queensland University of Technology, School of Psychology and Counseling, Brisbane, QLD, Australia
[206] The University of Queensland, Queensland Brain Institute, Brisbane, QLD, Australia
[207] University of Oslo, Institute of Clinical Medicine, Division of Mental Health and Addiction, Oslo, Norway
[208] Amsterdam UMC, Vrije Universiteit and GGZ inGeest, Department of Psychiatry, Amsterdam, Netherlands
[209] University of Granada, Department of Nursing, Faculty of Health Sciences and Biomedical Research Centre (CIBM), Granada, Spain
[210] Norwegian University of Science and Technology - NTNU, Mental Health, Faculty of Medicine and Health Sciences, Trondheim, Norway
[211] St Olavs University Hospital, Psychiatry, Trondheim, Norway
[212] Aarhus University, Centre for Integrated Register-based Research, Aarhus, Denmark
[213] Munich Cluster for Systems Neurology (SyNergy), Munich, Germany
[214] University of Liverpool, Liverpool, UK
[215] University of Pittsburgh, Psychiatry and Human Genetics, Pittsburgh, PA, USA
[216] Erasmus University Medical Center, Psychiatry, Rotterdam, Netherlands

[217] Rutgers University, RWJMS, NJMS, UBHC, Pisctatway, NJ, USA
[218] Rutgers University, RWJMS, NJMS, Pisctatway, NJ, USA
[219] Amsterdam UMC, Vrije Universiteit, Department of Psychiatry and Amsterdam Neuroscience, Amsterdam, Netherlands
[220] Johns Hopkins University School of Medicine, Psychiatry, Baltimore, MD, USA
[221] BioMarin Pharmaceuticals, Genetics, London, UK
[222] University of Oxford, St Edmund Hall, Oxford, UK
[223] University of Oxford, Department of Psychiatry, Oxford, UK
[224] University Hospital Frankfurt, Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, Frankfurt, Germany
[225] Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Department of Genetic Epidemiology in Psychiatry, Mannheim, Baden-Württemberg, Germany
[226] University of Granada, Department of Biochemistry and Molecular Biology II and Institute of Neurosciences, Biomedical Research Centre (CIBM), Granada, Spain
[227] Harvard TH Chan School of Public Health, Department of Environmental Health, Boston, MA, USA
[228] McGill University, Faculty of Medicine, Department of Neurology and Neurosurgery, Montreal, QC, Canada
[229] Montreal Neurological Institute and Hospital, Montreal, QC, Canada
[230] Instituto de Ciencias Biomedicas Universidade de Sao Paulo, Department of Physiology and Biophysics, São Paulo, SP, Brazil
[231] Johns Hopkins University School of Medicine, Department of Psychiatry and Behavioral Sciences, Baltimore, MD, USA
[232] National Institute of Mental Health, Human Genetics Branch, Intramural Research Program, Bethesda, MD, USA
[233] University Medical Center Göttingen, Department of Psychiatry and Psychotherapy, Göttingen, Germany
[234] University of Bologna, Department of Biomedical and Neuro-Motor Sciences, Bologna, Italy
[235] Department of Human Genetics and Donders Institute for Brain, Cognition and Behavior, Radboud University, Nijmegen, The Netherlands.
[236] National Cancer Institute, Division of Cancer Epidemiology and Genetics, Bethesda, MD, USA.
