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ARTICLE

Physician Liability for Genetic Risk-Based Prescription Decisions

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Abstract

The use of AvertD, a genetic test to assess an individual's risk of developing opioid use disorder, will expose physicians to liability. Critics of the test argue that the test itself is unreliable, often resulting in false positives, which will lead to potential undertreatment of pain, and false negatives, which will lead to inappropriate opioid prescriptions. But if the test is available, physicians will use it. And often, due to a combination of genetic determinism and genetic illiteracy, physicians will rely on the test to make opioid prescription decisions without also looking to the environmental, socioeconomic, lifestyle, and other factors that contribute to an individual's opioid use disorder risk.

Genetic test results that purport to predict opioid use disorder — or really, any behavioral or psychiatric trait or diagnosis — may have enormous consequences for individual lives. When patients are harmed by physicians' negligent clinical decision making, they can often turn to tort law for a remedy. This article covers various physician liability scenarios, from inappropriate prescribing based on genetic test results to failure to test and informed consent issues. Physicians could face liability for prescribing opioids after a positive test result, or for denying pain medication due to false positive test results, or for prescribing opioids to patients despite negative results that prove false, or for failing to administer the test at all. This article concludes that existing tort frameworks offer insufficient protection for patients and fail to ensure appropriate integration of these tests into clinical practice. And relying on tort law will not mitigate the individual and societal harms raised by the introduction of a polygenic risk score test for opioid use disorder.

1. Introduction

In December 2023, the U.S. Food and Drug Administration (FDA) approved its first polygenic risk score (PGS) test.[1] The test, AvertD, was approved to assess an individual's genetic risk of developing opioid use

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[1]Press Release, Jeff Shuren, Dir., FDA Ctr. for Devices & Radiological Health, FDA Approves First Test to Help Identify Elevated Risk of Developing Opioid Use Disorder (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; David Ovalle, *DNA Test Says It Can Predict Opioid Addiction Risk. Skeptics Aren't So Sure*, Wash. Post (Mar. 25, 2024), https://www.washingtonpost.com/health/2024/03/25/dna-test-opioid-addiction/ [https://perma.cc/6X8G-HCJN]. These are sometimes referred to as PRS, when the "trait of interest is a binary trait of disease status." Chen Cao, Shuting Zhang, Jianhua Wang, Min Tian, Xiaolong Ji, Dandan Huang, Sheng Yang & Ning Gu, *PGS-Depot: A Comprehensive Resource for Polygenic Scores Constructed by Summary Statistics Based Methods*, 52 Nucleic Acids Rsch. D963, D963 (2024). The AvertD test identifies fifteen single nucleotide polymorphisms (SNPs) that, when analyzed together, could suggest an elevated risk of OUD. Solvd Health, AvertD: Package Insert Instructions For Use 10 (2024), https://avertdtest.com/wp-content/uploads/AvertD-Package-Insert-02-FEB-2024.pdf

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disorder (OUD).[2] OUD is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as a "problematic pattern of opioid use leading to problems or distress,"[3] and it may result in overdose and death. In 2021, 80,816 people died from overdose deaths involving opioids,[4] and overdose-related deaths nearly quadrupled between 2010 and 2021.[5] The CDC estimates that the opioid crisis in the United States has been responsible for almost 645,000 deaths over twenty years.[6]

[https://perma.cc/PW85-E9KY]. PGS tests analyze small genetic variations, which "may be insignificant on their own," but when combined may help predict risk susceptibility. Ovalle, *supra.* The development of PGS tests relies on genome-wide association studies (GWAS), which identify associations between SNPs and human diseases or traits. Carolyn Riley Chapman, *Ethical, Legal, and Social Implications of Genetic Risk Prediction for Multifactorial Disease: A Narrative Review Identifying Concerns about Interpretation and Use of Polygenic Scores*, 14 J. Cmty. Genetics 441, 442 (2023) (noting that most human traits including disease susceptibility are not only polygenic (arising from many genes) but also multifactorial, meaning that the probability and strength (expressivity) of the phenotype are influenced by variation in many genes as well as environmental and lifestyle factors). These tests provide aggregate estimates of genetic risk based on the evaluation of multiple variants. *Id.* at 442. In approving AvertD, the FDA determined the test to be safe and effective. *See* Shuren, *supra*. Further, "[t]his approval represents another step forward in the FDA's efforts to prevent new cases of OUD, support the treatment of those with the disorder and decrease the misuse of opioid analgesics." *Id.* (citations omitted).

[2]Shuren, *supra* note 1.

[3]The Diagnostic and Statistical Manual of Mental Disorders (DSM 5-TR) describes opioid use disorder as a "problematic pattern of opioid use" leading to problems or distress with at least two of the following occurring within a twelve-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurring physical or psychological problem likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of an opioid.

    . . . .
11. Withdrawal, as manifested by either of the following:
    a. The characteristic opioid withdrawal syndrome . . . .
    b. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

Am. Psychiatric Ass'n, Diagnostic and Statistical Manual of Mental Disorders 541–42 (5th ed. 2013). "Severity of the OUD is determined by the number of criteria met: mild (2 to 3 criteria); moderate (4 to 5 criteria); and severe (≥6 criteria)." *Id.* at 542.

[4]*U.S. Overdose Deaths in 2021 Increased Half as Much as in 2020 – But Are Still Up 15%*, Ctrs. for Disease Control & Prevention: Nat'l. Ctr. for Health Stats. (May 11, 2022), https://www.cdc.gov/nchs/pressroom/releases/20220511.html?CDC_AAref_Val=https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm [https://perma.cc/8TCC-LFUA].

[5]Sam Streuli, CJ Valasek, Cassidy Tomlinson & Amy Non, *Why Genetic Testing is a Tool – Not a Solution – to the Opioid Epidemic*, The Hill (Jan. 28, 2024, at 07:00 ET), https://thehill.com/opinion/healthcare/4432170-why-genetic-testing-is-a-tool-not-a-solution-to-the-opioid-epidemic/ [https://perma.cc/A9PP-MCTS] (citing *Drug Overdose Death Rates: Facts and Figures*, Nat'l. Inst. on Drug Abuse (Aug. 2024), https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates#:~:text=Opioid%2Dinvolved%20overdose%20deaths%20rose,with%2080%2C411%20reported%20overdose%20deaths [https://perma.cc/WYE8-VHP8]).

[6]Bokyung Kim, Minseog Kim & Geunyong Park, *The Opioid Crisis and the Role of Employers*, Stan. Inst. for Econ. Pol'y Rsch., Jan. 2024, at 1, 1. *See also US FDA Approves First Test to Identify Opioid Use Addiction Risk*, Reuters (Dec. 20, 2023, at 16:01 ET), https://www.reuters.com/business/healthcare-pharmaceuticals/us-fda-approves-first-test-identify-opioid-use-addiction-risk-2023-12-19/ ("The addictive potential of the painkillers has fueled an opioid epidemic that has caused more than half a million overdose deaths in the United States over a period spanning more than two decades."). In August 2022, the FDA introduced its Overdose Prevention Framework, which elucidates four overarching priorities to address the opioid crisis.

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In order to address the opioid crisis in novel and creative ways, policy makers and scholars argue that the opioid epidemic would be more effectively ameliorated by looking to "stop people from becoming addicted in the first place" rather than intervening only when individuals are already "in the throes of addiction."[7] The AvertD test's approval was predicated on "the urgent need for medical devices that can make a positive impact on the overdose crisis, and specifically devices that can help assess the risk of developing OUD."[8] Thus, those who champion the test view it as a weapon in the arsenal against opioid misuse, in order to avoid prescribing opioids to those patients who are most likely to develop OUD.[9] According to Keri Donaldson, CEO of SOLVD Health, the maker of the AvertD device, the test is "absolutely transformative in this space . . . in terms of the ability to inform patients and providers of the genetic risks prior to prescribing."[10]

However, SOLVD Health explains that because it is a PGS test, AvertD is not intended to diagnose OUD.[11] Instead, the test is a genetic risk assessment tool.[12] It is intended to provide more accurate

Press Release, U.S. Food & Drug Admin., FDA Takes Steps to Facilitate Innovation for Devices Intended to Treat Opioid Use Disorder (July 27, 2023), https://www.fda.gov/news-events/press-announcements/fda-takes-steps-facilitate-innovation-devices-intended-treat-opioid-use-disorder.

[7]Yael Cannon, *The Kids are Not Alright: Leveraging Existing Health Law to Attack the Opioid Crisis Upstream*, 71 Fla. L. Rev. 765, 765, 780 (2019) ("The opioid crisis similarly demands upstream responses that examine the connections between poor health and powerful institutions. Many of the current responses to the opioid crisis center on downstream approaches that fail to address the underlying cause of addiction or move efforts to protect the next generation forward."). Current upstream approaches include "regulation of overprescribing physician practices known as 'pill mills,' prevention of patient 'doctor shopping,' education of health care providers, and initiatives to engage the public in reducing the number of prescription drugs in households, such as prescription medication 'take-back programs.'" *Id.* at 780–81 (footnotes omitted).

[8]Shuren, *supra* note 1.

[9]*Id.* ("The opioid crisis . . . calls for innovative measures to prevent, diagnose and treat opioid use disorder . . . ."); *see also Some Experts Worry a New DNA Test for Opioid Risk 'Will Make the Opioid Crisis Worse'*, Advisory Bd. (Apr. 5, 2024), https://www.advisory.com/daily-briefing/2024/04/05/opioid-test [https://perma.cc/2YL3-2MJZ]. The other three priorities are: (1) encouraging harm reduction through innovation and education; (2) advancing development of evidence-based treatments for substance use disorders; and (3) protecting the public from unapproved, diverted, or counterfeit drugs presenting overdose risks. *Food and Drug Administration Overdose Prevention Framework*, U.S. Food & Drug Admin. (Mar. 12, 2025), https://www.fda.gov/drugs/drug-safety-and-availability/food-and-drug-administration-overdose-prevention-framework. A fourth listed priority, mirroring Shuren's language, is "[s]upporting primary prevention by eliminating unnecessary initial prescription drug exposure and inappropriate prolonged prescribing." *Id.*

[10]Liz Carey, *Solvd Health CEO Responds to Harsh Letter Addressing FDA, CMS*, LabPulse.com (Apr. 9, 2024), https://www.labpulse.com/diagnostic-technologies/article/15668192/solvd-health-ceo-responds-to-harsh-letter-addressing-fda-cms [https://web.archive.org/web/20250215003523/https://www.labpulse.com/diagnostic-technologies/article/15668192/solvd-health-ceo-responds-to-harsh-letter-addressing-fda-cms] ("Our test is not predicting opioid use disorder, rather it is informing a patient of their personal genetic risk prior to being prescribed a first prescription of oral opioids for acute, nonemergent pain – and it excludes patients being treated for chronic pain. The test has been shown to demonstrate an 18-fold difference in individuals that have an elevated genetic risk vs. nonelevated [sic] genetic risk.").

[11]U.S. Food & Drug Admin., Ctr. for Devices & Radiological Health, Medical Devices Advisory Comm., Chemistry and Toxicology Devices Panel 135 (Oct. 20, 2022), https://www.fda.gov/media/175344/download (quote from Joseph Garbely, DO, DFASAM, FAPA). In its guidelines for prescribing opioids for pain, the CDC provides some background on pain management.

> Acute pain is usually sudden in onset and time limited (defined in this clinical practice guideline as having a duration of <1 month) and often is caused by injury, trauma, or medical treatments such as surgery. Unresolved acute pain or subacute pain (defined in this clinical practice guideline as pain that has been present for 1–3 months) can evolve into chronic pain. Chronic pain typically lasts >3 months and can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or unknown cause. Approximately one in five U.S. adults had chronic pain in 2019 and approximately one in 14 adults experienced 'high-impact' chronic pain, defined as having pain on most days or every day during the past 3 months that limited life or work activities. Pain, especially chronic pain, can affect almost every aspect of a person's life, leading to impaired physical functioning, poor mental health, and reduced quality of life, and contributes to substantial morbidity each year.

Deborah Dowell, Kathleen R. Ragan, Christopher M. Jones, Grant T. Baldwin & Roger Chou, *CDC Clinical Practice Guidelines for Prescribing Opioids for Pain – United States, 2022*, Morbidity & Mortality Wkly. Rep. Recommendations & Reps. Nov. 4, 2022, at 1, 2 (footnotes omitted).

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predictions of who will develop OUD as a result of opioid prescriptions, particularly for patients being treated for acute pain,[13] such as those scheduled to undergo a planned surgical procedure.[14] Both the FDA and SOLVD Health have stressed that the test is intended to be used as part of a broader evaluation of patients.[15] SOLVD Health's CEO referred to the genetic information that AvertD provides a "missing piece of information" that can be used in better clinical decision-making.[16]

In its approval, the FDA provided guidance on the use of results of the AvertD test, warning that they are "not [to] be used in treatment decision-making in isolation but as part of the complete clinical evaluation process."[17] The FDA's approval requires that educational materials be provided to physicians who utilize the test to make opioid prescribing decisions.[18] "The test also includes a 'black box' warning on its label, which cautions patients about its limitations and emphasizes that it shouldn't be the only measure used to evaluate OUD risk."[19]

The FDA approved AvertD over the objections of its own advisory committee, which voted eleven to two against its approval.[20] And since then, experts have petitioned the FDA to rescind its approval and for the Centers for Medicare and Medicaid Services (CMS) to deny reimbursement for administration of the test.[21] They argue that AvertD is unreliable.[22] It often returns false positive results, which would lead to potential undertreatment of pain, and false negatives results, which would lead to inappropriate opioid prescriptions.[23]

[13]The "AvertD test is intended to be used for adult patients prior to first exposure to oral opioid pain medications in patients being considered for a 4–30-day prescription for the treatment of acute pain, such as in patients scheduled to undergo a planned surgical procedure." Alison Knopf, *FDA Approves First Genetic Test to Help Identify Risk for OUD*, Alcoholism & Drug Abuse Wkly., Jan. 2024, at 8, 8; *see* SOLVD Health, *supra* note 1 ("This test is only to be used prior to a first prescription of oral opioids for a course of 4-30 days for the treatment of acute pain. If you are considering prescribing oral opioid treatment outside the 4-30 day timeframe, this test should not be used.").

