Criminalizing Transgender Care

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ABSTRACT: Since 2021, twenty-four states, in extraordinarily quick succession, have enacted statutes banning physicians from prescribing puberty blockers and cross-sex hormones to minors for treatment of gender dysphoria. Although the Food and Drug Administration has not approved these drugs for this use, off-label prescribing is a common practice, and leading medical organizations all agree that this off-label use of puberty blockers and sex hormones is an essential component of transgender medical care. These state laws thus represent an extreme, and unprecedented, interference with the provision of standard-of-care medicine. This Article, after exploring the ongoing litigation challenging these bans, argues that they violate a fundamental right under the Due Process Clause of the Fourteenth Amendment—namely, the right to obtain standard-of-care treatment from a physician. It demonstrates that this right is deeply rooted in America's history and traditions by presenting the first-ever comprehensive review of state policies regarding off-label prescribing practices and showing that the states have virtually never interfered with physicians' prescribing decisions in this manner. Finally, in light of relevant judicial precedents, this Article shows why courts should strike down these unparalleled, oppressive state laws as unconstitutional.

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INTRODUCTION

Drugs known as puberty blockers and sex hormones are an essential component of medical care for adolescents experiencing gender dysphoria[1]—that is, "incongruence between experienced gender identity and the sex assigned at birth."[2] Adolescent gender dysphoria is a serious, increasingly common medical condition associated with suicidal ideation and attempts and other high-risk behaviors.[3] The Clinical Practice Guidelines of the Endocrine Society[4] and standards of care promulgated by the World Professional Association for Transgender Health ("WPATH")[5] recommend that specially trained, specialist physicians prescribe drugs to treat gender dysphoria in youth, when appropriate, following comprehensive biopsychological evaluations by multidisciplinary teams. Every major American medical association and world health authority recognizes the necessity of such pharmaceutical care.[6]

Outside the abortion context, American lawmakers are not in the habit of interfering with medical practices that medical experts endorse so widely. Yet starting with Arkansas in 2021, an accelerating wave of states has enacted laws that not only ban the provision of gender-affirming care to adolescents, but even in some instances *criminalize* it.[7] As of today, twenty-four states have

1. "Gender Dysphoria" is also sometimes referred to as Gender Incongruence ("GI"). The former term was included in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders in 2013, and the latter appeared in 2019 in the eleventh revision of the World Health Organization's International Classification of Diseases ("ICD-11"). Marc-Antoine Crocq, *How Gender Dysphoria and Incongruence Became Medical Diagnoses – A Historical Review*, 23 DIALOGUES CLINICAL NEUROSCI. 44, 44 (2021). In an effort to "depathologize" GI, the ICD-11 moved the condition from the chapter on Mental and Behavioural Disorders to the chapter on Sexual Health. *Id.* at 49. Although some people prefer the term GI for this reason, this Article will predominantly use "gender dysphoria" to emphasize that many people seeking gender-affirming care are in distress and thus need *medical* treatment.

2. Eli Coleman et al., *Standards of Care for the Health of Transgender and Gender Diverse People, Version 8*, 23 INT'L J. TRANSGENDER HEALTH S1, S59 (2022). For some people, including some adolescents, gender-affirming care culminates in sex-reassignment surgery, but this Article focuses solely on drug treatments. Wylie C. Hembree et al., *Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline*, 102 J. CLINICAL ENDOCRINOLOGY & METABOLISM 3869, 3872, 3894 (2017) [hereinafter *Endocrine Society Clinical Practice Guideline*]. *But see* Coleman et al., *supra*, at S65–66 (suggesting that although vaginoplasty may be appropriate for some minors, phalloplasty is not).

3. *See generally* Derek S. Day, John J. Saunders & Anu Matorin, *Gender Dysphoria and Suicidal Ideation: Clinical Observations from a Psychiatric Emergency Service*, CUREUS, Nov. 12, 2019, at 1; Marla E. Eisenberg et al., *Risk and Protective Factors in the Lives of Transgender/Gender Nonconforming Adolescents*, 61 J. ADOLESCENT HEALTH 521 (2017); Arnold H. Grossman & Anthony R. D'Augelli, *Transgender Youth and Life-Threatening Behaviors*, 37 SUICIDE & LIFE THREATENING BEHAV. 527 (2007).