[237] Kaiser Permanente Washington, Behavioral Health Services, Seattle, WA, USA
[238] Massachusetts General Hospital, Psychiatric and Neurodevelopmental Genetics Unit (PNGU), Boston, MA, USA
[239] King's College London, Institute of Psychology, Psychiatry & Neuroscience, London, UK
[240] Baylor College of Medicine, Houston, Menninger Department of Psychiatry and Behavioral Sciences, Houston, TX, USA
[241] IRCCS Santa Lucia Foundation, Rome, Laboratory of Neuropsychiatry, Rome, Italy
[242] Nofer Institute of Occupational Medicine, Department of Environmental Epidemiology, Lodz, Poland
[243] University of California, San Diego, Center for Behavioral Genomics, Department of Psychiatry, La Jolla, CA, USA
[244] McGill University, Department of Psychiatry, Montreal, QC, Canada
[245] Centre for Addiction and Mental Health, Molecular Brain Science, Toronto, ON, Canada
[246] University Medicine Greifswald, Institute for Community Medicine, Greifswald, Mecklenburg-Vorpommern, Germany
[247] Columbia University College of Physicians and Surgeons, New York, NY, USA
[248] New York State Psychiatric Institute, Division of Translational Epidemiology, New York, NY, USA
[249] Stanford University, Department of Psychiatry and Behavioral Sciences, Stanford, CA, USA
[250] University of Toronto, Institute of Medical Science, Toronto, ON, Canada
[251] Centre for Addiction and Mental Health, Molecular Brain Science, Campbell Family Mental Health Research Institute, Toronto, ON, Canada
[252] University of Toronto, Laboratory Medicine and Pathobiology, Toronto, ON, Canada
[253] iPSYCH, The Lundbeck Foundation Initiative for Integrative Psychiatric Research, Aarhus, Denmark
[254] Australian National University, Center of Mental Health Research, Canberra, Australia
[255] Johns Hopkins Bloomberg School of Public Health, Department of Mental Health, Baltimore, MD, USA
[256] Mental Health Centre Copenhagen, Danish Research Institute for Suicide Prevention, Copenhagen, Denmark
[257] Broad Institute, Program in Medical and Population Genetics, Cambridge, MA, USA
[258] University of Tartu, Estonian Genome Center, Institute of Genomics, Tartu, Estonia
[259] SUNY Upstate Medical University, Department of Psychiatry and Behavioral Sciences, Syracuse, NY, USA
[260] Statens Serum Institut, Center for Neonatal Screening, Department for Congenital Disorders, Copenhagen, Denmark
[261] National Taiwan University Hospital and College of Medicine, Department of Psychiatry, Taipei, Taiwan
[262] King's College London, Department of Medical & Molecular Genetics, London, UK
[263] Janssen Research & Development, LLC, Neuroscience, Titusville, NJ, USA
[264] Aarhus University Hospital, Risskov, Psychosis Research Unit, Aarhus, Denmark
[265] Copenhagen University Hospital, Mental Health Center Copenhagen, Copenhagen, Denmark
[266] QIMR Berghofer Medical Research Institute, Department of Population Health, Brisbane, QLD, Australia
[267] University of Edinburgh, Institute for Genetics and Molecular Medicine, Edinburgh, UK
[268] University of Edinburgh, Centre for Clinical Brain Sciences, Edinburgh, UK
[269] Regeneron Genetics Center, Analytical Genetics and Data Science, Tarrytown, NY, USA
[270] University of California San Diego, Department of Psychiatry and School of Public Health, La Jolla, CA, USA
[271] University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark
[272] University of Copenhagen, Lundbeck Foundation GeoGenetics Centre, GLOBE Institute, Copenhagen, Denmark
[273] University of Iowa, Department of Psychiatry, Iowa City, IA, USA
[274] University of Utah School of Medicine, Biomedical Informatics, Salt Lake City, UT, USA
[275] Durham Veterans Affairs Health Care System, VISN 6 Mid-Atlantic Mental Illness Research, Education, and Clinical Center, Durham, NC, USA
[276] Duke University School of Medicine, Department of Psychiatry and Behavioral Sciences, Durham, NC, USA
[277] Vanderbilt University Medical Center, Department of Biomedical Informatics, Nashville, TN, USA
[278] Vanderbilt University Medical Center, Department of Psychiatry and Behavioral Sciences, Nashville, TN, USA.

MVP Suicide Exemplar Workgroup consists of the following individuals: Silvia Crivelli, Ph.D. (Lawrence Berkeley National Laboratory), Michelle F. Dennis, B.A. (Durham Veterans Affairs Health Care System & Duke University School of Medicine), Phillip D. Harvey, Ph.D. (University of Miami Miller School of Medicine, Miami, FL), Bruce W. Carter (VA Medical Center), Jennifer E. Huffman, Ph.D. (Massachusetts Veterans Epidemiology Research and Information Center, VA Boston Healthcare System), Daniel Jacobson, Ph.D. (Oak Ridge National Laboratory), Ravi Madduri, Ph.D. (Argonne National Laboratory), and John

Pestian, Ph.D. (Oak Ridge National Laboratory).

