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THE OPPOSITE OF EMPOWERING

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ABSTRACT

Life expectancy in the United States is falling for the first time in over 70 years, due in large part to deaths caused by addiction, depression, and loneliness. However, rather than funding effective prevention and treatment of the root causes, in the United States neoliberal market forces drive the development of medical tests for their diagnosis and prediction, which will do very little to address the problem. The newest example of this comes from polygenic risk scores ("PRS") for mental health. Like other genetic tests, these tests are marketed as tools that empower individuals to combat disease.[1] In this article I explain how PRS tests alone will not empower individuals or improve population mental health. Indeed, as research demonstrates, the competition that results from capitalist markets is itself correlated with mental illness, so we cannot use the market to fight our way out of this. Finally, relying on PRS reinforces the cruel neoliberal narrative that each of us is responsible for diagnosing and treating ourselves.

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1. Eric T. Juengst, Michael A. Flatt & Richard A. Settersten, *Personalized Genomic Medicine and the Rhetoric of Empowerment*, 42 HASTINGS CTR. REP. 34, 35 (2012) ("[C]laims that, for example, 'getting to know your personal genome will empower you and provide you with a road map to improve your health' are ubiquitous.").

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Life expectancy in the US is falling for the first time in over seventy years, due in large part to deaths from suicide and drug use.[2] These deaths are now responsible for one American's death every five minutes.[3] While so-called "deaths of despair" are not exclusively caused by poverty, they are thought to have increased based on

2. *See* Dilip V. Jeste, Ellen E. Lee & Stephanie Cacioppo, *Battling the Modern Behavioral Epidemic of Loneliness: Suggestions for Research and Interventions*, 77 JAMA PSYCHIATRY 553, 553 (2020).

3. Jeste et al., *supra* note 2, at 553.

"hopelessness spawned by adverse social and economic circumstances."[4] Poverty and loneliness have been identified as key risk factors[5] for depression,[6] addiction, and suicide.[7] When we are lonely, we feel threatened, and loneliness is associated with poor physical, emotional, and cognitive functioning.[8]

In the last two decades, loneliness has increased exponentially in the United States.[9] In 2023, the Surgeon General issued a report detailing how "across many measures, Americans appear to be becoming less socially connected."[10] He identified loneliness as a public health crisis, highlighting that our networks of friends are getting smaller, we rely on them less, and we spend more time alone.[11] The epidemic of loneliness has hit older, impoverished, disabled, and single parent Americans the hardest, as communities have paid little attention to the value of building libraries, community centers, and social supports.[12]

Loneliness can be deadly.[13] Even controlling for depression, a systematic review found that loneliness is independently associated with higher risk of mortality.[14] It is believed that experiencing it activates

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4. Lilly Shanahan & William E. Copeland, *Psychiatry and Deaths of Despair*, 78 JAMA PSYCHIATRY 695, 695 (2021); *see also* Lixia Ge, Chun Wei Yap, Reuben Ong & Bee Hoon Heng, *Social Isolation, Loneliness and Their Relationships with Depressive Symptoms: A Population-Based Study*, 12 PLOS ONE, Aug. 23, 2017, at 1, 10.

5. Sofie Danneel, Flore Geukens, Marlies Maes, Margot Bastin, Patricia Bijttebier, Hilde Colpin et al., *Loneliness, Social Anxiety Symptoms, and Depressive Symptoms in Adolescence: Longitudinal Distinctiveness and Correlated Change*, 49 J. YOUTH ADOLESCENCE 2246, 2247 (2020).

6. Ge et al., *supra* note 4, at 1, 10.

7. Manfred E. Beutel, Eva M. Klein, Elmar Brähler, Iris Reiner, Claus Jünger, Matthias Michal et al., *Loneliness in the General Population: Prevalence, Determinants and Relations to Mental Health*, 17 BMC PSYCHIATRY, Mar. 20, 2017, at 6.

8. Lisa Boss, Duck-Hee Kang & Sandy Branson, *Loneliness and Cognitive Function in the Older Adult: A Systematic Review*, 27 INT'L. PSYCHOGERIATRICS. 541 (2015); *see also* Anabella Pinton, Kristen Wroblewski, L. Philip Schumm, Louise C. Hawkley & Megan Huisingh-Scheetz et al., *Relating Depression, Anxiety, Stress and Loneliness to 5-Year Decline in Physical Function and Frailty*, 115 ARCHIVES GERONTOLOGY GERIATRICS, Sept. 2023, at 1 (2023).

9. U.S. Dep't of Health & Hum. Servs., *Our Epidemic of Loneliness and Isolation: The U.S. Surgeon General's Advisory on the Healing Effects of Social Connection and Community*, at 12–13 (2023) [hereinafter Surgeon General].

10. *Id.*

11. Shoshana Magnet & Celeste E. Orr, *Feminist Loneliness Studies: An Introduction*, 23 FEMINIST THEORY 3, 6 (2022).

12. Kristian Wahlbeck, *Public Mental Health: The Time Is Ripe for Translation of Evidence into Practice*, 14 WORLD PSYCHIATRY 36 (2015).

13. Eleanor Wilkinson, *Loneliness Is a Feminist Issue*, 23 FEMINIST THEORY 23, 24 (2022). Feeling lonely is linked to higher rates of coronary heart disease, stroke, depression, cognitive decline, and Alzheimer's. *See* Julie Christiansen, Rikke Lund, Pamela Qualter, Christina Maar Andersen, Susanne S. Pedersen & Mathias Lasgaard, *Loneliness, Social Isolation, and Chronic Disease Outcomes*, 55 ANN. BEHAV. MED. 203, 203 (2021) (showing links between loneliness and cardiovascular disease and type 2 diabetes).

14. *See also* Laura Alejandra Rico-Uribe, Francisco Félix Caballero, Natalia Martín-María, María Cabello, José Luis Ayuso-Mateos & Marta Miret, *Association of Loneliness with All-*

the body's stress response, which increases cortisol production and inflammation, resulting in sickness and poor sleep.[15] Roughly 162,000 deaths each year in the United States are attributed to loneliness and social isolation, which is comparable to those from smoking and obesity, and exceeds the number of deaths from cancer or stroke.[16] In the first year of the COVID-19 pandemic, the World Health Organization reported that the global prevalence of anxiety and depression increased by a massive twenty-five percent, demonstrating the tight link between social isolation and these common mental illnesses.[17] Loneliness and depression have been found to be more common in individuals with lower incomes, women, and those living alone.[18]

Loneliness is a predictable outcome of poverty and underinvestment in community programs — that is, the sour fruits of neoliberalism. As Michel Foucault affirmed, a lonely life "is often the result of the poverty of possible relationships in our society, where institutions make insufficient and necessarily rare all relations that one could have with someone else."[19] The Surgeon General's report identified a lack of "social infrastructure" (such as libraries and parks), programs (such as volunteer organizations and member associations), and local policies (such as public transportation and housing) as contributing to the lack of social connection.[20]

II. NEOLIBERALISM IS PARTLY TO BLAME FOR OUR POOR MENTAL HEALTH

The newfound attention being given to loneliness and its effects on mental health is a positive step. However, meaningful improvements cannot be achieved without addressing the root causes. In recent years it is becoming clearer that the pandemic of loneliness can be traced to the "free market" neoliberal policies that have been adopted in the U.S.

Cause Mortality: A Meta-Analysis, 13 PLOS ONE e0190033, 13 (2018) (finding that loneliness is a risk factor for all-cause mortality, with the effect being slightly higher for men).

15. Mei-Hua Hall, Yunyu Xiao, Dost Ongur, John Torous & Dilip V. Jeste, *Social Isolation and Loneliness: Modern Pandemic of a Psychosocial Determinant of Health*, 54 PSYCHIATRIC ANNALS e196, e197 (2024). 197 (2024).

16. *Id.* at 196–97.

17. Luisar Wegner & Shuyan Liu, *Positive and Negative Experiences with the COVID-19 Pandemic Among Lonely and NonLonely Populations in Germany*, 10 FRONTIERS PUB. HEALTH, Mar. 2023, at 1, 2.

18. Robyn J. McQuaid, Sylvia M.L. Cox, Ayotola Ogunlana & Natalia Jaworska, *The Burden of Loneliness: Implications of the Social Determinants of Health During COVID-19*, 296 PSYCHIATRY RSCH., Feb. 2021, at 2.

19. Magnet & Orr, *supra* note 11, at 5.

20. Surgeon General, *supra* note 9.

since the 1980s.[21] I will briefly sketch these out below, before explaining their connection to poor mental health and loneliness.