[14]Approximately "48 million surgical procedures are performed each year in the inpatient hospital setting with an additional 53 million surgical and nonsurgical procedures are performed during surgery ambulatory visits." Debra B. Gordon, Oscar A. de Leon-Casasola, Christopher L. Wu, Kathleen A. Sluka, Timothy J. Brennan & Roger Chou, *Research Gaps in Practice Guidelines for Acute Postoperative Pain Management in Adults: Findings from a Review of the Evidence for an American Pain Society Clinical Practice Guidelin*e, 17 J. Pain 158, 159 (2016). Moreover, "[m]ore than 80% of patients who undergo surgical procedures experience acute postoperative pain and approximately 75% of those with postoperative pain report the severity as moderate, severe, or extreme." Roger Chou, Debra B. Gordon, Oscar A. de Leon-Casasola, Jack M. Rosenberg, Stephen Bickler, Tim Brennan, Todd Carter, Carla L. Cassidy, Eva Hall Chittenden, Ernest Degenhardt, Scott Griffith, Renee Manworren, Bill McCarberg, Robert Montgomery, Jamie Murphy, Melissa F. Perkal, Samanthanam Suresh, Kathleen Sluka, Scott Strassels, Richard Thirlby, Eugene Viscusi, Gary A. Walco, Lisa Warner, Steven J. Weisman & Christopher L. Wu, *Management of Postoperative Pain: A Clinical Practice Guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council*, 17 J. Pain 131, 132 (2016). "Evidence suggests that less than half of patients who undergo surgery report adequate postoperative pain relief." *Id.*

[15]*See* Advisory Bd., *supra* note 9.

[16]Carey, *supra* note 10.

[17]Chetak Shetty, *FDA Greenlights Genetic Test to Gauge Opioid Addiction Risk*, MedScape (Jan. 15, 2024), https://www.medscape.com/viewarticle/fda-greenlights-genetic-test-gauge-opioid-addiction-risk-2024a10000x7?form=fpf [https://perma.cc/3WVU-YSS9].

[18]Advisory Bd., *supra* note 9.

[19]*Id.*

[20]U.S. Food & Drug Admin., Brief Summary of the Clinical Chemistry and Clinical Toxicology Devices Panel of the Medical Devices Advisory Committee Meeting 4, 5 (2022).

[21]*See* Letter from Michael T. Abrams et al., to Robert M. Califf, Comm'r, U.S. Food & Drug Admin. (Apr. 4, 2024), https://www.supportprop.org/wp-content/uploads/2024/04/FDA-AvertD-Letter-4.4.24.pdf [https://perma.cc/AM65-ZJUT] [hereinafter Letter to FDA]; Letter from Michael T. Abrams et al., to Hon. Chiquita Brooks-LaSure, Adm'r, Ctrs. for Medicare & Medicaid Servs. (Apr. 4, 2024), https://www.supportprop.org/wp-content/uploads/2024/04/CMS-AvertD-Letter-4.4.24.pdf [https://perma.cc/ZA47-KD6R] [hereinafter Letter to CMS].

[22]*See* Letter to FDA, *supra* note 21; Letter to CMS, *supra* note 21.

[23]*See* Letter to FDA, *supra* note 21; Letter to CMS, *supra* note 21.

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But if the test is available, physicians will use it. And, in fact, due to a combination of genetic determinism and genetic illiteracy,[24] the test will be relied upon to make opioid prescription decisions without also looking to the environmental, socioeconomic, lifestyle, and other factors that contribute to an individual's OUD risk.[25]

Usually, when patients are harmed due to clinical decision making, they can turn to tort law.[26] Here, however, tort law is inadequate to addressing the potential harms associated with genetic risk testing in opioid prescribing. Physicians may face liability for either over-relying on or disregarding genetic test results, resulting in a "damned if you do, damned if you don't" dilemma.[27]

This article argues that relying on tort law will not mitigate the harms raised by the introduction of a PGS test for OUD. But the introduction of AvertD may expose physicians to liability, whether they rely on the test or not. Thus, this article covers various physician liability scenarios, from inappropriate prescribing based on genetic test results to failure to test and informed consent issues. It concludes that tort liability is ill-equipped to protect patients and ensure appropriate integration of these tests into clinical practice.

II. The AvertD Test

The AvertD test's unreliability and lack of clinical utility challenges the advisability of incorporating the test into clinical practice. The test's high rate of false positives could lead to potential undertreatment of pain, and its high risk of false negatives could lead to inappropriate opioid prescriptions.

A. Unreliability

While the AvertD test is the first PGS to be approved by the FDA, it has been widely understood that PGS are unreliable in making diagnostic and treatment decisions.[28] One study recently found "poor performance of polygenic risk scores in population screening, individual disease prediction, and population risk stratification" and concluded that the enthusiasm for PGS appears "disproportionate to their performance."[29] Experts warn that "currently there is no unequivocable proof of [PGS] clinical utility to improve patients' outcomes compared with the current standard of care."[30] Importantly, the utility of PGS in making medical decisions is limited because such scores "usually only account for the heritable component of a trait and ignore the etiological role of environment and lifestyle."[31]

[24]*See* Gary E. Marchant & Rachel A. Lindor, *Genomic Malpractice: An Emerging Tide or Gentle Ripple?*, 73 Food & Drug L.J. 1, 9 (2018) ("Most physicians practicing today have not had any significant training in medical genomics as medical schools have only started adding genetics to their curriculum in the past few years.").

[25]*See generally* Lynn R. Webster, *Risk Factors for Opioid-Use Disorder and Overdose*, 125 Anesthesia & Analgesia 1741 (2017) (discussing other risk factors for opioid misuse beyond genetic predisposition).

[26]*See* Marchant & Lindor, *supra* note 24, at 12–13.

[27]*See id.* at 9–14, 16–17.

[28]*See* Naomi R. Wray, Tian Lin, Jehannine Austin, John J. McGrath, Ian B. Hickie, Graham K. Murray & Peter M. Visscher, *From Basic Science to Clinical Application of Polygenic Risk Scores*, 78 [J]AMA Psychiatry 101, 101 (2021) ("As with many risk factors used in health care (e.g., cholesterol levels), these risk scores have limited predictive accuracy (i.e., they cannot confidently predict the clinical outcome of interest with precision at the individual patient level)."); Aroon D. Hingorani, Jasmine Gratton, Chris Finan, A. Floriaan Schmidt, Riyaz Patel, Reecha Sofat, Valerie Kuan, Claudia Langenberg, Harry Hemingway, Joan Morris & Nicholas J. Wald, *Performance of Polygenic Risk Scores in Screening, Prediction, and Risk Stratification: Secondary Analysis of Data in the Polygenic Score Catalog*, BMJ Med., Oct. 2023, at 1, 9–10.

[29]Hingorani et al., *supra* note 28 at 1, 9; *see also* Jessica L. Roberts & Sonia M. Suter, *Damned if You Do or Damned if You Don't: The Medical Malpractice Implications of Consumer-Generated Polygenic Risk Scores*, 38 Harv. J.L. & Tech. 417, 417 (2025).

[30]Lara Andreoli, Hilde Peeters, Kristel Van Steen & Kris Dierickx, *Taking the Risk: A Systematic Review of Ethical Reasons and Moral Arguments in the Clinical Use of Polygenic Risk Scores*, 194 Am. J. Med. Genetics, Mar. 2024, at 1, 2.

[31]Sebastian Koch, Jörg Schmidtke, Michael Krawczak & Amke Caliebe, *Clinical Utility of Polygenic Risk Scores: A Critical 2023 Appraisal*, 14 J. Cmty. Genetics 471, 471 (2023).

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Unlike certain genetic tests in which a single gene mutation indicates that patients will develop that disease,[32] PGS are intended to help predict the risk of developing a complex or multifactorial condition.[33] Thus, a test like AvertD can, at best, only aid in predicting the risk of developing OUD, but that risk is confounded by the interaction of genes with each other and with environmental and other factors.[34]

Despite concerns expressed by the Clinical Chemistry and Clinical Toxicology Devices Advisory Committee of the FDA's Medical Devices Advisory Committee of independent experts, the FDA approved AvertD in December 2023.[35] In October 2022, the Committee voted eleven to two to reject the test,[36] generally agreeing that there was not enough evidence to prove its efficacy. It stated, "[t]he panel agreed that the predictive power should be better and that genetic risk is only one component of risk and should be treated as such."[37] And it concluded that the test's risks outweighed its benefits, "for reasons ranging from the test's clinical study design to how its results could be misinterpreted by clinicians. Others cited uncertainty in the accuracy of its algorithms and in how the test's genetic criteria would translate to a larger and more diverse real-world population."[38]

In April 2024, after AvertD's approval, thirty-one scientists wrote to the FDA and CMS, asking the agencies to "agree with the expert consensus that that the decision to approve AvertD was a mistake."[39] In the letters, they asked FDA to rescind approval of AvertD and attempted to influence an anticipated CMS coverage decision on AvertD.[40] The letters "argued that fifteen genetic markers were not adequate to reliably predict a person's genetic risk of OUD and that the test failed to account for differences in geographic ancestry, which can skew results."[41] The scientists pointed to a critical review of gene-by-environment interaction research published in 2011 that concluded that algorithms that used the same fifteen genetic markers to predict opioid addiction performed no better than chance, and argued that the test's approval relied on "an approach that has been abandoned by mainstream genetics."[42] An

[32]*See, e.g.*, Sandra D. Taylor, *Predictive Genetic Test Decisions for Huntington's Disease: Context, Appraisal and New Moral Imperatives*, 58 Soc. Sci. & Med. 137, 138 (2004).

[33]*See, e.g.*, Ying Ma & Xiang Zhou, *Genetic Prediction of Complex Traits with Polygenic Scores: A Statistical Review*, 37 Trends in Genetics 995, 995–96 (2021).

[34]*See id.* at 1008–09.

[35]Ovalle, *supra* note 1. When FDA advisory committees advise against approval, the agency is likely to disagree with those recommendations (and approve the drug anyhow) thirty three percent of the time. *See* Genevieve P. Kanter, *The Real Question the FDA is Asking its Advisory Committees*, JAMA Health F., July 7, 2023, at 1, 1. In a study of 409 advisory committee meetings, overall, investigators found that eighty-eight percent of FDA regulatory actions aligned with advisory committee votes (262 of 298 votes). C. Joseph Ross Daval, Theodore W. Teng, Massimiliano Russo & Aaron S. Kesselheim, *Association of Advisory Committee Votes with US Food and Drug Administration Decision-Making on Prescription Drugs, 2010-2021*, JAMA Health F., July 7, 2023, at 1, 1.

[36]Advisory Bd., *supra* note 9.

[37]U.S. Food & Drug Admin., *supra* note 20, at 3. It continued, "[t]he panel was uncertain on a level of clinical performance that would be acceptable." *Id.* at 3.

[38]Conor Hale, *FDA Approves First Genetic Test to Screen for Opioid Use Disorder Risks*, Fierce Biotech (Dec. 21, 2023, at 10:18 ET), https://www.fiercebiotech.com/medtech/fda-approves-first-genetic-test-screen-opioid-use-disorder-risks [https://perma.cc/2ALJ-BDYX].

[39]Letter to FDA, *supra* note 21. *See also* Letter to CMS, *supra* note 21 (asking CMS to consider the expert consensus and deny coverage).

[40]Letter to FDA, *supra* note 21; Letter to CMS, *supra* note 21; Carey, *supra* note 10.

[41]Advisory Bd., *supra* note 9.

[42]Letter to FDA, *supra* note 21 (citing Laramie E. Duncan & Matthew C. Keller, *A Critical Review of the First 10 Years of Candidate Gene-by-Environment Interaction Research in Psychiatry*, 168 Am. J. Psychiatry 1041, 1045). *See also* Alexander S. Hatoum, Frank B. Wendt, Marco Galimberti, Renato Polimanti, Benjamin Neale, Henry R. Kranzler, Joel Gelernter, Howard J. Edenberg & Arpana Agrawal, *Ancestry May Confound Genetic Machine Learning: Candidate-Gene Prediction of Opioid Use Disorder as an Example*, 229 Drug & Alcohol Dependence, no. 109115, 2021, at 1, 6 (discussing that models based on random SNPs to predict random phenotypes, "at perfect confounding by major geographic ancestral group," predict "no better than a coin flip"). The authors continued, "[t]he largest well-powered and state of-the-art genome-wide studies of OUD to date demonstrate that even a full genome's worth of markers (roughly six-million) is not sufficient to predict OUD in a clinically useful way." *Id.* (footnote omitted); *see also* Christal N. Davis, N. Davis, Zeal Jinwala, Alexander S. Hatoum, Sylvanus Toikumo, Arpana Agrawal, Christopher T. Rentsch, Howard J. Edenberg, James W. Baurley, Emily E. Hartwell, Richard C. Crist, Joshua C. Gray, Amy C. Justice, Joel Gelernter, Rachel L. Kember & Henry R. Kranzler, *Utility of Candidate Genes from an Algorithm*

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independent evaluation of the "claim that the gene markers underlying AvertD can predict OUD" found that "the algorithm used for AvertD fell into known pitfalls of genetic prediction that give the appearance of predicting genetic risk, without being a true measure of genetic risk."[43] The authors asserted that "[c]urrent scientific knowledge about OUD genetics is strong enough for us to state that AvertD does not predict genetic risk of OUD."[44]

In early 2024, an independent group of scientists analyzed the fifteen genetic variants for OUD risk tested by the AvertD test.[45] The authors observed high rates of false positives and negatives, with almost half (47/100) of predicted cases or controls being incorrectly classified.[46] The authors recognized that clinicians, without reliance on the AvertD test, "could better predict OUD risk using an individual's age and sex than the 15 genetic variants."[47] Finally, they concluded that "although the test approved by the FDA is intended to complement standard clinical assessment, its use is unlikely to confer additional benefits and may instead give providers and patients false and potentially harmful information."[48]

B. False Test Results

The Advisory Committee that cautioned against the FDA's approval of AvertD, as well as the groups of experts that have called for the test to be removed from the market, all expressed concerns about the risks of the test reporting false results.[49] While false negative (wrongly categorizing an individual as "low risk" on the basis of their PGS) and false positive (wrongly categorizing an individual as "high risk" on the basis of their PGS) results can be expected with almost all PGS,[50] they are particularly concerning in the context of the AvertD test.