4. *Endocrine Society Clinical Practice Guideline*, *supra* note 2, at 3869–70.

5. Coleman et al., *supra* note 2, at S6.

6. *Medical Association Statements in Support of Health Care for Transgender People and Youth*, GLAAD (June 26, 2024), https://glaad.org/medical-association-statements-supporting-trans-youth-healthcare-and-against-discriminatory [https://perma.cc/HA85-35VQ].

7. The states that criminalize the provision of this care are Alabama, Florida, Idaho, North Dakota, and Oklahoma (South Carolina criminalizes surgery only). *Bans on Best Practice Medical*

passed laws prohibiting most or all provision of medication (and surgery) to youth for gender transition,[8] although courts have blocked four of these statutes from taking effect.[9] Although current state statutes prohibit such care only for minors younger than eighteen years old, bills have been introduced prohibiting it for young adults of various ages up to twenty-five years old,[10] and some advocates for the transgender community express fear that the current barrage of youth bans presages future attempts to ban it altogether.[11]

Transgender youth and their supporters have filed cases in state and federal court challenging about fifteen of the state bans on the use of puberty blockers and cross-sex hormones to treat gender dysphoria in minors

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Care for Transgender Youth, MOVEMENT ADVANCEMENT PROJECT, https://www.lgbtmap.org/equality-maps/healthcare_youth_medical_care_bans [https://perma.cc/FAS7-NL8Z].

8. ALA. CODE §§ 26-26-1 to -9 (LexisNexis Supp. 2023); ARK. CODE ANN. §§ 16-114-401 to -403 (Supp. 2023); FLA. STAT. ANN. § 456.52 (2023); GA. CODE ANN. § 31-7-3.5 (Supp. 2024) (banning hormone therapy but not puberty blockers); IDAHO CODE § 18-1506C (Supp. 2023); IND. CODE §§ 25-1-22-1 to -18 (Supp. 2024); IOWA CODE § 147.164 (2024); KY. REV. STAT. ANN. § 311.372 (West Supp. 2023); LA. STAT. ANN. §§ 40:1098.1–1099.1 (Supp. 2024); MISS. CODE ANN. §§ 41-141-1 to -9 (2023); MO. REV. STAT. § 191.1720 (Supp. 2023); MONT. CODE ANN. §§ 50-4-1001 to -1006 (Supp. 2023); NEB. REV. STAT. §§ 71-7301 to -7307 (Supp. 2023); N.C. GEN. STAT. §§ 90-21.150–154 (2023); N.D. CENT. CODE §§ 12.1-36.1-01 to -04 (Supp. 2023); OHIO REV. CODE ANN. § 3129.02 (West Supp. 2024); OKLA. STAT. ANN. tit. 63, § 2607.1 (West 2024); S.C. CODE ANN. § 44-42-310 (2024); S.D. CODIFIED LAWS §§ 34-24-33 to -38 (Supp. 2023); TENN. CODE ANN. §§ 68-33-101 to -109 (2023); TEX. HEALTH & SAFETY CODE ANN. §§ 161.701–706 (West Supp. 2023); UTAH CODE ANN. §§ 58-1-603, 78B-3-427 (LexisNexis Supp. 2024); W. VA. CODE § 30-14-17 (2023); H.B. 0156, 67th Leg., 2024 Budget Sess. (Wyo. 2024). Arizona bans only surgery. ARIZ. REV. STAT. ANN. § 32-3230 (Supp. 2023). In two additional states (Kansas and Wisconsin), the governor vetoed legislation banning medical care for transgender youth, and the legislature failed to override the veto. Harm Venhuizen, *Democratic Wisconsin Governor Vetoes Bill to Ban Gender-Affirming Care for Kids*, AP NEWS (Dec. 6, 2023, 10:09 AM), https://apnews.com/article/wisconsin-governor-veto-transgender-care-ban-68b0968cd63e20f5ce727b0c932ba4dd [https://perma.cc/EAX2-5RXQ]; John Hanna, *Kansas Bill to Limit Gender-Affirming Care for Transgender Minors Dies After Failed Veto Override*, AP NEWS (Apr. 29, 2024, 11:11 PM), https://apnews.com/article/gender-affirming-care-minors-ban-kansas-veto-b63daeec39cf26e0741569b03aa9ebe9 [https://perma.cc/RG94-YHGP].