Ronald Reagan enacted several neoliberal policies as President, that strengthened corporations at the expense of communities.[22] These policies, that now have expanded into every corner of society, champion the free market and individual autonomy,[23] while cruelly ignoring baseline power differentials that can render this freedom elusive. Neoliberal policies generally involve cutting taxes, limiting government spending on social programs, stagnating wages, privatizing consumer protection agencies,[24] eliminating decent paying jobs and work benefits for the majority of Americans (which increases income inequality),[25] and "slashing regulations to create a social, legal, and political environment that is conducive to business."[26] A certain kind of neoliberalism is so pervasive it is now simply a part of the air we breathe.[27]

Neoliberalism is unabashedly competitive and promotes "survival of the fittest."[28] Because people are thought to succeed in the (fair) market based on superior decision-making,[29] the suffering of the poor is often attributed to their own "weaknesses,"[30] and personal failures.[31] Given this competitive spirit, to be financially successful, neoliberal societies squeeze every ounce of labor out of individuals, leaving them with little time or money to invest in their friendships or mental well-being.[32]

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21. Kiffer G. Card & Kirk J. Hepburn, *Is Neoliberalism Killing Us? A Cross Sectional Study of the Impact of Neoliberal Beliefs on Health and Social Wellbeing in the Midst of the COVID-19 Pandemic*, 53 INT'L J. SOC. DETERMINANTS HEALTH & HEALTH SERVS. 363 (2023).

22. Anna Zeira, *Mental Health Challenges Related to Neoliberal Capitalism in the United States*, 58 CMTY. MENTAL HEALTH J. 205, 206 (2022).

23. John Tomasi, *Democratic Legitimacy and Economic Liberty*, 29 SOC. PHIL. & POL'Y 50, 50 (2012).

24. Karim Bettache & Chi-Yue Chiu, *The Invisible Hand Is an Ideology: Toward a Social Psychology of Neoliberalism*, 75 J. SOC. ISSUES 8, 11 (2019) (describing how neoliberal policies lead to stagnating wages and privatizing the work of regulating agencies).

25. Zeira, *supra* note 22, at 206.

26. Luigi Esposito & Fernando M. Perez, *Neoliberalism and the Commodification of Mental Health*, 38 HUMANITY & SOC'Y 414, 418, 426 (2014).

27. Giovanni Rubeis, *Liquid Health. Medicine in the Age of Surveillance Capitalism*, 322 SOC. SCI. & MED., Apr. 2023, at 3; *see also* Jedediah Britton-Purdy, David Singh Grewal, Amy Kapczynski & K. Sabeel Rahman, *Building A Law-and-Political-Economy Framework: Beyond the Twentieth-Century Synthesis*, 129 YALE L.J. 1784, 1791 (2020) (describing the hegemonic shift toward neoliberal frames of thought in the law as the "Twentieth-Century Synthesis" and just part of the "air we breathe").

28. Carla Ibled, *The 'Optimistic Cruelty' of Hayek's Market Order: Neoliberalism, Pain and Social Selection*, 40 THEORY CULT. SOC. 81, 86 (2023).

29. *Id.* at 86–87.

30. *Id.*

31. Bettache & Chiu, *supra* note 24, at 217.

32. *See* Ilana Gershon, *"Neoliberal Agency,"* 52 CURRENT ANTHROPOLOGY 537, 539 (2011).

While some posited that neoliberal policies might advance agency, freedom, and personal growth, social scientists have now documented its overall devastating effects on mental health.[33] Put simply, neoliberalism makes corporations healthy and individuals sick.[34] Neoliberal beliefs are correlated with justifying unfair systems, excluding socially disadvantaged groups, and refusing to fight social and wealth inequality.[35] In addition to the direct stressors of having to work harder for less pay, deregulation and decreased public sector spending have triggered massive wealth inequality and job insecurity resulting in "severe emotional distress."[36] Underscoring this point, countries that adopted neoliberal policies in response to the COVID-19 pandemic faired much worse and had higher rates of mental illness than countries that immediately amplified their social services to meet their citizens' needs through structural interventions like paid sick leave.[37]

Perhaps this is not surprising, as neoliberal societies have many more mental health risk factors including poor educational achievement and parental attachment,[38] as well as high rates of imprisonment, obesity, violence,[39] and wealth inequality.[40] Neoliberalism has been linked to "increasing levels of stress, depression, financial insecurity, worker dissatisfaction, and declining levels of happiness compared to 30 years ago."[41] And while the evidence at the societal level is impressive, a growing body of work demonstrates that the interpersonal competition at the root of neoliberalism and its "imperative for personal growth and fulfillment" has made individuals lonelier and more depressed.[42] To

33. *See* Card & Hepburn, *supra* note 21, at 366.

34. Glenn Adams, Sara Estrada-Villalta, Daniel Sullivan & Hazel Rose Markus, *The Psychology of Neoliberalism and the Neoliberalism of Psychology*, 75 J. SOC. ISSUES 189, 190 (2019). Neoliberal systems build on and reinforce characteristic psychological tendencies of liberal individualism — including radical abstraction of self from context, an entrepreneurial understanding of self as an ongoing development project, an imperative for personal growth and fulfillment, and an emphasis on affect management for self-regulation — that increasingly inform dominant conceptions of mind-in-general.

35. *See* Bettache & Chiu, *supra* note 24, at 5.

36. Zeira, *supra* note 22, at 205–06.

37. Matthew Sparke & Owain David Williams, *Neoliberal Disease: COVID-19, Co-Pathogenesis and Global Health Insecurities*, 54 ENV'T PLAN. A: ECON. & SPACE 15, 16, 17, 20, 21, 26 (2022).

38. Micah Hartwell, Amy Hendrix-Dicken, Rachel Terry, Sadie Schiffmacher, Lauren Conway & Julie M. Croff, *Trends and Forecasted Rates of Adverse Childhood Experiences Among Adults in the United States: An Analysis of the Behavioral Risk Factor Surveillance System*, 123 J. OSTEOPATHIC MED. 357, 359 (2023).

39. *Id.*

40. Anna Zeira, *Mental Health Challenges Related to Neoliberal Capitalism in the United States*, 58 CMTY. MENTAL HEALTH J. 205, 207 (2022).

41. Esposito & Perez, *supra* note 26, at 426.

42. Glenn Adams, Sara Estrada-Villalta, Daniel Sullivan & Hazel Rose Markus, *The Psychology of Neoliberalism and the Neoliberalism of Psychology*, 75 J. SOC. ISSUES 189, 189 (2019).

improve mental health, governments must remove the dog-eat-dog mentality that the free market fosters.

III. COMMERCIALIZING ILLNESS

Since neoliberal goals are deeply embedded in our economy, it logically follows that our health care system also advances neoliberal objectives. For-profit health care administrators view everyone as a potential consumer, not just those who are pathologically unwell.[43] There are only so many *truly* sick people — but the market for enhancement is vast.[44] This is partly why investments in psychiatric research and the diagnostic criteria have shifted from treating mental illness to optimizing healthy, productive individuals.[45] The most commonly prescribed psychiatric drugs can be seen as attempts to match "normative patterns of neoliberal agency" by suppressing depression and anxiety to enhance competition and market productivity, rather than to merely treat severely atypical dysfunction.[46] As a result, the norms for treatment have shifted. We are no longer expected to seek treatment just to treat severe pathology. Now, we are expected to enhance our mental health in ways that will maximize our market potential, by increasing our selfishness, wealth, and status.[47] To accommodate the "prevailing market society" psychiatry has normalized the idea that individuals must correct feelings of anxiety, depression, and loneliness with psychoactive drugs.[48] Preventing sickness is now our personal responsibility.

With psychiatry's neoliberal orientation, the development of precision medicine only added fuel to the fire.[49] Precision or personalized medicine contrasts "[t]raditional, one-size-fits-all medicine . . . [which] treats us all as if we're the same . . . ." Instead, it "tracks the molecular-genetic differences between us to deliver the right treatment, to the right patient, at the right time."[50] Genetic sequencing made precision

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43. *See* Esposito & Perez, *supra* note 26, at 415–16.

44. *See* Adele E. Clarke, Melanie Jeske, Laura Mamo & Janet K. Shim, *Biomedicalization Revisited*, *in* THE WILEY BLACKWELL COMPANION TO MEDICAL SOCIOLOGY 125, 126–27 (William C. Cockerham ed., 2021).

45. Thomas R. Insel, *Psychiatrists' Relationships With Pharmaceutical Companies: Part of the Problem or Part of the Solution?*, 303 JAMA 1192 (2010); Adams et al., *supra* note 42, at 189; Lisa Cosgrove, *Financial Conflicts of Interest in the DSM — a Persistent Problem*, BMJ, Jan. 2024, at 1.

46. *See* Esposito & Perez, *supra* note 26, at 416.