VA Million Veteran Program (MVP) consists of the following individuals:

J. Michael Gaziano, M.D., M.P.H. (co-chair, VA Boston Healthcare System), Sumitra Muralidhar, Ph.D. (co-chair, U.S. Department of Veterans Affairs), Rachel Ramoni, D.M.D., Sc.D. (U.S. Department of Veterans Affairs), Jean Beckham, Ph.D. (Durham VA Medical Center), Kyong-Mi Chang, M.D. (Philadelphia VA Medical Center), Christopher J. O'Donnell, M.D., M.P.H. (VA Boston Healthcare System), Philip S. Tsao, Ph.D. (VA Palo Alto Health Care System), James Breeling, M.D. (Ex-Officio, U.S. Department of Veterans Affairs), Grant Huang, Ph.D. (Ex-Officio, U.S. Department of Veterans Affairs), and J.P. Casas Romero, M.D., Ph.D. (Ex-Officio, VA Boston Healthcare System). MVP Program Office: Sumitra Muralidhar, Ph.D., and Jennifer Moser, Ph.D., both of U.S. Department of Veterans Affairs. MVP Recruitment/Enrollment: Recruitment/Enrollment Director/Deputy Director, Boston—-Stacey B. Whitbourne, Ph.D., Jessica V. Brewer, M.P.H. (VA Boston Healthcare System). MVP Coordinating Centers: Clinical Epidemiology Research Center (CERC), West Haven—Mihaela Aslan, Ph.D. (West Haven VA Medical Center). Cooperative Studies Program Clinical Research Pharmacy Coordinating Center, Albuquerque—Todd Connor, Pharm.D., Dean P. Argyres, B.S., M.S. (New Mexico VA Health Care System). Genomics Coordinating Center, Palo Alto—Philip S. Tsao, Ph. D. (VA Palo Alto Health Care System). MVP Boston Coordinating Center, Boston—J. Michael Gaziano, M.D., M.P.H. (VA Boston Healthcare System). MVP Information Center, Canandaigua—Brady Stephens, M.S. (Canandaigua VA Medical Center). VA Central Biorepository, Boston—Mary T. Brophy, M.D., M.P.H., Donald E. Humphries, Ph.D., Luis E. Selva, Ph.D. (VA Boston Healthcare System). MVP Informatics, Boston—Nhan Do, M.D., Shahpoor Shayan (VA Boston Healthcare System). MVP Data Operations/Analytics, Boston—Kelly Cho, Ph.D. (VA Boston Healthcare System). MVP Science: Science Operations—Christopher J. O'Donnell, M.D., M.P.H. (VA Boston Healthcare System). Genomics Core— Christopher J. O'Donnell, M.D., M.P.H., Saiju Pyarajan, Ph.D. (VA Boston Healthcare System), Philip S. Tsao, Ph.D. (VA Palo Alto Health Care System). Phenomics Core—Kelly Cho, M.P.H., Ph.D. (VA Boston Healthcare System). Data and Computational Sciences—Saiju Pyarajan, Ph.D. (VA Boston Healthcare System). Statistical Genetics—Elizabeth Hauser, Ph.D. (Durham VA Medical Center). Yan Sun, Ph. D. (Atlanta VA Medical Center). Hongyu Zhao, Ph.D. (West Haven VA Medical Center. Current MVP Local Site Investigators: Peter Wilson, M. D. (Atlanta VA Medical Center); Rachel McArdle, Ph.D. (Bay Pines VA Healthcare System); Louis Dellitalia, M.D. (Birmingham VA Medical Center); Kristin Mattocks, Ph.D., M.P.H. (Central Western Massachusetts Healthcare System); John Harley, M.D., Ph.D. (Cincinnati VA Medical Center); Clement J. Zablocki (VA Medical Center); Jeffrey Whittle, M.D., M.P.H.; Frank Jacono, M.D. (VA Northeast Ohio Healthcare System); Jean Beckham, Ph.D. (Durham VA Medical Center); Edith Nourse Rogers Memorial Veterans Hospital; Salvador Gutierrez, M.D. (Edward Hines, Jr. VA Medical Center); Gretchen Gibson, D.D.S., M.P.H. (Veterans Health Care System of the Ozarks); Kimberly