9. Brandt v. Rutledge, 551 F. Supp. 3d 882, 894 (E.D. Ark. 2021), *aff'd*, 47 F.4th 661 (8th Cir. 2022); Doe v. Ladapo, 676 F. Supp. 3d 1205, 1226 (N.D. Fla. 2023); Poe *ex rel.* Poe v. Labrador, 709 F. Supp. 3d 1169, 1199–200 (D. Idaho 2023); Ord. Granting Plaintiff's Motion for Preliminary Injunction at 47, van Garderen v. State, No. DV-23-541 (Mont. Dist. Ct. Sept. 27, 2023). For current status of all litigation, see *Bans on Best Practice Medical Care for Transgender Youth*, *supra* note 7.

10. Brooke Migdon, *Oklahoma Lawmaker Lowers Age Limit in Proposed Gender-Affirming Care Ban*, HILL (Feb. 8, 2023, 2:35 PM), https://thehill.com/homenews/state-watch/3849734-oklahoma-lawmaker-lowers-age-limit-in-proposed-gender-affirming-care-ban [https://perma.cc/TV3U-SQAF]; Maggie Astor, *G.O.P. State Lawmakers Push a Growing Wave of Anti-Transgender Bills*, N.Y. TIMES (June 20, 2023), https://www.nytimes.com/2023/01/25/us/politics/transgender-laws-republicans.html (on file with the *Iowa Law Review*).

11. Orion Rummler, *Health Care for Transgender Adults Remains Legal, but States Are Quietly Trying to Limit Access*, 19TH (Oct. 3, 2022, 5:00 AM), https://19thnews.org/2022/10/transgender-healthcare-adults-limit-restrict [https://perma.cc/Z5YT-38FH].

("PB/CSH bans").[12] The federal lawsuits,[13] as well as some of the state lawsuits,[14] assert that the bans violate the Equal Protection Clause and Due Process Clause of the U.S. Constitution. The equal protection claims contend that these bans discriminate on the basis of sex and transgender status and are thus subject to intermediate judicial scrutiny, which the laws cannot survive. The due process argument is that parents have a fundamental right to direct the medical care of their children and thus to obtain PB/CSH treatments for them. Under this theory, because the bans violate a fundamental right, they are subject to strict scrutiny.

These suits were initially successful; at least a dozen U.S. district courts and state courts issued preliminary injunctions blocking the enforcement of these laws.[15] In the summer of 2023, however, transgender rights advocates experienced two major setbacks, when the U.S. Courts of Appeals for the Sixth and Eleventh Circuits (together comprising five of the states with bans) held that U.S. district courts within their purview had abused their discretion in enjoining state bans.[16] The circuit courts denied that these laws discriminated on the basis of sex or transgender status and that they implicated a fundamental right subject to strict scrutiny under the Due Process Clause. With respect to the due process claims, both circuit courts applied a test regarding the

12. Ernesto Londoño & Mitch Smith, *Young People Left in Limbo as Battle over Transgender Care Shifts to Court*, N.Y. TIMES (Oct. 3, 2023), https://www.nytimes.com/2023/10/03/us/transgender-care-lawsuits-courts.html (on file with the *Iowa Law Review*) (lawsuits challenging the youth care bans filed in "at least [fourteen] states"); *Bans on Best Practice Medical Care for Transgender Youth*, *supra* note 7.