47. *Id.*

48. *Id.* at 425.

49. THOMAS R. INSEL, HEALING: OUR PATH FROM MENTAL ILLNESS TO MENTAL HEALTH 123–25 (2022).

50. James Tabery, *The Aftermath of a 'Miracle Cure' for a Rare Cancer*, WIRED (Sept. 4, 2023), https://www.wired.com/story/tyranny-of-the-gene-james-tabery-excerpt/

medicine possible by pairing massive amounts of patient genetic data with individual health outcomes. This enabled predictions about individual health futures, based on one's genes.

President Obama galvanized investment in precision medicine when he announced the Precision Medicine Initiative through the National Institutes of Health[51] (later to be called the "All of Us" initiative).[52] The All of Us project was funded mostly by private pharmaceutical and genetics companies that were allowed to direct the research priorities in exchange for providing technological infrastructure.[53] The large-scale project identified "genes associated with twenty common diseases, which paved the way for pharmaceutical interventions."[54] This spurred other public-private partnerships[55] and energized the precision medicine juggernaut.[56]

The successful commercialization of genetic tests revealed "what can happen in biomedicine when corporate competition plays out in a free market."[57] Something of a "bandwagon effect" developed.[58] This precision genetics boom, and the federal funding supporting it, was "welcomed by conservatives because of its straightforward embrace of individualism . . . which ideologically resonated with neoliberals."[59] That is, precision medicine and the genetic tests that enable it tickle both the neoliberal itch to measure individual differences and ignore what is shared, and the desire to use rational self-interest to improve ourselves.[60] These tests also play into biomedicalization as a means of surveilling and controlling bodies,[61] while their development offered a

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[https://perma.cc/R58H-AVEQ]; *see also* Edward Abrahams, *Right Drug — Right Patient — Right Time: Personalized Medicine Coalition*, 1 CLINICAL TRANSLATIONAL SCI. 11, 11 (2008).

51. JAMES TABERY, TYRANNY OF THE GENE: PERSONALIZED MEDICINE AND ITS THREAT TO PUBLIC HEALTH 235 (2023).

52. Joshua C. Denny & Francis S. Collins, *Precision Medicine in 2030 — Seven Ways to Transform Healthcare*, 184 CELL 1415, 1415 (2021).

53. TABERY, *supra* note 51, at 82 (discussing how Francis Collins, director of the Human Genome Project, offered Pfizer and genetic testing company Perlegen "access to dozens of existing cohorts of research participants from studies spread out across the NIH" in exchange for Perlegen to have an exclusive contract to use its technologies "to perform the genome-wide association studies on the thousands of samples from the NIH cohorts.").

54. *Id.*

55. *Id.* at 38.

56. Pui-Yan Kwok & Zhijie Gu, *Single Nucleotide Polymorphism Libraries: Why and How Are We Building Them?*, 5 MOLECULAR MED. TODAY 538 (1999); TABERY, *supra* note 51, at 82.

57. TABERY, *supra* note 51, at 162.

58. Merlin Chowkwanyun, Ronald Bayer & Sandro Galea, *"Precision" Public Health — Between Novelty and Hype*, 379 NEW ENG. J. MED. 1398, 1398 (2018).

59. TABERY, *supra* note 51, at 130.

60. *Id.*

61. Mark A. Rothstein, *Big Data, Surveillance Capitalism, and Precision Medicine: Challenges for Privacy*, 49 J.L. MED. & ETHICS 666, 667 (2021); *see generally* Rubeis, *supra* note 27.

way to *make money* on this surveillance. What is more neoliberal than *that*?

IV. WHAT POLYGENIC RISK SCORES CAN AND CANNOT SAY

Many claimed that genetics tests would radically improve the way we screen, diagnose, and treat mental illness[62] as there are no reliable biomarkers for mental illness, and the symptoms may vary significantly between people. When polygenic risk scores began to be calculated for all types of illness, this seemed like the perfect product to add precision and objectivity to mental illness screening.[63] In the future, after taking a patient's medical history, the results of a PRS for a range of mental illnesses might help clinicians narrow the pool of potential diagnoses.[64] This may result in a more efficient treatment plan. Risk scores might also help determine the best course of treatment, given someone's uniquely predicted reaction to a particular drug.

So, what is a polygenic risk score, and how might it achieve these goals? Polygenic risk scores "look at thousands of genetic variants across a person's genome to estimate their risk of developing a specific disease" such as diabetes, depression, or colon cancer.[65] While each single mutation (called a single nucleotide polymorphism, or SNP) has a tiny effect on a person's risk of developing disease, "by looking at all the variants together, something clinically meaningful might be said about their *overall* risk of developing a disease."[66] They build upon research called "genome-wide association studies," ("GWAS") which scanned hundreds of thousands of genetic mutations at once. By pairing the mutations, weighted according to their predicted effect sizes, with symptoms and phenotypes that have been expressed in those individuals, companies can then generate a risk score for each individual.[67] This risk data might speak to your likelihood of developing a disorder, the age of onset, or potential responses to particular drugs.[68] These PRS tests can be developed for any disease that has a genetic component.

62. INSEL, *supra* note 49, at 123–26.

63. *Id.* at 664.

64. Graham K. Murray, Tian Lin, Jehannine Austin, John J. McGrath, Ian B. Hickie & Naomi R. Wray, *Could Polygenic Risk Scores Be Useful in Psychiatry?: A Review*, 78 JAMA PSYCHIATRY 210, 213 (2021).

65. Amit Sud, Aroon Hingorani, Ionna Tzoulaki & Richard Houlson, *Realistic Expectations Are Key to Realising the Benefits of Polygenic Scores*, 380 BMJ, Mar. 2023, at 1.

66. *Id.* (emphasis added).

67. Naomi R. Wray, Tian Lin, Jehannine Austin, John J. McGrath, Ian B. Hickie, Graham K. Murray et al., *From Basic Science to Clinical Application of Polygenic Risk Scores a Primer*, 78 JAMA PSYCHIATRY 101, 101–02 (2021).

68. Murray et al., *supra* note 64, at 214.

Importantly, the "PRS results do not provide a diagnosis, but instead provide a statistical prediction of increased risk."[69]

The market for polygenic risk scores has exploded.[70] In the context of mental illness, several tests have been commercialized for depression, anxiety, and addiction, and some are currently being developed for suicidality.[71] Many of these tests are offered directly to consumers ("DTC"), without a physician's involvement. In the United States, these tests cost around $100–500 out of pocket, and while this is changing, they are still rarely reimbursed by insurance.[72]

There is very little regulation of commercial polygenic risk score tests. This is likely due to the neoliberal idea that regulation kills enterprise, and the assumption that firms will voluntarily set best practices and compete over compliance.[73] But of course, competition requires transparency in terms of the quality, reliability, and validity of products, and the lack of competition between firms exposes the true nature of neoliberalism — which is not to promote free markets, but to promote corporate monopolies.[74] And while companies emphasize their origins in academic research centers,[75] once the risk calculators are commercialized, they become intellectual property. Transparency in each of these categories is therefore lacking with commercial PRS tests.

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69. Aya Abu-El-Haija, Honey V. Reddi, Hannah Wand, Nancy C. Rose, Mari Mori, Emily Qian et al., *The Clinical Application of Polygenic Risk Scores: A Points to Consider Statement of the American College of Medical Genetics and Genomics (ACMG)*, 25 GENETICS MED., 2023, at 2.

70. Jin K. Park & Christine Y. Lu, *Polygenic Scores in the Direct-to-Consumer Setting: Challenges and Opportunities for a New Era in Consumer Genetic Testing*, 13 J. PERSONALIZED MED. 573, 573 (2023). *See generally* Murray et al., *supra* note 64.

71. *See* Murray et al., *supra* note 64. For examples of the different companies offering polygenic risk score tests to guide treatment of depression or identification of risk for mental illnesses, see: NeoGenomics.com, ForeGenomics.com, Tempus.com, Genesight.com, 23andMe.com, DNA.Sequencing.com. The field is rapidly changing, with new companies appearing and disappearing every month.

72. Mary A. Majumder, Christi J. Guerrini & Amy L. McGuire, *Direct-to-Consumer Genetic Testing: Value and Risk*, 72 ANN. REV. MED. 151, 153 (2021).

73. Ian Maitland, *The Limits of Business Self-Regulation*, 27 CAL. MGMT. REV. 132, 133–34 (1985) (describing how despite being championed by neoliberalism, in many contexts industry self-regulation proved incapable of responding to the overpowering corporate pursuit of profit, and thus legal rules are necessary for compliance in the face of this).

74. Ian Bruff, *Detaching 'Neoliberalism' from 'Free Markets': Monopolistic Corporations as Neoliberalism's Ideal Market Form*, REV. SOC. ECON. 1, 4 (2024).