As part of its application to the FDA, SOLVD Health submitted sensitivity and specificity measures, which are intended to determine the effectiveness of the test.[51] The company reported that AvertD had

Designed to Predict Genetic Risk for Opioid Use Disorder, JAMA Network Open, Jan. 9, 2025, at 1, 7 (finding that for every hundred cases of OUD, the AvertD test misclassified forty-seven individuals).

[43]Letter to FDA, *supra* note 21 (citing Hatoum et al., *supra* note 42, at 7).

[44]Letter to FDA, *supra* note 21 (citing Joseph Deak, Hang Zhou, Marco Galimberti, Daniel F. Levey, Frank r. Wendt, Sandra Sanchez-Roige, Alexander S. Hatoum, Emma C. Johnson, Yaira Z. Nunez, Ditte Demontis, Anders D. Børglum, Veera M. Rajagopal, Mariela V. Jennings, Rachel L. Kember, Amy C. Justice, Howard J. Edenberg, Arpana Agrawal, Renato Polimanti, Henry R. Kranzler & Joel Gelernter, *Genome-wide Association Study in Individuals of European and African Ancestry and Multi-trait Analysis of Opioid Use Disorder Identifies 19 Independent Genome-wide Significant Risk Loci*, 27 Mol. Psychiatry 3970, 3970–79 (2022); Rachel Kember, Rachel Vickers-Smith, Heng Xu, Sylvanus Toikumo, Maria Niarchou, Hang Zhou, Emily E. Hartwell, Richard C. Crist, Christopher T. Rentsch, Million Veteran Program, Lea K. Davis, Amy C. Justice, Sandra Sanchez-Roige, Kyle M. Kampman, Joel Gelernter & Henry R. Kranzler, *Cross-Ancestry Meta-analysis of Opioid Use Disorder Uncovers Novel Loci with Predominant Effects in Brain Regions Associated with Addiction*, 25(10) Nature Neuroscience 1279, 1279–87 (2022)).

[45]*See generally* Davis et al., *supra* note 42.

[46]*Id.* at 7. The authors observed that the accuracy of the model of identifying OUD risk "was slightly greater than random guessing." *Id.* at 6 (statistics omitted).

[47]*Id.* at 7.

[48]*Id.* at 7.

[49]*See* Berkeley Lovelace Jr., *FDA Faces Backlash Over Approval of Genetic Test for Opioid Addiction Risk*, NBC News (Apr. 4, 2024, at 15:29 ET), https://www.nbcnews.com/health/health-news/fda-faces-backlash-approval-genetic-test-opioid-addiction-risk-rcna146178 [https://perma.cc/KA48-C97H].

[50]*See* Adebowale Adeyemo, Mary K. Balaconis, Deanna R. Darnes, Segun Fatumo, Palmira Granados Moreno, Chani J. Hodonsky, Michael Inouye, Masahiro Kana, Kazuto Kato, Bartha M. Knoppers, Anna C. F. Lewis, Alicia R. Martin, Mark I. McCarthy, Michelle N. Meyer, Yukinori Okada, J. Brent Richards, Lucas Richter, Samuli Ripatti, Charles N. Rotimi, Saskia C. Sanderson, Amy C. Sturm, Ricardo A. Verdugo, Elisabeth Widen, Cristen J. Willer, Genevieve L. Wojcik & Alicia Zhou, *Responsible Use of Polygenic Risk Scores in the Clinic: Potential Benefits, Risks and Gaps*, 27 Nature Med. 1876, 1878 (2021).

[51]Advisory Bd., *supra* note 9. According to Dr. Andrew Saxon, a professor of psychiatry and behavioral sciences at the University of Washington School of Medicine, "[a] highly sensitive test accurately identifies people with the condition, minimizing false negatives, while a highly specific test accurately rules out people without the condition, minimizing false positives." Lovelace, *supra* note 49. Saxon explained, "[i]f your specificity were 75%, it would mean a quarter of the people who you identify in the test as possibly having this disorder did not have this disorder." *Id.* (internal quotations omitted).

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demonstrated a sensitivity of approximately 82.5 percent and a specificity of 79.5 percent.[52] In other words, comparing the test's predictions to a clinician's diagnosis, those numbers suggest that approximately twenty percent of results would be false negatives and twenty percent of results would be false positives.[53] Based on these numbers, in its deliberations in October 2022, the FDA advisory committee concluded "that results of a genetic test could lead to over reliance on the result to change prescribing behaviors. Patients receiving a 'high risk' result may not be prescribed much needed opioids, and patients receiving a 'low risk' result may be over-prescribed opioids based on a sense of security."[54]

False positive test results can result in patients being denied appropriate pain relief, resulting in un- or undertreated pain. In October 2021, the Pew Charitable Trusts identified "real risks" associated with genetic tests, explaining that "[a]ccording to FDA, inaccurate tests could cause patients to undergo unnecessary, costly, and risky treatment when tests return false-positive results."[55] Interestingly, in most instances, a "false positive" medical test results in mis- or overtreatment, because the patient will be (inappropriately) diagnosed with a disease that has a particular treatment protocol.[56] However, a false positive AvertD result — one that inaccurately predicts that a patient has a higher-than-normal risk of developing OUD — could result in denying patients access to opioids when they are the best, or only, available approach for acute pain. Thus, in the case of AvertD, a false positive result can, for some patients, lead to inadequate pain management due to avoidance of opioids, "which may prevent patients from receiving optimal medical care to treat their acute pain."[57]

This is not to say that there are no alternatives to opioid treatment for acute pain. Physicians can prescribe non-steroidal drugs such as acetaminophen, gabapentin, or non-steroidal anti-inflammatory drugs, or regional anesthetic techniques (for example, epidural catheters and peripheral nerve blocks), to help reduce or eliminate the need for prescription opioids.[58] But in some instances, and for some indications, these alternatives will not adequately address a patient's pain.

Experts note "real and substantial harms associated with overestimating a patient's overdose risk."[59] The risks related to untreated and undertreated pain[60] include physical risks:

[52]Keri Donaldson, David Cardomone, Michael Genovese, Joseph Garbely & Lawrence Demers, *Clinical Performance of a Gene-Based Machine Learning Classifier in Assessing Risk of Developing OUD in Subjects Taking Oral Opioids: A Prospective Observational Study*, 51 Annals Clinical & Lab'y Sci. 451, 451 (2021); K. Melodi Gussow, Toxicology Team Lead, FDA, Clinical Chemistry and Toxicology Panel Meeting: SOLVD Health, AvertD 36 (2022), https://www.fda.gov/media/162585/download.

[53]*See* Lovelace, *supra* note 49.

[54]U.S. Food & Drug Admin., *supra* note 20, at 3. Similarly, experts who call for FDA to rescind its approval of AvertD argue, "a false negative result could lead to a false sense of security for a patient at increased risk of OUD, while a false positive result could result in inadequate pain management due to opioid avoidance." Shetty, *supra* note 17. This concern was repeated by the scientists calling for rescinding of the AvertD test from the market. Letter to FDA, *supra* note 21.

[55]*Diagnostic Tests Not Reviewed by FDA Present Growing Risks to Patients*, Pew Rsch. (Oct. 22, 2021), https://www.pew.org/en/research-and-analysis/fact-sheets/2021/10/diagnostic-tests-not-reviewed-by-fda-present-growing-risks-to-patients [https://perma.cc/TH95-FPZF].

[56]*See id.*

[57]*See* Shuren, *supra* note 1.

[58]Mark C. Bicket, Lewei A. Lin & Jennifer Waljee, *New Persistent Opioid Use After Surgery: A Risk Factor for Opioid Use Disorder?*, 275 Annals Surgery e288, e289 (2022); Mark D. Neuman, Brian T. Bateman & Hannah Wunsch, *Inappropriate Opioid Prescription After Surgery*, 393 Lancet 1547, 1549, 1551 (2019).

[59]Michele J. Buonora, Sydney A. Axson, Shawn M. Cohen & William C. Becker, *Paths Forward for Clinicians Amidst the Rise of Unregulated Clinical Decision Support Software: Our Perspective on NarxCare*, 39 J. Gen. Internal Med. 858, 859 (2023).

[60]*See generally* Karen O. Anderson, Carmen R. Green & Richard Payne, *Racial and Ethnic Disparities in Pain: Causes and Consequences of Unequal Care*, 10 J. Pain 1187 (2009); Comm. on Advancing Pain Rsch., Care & Educ., Bd. on Health Scis. Pol'y & Inst. Med., Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research 1 (2011). Interestingly, a false positive AvertD test result may have the opposite effect a false positive test result may have in other circumstances, leading to undertreatment rather than overtreatment. *Compare* Samuel A. Lambert, Gad Abraham & Michael Inouye, *Towards Clinical Utility of Polygenic Risk Scores*, 28 Hum. Molecular Genetics R133, R135 (2019), *with* Shuren, *supra* note 1.

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> A body in pain produces high levels of hormones that cause stress to the heart and lungs. Pain can cause blood pressure to spike, leading to heart attacks and strokes. Pain can also consume so much of the body's energy that the immune system degrades. Severe chronic pain sometimes leads to suicide.[61]

As Professors Kelly Dineen and James DuBois explain, "[t]he failure to utilize opioids in appropriate circumstances causes suffering and creates a barrier to effective pain care."[62] Professor Ben Rich has argued that "undertreatment of pain [is] a major ethical, and not merely a clinical, failing of the medical profession."[63] Studies have shown that undertreatment of pain can have major economic impacts as well, resulting in "over $70 billion per year in health care spending and lost productivity."[64]

When patients are denied adequate pain control, they may seek pain relief in other ways. Patients with unmet post-surgical pain control needs as a result of refusal of appropriate medication due to false positive AvertD test results "may be driven to the illegal market, where counterfeits and illicit substances are increasingly being adulterated with fentanyl and other potential lethal consequences."[65]

Conversely, a false negative test result could give individuals "false reassurance,"[66] leading to opioid addiction because the test indicated they were not at increased risk for opioid use disorder.[67] In fact, "[g]etting it wrong has consequences: A test that fails to identify a person at risk may give both the patient and the doctor a false sense of security about opioid use."[68] One of the authors of the letters calling for the

[61]Tina Rosenberg, *When is a Pain Doctor a Drug Pusher?*, N.Y. Times Mag. (June 17, 2007), https://www.nytimes.com/2007/06/17/magazine/17pain-t.html.

[62]Kelly K. Dineen & James M. DuBois, *Between a Rock and a Hard Place: Can Physicians Prescribe Opioids to Treat Pain Adequately While Avoiding Legal Sanctions*, 42 Am. J.L. & Med. 7, 7 (2016) (citing Martin D. Cheatle & Seddon R. Savage, *Informed Consent in Opioid Therapy: A Potential Obligation and Opportunity* 44 J. Pain Symptom Mgmt. 105, 106 (2012)).

[63]Ben A. Rich, *A Legacy of Silence: Bioethics and the Culture of Pain*, 18 J. Med. Hums. 233, 233 (1997).

[64]Michael J. Reynolds, *Morphine or Malpractice: Should Courts Recognize a Legal Duty to Prescribe Opiates for Treating Chronic Pain*, 15 J. Civ. Rights & Econ. Develop. 79, 79 (2000) (citing John J. Bonica, *Status of Pain Research and Therapy*, 5 Seminars in Anesthesia 82, 83 (1986) and Fenella Rouse, *Decision Making About Medical Innovation: Role of the Advocate*, 57 Alb. L. Rev. 607, 608 (1994)). For further discussion of pain treatment, see generally J. David Haddox & Gerald M. Aronoff, Commentary, *The Potential for Unintended Consequences From Public Policy Shifts in the Treatment of Pain*, 26 J.L. Med. & Ethics 350, 351 (1998); Sandra H. Johnson, *End-Of-Life Decision Making: What We Don't Know, We Make Up; What We Do Know, We Ignore*, 31 Ind. L. Rev. 12, 33 (1998); Alfred F. Connors et al., *A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients: The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT)*, 274 [J]AMA 1591, 1594–97 (1995); Bruce A. Ferrell, Betty R. Ferrell & Dan Osterweil, *Pain in the Nursing Home*, 38 J. Am. Geriatric Soc'y 409 (1990); Russell K. Portenoy, *Opioid Therapy for Chronic Nonmalignant Pain: A Review of the Critical Issues*, 11 J. Pain & Symptom Mgmt. 203 (1996); J. David Haddox, David Joranson, Robert T. Angarola, Albert Brady, Daniel B. Carr, E. Richard Blonsky, Kim Burchiel, Melvin Gitlin, Matthew Midcap, Richard Payne, Dana Simon, Sridhar Vasudevan & Peter Wilson, *The Use of Opioids for the Treatment of Chronic Pain: A Consensus Statement from the American Academy of Pain Medicine and the American Pain Society*, 13 Clin. J. Pain 6 (1997); Interview by John C. Liebeskind with John J. Bonica, in Honolulu, Hi. (Mar. 9–12, 1992) (transcript at 82, 83), https://www.iasp-pain.org/wp-content/uploads/2023/06/final_bonica.pdf [https://perma.cc/5PFT-9U3M]; Fenella Rouse, *Decision Making About Medical Innovation: The Role of the Advocate*, 57 Alb. L. Rev. 607, 608 (1994).