13. *See generally* Eknes-Tucker v. Marshall, 603 F. Supp. 3d 1131 (M.D. Ala. 2022), *vacated sub nom.* Eknes-Tucker v. Governor of Ala., 80 F.4th 1205 (11th Cir. 2023); Brandt v. Rutledge, 551 F. Supp. 3d 882 (E.D. Ark. 2021), *aff'd*, 47 F.4th 661 (2022); Doe v. Ladapo, 676 F. Supp. 3d 1205 (N.D. Fla. 2023); Koe v. Noggle, 688 F. Supp. 3d 1321 (N.D. Ga. 2023); Poe *ex rel.* Poe v. Labrador, 709 F. Supp. 3d 1169 (D. Idaho 2023); K.C. v. Individual Members of Med. Licensing Bd. of Ind., No. 23-cv-00595, 2023 WL 4054086 (S.D. Ind. June 16, 2023), *stayed*, 2024 WL 811523 (7th Cir. Feb. 27, 2024); Doe 1 v. Thornbury, 679 F. Supp. 3d 576 (W.D. Ky. 2023), *rev'd and remanded sub nom.* L.W. *ex rel.* Williams v. Skrmetti, 83 F.4th 460 (6th Cir. 2023); Complaint for Declaratory & Injunctive Relief, Voe v. Mansfield, No. 23-cv-00864 (M.D.N.C. Oct. 11, 2023); Poe v. Drummond, No. 23-cv-177, 2023 WL 6516449 (N.D. Okla. Oct. 5, 2023); L.W. *ex rel.* Williams v. Skrmetti, 679 F. Supp. 3d 668 (M.D. Tenn. 2023), *rev'd and remanded*, 83 F.4th 460 (6th Cir. 2023).

14. *See generally* Motion for Preliminary Injunction, Noe v. Parson, No. 23AC-CC04530 (Mo. Cir. Ct. July 25, 2023); Ord. Granting Plaintiff's Motion for Preliminary Injunction, *supra* note 9.

15. *See* cases cited *supra* note 13; *see also* MOVEMENT ADVANCEMENT PROJECT, HEALTHCARE LAWS AND POLICIES: BANS ON BEST PRACTICE MEDICAL CARE FOR TRANSGENDER YOUTH 3–6 (2024), https://www.lgbtmap.org/img/maps/citations-youth-medical-care-bans.pdf [https://perma.cc/94UL-2MJG].

16. *See generally* L.W. *ex rel.* Williams v. Skrmetti, 73 F.4th 408 (6th Cir. 2023) (staying Tennessee injunction), *rev'd and remanded*, 83 F.4th 460 (6th Cir. 2023) (reversing Tennessee and Kentucky injunctions); Eknes-Tucker v. Governor of Ala., 80 F.4th 1205 (11th Cir. 2023) (vacating Alabama injunction). In addition, on February 27, 2024, the Seventh Circuit issued a stay on the district court's order enjoining enforcement of the Indiana ban, with no explanation but with an announcement that an opinion and judgment will follow. *See Seventh Circuit Allows Indiana's Ban on Care for Transgender Youth to Take Effect*, ACLU (Feb. 27, 2024, 6:46 PM), https://www.aclu.org/press-releases/seventh-circuit-allows-indianas-ban-on-care-for-transgender-youth-to-take-effect [https://perma.cc/X9DC-9A5G].

identification of fundamental rights which asks, among other things, whether the right is "deeply rooted in this Nation's history and tradition." The U.S. Supreme Court articulated this test in *Washington v. Glucksberg*,[17] a 1997 case denying the existence of a fundamental right to obtain physician-assisted suicide, and reaffirmed it in *Dobbs v. Jackson Women's Health Organization*,[18] the 2022 decision rejecting a fundamental right to obtain an abortion. As this Article was being edited for publication, the U.S. Supreme Court agreed to hear the Sixth Circuit case concerning the constitutionality of the Tennessee ban in its next term, although it will only consider the equal protection arguments.[19]

In the ongoing litigation, states have defended their PB/CSH bans based purely on medical and scientific grounds, not with cultural or moral arguments. While pointing to studies that (they contend) undermine the Endocrine Society and WPATH's recommendations, the states also emphasize that the use of these drugs for transgender care in youth is "experimental," in part because the Food and Drug Administration ("FDA") has not approved them for this use. Consider, for example, the opening of Arkansas's brief justifying its ban:

> Contrary to the story that Plaintiffs tell, there is no scientific consensus that children ought to undergo the irreversible, experimental gender-transition procedures regulated by the . . . Act. Indeed, there is no dispute that the procedures at issue here are entirely experimental: They have *never* been approved—or evaluated—by the [FDA] as a method of gender transition in children.[20]

When FDA approves a drug, it does not approve the substance for all uses, but only for those adequately supported by clinical studies submitted to and reviewed by the agency. These approved uses are set forth in the "Indications" section of the drug's approved labeling. But federal law, with rare exceptions, does not interfere with physicians' authority to prescribe drugs for additional uses based on their professional judgment.[21] Indeed, off-

17. Washington v. Glucksberg, 521 U.S. 702, 720 (1997).

18. Dobbs v. Jackson Women's Health Org., 597 U.S. 215, 237 (2022).

19. United States v. Skrmetti, 144 S. Ct. 2679 (2024) (mem.) (granting certiorari); Amy Howe, *Supreme Court Takes Up Challenge to Ban on Gender-Affirming Care*, SCOTUSBLOG (June 24, 2024, 10:03 AM), https://www.scotusblog.com/2024/06/supreme-court-takes-up-challenge-to-ban-on-gender-affirming-care [https://perma.cc/EZ79-FLB5]. The petition for the United States granted by the Supreme Court focuses only on the equal protection argument because the United States intervened in the case under 42 U.S.C. § 2000h-2, which applies to suits "seeking relief from the denial of equal protection of the laws." United States' Petition for Writ of Certiorari at 12 n.4, United States v. Skrmetti, No. 23-477 (U.S. Nov. 6, 2023), 2023 WL 7327440.

20. Defendants' Combined Brief in Opposition to Plaintiffs' Motion for Preliminary Injunction; Reply in Support of Defendants' Motion to Dismiss at 1, Brandt v. Rutledge, 551 F. Supp. 3d 882 (E.D. Ark. 2021) (No. 21-cv-00450) [hereinafter Rutledge Brief in Opposition]; *see also, e.g.*, Combined Memorandum of L. in Opposition to Motion for Preliminary Injunction & in Support of Motion to Dismiss at 17–19, Poe *ex rel.* Poe v. Labrador, 709 F. Supp. 3d 1169 (D. Idaho Oct. 2, 2023), 2023 WL 8850770; Defendants' Response in Opposition to Plaintiff's Motion for Preliminary Injunction at 27–29, van Garderen v. Montana, No. 2023-0541 (Mont. Dist. Ct. Missoula Cnty. Sept. 1, 2023).

21. *See* discussion *infra* Section III.A.

label prescribing is extremely common.[22] Moreover, off-label uses of drugs are not necessarily "experimental." To the contrary, they are often supported by significant evidence and constitute the standard of care; that is, physicians would frequently be committing medical malpractice by *not* prescribing a drug off-label.[23]

As a general matter, the federal Food, Drug, and Cosmetic Act ("FDCA") implicitly cedes to states the power to restrict the off-label use of drugs as part of their authority over the "practice of medicine" within their borders.[24] As this Article will show, however, states almost never exercise this power. Thus, although the states frame their PB/CSH bans as run-of-the-mill health regulations protecting children from "dangerous and unproven treatments,"[25] they are, in fact, extraordinary. Even in those extremely rare instances when states have interfered with off-label prescribing, they have never previously (outside the context of abortion medication) prohibited an off-label use of a drug that orthodox medical experts widely embrace as the standard of care. Nor (outside the abortion context) has a state ever before made off-label prescribing of a drug for a medical use a *crime*.

In defense of their bans, the states point to other western nations that have severely restricted the use of these treatments in minors.[26] But none of these countries *ban* pharmaceutical treatment for gender dysphoria for minors.[27] If American states were truly concerned about the health and safety of transgender youth, they could limit and regulate the use of puberty blockers and cross-sex hormones in various ways. Instead, they have entirely prohibited this care. It would be absurd to contend that such prescriptions are *never* consistent with the standard of care—even when, for example, a multidisciplinary team of specially trained physicians determines that a seventeen-year-old is likely to commit suicide without such treatment. A total ban on a standard-of-care treatment embraced by the medical profession is an astonishing invasion of people's right to bodily integrity that, I will argue, is unconstitutional under the Due Process Clause of the Fourteenth Amendment.