75. See TruDiagnostic's page "The Science" where they proclaim that their tests were "[c]reated with science from Harvard, Yale, and Duke, the TruAge test measures +75 key biomarkers for longevity to give you the most precise, accurate, and actionable insights about your aging." *The Science*, TRUDIAGNOSTIC, https://www.trudiagnostic.com/science [https://perma.cc/5BRJ-MYM2]; *see also About Our DNA Test*, DNA COMPLETE, https://dnacomplete.com/science-and-technology/ [https://perma.cc/2FBK-PETR] (emphasizing that the polygenic risk score tests from Nebula Genomics and DNA Complete were developed by researchers from Harvard Medical School).

As the market for direct-to-consumer polygenic risk score testing expands, this has led some to ask a deeper question "what is it for?"[76] Despite their promise, polygenic risk scores have not been routinely adopted into practice.[77] The "[i]nitial expectations that genomics would rapidly transform and personalise medicine have been largely unmet."[78] This is because diseases are more genetically complex than initially expected,[79] and PRS tests themselves possess significant interpretive limitations.[80]

For starters, the majority of the research participants that generated the genome-wide data used in PRS tests are of European descent and from relatively higher socio-economic groups.[81] Participation bias like this limits the generalizability of the risk data to other populations.[82] As a result, the scores do not "port" well across populations; PRS generated for people of color "can be multiple times less predictive" than the same score in white, European populations.[83]

Additionally, for most mental illnesses PRS can only predict a *tiny* amount of the overall variation between groups. This is due in part to low population base rates of the tested-for diseases as well as the overwhelming majority of the risk being due to causes we have not yet identified. For example, in psychiatry, the best and strongest genetic risk data gathered is for schizophrenia. Even so, at present PRS can only predict about eleven percent of the variance in that condition.[84] This means that the overwhelming majority of the risk of developing schizophrenia (89%) is at present attributed to non-genetic factors. And while those who test in the top ten percent of the population have an almost *threefold* increase in the risk of developing schizophrenia over the general population, only about three percent of those in this highest risk category are expected to actually develop schizophrenia, because the overall lifetime risk is still so low.[85] Put differently, if base rates are

76. Park & Lu, *supra* note 70, at 1; Anna C. F. Lewis & Robert C. Green, *Polygenic Risk Scores in the Clinic: New Perspectives Needed on Familiar Ethical Issues*, 13 GENOME MED. 14 (2021).

77. Benjamin Cross, Richard Turner & Munir Pirmohamed, *Polygenic Risk Scores: An Overview from Bench to Bedside for Personalised Medicine*, 13 FRONTIERS GENETICS, Nov. 2022, at 1.

78. *Id.*

79. *Id.*

80. Park & Lu, *supra* note 70, at 3–4 ("While there are now many open-source algorithms for the calculation of PGS, there is still significant room for variability in choosing optimally performing PGS given specified parameters.").

81. Lewis & Green, *supra* note 76, at 2.

82. Laura Fusar-Poli, Bart P. F. Rutten, Jim van Os, Eugenio Aguglia & Sinan Guloksuz, *Polygenic Risk Scores for Predicting Outcomes and Treatment Response in Psychiatry: Hope or Hype?*, 34 INT'L REV. PSYCHIATRY 663, 668 (2022); Abdel Abdellaoui, Loic Yengo, Karin J.H. Verweij & Peter M. Visscher, *15 Years of GWAS Discovery: Realizing the Promise*, 110 AM. J. HUM. GENETICS 179, 182 (2023).

83. Lewis & Green, *supra* note 76, at 2.

84. Murray et al., *supra* note 64.

85. *Id.* at 212.

low and you begin with a lifetime risk of developing a mental illness that is .5%, doubling that risk sounds meaningful. But because the disease is rare and environmental factors have a substantial causal role, the doubled risk translates to having a 1% lifetime risk, which remains quite low. Clinicians continue to question whether PRS will ever make a meaningful impact on public mental health policy, "given that nearly all of the people in each stratum will never get the disorder" due to low absolute risk.[86]

For diseases with higher base rates and absolute risk, PRS tests might be more meaningful to a very small number of individuals who score at the very tail end of the curve. Because major depressive disorder is much more common than schizophrenia, those in the top one percent of depression PRS scores have roughly a thirty percent chance of developing depression in their lifetime. This represents roughly a *two-fold* increased risk compared with a randomly selected person. The relative risk data is remarkable for this group at extreme end of the distribution, but still not very valuable to the vast majority of people tested, who are not in the top 1%. Even so, many would like to know about this two-fold increase in risk, even if it does not change the way they are treated clinically.

In addition to having small effect sizes, disease-causing genes are expressed differentially based on the *other* inherited genes and one's environmental exposures.[87] This means psychiatrists are "not yet sure what conclusions can be drawn from them."[88] The predictive value of PRS is severely hamstrung by their focus on only the nature side of things, completing ignoring the critical role of nurture. And it turns out that when it comes to mental illness, our environmental exposures are every bit as important as our genes.

V. THE PROMISE OF PRS FOR MENTAL HEALTH DIAGNOSIS AND TREATMENT

In the introduction, I explained how suicide, overdoses, and depression are at all-time highs, and in some studies loneliness has been shown to be the biggest risk factor for each.[89] Rather than adopting evidence-based public health interventions, in the United States, funding agencies have disproportionately financed biomedical market

86. *Id.* at 212.

87. Wray et al., *supra* note 67, at 101.

88. Park & Lu, *supra* note 70, at 3–4 ("While there are now many open-source algorithms for the calculation of PGS, there is still significant room for variability in choosing optimally performing PGS given specified parameters.").

89. Yuval Palgi, Amit Shrira, Lia Ring, Ehud Bodner, Sharon Avidor, Yoav Bergman et al., *The Loneliness Pandemic: Loneliness and Other Concomitants of Depression, Anxiety and Their Comorbidity During the COVID-19 Outbreak*, 275 J. AFFECTIVE DISORDERS 109, 110 (2020).

solutions[90] and encouraged services to be delivered through the non-profit sector.[91] Given the tremendous role of the environment in mental illness risk, these market solutions alone will be wholly inadequate. In the next section, I briefly describe three major mental illnesses that are driving up mortality rates. I will survey the current understanding of the genetic bases for each. Then, I will explain how despite their promise, the inability of genetic tests to capture substantial environmental risks will severely and permanently limit their clinical utility.

A. What Polygenic Risk Scores Can Tell Us About Depression

Major depressive disorder ("MDD") is a common mood disorder (with a lifetime prevalence of approximately fifteen percent) consisting of persistent feelings of hopelessness and sadness.[92] Those affected lose interest in activities they once enjoyed.[93] While it can present very differently across individuals in its many forms, it is now the leading causes of global disability.[94] Between 2010 and 2018, the proportion of U.S. adults with severe depression who are in the age range 18–34 increased from 34.6 to 47.5 percent.[95] Not only can MDD be debilitating, but it has massive economic impacts both in health care and workplace costs. In the last decade, the incremental economic burden of adults with MDD increased by 37.9% from $236.6 billion to 326.2 billion (year 2020 values).[96] The public health burden of depression is enormous.

Depression is considered "moderately heritable" meaning that it has significant environmental and genetic causal components.[97] Early twin studies suggested that the expression of depression had more to do with the shared environment than genes.[98] However, heritability

90. Laura Finney & Luigi Esposito, *Neoliberalism and the Non-Profit Industrial Complex: The Limits of a Market Approach to Service Delivery*, 5 PEACE STUD. J. 4, 6 (2012).

91. Mary A. Caplan & Lauren Ricciardelli, *Institutionalizing Neoliberalism: 21st-Century Capitalism, Market Sprawl, and Social Policy in the United States: Institutionalizing Neoliberalism*, 8 POVERTY PUB. POL'Y 20, 20–21 (2016).

92. Johan Ormel, Catharina A. Hartman & Harold Snieder, *The Genetics of Depression: Successful Genome-Wide Association Studies Introduce New Challenges*, 9 TRANSLATIONAL PSYCHIATRY, 2019, at 114.

93. *Id.*

94. Paul E. Greenberg, Andree-Anne Fournier, Tammy Sisitsky, Mark Simes, Richard Berman, Sarah H. Koenigsberg et al., *The Economic Burden of Adults with Major Depressive Disorder in the United States (2010 and 2018)*, 39 PHARMACOECONOMICS 653 (2021); Brittany L. Mitchell, Jackson G. Thorp, Yeda Wu, Adrian I. Campos, Dale R. Nyholt, Scott D. Gordon et al., *Polygenic Risk Scores Derived from Varying Definitions of Depression and Risk of Depression*, 78 JAMA PSYCHIATRY 1152, 1152 (2021).