[65]Ctr. for U.S. Pol'y, CUSP FDA Citizen Petition to Protect Patients 6 (2023), https://centerforuspolicy.org/fdacp2023-2/ [https://perma.cc/WKX8-NNJF] (discussing the impacts of patients having unmet medical needs). In May 2023, the Center for U.S. Policy petitioned the FDA to remove NarxCare from the market, alleging that the company violates the Federal Food, Drug and Cosmetic Act (FDCA) by not complying with FDA requirements for medical devices. *Id.* at 1. Critics have noted that NarxCare was found to have a seventeen-percent false positive rate and a thirteen-percent false negative rate. Gerald Cochran, Jennifer Brown, Ziji Yu, Stacey Frede, M. Aryana Bryan, Andrew Ferguson, Nadia Bayyari, Brooke Taylor, Margie E. Snyder, Elizabeth Charron, Omolola A. Adeoye-Olatunde, Udi E. Ghitza & T. Winhusen, *Validation and Threshold Identification of a Prescription Drug Monitoring Program Clinical Opioid Risk Metric with the WHO Alcohol, Smoking, and Substance Involvement Screening Test*, 228 Drug & Alcohol Dependence, no. 109067, 2021, at 1, 5–7.

[66]Anna C.F. Lewis & Robert C. Green, *Polygenic Risk Scores in the Clinic: New Perspectives Needed on Familiar Ethical Issues*, 13 Genome Med., no. 14, 2021, at 1, 4.

[67]Shuren, *supra* note 1.

[68]Lovelace, *supra* note 49.

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FDA to rescind AvertD from the market worries, "[m]ost people who take this test are going to test negative and be left with the impression that they don't have to worry about getting addicted . . . and if they subsequently take opioids more aggressively for that reason, they are going to be more likely to get addicted."[69]

III. Physician Liability for Relying on a Genetic Test to Predict OUD

As demonstrated in Section II, polygenic risk scores for OUD are not a great predictor of addiction. Despite the unreliability of tests such as AvertD, physicians will likely (over)rely on genetic test results to make decisions about who will and will not receive access to opioids. But physicians are woefully untrained in genetics.[70] Thus, they may be ill-equipped to contextualize the (limited) utility of a "genetic test for opioid use" in an appropriate, moderated way. And although the AvertD test has only been approved for use in making decisions about opioid prescriptions for acute pain (e.g., post-surgical pain) for the opioid-naïve, it is predictable that physicians will rely on these tests in other contexts (e.g., for making prescription decisions to address chronic pain).

Genetic test results that purport to predict OUD — or really, any behavioral or psychiatric trait or diagnosis — may have enormous consequences for individual lives. Some of these concerns, such as the potential denial of appropriate pain relief or triggering of an OUD, could potentially be addressed through tort law remedies.

But tort law is inadequate to address the potential harms associated with genetic risk testing in opioid prescribing. Regardless of whether they rely on the AvertD test or not, the introduction of the test exposes physicians to liability, resulting in a "damned if you do, damned if you don't" dilemma.[71] And looking to tort law will not mitigate the individual and systemic issues raised by the introduction of a PGS test for OUD. Tort liability is ill-equipped to protect patients and ensure appropriate integration of these tests into clinical practice.

A. Tort Law

Tort law is "the law of wrongs."[72] Tort law is generally described as having two main goals (or at least two primary effects): deterring harms and compensating those who have been injured by others.[73] Professors David M. Studdert, Michelle M. Mello, and Troyen Brennan have explained that the goals of malpractice litigation are "to deter unsafe practices, to compensate persons injured through negligence, and to exact corrective justice."[74] These goals are echoed by Gary Marchant and colleagues in their analysis of liability in the context of genomics.[75] They explain that medical malpractice liability

[69]Mark Herz, *Scientists Blast FDA Approval of Genetic Test for Opioid Addiction*, GBH News (Apr. 4, 2024), https://www.wgbh.org/news/health/2024-04-04/scientists-blast-fda-approval-of-genetic-test-for-opioid-addiction [https://perma.cc/KQD2-9T5P] (quoting Dr. Andrew Kolodny, the medical director for opioid policy research at Brandeis University).

[70]*See generally* Marchant & Lindor, *supra* note 24. *See also* Tatiane Yanes, Courtney K. Wallingford, Mary-Anne Young, Aideen M. McInerney-Leo, Amanda M. Willis, Lauren McKnight, Bronwynn Terrill, Simone McInerny, Laura E. Forrest, Linda Cicciarelli, Rachel Williams, Holly Keane & Paul A. James, *Development and Evaluation of a Novel Educational Program for Providers on the Use of Polygenic Risk Scores*, 25 Genetics Med., no. 100876, 2023, at 1, 2 ("The lack of knowledge among providers is a significant barrier to successful evaluation and implementation of PRS and personalized risk assessment.").

[71]*See* Marchant & Lindor, *supra* note 24, at 8.

[72]John C.P. Goldberg & Benjamin C. Zipursky, Recognizing Wrongs 2 (2020).

[73]John C.P. Goldberg, *Twentieth-Century Tort Theory*, 91 Geo. L.J. 513, 525 (2003). Professors Goldberg and Zipursky posit that deterrence and compensation are not the goals of the tort system, but instead are the "beneficial effects of having tort law." Goldberg & Zipursky, *supra* note 72, at 29. Rather, the purpose of tort is to redress wrongs. *See id.* at 29–30.

[74]M. Studdert, Michelle M. Mello & Troyen Brennan, *Medical Malpractice*, 350 NEJM 283, 283 (2004) (citing W. Page Keeton et al., Prosser and Keeton on the Law of Torts 164–65 (5th ed. 1984)).

[75]*See* Gary Marchant, Mark Barnes, James P. Evans, Bonnie LeRoy & Susan M. Wolf, *From Genetics to Genomics: Facing the Liability Implications in Clinical Care*, 48 J.L. Med. & Ethics 11, 16 (2020) [hereinafter *Genetics to Genomics*].

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"is intended to deter health care providers from engaging in substandard and unreasonable health care practices, while incentivizing appropriate uptake of improved medical technologies and practices. Second, medical malpractice liability is intended to compensate those patients who are injured by negligent medical care."[76]

Professor Barry Furrow has argued that medical malpractice law serves four primary functions.[77] It "reinforces good medical practice," protects patients by giving a voice to those "who have been patronized, ignored, actively manipulated, or cruelly treated by physicians," guides more consistent practice based on empirically validated clinical practice guidelines,[78] and "articulates new duties of care for providers."[79]

A claim alleging medical malpractice must prove the classic four elements of a tort claim: (1) a duty of care owed by the defendant to use reasonable care to prevent harm to the plaintiff, (2) breach of that duty by failing to adhere to the standard of care, (3) harm or injury to the plaintiff, and (4) a causal link between the injury and the breach of duty.[80] Most jurisdictions define the standard of care for medical malpractice as based on what "the average careful, diligent and skillful physician in the community or like communities, would do or not do in the care of similar cases."[81] Proving the second element — breach of the duty of care — has historically been achieved through expert testimony showing that the physician's actions were not in accord with the customary practice of physicians in the same specialty in that same locality.[82] However,

> [T]he locality rule is being replaced in a number of jurisdictions with a national standard of care, in which a physician is not judged solely against similar practitioners in the same geographic region, but rather against doctors across the nation. Second, the standard of care based on custom (i.e., what other doctors are doing) is giving way in many jurisdictions to a more objective "reasonableness" standard in which the jury gets to determine whether a physician's actions were reasonable, regardless of the practice patterns of other physicians.[83]

Technological innovation often pushes tort law to evolve in novel ways. In fact, research has shown that scientific advances, particularly in genomics, has driven malpractice liability.[84] Professor Gary Marchant and colleagues explain that this "is because physicians and other providers are often unfamiliar with the new technologies and thus make more frequent mistakes, plus there is differential uptake of the

[76] *Id.* at 16.

[77] Barry R. Furrow, *Pain Management and Provider Liability: No More Excuses*, 29 J.L. Med. & Ethics 28, 30 (2001) (advocating for new cause of action against medical care providers who fail to appropriately treat pain).

[78] *Id.* at 30; *see, e.g.*, Deborah Dowell, Tamara M. Haegerich & Roger Chou, *CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016*, 315 [J]AMA 1624, 1624 (2016); Teryl K. Nuckols, Laura Anderson, Ioana Popescu, Allison L. Diamant, Brian Doyle, Paul Di Capua & Roger Chou, *Opioid Prescribing: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain*, 160 Annals Internal Med. 38, 38 (2014).

[79] Furrow, *supra* note 77, at 30.

[80] See Jessica W. Berg, Charles W. Lidz, Lisa S. Parker & Paul S. Appelbaum, Informed Consent: Legal Theory and Clinical Practice 156 (2d ed. 2001) (ebook); Studdert et al., *supra* note 74, at 283 ("The standard traditionally used to evaluate whether the breach in question rises to the level of negligence is medical custom — the quality of care that would be expected of a reasonable practitioner in similar circumstances.").

[81] Allan H. McCoid, *The Care Required of Medical Practitioners*, 12 Vand. L. Rev. 549, 558 (1959).

[82] Gary E. Marchant, Doug E. Campos-Outcalt & Rachel A. Lindor, *Physician Liability: The Next Big Thing for Personalized Medicine?*, 8 Personalized Med. 457, 459 (2011).

[83] *Id.* at 459 (footnotes omitted); Studdert et al., *supra* note 74, at 283 ("The standard traditionally used to evaluate whether the breach in question rises to the level of negligence is medical custom — the quality of care that would be expected of a reasonable practitioner in similar circumstances.").

[84] *Genetics to Genomics*, *supra* note 75, at 16 (citing William M. Sage, *Medical Liability and Patient Safety*, 22 Health Affs., no. 4, 2003, at 26, 28; Kennethe De Ville, *Medical Malpractice in Twentieth Century United States: The Interaction of Technology, Law and Culture*, 14 Int'l J. Tech. Assessment in Health Care 197, 197 (1998)).

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technologies, which can lead to disputes over whether the standard of care at a given time requires use of the new technology."[85] Even before the AvertD test was introduced, scholars recognized that

> Many genomic tests will give probabilistic rather than deterministic outcome — in other words, the test will indicate that patients may have a certain risk. The fact that an individual patient has a bad outcome is not in and of itself evidence of negligence, and in this area of clinical practice as in others, the clinician cannot be a guarantor of the patient's positive outcome. Rather, the negligence inquiry should focus on whether the clinician's recommendation of and reliance on a test was reasonable in the circumstances of the individual patient and consistent with the prevailing standard of care.[86]

B. AvertD as the Standard of Care

The FDA's approval of AvertD was predicated on the expectation that physicians exercise their best judgment in relying on the test results, in conjunction with all other information about the patient, to inform their decisions about whether to prescribe opioids to a patient.[87] The AvertD test is intended to provide probabilistic insights into a patient's risk of OUD.[88] It is not a definitive diagnostic tool. Physicians relying solely on the test's results without considering the broader clinical picture may expose themselves to liability if adverse outcomes occur. This underscores the importance of using the test as one component of a comprehensive assessment.

However, physicians may ignore or override the test results at their own risk. Because AvertD is a very new (and unproven) PGS test, it cannot be argued that it is the standard of care, because it has not been around long enough for a custom to develop.[89] However, using and relying on a diagnostic test — genetic or otherwise — can quickly become the standard of care.[90] With the introduction of the AvertD test, a physician may still, despite a positive test result, prescribe a patient experiencing acute pain an opioid, with adverse results. In such a case, the positive test result may be evidence that the physician, rather than simply exercising her professional judgment, violated the standard of care. As the test becomes more accepted amongst treating physicians, a doctor may be judged to be bucking custom by prescribing opioids despite a test result indicating a higher risk of OUD. Or a jury might find that a reasonable physician would have relied on these test results, particularly if the patient did, in fact, develop an OUD as a result of their opioid use. And if a professional society endorses AvertD (or a similar genetic test) to predict the likelihood of a patient developing OUD, physicians' "best judgment" could be quickly replaced by an expectation that the test be used to make opioid prescription decisions. To the extent that making opioid prescription decisions in reliance of the AvertD test results becomes the standard of care, physicians may avoid making decisions that are more patient-specific to evade liability.

By way of analogy, Professor Sonia Suter describes a situation where, despite warnings that a new prenatal test was "of uncertain value," a professional society's endorsement of the test led to it quickly becoming the standard of care, "not for medical reasons, but in response to liability concerns."[91] She describes an "alert" issued by the American College of Obstetrics and Gynecology ("ACOG")'s

[85] *Id.* at 16 (citing Michael D. Greenberg, *Medical Malpractice and New Devices: Defining an Elusive Standard of Care*, 19 Health Matrix 423, 424 (2009); Amy Jurevic Sokol & Christopher J. Molzen, *The Changing Standard of Care in Medicine: E-Health, Medical Errors, and Technology Add New Obstacles*, 23 J. Legal Med. 449, 450 (2002)).

[86] *Id.* at 22.