These bans prohibit the off-label use of FDA-approved drugs for transgender care even when adolescent patients, their parents, and their physicians all desire these treatments. They are thus in tension with Americans' broad historical embrace of freedom of therapeutic choice without government interference.[28] More importantly, they conflict with the country's unwavering commitment to freedom of choice among remedies accepted by the orthodox

22. *See* discussion *infra* Section III.B.

23. *See infra* notes 183–86 and accompanying text.

24. *See* discussion *infra* Section III.A.

25. *See, e.g.*, Defendants' Response in Opposition to Plaintiffs' Motion for a Preliminary Injunction at 1, L.W. *ex rel.* Williams v. Skrmetti, 679 F. Supp. 3d 668 (M.D. Tenn. 2023) (No. 23-cv-00376).

26. *See, e.g.*, *id.* at 15; Rutledge Brief in Opposition, *supra* note 20, at 20–30.

27. *See infra* note 395 and accompanying text.

28. *See* LEWIS A. GROSSMAN, CHOOSE YOUR MEDICINE: FREEDOM OF THERAPEUTIC CHOICE IN AMERICA 291 (2021).

medical profession. Notably, the bans have emerged from states that, in other contexts, have been at the forefront of *noninterference* with physician prescribing practices.[29] The stark inconsistency of these bans with the same states' other policies highlights their arbitrariness and discriminatory motivation.

In short, the state prohibitions on prescribing puberty blockers and hormones to minors suffering from gender dysphoria constitute an indefensible abuse of the states' power to regulate the practice of medicine and violate these patients' fundamental right to obtain standard-of-care medical treatment. These laws constitute the first time that any government of the United States, federal or state, has completely banned a standard-of-care off-label use of a drug—or any standard-of-care treatment—outside the abortion context. And abortion care is distinguishable; the *Dobbs* court emphasized that abortion raises unique substantive due process questions because of the state's interest in protecting "potential life."[30]

Although the plaintiffs in lawsuits challenging these bans also rely on the Equal Protection Clause, and the Supreme Court recently granted certiorari only on the equal protection issues,[31] this Article focuses on the plaintiffs' due process claims and argues that these claims are cogent, even under the constrained approach to substantive due process the Supreme Court manifested most recently in *Dobbs*. Nevertheless, much of the information and analysis in this Article is relevant to the equal protection claims, as well.

This Article will proceed as follows. Part I provides the medical background regarding the off-label use of puberty blockers and sex hormones in the treatment of gender dysphoria in adolescents. It also discusses disputes regarding what constitutes the "standard of care" for treatment of gender dysphoria in adolescents and explains why it is not necessary to resolve this dispute to conclude that complete bans on the use of drugs for this indication are unconstitutional. Part II describes the state bans themselves and the substantive due process challenges to them, with special focus on the litigation in Alabama, Tennessee, and Kentucky.

The remainder of the Article seeks to undermine the Sixth Circuit's and Eleventh Circuit's reasoning in rejecting due process claims. Part III examines the true significance of FDA approval of a drug for a particular use, discusses the agency's almost total noninterference with off-label prescribing, and explains why many uses remain off-label even though they are extremely common and backed by extensive scientific evidence. Part IV shows that the states also have a long tradition of noninterference with off-label prescribing—and sometimes with physician prescribing of drugs that FDA has not approved for *any* use. Part V of the Article then highlights the hypocritical and arbitrary enactment in some of the very same states that have enacted PB/CSH bans of laws that explicitly protect off-label prescribing of other drugs (and the

29. *See* discussion *infra* Section IV.C.

30. Dobbs v. Jackson Women's Health Org., 597 U.S. 215, 262–63 (2022) (criticizing the dissenters' stoking of "unfounded fear" that the Court's decision will imperil other substantive due process rights).