95. Greenberg et al., *supra* note 95, at 653.

96. *Id.* at 653–357.

97. Ormel et al., *supra* note 9293, at 5.

98. Arvid Harder, Thuy-Dung Nguyen, Joëlle A. Pasman, Miriam A. Mosing, Sara Hägg & Yi Lu, *Genetics of Age-at-Onset in Major Depression*, 12 TRANSLATIONAL PSYCHIATRY 124, 124 (2022).

estimates operate at the population level and say nothing about an individual's risk. The largest published genome-wide association study to date has identified 178 independent loci associated with risk of developing depression.[99] Using multiple different ways of diagnosing depression, a review of several GWAS studies identifies a particular role for mutations on loci16.[100]

Researchers have assessed the utility of PRS of major depressive disorder to move from population heritability to predicting individual treatment outcomes. A review of these studies was found to be "substantially inconclusive" as many yielded no significant predictive value.[101] However, a couple studies found associations between patients being in the highest PRS quintile and being unable to achieve remission.[102] Another study found that if patients had a higher polygenic loading for depressive symptoms, they were more likely to respond to ketamine treatment.[103] One large population study found significant associations between having a higher PRS and an earlier onset and more severe symptoms of depression.[104] This data is not clinically useful for individuals just yet, but might justify early intervention efforts in the future or targeted treatment protocols based on one's unique PRS.

One of the reasons meta-analyses produce inconclusive results is that the phenotype of depression is heterogenous "in timing of onset, symptom profile, course, response to treatment, and both psychiatric and physical comorbidities."[105] This has led researchers to limit their studied populations to those with the most severe presentations. But by massively increasing the sample sizes and permitting a more phenotypically rich group (i.e., using diagnostic questionnaires rather than self-reports) researchers hope that the genetic architecture of depression can be more precisely mapped out.[106] That is, if a broader definition of depression is used that is more consistent with how the term is used in regular clinical practice, the results will better capture the true risk of

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99. Daniel F. Levey, Murray B. Stein, Frank R. Wendt, Gita A. Pathak, Hang Zhou, Mihaela Aslan et al., *Bi-Ancestral Depression GWAS in the Million Veteran Program and Meta-Analysis in >1.2 Million Individuals Highlight New Therapeutic Directions*, 24 NATURE NEUROSCIENCE 954, 954 (2021).

100. Brittany L. Mitchell, Jackson G. Thorp, Yeda Wu, Adrian I. Campos, Dale R. Nyholt, Scott D. Gordon et al., *Polygenic Risk Scores Derived from Varying Definitions of Depression and Risk of Depression*, 78 JAMA PSYCHIATRY 1152, 1152–53 (2021).

101. Laura Fusar-Poli, Bart P. F. Rutten, Jim van Os, Eugenio Aguglia & Sinan Guloksuz, *Polygenic Risk Scores for Predicting Outcomes and Treatment Response in Psychiatry: Hope or Hype?*, 34 INT'L REV. PSYCHIATRY 663, 668 (2022).

102. *Id.* at 666.

103. Julia J. Meerman, Sophie E. Ter Hark, Joost G.E. Janzing & Marieke J.H. Coenen, *The Potential of Polygenic Risk Scores to Predict Antidepressant Treatment Response in Major Depression: A Systematic Review*, 304 J. AFFECTIVE DISORDERS 1, 3 (2022).

104. Harder et al., *supra* note 98, at 5.

105. *See* Mitchell et al., *supra* note 94, at 1152.

106. Mitchell et al., *supra* note 100, at 1159.

developing depression. At present, the PRS is not thought to add actionable data for clinicians in treating individual patients.[107]

B. What Polygenic Risk Scores Can Tell Us About Addiction

U.S. drug overdose deaths increased thirty percent from 2019 to 2020 and fifteen percent in 2021, resulting in an estimated 108,000 deaths in 2021.[108] While the COVID-19 pandemic saw a surge in many different "deaths of despair," overdose deaths were already sharply increasing in the years leading up to it, due largely to fentanyl and alcohol.[109] These escalating overdose deaths have reversed the century-long trend of increasing life expectancy in the United States.[110]

Researchers have appreciated the sizable heritability of addiction for decades, due to studies where identical twins were reared apart.[111] The GWAS studies supplemented this understanding, by characterizing the polygenic architecture of addiction at the level of individual genes. Many of the significant genes that have been identified as increasing addiction risk are those known to regulate metabolism (such as ADH1B for alcohol and CYP2A6 for nicotine), and to encode binding sites for receptors (such as CHRNA5 for nicotine and OPRM1 for opioids).[112] Studies show that certain mutations are associated with broad-spectrum liability to addiction and others increase risk of developing addiction to particular drugs.[113] Perhaps because of our endogenous opioid analgesic system, the effect sizes of the mutations conferring risk of opioid use disorder ("OUD") "are an order of magnitude larger than those of variants that are common across addictions."[114]

While many clinicians still find the PRS data to be too noisy for individual clinical use, these larger effect sizes might be what motivated the Food and Drug Administration to approve a prescription PRS

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107. Fusar-Poli et al., *supra* note 82, at 666.

108. *Provisional Drug Overdose Death Counts*, CDC, https://www.cdc.gov/nchs/nvss/vsrr/drug-overdosedata.htm [https://perma.cc/3GK4-B7JJ] (acknowledging these are under-estimates as states are delayed in reporting their overdose deaths).

109. Elisabet Beseran, Juan M. Pericàa, Lucinda Cash-Gibson, Meritxell Ventura-Cots, Keshia M. Pollack Porter & Joan Benach, *Deaths of Despair: A Scoping Review on the Social Determinants of Drug Overdose, Alcohol-Related Liver Disease and Suicide*, 19 INT'L J. ENV'T RSCH. PUB. HEALTH Sept. 2022, at 1–2.

110. *Id.*

111. Karen A. Urbanoski & John F. Kelly, *Understanding Genetic Risk for Substance Use and Addiction: A Guide for Non-Geneticists*, 32 CLINICAL PSYCH. REV. 60, 61 (2012).

112. Ryan Bogdan, Alexander S. Hatoum, Emma C. Johnson & Arpana Agarwal, *The Genetically Informed Neurobiology of Addiction (GINA) Model*, 24 NAT'L. REV. NEUROSCIENCE 40, 43 (2023).

113. *Id.* at 40.

114. *Id.* at 44.

for risk of opioid addiction in December of 2023.[115] As a condition of approval, the FDA required the company, AutoGenomics, to conduct post-market studies to assess device performance and to train their health care workers to ensure proper use of the test in post-surgical, opioid-naïve patients.[116] Despite receiving FDA approval, clinicians have balked at the clinical utility of the test, saying "the likelihood that a commercially developed genetic test for OUD would have the kind of validity that you would need to really drive clinical practice, based on the broader scientific literature, seems like a stretch . . . [i]f you just ask people, 'Do you have a family history of addiction?' . . . that would be a better risk categorizer than this genetic test."[117]

The PRS test for opioid addiction is not supposed to be used in patients who have chronic pain. But it is intended to guide clinicians and patients in their prescription and consumption of opioids after surgery.[118] On the ground, however, one wonders whether this information will be used in any meaningful or helpful way. While it could lead to better opioid stewardship, it *could* also lead risk averse clinicians to under-prescribe even very short courses of treatment, based on the idea that elevated risk means that this person will almost certainly develop dependence and addiction. But of course, even the robust PRS tests for opioid use disorder only explain the very tip of the heritability iceberg.

C. What Polygenic Risk Scores Can Tell Us About Suicide

Every year, about 40,000 people die by suicide in the United States.[119] Nonfatal attempts and ideation are estimated to be several times more common.[120] Sadly, the prevalence of suicidal behavior ("SB") has gradually increased over the past two decades.[121] Attempted suicide is a major source of disability, reduced quality of life, and public

115. Jeff Shuren, *FDA Approves First Test to Help Identify Elevated Risk of Developing Opioid Use Disorder*, U.S. FOOD & DRUG ADMIN. (Dec. 19, 2023), https://www.fda.gov/medical-devices/medical-devices-news-and-events/fda-approves-first-test-help-identify-elevated-risk-developing-opioid-use-disorder [https://perma.cc/69UL-AKC2].

116. *Id.*

117. Deidre McPhillips, *FDA Approves First Test to Help Screen for Risk of Opioid Use Disorder*, CNN (Dec. 20, 2023, 2:24 PM EST), https://www.cnn.com/2023/12/20/health/opioid-use-disorder-test-avertd/index.html [https://perma.cc/26LY-WCD8].