[87] *See* U.S. Food & Drug Admin., Executive Summary Prepared for the Meeting of the Clinical Chemistry and Clinical Toxicology Devices Panel on AvertD and SOLVD Health 2 (2022) ("Results of the test are intended to be used in combination with clinical evaluation and assessment of the patient."); Ovalle, *supra* note 1.

[88] *See* Ovalle, *supra* note 1 (discussing that patients with positive results are eighteen times more likely to develop an addiction after taking an opioid).

[89] Roberts & Suter, *supra* note 29, at 427 ("With any new technology, there is no clear standard of care because the practice has not been around long enough for a custom to develop.").

[90] *See id.* at 427 (discussing the emergence of common practices as a technology is more widely used).

[91] Sonia M. Suter, *Genomic Medicine – New Norms Regarding Genetic Information*, 15 Hou. J. Health L. & Pol'y 83, 111 (2015).

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Department of Liability, which warned that it was *imperative* that every prenatal patient be advised about the availability of this test" and that discussion about the test and the patient's decision with respect to the test be documented in the patient's chart.[92]

Moreover, in the context of opioids, physician prescribing behavior is already under a microscope.[93] Thus, for example, the decision to prescribe opioids despite a positive test result might be heavily scrutinized, and physicians may need to justify their prescribing decisions at a much higher evidentiary level — despite the fact that the test itself is in no way conclusive about its ability to predict a patient's likelihood of developing OUD.

C. Tort Law Claims that May Arise from Relying on AvertD in Clinical Practice

Prior to the recognition of the U.S. opioid epidemic, a consensus had begun to emerge that physicians were overly cautious in treating pain.[94] Scholars and policy makers argued that physicians have a duty to adequately treat pain[95] and that "the courts, through malpractice cases, should force the adoption of the new practices by imposing them now as the standards of care, thus holding physicians liable when a patient unnecessarily suffers pain."[96] They pointed to clinical practice guidelines as establishing a new standard of care for pain management,[97] and noted that the medical community seemed to be constantly underutilizing pain medication, a condition that some termed "opiophobia."[98]

However, as the opioid epidemic intensified, physicians began to face both civil and criminal liability for their prescribing decisions.[99] These efforts were intended to check inappropriate prescription decisions, with the hope of reducing the risk of developing OUD.[100] However, restricting opioid

[92]*Id.* at 111 (citing Sherman Elias, George L. Annas & Joe Leigh Simpson, *Carrier Screening for Cystic Fibrosis: A Case Study in Setting Standards of Medical Practice*, *in* Gene Mapping: Using Law and Ethics as Guides 186, 197 (George J. Annas & Sherman Elias eds., 1992) (emphasis added)).

[93]*See* Sari Horwitz & Scott Higham, *DEA Launches New Crackdown on Pharmacies and Opioid Over-Prescribers*, Wash. Post (Jan. 30, 2018), https://www.washingtonpost.com/world/national-security/dea-launches-new-crackdown-on-pharmacies-and-opioid-over-prescribers/2018/01/30/14cc20be-0600-11e8-94e8-e8b8600ade23_story.html [https://perma.cc/79FT-WJCS]. Opioid prescriptions are already policed at a higher level than almost all other medications. The Controlled Substances Act (CSA) (Pub. L. No. 91-513, 84 Stat. 1236 (1970) (codified as amended at 21 U.S.C. §§ 801–971) is administered by the Drug Enforcement Administration (DEA) (21 C.F.R. §§ 1306.04(a), 1306.07(c) (2025)). *See also* Gilah R. Mayer, *Bergman v. Chin: Why an Elder Abuse Case is a Stride in the Direction of Civil Culpability for Physicians who Undertreat Patients Suffering from Terminal Pain*, 37 New Eng. L. Rev. 313, 319 (2003). Under the CSA, the DEA is increasingly prosecuting physicians who knowingly and intentionally prescribe drugs outside of the usual course of medical practice or for non-legitimate medical purposes. *See id.* at 315. 21 U.S.C. § 841(b) contains a penalty enhancement for cases where distribution of controlled substance(s) in violation of § 841(a) results in death or serious injury. In 2018, the DEA announced a crackdown on prescribers for inappropriate dispensation of opioids, to deter over-prescribing the drugs. 21 C.F.R. § 1306 (2025). Opiates fall under Schedule II of the CSA because of their high potential for abuse, further fueling the public perception that opiates are dangerous. Mayer, *supra* at 319–20.

[94]*See* Mayer, *supra* note 93, at 314; Furrow, *supra* note 77, at 33–41; Reynolds, *supra* note 64, at 79.

[95]AMA Council on Ethical and Jud. Affs., *AMA* Code of Medical Ethics' *Opinions on Care at the End of Life*, 13 Virtual Mentor 1038, 1039 (2013). The Code of Medical Ethics issued by the Council on Ethical and Judicial Affairs of the American Medical Association provides, "Physicians have an obligation to relieve pain and suffering and to promote the dignity and autonomy of dying patients in their care." *Id.* at 1039. Professor Ben Rich has opined, "It would be a mistake, I believe, to interpret this provision as creating an ethical responsibility of physicians to effectively manage the pain experienced by patients only when they are dying." Rich, *supra* note 63, at 236. Although the language appears in a section of the Code of Ethics about care at the end of life, he opined that it is "most likely an acknowledgment of the fact that pain and suffering may be at their most acute in that context." *Id.* at 236.

[96]James R. Blaufuss, Note, *A Painful Catch-22: Why Tort Liability for Inadequate Pain Management Will Make for Bad Medicine*, 31 Wm. Mitchell L. Rev. 1093, 1095 (2005).

[97]Reynolds, *supra* note 64, at 95.

[98]Mayer, *supra* note 93, at n.11.

[99]*See generally* Dineen & DuBois, *supra* note 62.

[100]*See id.* at 36.

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prescriptions could also lead to undertreated pain.[101] It quickly became clear that, "[w]hile liability can serve to deter physicians with reckless prescribing behaviors . . . it may also discourage well-intentioned prescribers and compromise patient pain management."[102]

Today, physicians bear heightened responsibility when prescribing opioids compared to other medications, as "[p]hysicians can face serious legal sanctions for inappropriate prescribing, including malpractice liability, medical board discipline, and criminal convictions."[103]

With the introduction of a polygenic risk score that purports to predict an individual's likelihood of developing opioid use disorder, physicians will be in a "damned if you do, damned if you don't" situation. Ignoring test results (e.g., prescribing opioids after a positive result or denying opioids after a negative result) may lead to liability; but relying on the test results could also result in liability. Thus, physicians may face liability if they fail to treat patients with opioids in reliance on a positive test result. Or they may face liability if they treat patients despite a positive result. Or they may even face liability for decisions to prescribe a patient opioids in reliance of a negative test result.

Table 1 enumerates some of the possible tort claims to which a physician may be exposed with the introduction of a genetic test for OUD to clinical practice, as well as possible outcomes. The following sections will address each of these in turn.

Table 1. Potential Legal Outcomes Related to Genetic Risk-Based Prescription Decisions[104]

Test recommends:	Which is:	Physician:	Result:	Liability
No Opioid (high risk)	Correct	Follows advice	No OUD	No liability (no injury)
		Rejects advice	OUD	**Liability ?** [***scenario A***]
	Incorrect (false positive)	Follows advice	No OUD, but unnecessary pain	**Injury (pain); Liability?** [***scenario B***]
		Rejects advice	Opioid Rx, but no OUD	No liability (no injury)
OK Opioid (low risk)	Correct	Follows advice	Opioid Rx, but no OUD	No liability (no injury)
		Rejects advice	Unnecessary pain	**Injury (pain); Liability?** [***scenario C***]
	Incorrect (false negative)	Follows advice	OUD	**Liability?** [***scenario D***]
		Rejects advice	No OUD (but unnecessary pain)	**Injury (pain); Liability?** [***scenario E***]

[101]Jacob B. Nist, *Liability for Overprescription of Controlled Substances: Can It Be Justified in Light of the Current Practice of Undertreating Pain?*, 23 J. Legal Med. 85, 87 (2002).

[102]Y. Tony Yang, Marc R. Larochelle & Rebecca L. Haffajee, *Managing Increasing Liability Risks Related to Opioid Prescribing*, 130 Am. J. Med. 249, 249 (2017) (alteration in original).

[103]Dineen & DuBois, *supra* note 62, at 12 (alteration in original); Carol L. Galletly, Erika A. Chirstenson, Jessica Ohlrich & Julia Dickson-Gomez, *Out of Bounds: Physician Licensing Board Disciplinary Cases Related to Opioid Prescribing*, 52 J.L. Med. & Ethics 679, 680 (2024) ("Evidence suggest that concerns about potential entanglement in legal processes related to alleged opioid misprescribing [sic] make some physicians reluctant to prescribe opioids. This can result in under-treatment of pain and/or reluctance to treat patients with pain or opioid use disorders.").

[104]*See* W. Nicholson Price II, Sara Gerke & I. Glenn Cohen, *Potential Liability for Physicians Using Artificial Intelligence*, 322 [J]AMA 1765, 1766 (2019). *See also* W. Nicholson Price II, Sara Gerke & I. Glenn Cohen, *Liability for Use of Artificial Intelligence in Medicine*, *in* Research Handbook on Health, AI and the Law 150, 152 (Barry Solaiman & I. Glenn Cohen eds., 2024) (considering "styli[z]ed fact pattern, adapted from prior work, where AI makes a recommendation either according to the standard of care or not, the recommendation is correct or not, and the physician follows it or not."). The authors explain

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1. Failure to Provide the Test

Beyond the possible outcomes of administering and relying — or not relying — on the AvertD test outlined in Table 1, physicians may face liability for failure to provide the test when making opioid prescription decisions.

Even before the AvertD test was approved, physicians could be found liable for failure to administer a genetic test that could yield actionable results.[105] For example, in one case, a breast cancer patient brought a medical malpractice lawsuit against her physician for failing to recommend a genetic test — an Oncotype Dx assay.[106] She had been diagnosed with non-invasive cancer, which was treated but later returned and metastasized.[107] The patient alleged that had the genetic test been administered, the test results would have indicated the need for chemotherapy, which may have prevented the tumor recurrence.[108] The case was settled for 1.5 million dollars.[109]

Likewise, a patient who is prescribed opioids and subsequently develops an OUD could allege that, had the physician administered a genetic test (that would have yielded a positive result), they would not have been prescribed the drugs and developed a dependence. As the test becomes more accepted and incorporated into clinical practice, it will become increasingly possible that physicians who do not use the test will be susceptible to claims that they violated the standard of care.

2. Informed Consent

As a medical intervention, the law requires that patients must consent to administration of a genetic test.[110] Such consent includes disclosures of a "general description of the test, including the purpose of the test and the condition for which the testing is being performed," how the test will be administered, what test results could mean, the possibility of uninformative or false positive or negative test results, and physical or emotional risks of the test.[111]

Interestingly, despite the general liability rule that a physician must obtain informed consent before administering a test for a genetic mutation, the AvertD package insert explicitly calls for consent for the test to be administered.[112] This appears to be an outlier, as most package inserts do not include such language.[113]

However, one might question whether true informed consent is even possible with the administration of the AvertD test. Is it possible for a patient to consent to administration of the test if she worries that her refusal will result in the physician believing the patient to be a "drug seeker"? Physicians may easily deny the patient opioid pain relief because of negative assumptions resulting from the patient's refusal.

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that the "fact pattern is highly styli[z]ed to make points clearer; in the real world, these decisions are shrouded in probabilities and more complex points which we explore below. Moreover, we use very simplified binary language such as healed/injured and right choice/wrong choice just for illustrative purposes."

[105] *Genetics to Genomics*, *supra* note 75, at 18 (noting that "such a failure will result in liability only if it fails to meet the standard of care — not all adverse outcomes or wrong choices are the result of negligence.").

[106] *Id.* at 22.

[107] *Id.* at 22.

[108] *Id.* at 22 (discussing *Metastatic Cancer Settlement Case*, *infra* note 109).

[109] *Metastatic Cancer Originally Diaganosed [sic] as Non-invasive – $1,500,000 Settlement*, Va. Laws. Wkly (Dec. 29, 2014), https://valawyersweekly.com/2014/12/29/metastatic-cancer-originally-diaganosed-as-non-invasive-1500000-settlement/ [https://perma.cc/C3FS-URBK] [hereinafter *Metastatic Cancer Settlement Case*].

[110] *See* Kayte Spector-Bagdady, Anya Prince, Joon-Ho Yu & Paul S. Appelbaum, *Analysis of State Laws on Informed Consent for Clinical Genetic Testing in the Era of Genomic Sequencing*, 178 Am. J. Med. Genetics Part C 81, 81–86 (2019) (examining state laws specific to informed consent for genetic testing from fifteen states, focusing on scope and content of informed consent protections and disclosures).

[111] *What is Informed Consent?*, Medline Plus (July 28, 2021), https://medlineplus.gov/genetics/understanding/testing/informedconsent/ [https://perma.cc/T6AP-WJN5].

[112] Solvd Health, *supra* note 1 ("The test is indicated for use only in patients prior to receiving a first prescription of oral opioids for four-to-thirty days for acute pain, such as in patients scheduled to undergo a planned surgical procedure and ***who consent to having the test performed***." (emphasis added)).