Hammer, Ph.D. (Fargo VA Health Care System); Laurence Kaminsky, Ph.D. (VA Health Care Upstate New York); Gerardo Villareal, M.D. (New Mexico VA Health Care System); Scott Kinlay, M.B.B.S., Ph.D. (VA Boston Healthcare System); Junzhe Xu, M.D. (VA Western New York Healthcare System); Mark Hamner, M.D. (Ralph H. Johnson VA Medical Center); Roy Mathew, M. D. (Columbia VA Health Care System); Sujata Bhushan, M.D. (VA North Texas Health Care System); Pran Iruvanti, DO, Ph.D. (Hampton VA Medical Center); Michael Godschalk, M.D. (Richmond VA Medical Center); Zuhair Ballas, M.D. (Iowa City VA Health Care System); Douglas Ivins, M.D. (Eastern Oklahoma VA Health Care System); Stephen Mastorides, M.D. (James A. Haley Veterans' Hospital); Jonathan Moorman, M.D., Ph.D. (James H. Quillen VA Medical Center); Saib Gappy, M.D. (John D. Dingell VA Medical Center); Jon Klein, M.D., Ph.D. (Louisville VA Medical Center); Nora Ratcliffe, M.D. (Manchester VA Medical Center); Hermes Florez, M.D., Ph.D. (Miami VA Health Care System); Olaoluwa Okusaga, M.D. (Michael E. DeBakey VA Medical Center); Maureen Murdoch, M.D., M.P.H. (Minneapolis VA Health Care System); Peruvemba Sriram, M.D. (N FL/S GA Veterans Health System); Shing Shing Yeh, Ph.D., M.D. (Northport VA Medical Center); Neeraj Tandon, M.D. (Overton Brooks VA Medical Center); Darshana Jhala, M.D. (Philadelphia VA Medical Center); Samuel Aguayo, M.D. (Phoenix VA Health Care System); David Cohen, M.D. (Portland VA Medical Center); Satish Sharma, M.D. (Providence VA Medical Center); Suthat Liangpunsakul, M.D., M.P.H. (Richard Roudebush VA Medical Center); Kris Ann Oursler, M.D. (Salem VA Medical Center); Mary Whooley, M.D. (San Francisco VA Health Care System); Sunil Ahuja, M.D. (South Texas Veterans Health Care System); Joseph Constans, Ph.D. (Southeast Louisiana Veterans Health Care System); Paul Meyer, M.D., Ph.D. (Southern Arizona VA Health Care System); Jennifer Greco, M.D. (Sioux Falls VA Health Care System); Michael Rauchman, M.D. (St. Louis VA Health Care System); Richard Servatius, Ph.D. (Syracuse VA Medical Center); Melinda Gaddy, Ph.D. (VA Eastern Kansas Health Care System); Agnes Wallbom, M.D., M.S. (VA Greater Los Angeles Health Care System); Timothy Morgan, M.D. (VA Long Beach Healthcare System); Todd Stapley, D.O. (VA Maine Healthcare System); Scott Sherman, M.D., M.P. H. (VA New York Harbor Healthcare System); George Ross, M.D. (VA Pacific Islands Health Care System); Philip Tsao, Ph.D. (VA Palo Alto Health Care System); Patrick Strollo Jr., M.D. (VA Pittsburgh Health Care System); Edward Boyko, M.D. (VA Puget Sound Health Care System); Laurence Meyer, M.D., Ph.D. (VA Salt Lake City Health Care System); Samir Gupta, M.D., M.S.C.S. (VA San Diego Healthcare System); Mostaqul Huq, Pharm.D., Ph.D. (VA Sierra Nevada Health Care System); Joseph Fayad, M.D. (VA Southern Nevada Healthcare System); Adriana Hung, M.D., M.P.H. (VA Tennessee Valley Healthcare System); Jack Lichy, M.D., Ph.D. (Washington, DC VA Medical Center); Robin Hurley, M.D. (W.G., Bill Hefner VA Medical Center); Brooks Robey, M.D. (White River Junction VA Medical Center); and Robert Striker, M.D., Ph. D. (William S. Middleton Memorial Veterans Hospital).

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