118. *Id.*

119. Douglas M. Ruderfer, Colin G. Walsh, Matthew W. Aguirre, Yosuke Tanigawa, Jessica D. Ribeiro, Joseph C. Franklin et al., *Significant Shared Heritability Underlies Suicide Attempt and Clinically Predicted Probability of Attempting Suicide*, 25 MOLECULAR PSYCHIATRY 2422, 2422 (2020).

120. *Id.*

121. *Id.*

health burden.[122] While other psychiatric disorders elevate the risk of SB, its heritability is high even when controlling for depression and related illnesses. Using the same GWAS methodology, one research team found a mutation in neuroligin 1 ("NLGN1") that passed significance thresholds for strength, even when accounting for co-occurrence with severe depression, suggesting that this mutation confers risk that is specific to suicidality.[123] Other significant mutations for suicide risk have been found on chromosome 20.[124]

Additionally, using medical records data and confirmed cases of completed suicide, Utah researchers identified high-risk extended families (7–9 generations) with significant familial risk.[125] Aggregating across generations minimized the effects of shared environment while providing a more genetically similar within-family group. Researchers were able to identify four additional significant variants that increase the risk of completing suicide (on genes *SP110*, *AGBL2*, *SUCLA2*, *APH1B*).[126] Researchers are beginning to assess the role of dysregulated gene expression and epigenetics in the risk of suicide death. Analyzing brain expression quantitative trait loci ("eQTLs"), a team found lower expression of RFPL3S, a gene that is critical for the development of the neocortex and implicated in arousal.[127] Importantly, the PRS tests available at present do not account for the different ways genes might be expressed or "turned on."[128] And just as with depression and addiction, any resulting PRS score would only capture a tiny amount of the variance between people due to the large and unmeasured environmental risk factors. This has led many researchers, including myself, to question the ethics of providing families with this PRS data.[129]

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122. Qingqin S. Li, Andrey A. Shabalin, Emily DiBlasi, Srihari Gopal, Carla M. Canuso, FinnGen et al., *Genome-Wide Association Study Meta-Analysis of Suicide Death and Suicidal Behavior*, 28 MOLECULAR PSYCHIATRY 891, 891 (2023).

123. *Id.* at 897.

124. Annette Erlangsen, Vivek Appadurai, Yunpeng Wang, Gustavo Turecki, Ole Mors, Thomas Werge et al., *Genetics of Suicide Attempts in Individuals with and without Mental Disorders: A Population-Based Genome-Wide Association Study*, 25 MOLECULAR PSYCHIATRY 2410, 2413, 2415 (2020).

125. Hilary Coon, Todd M. Darlington, Emily DiBlasi, W. Brandon Callor, Elliott Ferris, Alison Fraser et al., *Genome-Wide Significant Regions in 43 Utah High-Risk Families Implicate Multiple Genes Involved in Risk for Completed Suicide*, 25 MOLECULAR PSYCHIATRY 3077, 3077 (2020).

126. *Id.* at 3087.

127. Seonggyun Han, Emily DiBlasi, Eric T. Monson, Andrey Shabalin, Elliott Ferris, Danli Chen et al., *Whole-Genome Sequencing Analysis of Suicide Deaths Integrating Brain-Regulatory eQTLs Data to Identify Risk Loci and Genes*, 28 MOLECULAR PSYCHIATRY 3909, 3909 (2023).

128. *Id.* at 3917.

129. Brent M. Kious, Anna R. Docherty, Jeffrey R. Botkin, Teneille R. Brown, Leslie P. Francis, Douglas D. Gray et al., *Ethical and Public Health Implications of Genetic Testing for Suicide Risk: Family and Survivor Perspectives*, 23 GENETICS MED. 289 (2021).

VI. PRS DO NOT CAPTURE ENVIRONMENTAL AND SOCIAL RISKS

In the context of mental illnesses, the evidence of improved clinical outcomes based on the use of PRS is extremely limited.[130] As compared to family history, PRS do not contribute much to overall risk prediction. Right now, they explain less than five percent of the variance in time until diagnosis.[131] Their weak predictive value has led experts to say that PRS tests "currently have a relatively small role to play" in the treatment and prevention of mental illness.[132]

Some of these data limitations will be overcome as more nuanced phenotypic data is matched with larger sets of genomic data. But by far the larger limitation on PRS tests has to do with their inability to capture the exposome — the diverse and important environmental factors that contribute significantly to mental illnesses like depression, suicide, and addiction risk.[133] The focus on the genome is deeply unfortunate because environmental factors play a huge role in predicting mental illness.

By far the biggest limitation in the clinical utility of PRS lies with their inability to capture weighty environmental factors such as trauma, poverty, or nutrition.[134] This is particularly troublesome in the context of mental illnesses, which are deeply impacted by these things. As a result, the PRS data in this domain can only explain a small amount of the variance between people who do and do not develop depression, addiction, or suicidality.

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130. Sebastian Koch, Jörg Schmidtke, Michael Krawczak & Amke Caliebe, *Clinical Utility of Polygenic Risk Scores: A Critical 2023 Appraisal*, 14 J. CMTY. GENETICS 471 (2023) (finding that across domains of psychiatry, oncology and internal medicine, the "diagnostic and prognostic performance of PRSs alone is consistently low"); *see also* Masashi Ikeda, Takeo Saito, Tetsufumi Kanazawa & Nakao Iwata, *Polygenic Risk Score as Clinical Utility in Psychiatry: A Clinical Viewpoint*, 66 J. HUM. GENETICS 53 (2021) (finding that the "insufficient" discriminative power of PRS renders them not useful at the individual level for clinical use).

131. Joanna M. Biernacka, *Do Polygenic Scores Inform Psychiatric Disease Risk After Considering Family History?*, 180 AM. J. PSYCHIATRY 256, 257 (2023).

132. Murray et al., *supra* note 64, at 214.

133. Fusar-Poli et al., *supra* note 82, at 668–69.

134. Sud et al., *supra* note 65, at 5.

Researchers have identified that variables like pollution,[135] sex,[136] socio-economic factors,[137] age, nutrition,[138] stress, infection, and inflammation[139] all play key causal roles in how the genes we inherit are expressed — specifically in mental illness and psychosis.[140] Environmental factors have been linked to increased risk of suicide,[141] depression, and addiction. Until studies incorporate the exposome into their causal models of mental illness, "the stand-alone applicability of PRS in clinical practice [will remain] very limited."[142] The PRS data is not garbage; it is a reliable measure of something.[143] The question is: *of what*? Before they can be used to disambiguate amorphous psychological symptoms or predict onset or severity of symptoms or treatment outcomes, researchers will need to include many other rich social and environmental causal factors into the models.[144]

VII. PRS ARE NOT EMPOWERING: INFORMATION ALONE DOES NOT EMPOWER

Providing people with PRS results might seem empowering because people are given data to analyze and control their own health.[145] This was the marketing strategy of direct-to-consumer companies like 23andMe, that claimed to promote consumer empowerment through

135. Aaron Reuben, Jonathan D. Schaefer, Terrie E. Moffitt, Jonathan Broadbent, Honalee Harrington, Renate M. Houts et al., *Association of Childhood Lead Exposure With Adult Personality Traits and Lifelong Mental Health*, 76 JAMA PSYCHIATRY 418, 419 (2019); Isabella Annesi-Maesano, Cara Nichole Maesano, Benedetta Biagioni, Gennaro D'Amato & Lorenzo Cecchi, *Call to Action: Air Pollution, Asthma, and Allergy in the Exposome Era*, 148 J. OF ALLERGY AND CLINICAL IMMUNOLOGY 70, 70 (2021); Tamas Pandics, David Major, Vince Fazekas-Pongor, Zsofia Szarvas, Anna Peterfi, Peter Mukli et al., *Exposome and Unhealthy Aging: Environmental Drivers from Air Pollution to Occupational Exposures*, 45 GEROSCIENCE 3381, 3381, 3382, 3384 (2023).

136. Fusar-Poli et al., *supra* note 82, at 669.

137. Ka Kei Sum, Mya Thway Tint, Rosana Aguilera, Borame Sue Lee Dickens, Sue Choo, Li Ting Ang et al., *The Socioeconomic Landscape of the Exposome During Pregnancy*, 163 ENV'T INT'L, Mar. 2022, at 2.

138. Yichao Huang & Mingliang Fang, *Nutritional and Environmental Contaminant Exposure: A Tale of Two Co-Existing Factors for Disease Risks*, 54 ENV'T SCI. TECH. 14793, 14793–94 (2020).

139. Nadia Lampiasi, Rosa Bonaventura, Irene Deidda, Francesca Zita & Roberta Russo, *Inflammation and the Potential Implication of Macrophage-Microglia Polarization in Human ASD: An Overview*, 24 INT'L J. MOLECULAR SCI. Jan. 2023, at 2.