[113] Google, "package insert device consent to having the test performed", 181,000,000 results (Sep. 30, 2024) (on file with the American Journal of Law and Medicine). Apart from yielding results of generic consent templates, AvertD's documentation was the only specific result of package inserts containing consent language. *Id.*

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Elizabeth Joniak-Grant, a non-voting member of the AvertD advisory committee that voted against its approval, similarly worried that pain patients might be treated unfairly if they decline to use AvertD.[114] And others have opined, "this is unlikely to be a genuinely free choice: patients may fear being stigmatized as potentially addicted if they don't agree to be tested."[115]

Similar concerns have been raised with regard to proposed brain scans that are intended to predict and measure chronic pain. Critics have cautioned,

> Whether refusal to undergo a scan should result in adverse inferences and legal consequences depends, in part, on the reliability of any brain imaging tests that are introduced. Unless the technology is highly accurate, adverse inferences should not be made about claimants who refuse to undergo the scan, and no legal requirement should be put in place. Any legal requirement to have a brain scan must also balance issues of autonomy, efficiency, and resource allocation.[116]

3. Physician Liability for Prescribing Opioids Despite a Positive Genetic Test Result [Scenario A]

Medical malpractice can attach when physicians fail to act on clinically significant information, particularly when there is "medical consensus regarding how to respond."[117] So, if the genetic test becomes so widely adopted that using it becomes the standard of care, a physician could be liable for failure to withhold opioid medications after a positive test result. The patient (or the patient's estate) may claim that the physician knew or should have known, based on the genetic test result, that prescribing the controlled substances would lead to addiction.

Already, in the absence of an FDA-approved genetic test that purports to predict OUD risk, physicians face civil and criminal liability for the harm that can occur when a patient is prescribed opioids.[118] For example, in February 2002, a Florida jury convicted Dr. James Graves of manslaughter in the deaths of four patients for whom he prescribed oxycontin for chronic pain relief, sentencing him to 62.9 years in prison.[119]

The introduction of the AvertD test may increase the possibility that a physician faces liability for opioid prescription decisions if the patient develops OUD. A test result indicating that a patient has a genetic predisposition to OUD could be relied on as evidence that the physician acted negligently in prescribing that particular patient an opioid for her pain control. Even though physicians are instructed to use discretion in making prescription decisions and to rely on the AvertD test results in context with environmental and other risk factors, it is foreseeable that a physician who prescribes an opioid to a patient despite a positive test result will face liability.

4. Physician Liability for Not Prescribing Opioids in Reliance of a False Positive Genetic Test Result [Scenario B]; Physician Liability for Not Prescribing Opioids Despite a Negative Test Result [Scenario C]; and Physician Liability for Treating Despite a False Negative Genetic Test Result [Scenario E]

If a patient receives a positive AvertD test result, a physician may rely on that result to abstain from prescribing that patient opioids, for fear of the patient developing OUD. However, in the event that the

[114]Ovalle, *supra* note 1 ("'Refusing the test could be interpreted by clinicians as a patient being drug-seeking,' she said.").

[115]Maia Szalavitz, *Say Hello to Your Addiction Risk Score – Courtesy of the Tech Industry*, N.Y. Times (Apr. 20, 2024), https://www.nytimes.com/2024/04/20/opinion/addiction-risk-score-avertd-narxcare.html [https://perma.cc/XM3B-HZRY].

[116]Karen D. Davis, Herta Flor, Henry T. Greely, Gian Domenico Iannetti, Sean Mackey, Markus Ploner, Amanda Pustilnik, Irene Tracey, Rolf-Detlef Treede & and Tor D. Wager, *Brain Imaging Tests for Chronic Pain: Medical, Legal and Ethical Issues and Recommendations*, 13 Nature 624, 635 (2017).

[117]Roberts & Suter, *supra* note 29, at 424. The authors note that medical malpractice does not distinguish between acting and failing to act. *Id.* at 424.

[118]*See* Robert Capodilupo & Jacob James Rich, *The Misinformed & Misguided Prescription Abuse Prevention Act: A Response to Delfino*, 2023 Yale L. & Pol'y Rev. Inter Alia 1, 15. As a result of the Controlled Substances Act, physicians are also reluctant to "provide legitimate opioid treatments for patients, out of fear of prosecution." *Id.* at 15.

[119]Diane E. Hoffmann, *Treating Pain v. Reducing Drug Diversion and Abuse: Recalibrating the Balance in Our Drug Control Laws and Policies*, 1 St. Louis Univ. J. Health L. & Pol'y 231, 237–38, 238 n.26 (2008).

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test resulted in a false positive, a patient may be denied pain medication and suffer from unnecessary or undertreated pain. Similarly, if a patient receives a negative test result, but the physician still decides to refuse to prescribe opioids, the patient may suffer from undertreated pain. Or (to consider an even more complex scenario), a physician may administer a genetic test that falsely indicates that the patient is not at a high risk of developing OUD, the physician rejects the false results (by exercising her professional judgment) and does not prescribe opioids anyhow. In all three scenarios, the patient does not receive opioids (and therefore, presumably, does not develop an OUD), but may suffer unnecessary pain as a result. Thus, Scenarios B, C, and E will be considered together.

Tort law's customary practice sets the medical standard of care, without focusing on "the effectiveness of that practice."[120] As discussed above, medical custom has been to undertreat pain.[121] And, "[b]ecause undertreatment of pain often constitutes the prevailing practice amongst physicians, adhering to that practice does not violate any professional duty imposed by law on the physician."[122] In fact, physicians are much more likely to be sued or held liable for over-prescribing opioids than under-prescribing them.[123]

Historically, it has been widely acknowledged that "there is no medical malpractice cause of action for failure to adequately treat pain."[124] As a general rule, treatment decisions that result in un- or undertreated pain are not legally actionable harms.[125] In other words, "a physician's failure to adequately treat pain does not expose that physician to liability for medical malpractice."[126] And, in practice, patients have been unsuccessful in claiming that physicians ineffectively managed their pain.[127]

Over the years, however, some scholars have advocated "that chronic pain patients should utilize tort law to vindicate their rights" by recognizing "a tort claim in medical malpractice against physicians who under-prescribe [sic] opioid medications for those suffering chronic pain."[128] They argue that "for a population whose pain remains undertreated, legal remedies that ensure access to appropriate analgesia is indicated."[129]

[120]Furrow, *supra* note 77, at 31; Mayer, *supra* note 93, at 316 ("Common sense and public policy dictate that to protect the health and lives of the public, physicians must be held liable to their patients for failure to practice medicine with the requisite degree of care, skill, or knowledge. A physician is reasonably expected to possess the medical knowledge commonly possessed in the same specialty or general field of practice throughout the United States. The traditional view, followed by a majority of the jurisdictions, is that the usual and customary practice sets the standard of care for physicians.") (footnotes omitted).

[121]Reynolds, *supra* note 64, at 89 ("Since under-treating pain has been the *accepted* practice within the medical community, peers have exerted minimal pressure to change the norm") (citing Ann M. Martino, *In Search of a New Ethic For Treating Patients With Chronic Pain: What Can Medical Boards Do?*, 26 J.L. Med. & Ethics 332, 339–41 (1998) ("describing how institutionalized pressures reinforce ethic of under-prescribing")).

[122]Mayer, *supra* note 93, at 316.

[123]Reynolds, *supra* note 64, at 89, n.63.

[124]Mayer, *supra* note 93, at 315, n.25. Instead, "[p]ain as a component of a tort suit shows up primarily in pain and suffering awards for a physician's negligent treatment or diagnosis of a patient that leads to physical harm and accompanying pain . . . If, however, a physician's treatment of the patient's illness meets the medical standard of care, then the pain attendant on the normal course of illness has typically not been the subject of tort damages. What is needed is recognition that the standard of care in treating patients includes pain management as much as it does treatment of the disease." Furrow, *supra* note 77, at 28.

[125]*See* Blaufuss, *supra* note 96, at 1094–95 (describing legal liability for inappropriate pain treatment as a "new cause of action").

[126]Mayer, *supra* note 76, at 316, nn.28–33.

[127]*See, e.g.*, McGregor v. Hospice Care of La. in Baton Rouge L.L.C., 36 So. 3d 281, 285–86 (La. App. 1 Cir. 2010) (relying on expert testimony to find that doctors did not breach standard of care where plaintiffs alleged negligence in under-prescription of pain medication).

[128]Reynolds, *supra* note 64, at 81; Rima J. Oken, Note, *Curing Healthcare Providers' Failure to Administer Opioids in the Treatment of Severe Pain*, 23 Cardozo L. Rev. 1917, 1923, 1982–91 (2002) (proposing model legislation to impose liability on health care providers for failure to administer proper pain management).

[129]Joseph J. Fins & Zachary E. Shapiro, *Pain Management, Disorders of Consciousness, and Tort Law: An Emergent Tort to Fix a Longstanding Injustice*, 98 Ind. L.J. 693, 707 (2023) (arguing for a novel tort for failure to treat pain in patients with disorders of consciousness). In contrast, James Blaufuss has argued against a tort cause of action for failure to adequately treat pain. *See* Blaufuss, *supra* note 96, at 1096–97. He claims that "[i]nadequate pain treatment does not fit within the traditional notion of medical malpractice because a patient could not say that the physician caused the pain. Rather, the physician simply failed to alleviate the patient's pre-existing pain." *Id.* at 1097. While this may be true for pre-existing chronic pain, this argument against tort liability for adequate pain control may not apply for post-surgical pain. When a patient's pain is the direct result of a physician's surgical intervention, the patient has a stronger argument that the physician's duty has not be met. *See* Howard

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Although these proposals had already begun to lose traction as the opioid epidemic took hold,[130] recently, courts have demonstrated a bit more openness to claims against physicians for under prescribing pain medication.[131] They have begun to entertain the possibility of malpractice liability for inadequate pain control.[132] That said, most cases that have allowed a patient to recover have involved patients suffering from chronic pain who are often at the end of life. For example, in 1991, a jury returned a fifteen million dollar verdict against a nursing home and its nursing staff for failure to provide appropriate pain management to a terminally ill patient with metastatic prostate cancer.[133] They withheld medication due to concerns that the patient was "addicted to morphine."[134] The court noted that its decision was based on the allegation that the defendants "caused increased pain and suffering."[135]

Likewise, in 2000, a jury found a physician liable for under-treatment of pain.[136] In *Bergman v. Chin*, the jury awarded the patient's family 1.5 million dollars for their father's pain and suffering, which was reduced to 250,000 dollars due to the state's cap on noneconomic damages under the Elder Abuse Act.[137] Again, the case involved chronic — rather than acute — pain management. In 1998, eighty-five-year-old William Bergman was hospitalized after presenting to the emergency room with severe pain.[138] The attending physician, Dr. Chin, testified that he typically gauged patients' pain by asking them how they are feeling and observing their demeanor.[139] However, despite reporting that his pain was a "10 on a 10-point scale[,] the worst pain imaginable," Dr. Chin planned to discharge Bergman from the hospital without a medication strong enough to control the pain.[140] Only after the patient's daughter objected "did Dr. Chin order another administration of Demerol and prescribe a fentanyl patch."[141] However, after Bergman was discharged, Dr. Chin refused to prescribe morphine for Mr. Bergman's pain.[142] Bergman died of advanced lung cancer three days later.[143]

Supported by the national Compassion in Dying Federation, Bergman's daughter filed suit against Dr. Chin for failure to adequately manage her father's pain.[144] Because, in California, medical malpractice

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Y. Park, Richard Hwang, William L. Sheppard, Gideon Blumstein, Akash A. Shah Jesus A. Medina, Melani N. Cargle, Amador Bugarin, Christopher D. Hamad, Joshua D. Proal, Ryan Smith, Nicholas M. Bernthal, A. Nick Shamie & Don Y. Park, *Predictors of Medical Malpractice Outcomes After Spine Surgery: A Comprehensive Analysis From 2010 to 2019*, 34 Clin. Spine Surgery 228, 228, 230–31 (finding that in cases where plaintiffs alleged improper postoperative management as a reason for litigation following spine surgery, plaintiffs obtained statistically significantly higher median verdict awards; however, equal percentages of cases were decided in favor of plaintiffs whether or not pain and suffering were a result of the alleged negligence). In other words, if the physician had not performed the surgical intervention, the patient would not have experienced the pain, requiring amelioration.

[130]Fins & Shapiro, *supra* note 129, at 706–07 ("The notion of a tort for inadequate pain amelioration has fallen by the wayside, especially given the emergent information about the risk of opioid addiction with drugs like OxyContin and Fentanyl.").

[131]*See, e.g.*, Garcia v. Sleeley, No. 3:14-cv-01525-JLS-PCL, 2018 WL 3303013, at *11 (S.D. Cal. July 5, 2018) (finding that defendant doctors "were not deliberately indifferent toward Garcia's pain; but instead responded to Plaintiff's medical needs in a way they saw fit" when faced with allegations that "they undermedicated Plaintiff with 'weak' pain relieving medications").

[132]*See* Davis v. City of Phila., 284 F. Supp. 3d 744, 747, 757–58 (E.D. Pa. 2018) (finding that detainee plaintiff had sufficiently stated medical malpractice claim where complaints of severe pain stemming from wrist fracture were treated only with over-the-counter pain medication without additional consultation from specialist).

[133]Oken, *supra* note 128, at 1977–78.

[134]*Id.* at 1977–78.

[135]*Id.* at 1978 (discussing case as a rare instance of recovery in inadequate palliative care suit).

[136]*Id.* at 1978.

[137]*Judge Reduces 'Landmark' Pain Management Award to $250,000*, Cal. Healthline (Aug. 23, 2001), https://californiahealthline.org/morning-breakout/judge-reduces-landmark-pain-management-award-to-250000/ [https://perma.cc/MFG2-X2G4]. *See also* Cal. Civ. Code § 3333.2.

[138]*See* Ben A. Rich, *Moral Conundrums in the Courtroom: Reflections on a Decade in the Culture of Pain*, 11 Cambridge Q. Healthcare Ethics 180, 181.

[139]*Id.* at 182.

[140]*Id.* at 182.

[141]*Id.* at 182.

[142]*Id.* at 183.