140. Fusar-Poli et al., *supra* note 82, at 669.

141. Ran Barzilay, Tyler M. Moore, Monica E. Calkins, Lydia Maliackel, Jason D. Jones, Rhonda C. Boyd et al., *Deconstructing the Role of the Exposome in Youth Suicidal Ideation: Trauma, Neighborhood Environment, Developmental and Gender Effects*, 14 NEUROBIOLOGY STRESS Mar. 2021, at 1.

142. Fusar-Poli et al., *supra* note 82, at 668.

143. Wray et al., *supra* note 67, at 101.

144. Phil H. Lee, Alysa E. Doyle, Micah Silberstein, Jae-Yoon Jung, Richard T. Liu, Roy H. Perlis et al., *Associations Between Genetic Risk for Adult Suicide Attempt and Suicidal Behaviors in Young Children in the US*, 79 JAMA PSYCHIATRY 971, 978 (2022).

145. *See generally* Juengst et al., *supra* note 1.

"democratization of genomic information."[146] But information alone is not empowering. Indeed, the way that polygenic risk scores have been developed and marketed is the *opposite* of empowering, as I will explain.

These genetic databases were populated by exhorting us to become citizen-scientists and "join an effort to translate basic research into improved health care for everyone."[147] The creation of the early databases relied on thousands of individuals to exchange their immutable DNA for information about their ancestors and whether they had wet earwax.[148] Despite significant implications for individual privacy,[149] there was never any commitment either by the government or DTC genetic testing companies to ensure that participants would benefit from donating their genomes to these large biobanks.[150] Rather, due to weak informed consent requirements for consumer genetics, most people did not realize they were opting in to a lopsided bargain.[151]

The subtle pressure to canvass our genetic risk has changed the way we are expected to think about our health.[152] By assuming people should be "active participants in reacting to their genomic risk profiles in the prevention of disease and improvement of human health,"[153] we are given responsibility over yet another bit of data that we must then monitor and interpret. Good citizens must do more than seek treatment when they are sick — they must keep track of all future health risks too. Health has become "a fragile state constantly in danger, permanently at risk" and needing to be closely monitored.[154]

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146. Sandra Soo-Jin Lee, *American DNA: The Politics of Potentiality in a Genomic Age*, 54 CURRENT ANTHROPOLOGY S78 (2013).

147. J. Patrick Woolley, Michelle L. McGowan, Harriet J. A. Teare, Victoria Coathup, Jennifer R. Fishman, Richard A. Settersten Jr. et al., *Citizen Science or Scientific Citizenship? Disentangling the Uses of Public Engagement Rhetoric in National Research Initiatives*, 17 BMC MED. ETHICS 2016, at 6.

148. Jeanne Lenzer & Shannon Brownlee, *Knowing Me, Knowing You*, 336 BMJ 858, 858 (2008).

149. Ellen Wright Clayton, Barbara J. Evans, James W. Hazel & Mark A. Rothstein, *The Law of Genetic Privacy: Applications, Implications, and Limitations*, 6 J.L. BIOSCIENCES 2019, at 2–3.

150. Clarke et al., *supra* note 44, at 136.

151. Emilia Niemiec, Danya F. Vears, Pascal Borry & Heidi Carmen Howard, *Readability of Informed Consent Forms for Whole-Exome and Whole-Genome Sequencing*, 9 J. CMTY. GENETICS 143, 143 (2018); Eline M. Bunnik, A. Cecile J.W. Janssens & Maartje H.N. Schermer, *Informed Consent in Direct-to-Consumer Personal Genome Testing: The Outline of a Model Between Specific and Generic Consent: Informed Consent in Direct-to-Consumer Personal Genome Testing*, 28 BIOETHICS 343 (2014).

152. Sandra Soo-Jin Lee, *Consuming DNA: The Good Citizen in the Age of Precision Medicine*, 46 ANN. REV. ANTHROPOLOGY 33, 34 (2017).

153. Lee, *supra* note 152, at 78.

154. Rubeis, *supra* note 27, at 4.

The need to be vigilant about which tests are available and what the risks mean sacrifices our ability to relax about our health.[155] The threat of missing out on a red flag — that might predict cancer or a mental breakdown — is everywhere. In addition to causing anxiety, this situates the problem of mental illness "within individuals who are responsible for 'fixing' themselves."[156]

VIII. PRS ARE NOT EMPOWERING: THEY OBFUSCATE THE SUBSTANTIAL ROLE OF THE ENVIRONMENT

We already know a great deal about the significant root causes of mental illness, and they are not genetic — they are environmental. At present, the most effective ways of preventing mental illness employ non-medical interventions.[157] Specifically, reducing poverty, improving prenatal nutrition, minimizing exposure to toxic substances, treating maternal depression, reducing neglect, minimizing abuse and trauma, and encouraging nurturing bonds between caregivers and children[158] would have an enormous positive impact on population mental health.[159]

As one team observed, "there is no longer a debate as to whether poverty negatively impacts on mental health — the debate is about which aspects of poverty and deprivation are the strongest drivers."[160] Neoliberal policies that outsource jobs to cheaper, exploitative foreign labor and to technology platforms leave many workers in precarious financial situations.[161] This financial instability then increases stress, loneliness, and isolation.[162] Relatedly, work conditions that encourage intense competition, few opportunities for advancement, and inflexible working hours all contribute to poor mental health.[163]

Capitalist market pressures that build on archetypes of extreme self-reliance are toxic to mental health because they engender blame[164]

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155. Silja Samerski, Individuals on Alert: Digital Epidemiology and the Individualization of Surveillance, 14 LIFE SCI. SOC'Y & POLICY 2018, at 3–4.

156. Bettache & Chiu, *supra* note 24, at 217.

157. Wahlbeck et al., *supra* note 12, at 38–39.

158. J. K. Burns, *Poverty, Inequality and a Political Economy of Mental Health*, 24 EPIDEMIOLOGY & PSYCHIATRIC SCIS. 107, 107 (2015).

159. Rosana E. Norman, Munkhtsetseg Byambaa, Rumna De, Alexander Butchart, James Scott & Theo Vos, *The Long-Term Health Consequences of Child Physical Abuse, Emotional Abuse, and Neglect: A Systematic Review and Meta-Analysis*, 9 PLOS MED., Nov. 2012, at 1.

160. Burns, *supra* note 158, at 107.

161. Carles Muntaner, *Digital Platforms, Gig Economy, Precarious Employment, and the Invisible Hand of Social Class*, 48 INT'L J. HEALTH SERVS. 597, 597 (2018).

162. Paul Glavin, Alex Bierman & Scott Schieman, *Über-Alienated: Powerless and Alone in the Gig Economy*, 48 WORK & OCCUPATIONS 399, 421–22 (2021).

163. Wahlbeck et al., *supra* note 12, at 37.

164. Adams et al., *supra* note 34 at 203.

and shame when individuals *necessarily* fail.[165] Neoliberal policies are making us sick, especially those that endorse starvation wages, unaffordable childcare, expectations that parents to return to work immediately after giving birth, the relentless pursuit of competition, and inadequate consumer safety and environmental protections.[166] Each of these contribute to stress, depression, and social isolation, while tearing apart the social safety nets of governmental support.

One of the most significant environmental contributors to poor adult mental health are adverse childhood experiences ("ACEs").[167] A meta-analysis found that approximately twenty-five percent of mood disorders among US adults are attributable to the ACEs of childhood sexual abuse, physical abuse, and witnessing domestic violence.[168] Economic policies that reduce sexual and physical abuse and domestic violence will significantly reduce the adult mental health burden.[169] And because domestic violence is connected to stress from poverty and income inequality,[170] reducing poverty will reduce domestic violence, which will dramatically improve population mental health.

A whopping eighty-one percent of US adults ages 18–21 say that financial anxiety is a substantial cause of their distress, and the number is not much better for the rest of the adult population (sixty-four percent).[171] Research shows that "policies that promote financial and housing security among low-income populations could produce mental health benefits by reducing exposure to chronic stressors."[172] Because so much adversity can be explained by poverty, the most effective thing governments can do to improve mental health is to increase the minimum wage and extend the earned income tax credit for the poor. Such policies are vehemently opposed by neoliberals.

In addition to reducing poverty, significant gains could be made to mental health by removing toxins from the air and increasing access to green spaces. Studies have demonstrated that just having a usable green

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165. Felicity Thomas, Katrina Wyatt & Lorraine Hansford, *The Violence of Narrative: Embodying Responsibility for Poverty-Related Stress*, 42 SOCIO. HEALTH ILLNESS 1123, 1123 (2020); Rubeis, *supra* note 27, at 3.

166. *See, e.g.*, Jacob D. King, Shuo Zhang & Alex Cohen, *Air Pollution and Mental Health: Associations, Mechanisms and Methods*, 35 CURRENT OP. PSYCHIATRY 192 (2022).

167. Alexander C. McFarlane, *The Long-Term Costs of Traumatic Stress: Intertwined Physical and Psychological Consequences*, 9 WORLD PSYCHIATRY 3, 3, 5 (2010).

168. Jonathan Purtle, Katherine L. Nelson, Nathaniel Z. Counts & Michael Yudell, *Population-Based Approaches to Mental Health: History, Strategies, and Evidence*, 41 ANN. REV. PUB. HEALTH 201, 206–07 (2020).

169. *Id.* at 203, 206.

170. Murray A. Straus, *Social Stress and Martial Violence in a National Sample of American Families*, 347 ANN. N.Y. ACAD. SCIS. 229 (1980); Jenevieve Mannell, Hattie Lowe, Laura Brown, Reshmi Mukerji, Delan Devakumar, Lu Gram et al., *Risk Factors for Violence Against Women in High-Prevalence Settings: A Mixed-Methods Systematic Review and Meta-Synthesis*, 7 BMJ GLOB. HEALTH e007704, 4 (2022).

171. Purtle et al., *supra* note 168, at 207.

172. *Id.*

space nearby significantly reduces anxiety in the surrounding community.[173] Others have found "consistent longitudinal associations of long-term exposure to air pollutants (NO_2, NO_x and $PM_{2.5}$) with mental disorders."[174] This is yet another way that the neoliberal resistance to environmental regulation and the antagonism to public spaces is hurting population mental health.

While mental health interventions may be expensive, ignoring them likely has even greater long-term population costs. And interventions need not break the bank. As more people age in cities, the impact of excessive ambient light at night can also increase mental health disorders by compromising sleep.[175] Something small like incentivizing the installation of blackout curtains for older adults could produce huge benefits for mental health.[176]

In his masterful book on the topic, James Tabery refers to the myopic focus on precision genetics — at the exclusion of these public health interventions — as the "tyranny of the gene."[177] By focusing on objective, genetic differences through the development of PRS, we have glorified the gene and ignored important environmental factors like poverty and pollution. Ignoring the social determinants of health will impact communities of color the most, as "[h]ealth disparities, it is abundantly clear, are caused by differences in our environments, not differences in our genes."[178] And poor, minority neighborhoods "tend to be the ones who are closest to the factories, landfills, and highways . . . and are less likely to have reliable access to healthy foods, green spaces, and walkable neighborhoods."[179] But if none of these important social and environmental variables are measured, they cannot be diagnosed as a cause.

IX. PRS ARE NOT EMPOWERING: MENTAL HEALTH TREATMENT IS UNAFFORDABLE AND INACCESSIBLE

It is a bit cruel to inform people of their risks of depression, addiction, and suicide when they cannot afford to obtain any treatment.

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173. D. Nutsford, A.L. Pearson & S. Kingham, *An Ecological Study Investigating the Association Between Access to Urban Green Space and Mental Health*, 127 PUB. HEALTH 1005, 1008 (2013); Roland Sturm & Deborah Cohen, *Proximity to Urban Parks and Mental Health*, 17 J. MENTAL HEALTH POL'Y ECON. 19 (2014).

174. Ioannis Bakolis et al., *Mental Health Consequences of Urban Air Pollution: Prospective Population-Based Longitudinal Survey*, 56 SOC. PSYCHIATRY & PSYCHIATRIC EPIDEMIOLOGY 1587, 1593 (2021).

175. Purtle et al., *supra* note 168, at 207.

176. *Id.*

177. *See generally* TABERY, *supra* note 51.

178. *Id.* at 11.

179. *Id.*

Unfortunately, this is the case for many Americans.[180] Mental health counseling and treatment is hard to find, unavailable when we can find it, and unaffordable.[181] Twenty percent of U.S. adults with mental health issues lack a reliable source of care, and more than half report cost barriers to accessing treatment.[182] The system "wait[s] for clients to seek treatment," and there is very little screening that takes place in primary care settings.[183] When people do seek treatment, those who need it the most — those experiencing financial stress — are the least capable of overcoming the barriers to receive it.[184]

There are not enough mental health providers to meet the population needs. Over a hundred million Americans live in "mental health deserts," and roughly half of those who receive care have to travel more than one hour to see a therapist.[185] Training more mental health workers and incentivizing them to work in rural areas will improve population mental health.[186] And while telemedicine can bridge some of this gap, technology limitations in rural and high-need areas have hamstrung these efforts.[187]

Despite parity requirements in the Affordable Care Act mandating that insurance plans cover mental health to the same extent as physical health,[188] these laws are under-enforced and fail to deliver on their promise.[189] Stigma, complications navigating the healthcare system, and cost present huge barriers to receiving adequate mental health treatment in the United States. Indeed, a large multi-country study found that people with mental illness in the U.S. experience much larger treatment barriers than those in several other developed countries.[190]

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180. Nicholas C. Coombs, Wyatt E. Meriwether, James Caringi & Sophia R. Newcomer, *Barriers to Healthcare Access among U.S. Adults with Mental Health Challenges: A Population-Based Study*, 15 SSM — POPULATION HEALTH 1, 2 (2021).

181. *Id.* at 6.

182. *Id.* at 2.

183. Joshua P. Mersky, James Topitzes, Jeffery Langlieb & Kenneth A. Dodge, *Increasing Mental Health Treatment Access and Equity Through Trauma-Responsive Care*, 91 AM. J. ORTHOPSYCHIATRY 703, 703 (2021).

184. *Id.* at 710.

185. John Auerbach & Benjamin F. Miller, *COVID-19 Exposes the Cracks in Our Already Fragile Mental Health System*, 110 AM. J. PUB. HEALTH 969, 969 (2020).

186. *Id.*

187. *Id.*

188. Kirsten Beronio, Sherry Glied & Richard Frank, *How the Affordable Care Act and Mental Health Parity and Addiction Equity Act Greatly Expand Coverage of Behavioral Health Care*, 41 J BEHAV. HEALTH SERVS. RSCH. 410, 410 (2014) (providing that the ACA "will expand coverage of mental health and substance use disorder benefits and federal parity protections to over 60 million Americans. The key to this expansion is the essential health benefit provision in the ACA that requires coverage of mental health and substance use disorder services at parity with general medical benefits").

189. *See* Kathleen C. Thomas, Adele Shartzer, Noelle K. Kurth & Jean P. Hall, *Impact of ACA Health Reforms for People with Mental Health Conditions*, 69 PSYCHIATRIC SERVS. 231, 234 (2018).

190. Coombs et al., *supra* note 180, at 2.

X. CONCLUSION

In this article I hoped to explain how PRS tests fall quite short of realizing their "empowerment" goals. Indeed, in many ways, they are the pinnacle of neoliberalism. If they are marketed and delivered in a context where most people cannot access or afford mental health treatment, or where the bulk of the risk can be explained by poverty, pollution, and trauma, then they stand to do more harm than good.

Research shows that we need more time with our loved ones, better wages and workplace conditions, affordable housing, clean environments, and access to affordable mental health care.[191] We do not need poorly predictive genetic data. This is what polygenic risk scores give us — an illusion of personal empowerment and control, while dodging the real target: the need for governments to invest in the social determinants of mental health. Of course, it need not be an either/or phenomenon. Governments can and should fund biomedical models of disease while simultaneously investing in social policies that promote mental health.[192] But because of our neoliberal political commitments, social and environmental interventions are highly disfavored over market-based ones.

Polygenic risk scores combine an obsession with individual uniqueness and freedom from regulation, with an exploitative business model that oversells on its potential. These tests provide feeble predictions (for those who can afford the expense), while offering nothing by way of concrete steps we can take. This is the opposite of empowering. Indeed, results from PRS tests will likely create greater anxiety as we are expected to interpret and act upon the complex data by ourselves. They perpetuate the neoliberal idea that mental illnesses are "self-contained ailments that can be resolved individually through pharmaceutical drugs" rather than being products of a neoliberal society where "competition erodes social bonds and promotes alienation."[193] Put simply, because neoliberalism is the cause of much of our population mental illness, it cannot also be the cure.

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191. Paula M. Lantz, Daniel S. Goldberg & Sarah E. Gollust, *The Perils of Medicalization for Population Health and Health Equity*, 101 MILBANK Q. 61, 62, 65 (2023).

192. Emilia Kaczmarek, *How to Distinguish Medicalization from Over-Medicalization?*, 22 MED. HEALTH CARE & PHIL. 119, 126–27 (2019).

193. Esposito & Perez, *supra* note 26, at 416.