[143]*Id.* at 183.

[144]*Id.* at 183. The patient's daughter, Beverly, first sought a response from the state Medical Board to address Dr. Chin's alleged undertreatment of Bergman's pain. *Id.* at 183. However, even though the Medical Board of California acknowledged that "pain management for your father was indeed inadequate," it stated, "there is insufficient evidence at this time to warrant

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damages for pain and suffering are not available following a patient's death, she instead relied on the state's Elder Abuse Law.[145] The jury found Dr. Chin liable for gross negligence.[146]

The verdict in *Bergman* may be an outlier, as California's elder abuse statute is somewhat anomalous.[147] However, despite the fact that most states do not have similar laws, the decision may still have affected medical practice across the country. In response to this case, Professor Robyn Shapiro opined, "So I find it exciting . . . . It sends a message to physicians and other health care providers that pain management has to be an integral part in what they need to think about to provide adequate care."[148] Scholars argue that in such cases, physicians

> are between a rock and a hard place, damned if they do and damned if they don't. The suggestion here is that when physicians are aggressive in their use of opioid analgesics, they are disciplined by medical boards or at risk of prosecution under the criminal law. When they are cautious and conservative (presumably like Dr. Chin) in prescribing such narcotics, they are vulnerable to lawsuits by patients or families and the wrath of juries.[149]

However, all these cases address the failure to provide pain control for chronic (and often end-of-life) pain. In contrast, courts have not yet opined on undertreatment of acute pain. As policy statements and clinical practice guidelines that delineate standards for appropriate pain management continue to be developed, it may be more likely that courts will find that the failure to address a patient's pain constitutes medical negligence. When a patient's un- or undertreated pain is the direct result of a physician's surgical intervention, the patient has a stronger argument that the physician's duty has not been met.[150] In other words, if the physician had not performed the surgical intervention, the patient would not have experienced the pain, thereby requiring amelioration.

Proposals to impose liability on health care providers for failure to administer proper pain management may face a steeper challenge if the decisions to refuse to prescribe opioids is premised on genetic test results. This is particularly true where, due to genetic test results that indicate that the patient is not at risk of developing OUD (Scenario C), the physician has less justification for withholding opioids for acute pain control. The introduction of the AvertD test bares striking similarities to the reliance on NarxCare, a "clinical decision support [CDS] and analytics solution" that "helps clinicians and care team members evaluate controlled substance data from government managed and regulated prescription drug monitoring programs to make more informed prescribing decisions"[151] to guide opioid prescription decisions, in which patients can be denied certain pain care — apparently without recourse — even when such care is medically indicated.[152] As Maia Szalavitz reported, NarxCare returned potentially incorrect risk assessments, and medical staff members operated in fear about disregarding NarxCare scores.[153] Physicians may similarly be concerned about liability for failure to rely on AvertD test results, even when they would pursue a different treatment approach in its absence.

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pursuing further action in this case." Susan Okie, *Doctor's Duty to Ease Pain at Issue in Calif. Lawsuit; Physicians are Wary in Prescribing Narcotics*, Wash. Post (May 6, 2001), https://www.washingtonpost.com/archive/politics/2001/05/07/doctors-duty-to-ease-pain-at-issue-in-calif-lawsuit/c5cce996-344e-40d3-b656-c5da7338e050/ [https://perma.cc/4FPU-DKYM].

[145] *See* Mayer, *supra* note 93, at 330.

[146] Rich, *supra* note 138, at 187.

[147] *See* Maria L. La Ganga & Terence MonManey, *Doctor Found Liable in Suit Over Pain*, L.A. Times (June 15, 2000, at 00:00 PT), https://www.latimes.com/archives/la-xpm-2001-jun-15-mn-10726-story.html [https://perma.cc/FQ47-B6TG].

[148] *Id.*

[149] Rich, *supra* note 138, at 187 (footnote omitted).

[150] *See* Park et al., *supra* note 129, at 230–31 (finding that in cases where plaintiffs alleged improper postoperative management as reason for litigation following spine surgery, plaintiffs obtained statistically significantly higher median verdict awards; however, equal percentages of cases were decided in favor of plaintiffs whether or not pain and suffering were result of alleged negligence).

[151] NarxCare, https://bamboohealth.com/solutions/narxcare/ [https://perma.cc/Z2BC-XJK2] (last visited July 24, 2024).

[152] *See* Szalavitz, *supra* note 115.

[153] *Id.* ("I heard from patients who were left in agony. One said that she had her opioids stopped in the hospital and was then dismissed from care by her gynecologist during treatment for painful endometriosis, because of a high score. She didn't have a

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Even if a court were to recognize a claim for undertreatment of pain due to reliance on a genetic test for OUD, proving pain as damages may prove daunting. In such a case, the patient's pain is not caused directly by the physician's intervention, but rather by her passivity. In contrast,

> In the normal tort case, pain is the result of a bodily injury caused by the defendant. The court is willing to instruct juries on pain and suffering when the plaintiff has suffered tangible injury due to the defendant. In the medical setting, pain from a missed diagnosis and lost opportunity to treat can be part of damages. The pain management failures are more complicated: The physician or provider is responsible not for the patient's condition, but for the mismanagement of pain, which is a by-product and symptom of an underlying disease. Pain, therefore, becomes the only component of damages, by analogy to the mental distress torts. The loss of enjoyment of life, as a corollary of the pain, may be allowed as a separate component of damages. The plaintiff's reactions to the pain and his or her sense of loss as a result may also be compensable.[154]

5. Physician Liability for Not Treating in Reliance of a False Negative Genetic Test Result [Scenario D]

When an AvertD test returns a false negative genetic test result, and the physician prescribes the patient opioids in reliance of those results, they may face liability if the patient nevertheless develops an OUD. In other words, relying on an FDA-approved genetic test may not be enough to obviate physician liability. In the event a physician prescribes a patient opioids, relying solely on genetic test results that indicate a normal likelihood that the patient will develop an OUD, without considering the non-genetic factors that contribute to OUD risk, the physician may be liable — particularly if the test returned a false negative result.

By way of analogy, physicians have been unable to avoid liability by arguing that they relied on electronic health records (EHRs) or clinical algorithms to make their treatment and prescribing decisions. For example, "[t]he case law on EHRs . . . establishes that 'physicians can be held liable for harm that could have been averted had they more carefully studied their patients' medical records.' Use of the models could cause clinicians to reduce the time they spend with those medical records and thus increase their liability."[155] Liability can still be found due to courts' concern that physicians will over-rely on the results of tests or records, instead of considering the whole patient.[156] In the case of the AvertD test, solely relying on the test results to make treatment decisions is particularly problematic because genetics is only one contributing factor, and, as discussed in Section II, test results are intended to be considered within the context of all the other factors that may contribute to a patient's likelihood of developing OUD.

The AvertD test's high return of false negative and false positive test results also opens physicians up to increased liability when they rely on the tests to make treatment decisions. Similarly, "[i]n the case of computer decision support software more generally, some legal scholars suggest that courts are likely to fault a physician for failing to question bad advice given by the software — even if the error was in the software — because courts would assume that physicians would ultimately rely on their own judgment and professional knowledge."[157]

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drug problem; her score seems to have been elevated because prescriptions for her two medically needy rescue dogs were recorded under her name, making it appear she was doctor shopping. Another high-scoring patient had his addiction treatment medication prescription repeatedly rejected by pharmacies, even though such medications are the only treatment proven to reduce overdose risk.").

[154]Furrow, *supra* note 77, at 36 (citing Dan B. Dobbs, Law of Torts 1050, 1052 (2000)).

[155]I. Glenn Cohen, Ruben Amarasingham, Anand Shah, Bin Xie & Bernard Lo, *The Legal and Ethical Concerns that Arise from Using Complex Predictive Analytics in Health Care*, 33 Health Affs. 1139, 1144 (2014) (citing Sharona Hoffman & Andy Podgurski, *E-Health Hazards: Provider Liability and Electronic Health Record Systems*, 24 Berkeley Tech. L.J. 1524, 1541 (2009)) (footnotes omitted).

[156]*See id.* at 1144.

[157]*Id.* at 1144 (citing MS Ridgely & MD Greenberg, *Too Many Alerts, Too Much Liability: Sorting Through the Malpractice Implications of Drug-Drug Interaction Clinical Decision Support*, 5 St. Louis Univ. J. Health L. Pol'y 257, 267 (2012)).

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In such cases, it may be useful to look to another area of torts where genetic knowledge is transforming how the law approaches liability: toxic tort liability. In the context of toxic tort liability, genetic testing is used to demonstrate that a manufacturer was not responsible for the outcome because the individual had a preexisting genetic susceptibility.[158] Like toxic tort cases, where the question of liability focuses on whether a particular toxic substance — or an individual's individual genetic makeup — produced the disease in a particular individual,[159] here, the question is whether an individual's genetic makeup led to the patient's OUD.

Like in toxic tort cases, however, proving causation may be challenging.[160] First, the patient would have to show that the original test, administered by the prescribing physician, returned a false negative result — presumably by taking another genetic test that yielded a different result.[161] In other words, the plaintiff would have to demonstrate that she, in fact, had the relevant genetic susceptibility to OUD. Further, the patient would need to demonstrate that her (misdiagnosed) genetic predisposition caused her OUD, rather than any other number of other epigenetic and environmental causes.[162] In other words, she would then have to prove that, had the physician taken other factors into consideration, such as environmental and lifestyle factors, the physicians would have abstained from prescribing opioids to the patient, thereby avoiding the patient's OUD. She would have to show that, but for the test, she would have received different treatment.

In toxic tort cases, "[t]o satisfy this causation requirement, some (but not all) courts require that plaintiffs demonstrate that the defendant's action doubled their background risk (i.e., relative risk > 2.0) such that the exposure was 'more likely than not' the cause of the illness in the individual."[163] The AvertD marketing materials state that "Patients with Elevated Genetic Risk were shown to be *eighteen times more likely* to develop OUD than patients with a Non-Elevated Genetic Risk."[164]

As discussed above, it is likely that, eventually, reliance on PGS for OUD (and other behavioral traits or psychiatric illnesses[165]) will become the standard of care.[166] If this becomes the case, the physician's reliance on the test, even with the false negative result, may protect the physician from liability. This result is particularly problematic in cases where the tests are not highly accurate or are only partially informative of one's true risk, and it undermines arguments that physicians should be

[158]Diane E. Hoffmann & Karen H. Rothenberg, *Judging Genes: Implications of the Second Generation of Genetic Tests in the Courtroom*, 66 Md. L. Rev. 858, 867 (2007) (citing Severson v. Allied Chems. Co., No. 1-90-CV-698517 (Cal. Super. Ct. Dec. 18, 1995) (demonstrating that courts have ordered genetic testing to determine whether genetic disorder or mother's exposure to chemical solvent at work during pregnancy was cause of plaintiff-child's disability). Similarly, in medical malpractice cases, genetic testing has proven useful and has been compelled where the results could show that the physician was not responsible for disabilities of a newborn infant. Jennifer M. Champagne, *Genetic Testing and Testimony in Toxic Tort Litigation: 'Admissibility and Evaluation'*, 13 N.C. J.L. & Tech. 1, 6 (2011) (citing Harris v. Mercy Hosp., 596 N.E.2d 160, 163 (111. App. Ct. 1992)).

[159]*See* Gary E. Marchant, *Genetic Data in Toxic Tort Litigation*, 14 J.L. & Pol'y 7, 8 (2005) [hereinafter Marchant, *Toxic Tort*].

[160]*See id.* at 9–10 ("Plaintiffs in toxic tort lawsuits must prove that the toxic substances to which they were exposed caused their illness.").

[161]*See* Champagne, *supra* note 158, at 9–11 (discussing how similar process is used for establishing causation in toxic tort litigation).

[162]*See id.* at 9–11.

[163]Marchant, *Toxic Tort*, *supra* note 159, at 9 (citing Daubert v. Merrell Dow Pharm., Inc., 43 F.3d 1311, 1321 (9th Cir. 1995); Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1403–04 (D. Or. 1996); Russellyn S. Carruth & Bernard D. Goldstein, *Relative Risk Greater Than Two in Proof of Causation in Toxic Tort Litigation*, 41 Jurimetrics J. 195, 195 (2001)).

[164]*What is Genetic Risk?*, AvertD, https://avertdtest.com/for-providers/ [https://perma.cc/MQ6S-P8VJ] (last visited Oct. 23, 2025) (citing Donaldson et al., *supra* note 52).

[165]*See generally* Amanda L. Rodrigue, Samuel R. Mathias, Emma E.M. Knowles, Josephine Mollon, Laura Almasy, Laura Schultz, Jessica Turner, Vince Calhoun & David C. Glahn, *Specificity of Psychiatric Polygenic Risk Scores and Their Effects on Associated Risk Phenotypes*, 3 Biological Psychiatry 519 (2022) (citing Gunnar W. Reginsson, Andres Ingason, Jack Euesden, Gyda Bjornsdottir, Sigurgeir Olafsson, Engilbert Sigurdsson, Hogni Oskarsson, Thorarinn Tyrfingsson, Valgerdur Runarsdottir, Ingunn Hansdottir, Stacy Steinberg, Hreinn Stefansson, Daniel F. Gudbjartsson, Thorgeir E. Thorgeirsson & Kari Stefansson, *Polygenic Risk Scores for Schizophrenia and Bipolar Disorder Associate with Addiction*, 23 Addiction Biol. 485, 486–87 (2018); Caitlin E. Carey, Arpana Agrawal, Kathleen K. Bucholz, Sarah M. Hartz, Michael T. Lynskey, Elliot C. Nelson, Laura J. Bierut & Ryan Bogdan, *Associations between Polygenic Risk for Psychiatric Disorders and Substance Involvement*, 7 Frontiers in Genetics 1, 8 (2016)). Importantly, studies have also demonstrated that psychiatric PGS are related to "allied" phenotypes, such as substance use. *See id.* at 519.

[166]*See generally* Roberts & Suter, *supra* note 29 (discussing determination of standard of care).

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expected to exercise their best judgment in the context of all other contributing factors. More specifically, if a patient presents with other factors that indicate a probability of developing OUD, but the physician ignores those by relying solely on the AvertD test, then presumably there should be liability.

SolvD Health makes efforts to insulate itself from responsibility if a patient with an AvertD test result that indicates a "non-elevated genetic risk" for OUD develops or has an OUD, seemingly intending to shift the blame to physicians who rely on the test with problematic outcomes.[167] On its website describing the test to health care providers, it disclaims,

> Because genetic variations only account for a portion of a person's risk of developing OUD, it is possible that an individual with a "Non-Elevated Genetic Risk" result will develop OUD or may already have OUD. AvertD test results should not be used as the sole basis for treatment or patient management decisions, including prescribing oral opioids.[168]

6. Liability for Off-Label Uses

While AvertD was specifically approved for use in making decisions about opioid prescription for acute pain, there is no limiting how these tests could, in fact, be used. Not only is it likely that physicians will (over)rely on the AvertD test for its stated purpose of making opioid treatment decisions for opioid-naïve patients with acute pain, it is also likely that they will rely on the test for other off-label purposes. Because the FDA does not regulate the practice of medicine, physicians are free to use approved medical devices for other reasons beyond that for which they were approved.[169] Thus, while the FDA approved the test for a specific, narrow use with the stated goal of protecting patients and avoiding some of the concerns raised by the advisory committee when it recommended against the test's approval[170] physicians are privileged to administer the test for off-label use, or use not specified in the device's FDA-approved labeling. In fact, off-label use is an "important part of mainstream, legitimate medical practice."[171]

Once approved, physicians have the authority to rely on these tests for other decisions as well, including the treatment of chronic pain or for patients with a history of opioid use.[172] Even when physicians administer the test for its intended use,

> Patient advocates wonder if time-strapped doctors, despite FDA-mandated labeling, will lean too heavily on results instead of asking probing questions of patients. Will doctors prescribe the test off-label? Could a test indicating a risk for addiction be memorialized in medical records and used against a patient years later — in a custody dispute in court, or by an employer? Will someone with an elevated test come to believe they are prone to addictions of all sorts?[173]

The implications of relying on the AvertD test, or any genetic test for that matter, in the treatment of chronic pain are vast. For non-opioid-naïve patients, a positive AvertD test result could lead to concerning health decisions. Already, responses to the opioid epidemic have led to an increase in reports of long-term pain patients being abruptly tapered off their medication or abandoned of care

[167] *See What is Genetic Risk?*, *supra* note 164.

[168] *Id.*

[169] *FDA's Role in Regulating Medical Devices*, U.S. Food & Drug Admin., https://www.fda.gov/medical-devices/home-use-devices/fdas-role-regulating-medical-devices (last visited Oct. 23, 2025) ("FDA regulates the sale of medical device products . . . and monitors the safety of all regulated medical products . . . . The FDA does not have the authority to . . . [r]egulate a physician's or nurse's practice.").

[170] *See* Shuren, *supra* note 1 (discussing FDA approval of AvertD and some of the concerns of the advisory committee).

[171] Veronica Henry, *Off-Label Prescribing: Legal Implications*, 20 J. Legal Med. 365, 365 (1999).

[172] *See* Shuren *supra*, note 1 (discussing FDA intended uses of AvertD by practitioners).

[173] Ovalle, *supra* note 1.

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altogether.[174] And, "[a]s a result, patients report damage to their mental and physical health. Some are no longer able to work or function and have suffered financial devastation as a result. Others have resorted to the illegal market and even suicide when their medication or care is denied."[175] In response to a positive test result, physicians may modify patients' prescribed dosages or even stop providing care, like we have seen in response to NarxCare data.[176] Patients who are denied continued pain control are vulnerable to seeking care illegally or turning to street drugs.[177] Relying on a genetic test in making pain treatment decisions runs the risk of exacerbating these outcomes.[178]

Thus, reliance on these tests to deny individuals care upon which they have already become reliant may further exacerbate the very problem utilizing the test is intended to avoid. And just like with acute pain patients, physicians who continue to prescribe opioids to chronic pain patients who received a positive test result could open themselves up to increased liability.

IV. AvertD'ing Physician Liability

Although the introduction of AvertD may expose physicians to liability, relying on tort law will not mitigate the individual harms raised by the introduction of a PGS test for OUD. In cases where patients are denied access to opioid treatment due to AvertD test results that indicate a higher risk of developing OUD, patients are unlikely to succeed in cases alleging insufficient treatment, leading to uncontrolled pain.[179] In cases where patients are (inappropriately) prescribed opioids in reliance of the test, it will be difficult to prove causation.[180] Similarly, patients will have difficulty accessing claims alleging failure of informed consent.[181]

The delineation of clear rules often goes a long way in guiding consistent, ethical behavior. But in the case discussed here, it is difficult to imagine what a clear tort rule would look like. For example, it might be suggested that states implement liability protections for those who incorporate PGS tests for OUD into clinical practice by using them to guide opioid prescription decisions. Liability shields are invoked

[174]Kate M. Nicholson & Deborah Hellman, *Opioid Prescribing and the Ethical Duty to Do No Harm*, 46 Am. J.L. & Med. 297, 308 (2020).

[175]*Id.* at 308 (footnotes omitted). Legal scholars have argued that physicians could be liable for wrongful death based on negligent tapering of opioids, which could presumably be extended to wrongful death due to negligent refusal of opioids. *See generally* Mark A. Rothstein & Julia Irzyk, *Physician Liability for Suicide After Negligent Tapering of Opioids*, 50 J.L. Med. & Ethics 184 (2022).

[176]*See* Maia Szalavitz, *The Pain was Unbearable. So Why Did Doctors Turn Her Away?*, WIRED, https://www.wired.com/story/opioid-drug-addiction-algorithm-chronic-pain/ [https://perma.cc/94AU-CC8H] (last visited Aug. 10, 2021) (discussing how doctors are concerned about prescribing opioids to opioid addicts through NarxCare database containing information on patients who "doctor shop" and end up turning away patients).

[177]*Id.*; *see also* Ovalle, *supra* note 1 (discussing in part doctors writing fewer prescriptions and users turned to illegal street drugs).

[178]To illustrate, many state rules limit opioid dosages to ninety morphine milligram equivalents (MMEs) per day, based on CDC guidelines. Rita Rubin, *Limits on Opioid Prescribing Leave Patients with Chronic Pain Vulnerable*, 321 [J]AMA 2059, 2059 (2019). Although these rules "target prescribing for *acute* pain," it is recognized that they could affect prescribing for *chronic* pain as well. *Id.* at 2060. And this has had significant implications for the provision of adequate care to chronic pain patients, including the cessation of prescribing opioids for chronic pain. *See id.* at 2060. A North Carolina study found that some chronic pain patients had their physicians stop prescribing them opioids and provided them a copy of the Strengthen Opioid Misuse Prevention (STOP) Act, which limits prescriptions covering acute pain to five or seven days. *Id.* at 2060. "The STOP Act specifically states that the limits do not apply to chronic pain. And yet, a quarter (663) of the 2861 physicians who responded last fall to a survey by the North Carolina Medical Board said they had stopped prescribing opioids for chronic pain." *Id.* at 2060.

[179]*See generally* Valerie Gutmann Koch, *The Opioid Crisis Meets Genomics*, 56 Seton Hall L. Rev. 1 (2025) (discussing challenges patients will face in winning medical malpractice actions with the new AvertD test).

[180]*Id.* at 51.

[181]*See id.* at 9; *see also* Szalavitz, *supra* note 115 (discussing the difficulties arising from the informed consent requirement on the black box of the test and patients may feel stigmatized if they don't take the test).

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when policy makers seek to encourage certain behaviors or actions.[182] However, due to the unreliability of the AvertD test and the myriad ethical concerns that may arise,[183] in the case of AvertD, it would be inappropriate to incentivize the use of the test through liability protections.

Further, modifying tort rules would likely remain insufficient to changing physician behavior.[184] Other fears, such as threats of disciplinary and criminal actions, would continue to deter physicians from providing adequate pain relief.[185] As James Blaufuss explains, "[t]here is no evidence that the deterrence effect of tort liability can overcome or even mitigate the deterrence effect of imprisonment or loss of medical license that has deterred so many physicians into playing it safe — and, in effect, undertreating pain."[186]

To address the lack of clarity and consistency, prescribers may be well served if professional societies establish empirically validated clinical practice guidelines (CPGs) to guide the standard care in incorporating genetic tests like AvertD into medical decision-making. CPGs have been described as a "type of written industry standard,"[187] and are usually treated as "admissible, probative evidence of the defendant's duty."[188] CPGs issued by medical societies demonstrate professional consensus and therefore often establish custom,[189] or what a reasonable physician would do in such instances.[190] When done right, guidelines can help standardize care, protect physicians from liability, and ensure patient safety.[191] They can be relied upon by physicians who are accused of malpractice for their decisions to administer, or rely on, the PGS test, to determine the standard of care.[192] However, in crafting such position statements, caution should be exercised to avoid over-reliance on, over-use of, or misuse of these tests.[193]

[182]*See* Valerie Gutmann Koch, *Crisis Standards of Care and State Liability Shields*, 57 S.D. L. Rev. 973, 991–92 (2020) (discussing policymakers passing legislation providing civil immunity to practitioners during COVID-19 pandemic could encourage them to perform their best during difficult circumstances); *see also* Roberts & Suter, *supra* note 29, at 425 (discussing in part Virginia statute providing civil liability immunity for practitioners who fail to review certain lab results).

[183]*See* Koch, *supra* note 179, at 10 (discussing ethical questions at intersection of tort law, public health, and scientific innovation as well as unreliability of AvertD).

[184]Blaufuss, *supra* note 96, at 1096–97.

[185]*Id.* at 1096 ("Physicians are currently fearful of overprescribing opioids due to the potential for disciplinary actions and criminal proceedings, in addition to fears of possibly harming their patient.").

[186]*Id.* at 1109.

[187]Michelle M. Mello, *Of Swords and Shields: The Role of Clinical Practice Guidelines in Medical Malpractice Litigation*, 149 U. Pa. L. Rev. 645, 660 (2001).

[188]*Id.* at 660.

[189]Nicholson Price explains that "when a practice is too innovative to have many adherents . . . legislative action and practice guidelines set by professional organizations could be particularly influential." W. Nicholson Price, *Medical Malpractice and Black Box Medicine*, *in* Big Data, Health Law, and Bioethics 295, 301 (I. Glenn Cohen et al. eds., 2018). In terms of CPGs, the "general purpose of such guidelines is suggested by their definition, 'systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.'" Ben A. Rich, *A Prescription for the Pain: The Emerging Standard of Care for Pain Managemen*t, 26 Wm. Mitchell L. Rev. 1, 82 (2000). CPGs "can be used in litigation by an accused physician as a defense (exculpatory evidence) and by patients alleging a breach of the standard of care (inculpatory evidence)." Timothy K. Mackey & Bryan A. Liang, *The Role of Practice Guidelines in Medical Malpractice Litigation*, 13 Am. Med. Ass'n J. Ethics 36, 36 (2011).

[190]The 2000 revisions to the learned treatise doctrine "opened the door for the use of CPGs as admissible evidence as a 'learned treatise,' which allows consideration and admission of CPGs as a 'reliable authority' for use in expert testimony." Mackey & Liang, *supra* note 189, at 37.

[191]*See* Mello, *supra* note 187, at 647–48 (discussing the argument of how CPGs could help standardize care, decrease liability for practitioners, and enhance health care quality for patients).

[192]*Genetics to Genomics*, *supra* note 75, at 19.

[193]As Roberts and Suter note, "some professional organizations have already issued guidance regarding" PGS. Roberts & Suter, *supra* note 29, at 436. For example, the American Society of Human Genetics (ASHG) made three key recommendations in December 2022: (1) develop diverse research cohorts and analyses; (2) foster robustness in scientific development, validation, application, and interpretation of PGSs, and (3) accompany research products with communications materials for broad, non-specialist audiences. John Novembre, Catherine Stein, Samira Asgari, Claudia Gonzaga-Jauregui, Andrew Landstrom, Amy Lemke, Jun Li, Chloe Mighton, Matthew Taylor & Sarah Tishkoff, *Addressing the Challenges of Polygenic Scores in Human Genetic Research*, 109 Am. J. Hum. Genetics 2095, 2096 (2022); *see also ASHG Issues New Guidance on Addressing the Challenges of Polygenic Scores in Human Genetic Research*, Am. Soc'y of Hum. Genetics (Dec. 1, 2022), https://www.ashg.org/advocacy/statement-archive/new-guidance-on-the-challenges-of-polygenic-scores-in-human-genetic-research/ [https://perma.cc/T2KW-RU7R].

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CPGs should emphasize patient-centered care, ensuring that physicians do not over-rely on genetic tests at the expense of considering environmental, socioeconomic, and behavioral factors that influence addiction risk.

Overall, tort law is ill-equipped to protect patients and ensure appropriate integration of these tests into clinical practice. Existing liability rules are unlikely to have either a compensatory or deterrent effect, as there exists little threat of liability for over-relying on the test, even when doing so results in harm to the patient or the community.[194] The tort system offers patients little recourse for decisions that physicians make that could leave their pain un- or undertreated, or, on the other hand, that result in them developing avoidable OUDs.

[194] *See generally* Roberts & Suter, *supra* note 29, at 417.

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