31. *See* sources cited *supra* note 19.

prescribing of entirely unapproved drugs) even when these practices *violate* the standard of care.

Part VI examines the rare prior instances in which states have, by law or regulation, explicitly prohibited particular off-label uses. It shows that none of these laws (except for restrictions on abortion medication) have restricted off-label prescribing that conformed to the standard of care.

Part VII lays out the argument that patients have a fundamental right to obtain standard-of-care treatment without government interference, including standard-of-care off-label uses of drugs. Finally, Part VIII explains why courts must find the PB/CSH bans unconstitutional if they apply the strict judicial scrutiny required for invasions of fundamental rights—and why the bans might even fail rational basis review.

I. THE USE OF DRUGS FOR GENDER-AFFIRMING CARE

A. PUBERTY BLOCKERS, SEX HORMONES, AND TREATMENT OF GENDER DYSPHORIA

Puberty blockers, also known as gonadotropin-releasing hormone ("GnRH") analogues, inhibit the body's natural production of gonadal hormones: estrogen, progesterone, and testosterone.[32] FDA first approved a GnRH analogue for human use in the 1980s as a prostate cancer treatment.[33] Over the years, these drugs have also obtained FDA approval for various other indications, including endometriosis, uterine fibroids, breast cancer, and central precocious puberty—a condition where a child (more commonly a girl) reaches puberty at an abnormally early age.[34] Puberty blockers are not currently approved by FDA for treatment of gender dysphoria, and their use for this purpose is thus "off-label."

The medical use of estrogens (female sex hormones) has a much longer history.[35] The early twentieth century saw the emergence of a largely unregulated market for poorly characterized ovarian preparations and extracts. In 1933, Ayerst began selling the first modern pharmaceutical version of a sex hormone—

32. *Gonadotropin Releasing Hormone (GnRH) Analogues*, NAT'L LIBR. MED., NAT'L INST. HEALTH, http://www.ncbi.nlm.nih.gov/books/NBK547863 [https://perma.cc/SPU2-JN7B].

33. *See* FDA, FDA REVIEW PACKAGE FOR NDA 19010, at *4 (1985), https://www.accessdata.fda.gov/drugsatfda_docs/nda/pre96/019010Orig1sooorev.pdf [https://perma.cc/B7SH-RE4S].

34. *See, e.g.*, FDA, HIGHLIGHTS OF PRESCRIBING INFORMATION *1 (2023) [hereinafter LUPRON DEPOT PRESCRIBING INFORMATION], https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/020011Orig1s046;019943Orig1s039lbl.pdf [https://perma.cc/643N-CU6J]; FDA, HIGHLIGHTS OF PRESCRIBING INFORMATION *1 (2015) [hereinafter ZOLADEX PRESCRIBING INFORMATION], https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/019726s059,020578s037lbl.pdf [https://perma.cc/84Q3-E3HR]; PHARMA MARKETLETTER, NEW INDICATION FOR LUPRON DEPOT-PED 1 (1993) (on file with the *Iowa Law Review*); FDA., HIGHLIGHTS OF PRESCRIBING INFORMATION *1 (2022), https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/020263s050lbl.pdf [https://perma.cc/Y5A2-UDGF]; Melinda Chen & Erica A. Eugster, *Central Precocious Puberty: Update on Diagnosis and Treatment*, 17 PEDIATRIC DRUGS 273, 275–77 (2015).

35. *See generally* Grace E. Kohn, Katherine M. Rodriguez, James Hotaling & Alexander W. Pastuszak, *The History of Estrogen Therapy*, 7 SEXUAL MED. REVS. 416 (2019) (examining the history of menopausal hormone therapy since the 1800s).

a bio-identical estrogen therapy for treatment of menopausal symptoms (Emmenin® tablets).[36] In 1938, Congress began requiring the manufacturers of new drugs to submit new drug applications ("NDAs") to FDA, and it gave the agency the power to review the drugs for safety prior to marketing.[37] Soon afterward, the agency let NDAs become effective for two treatments for menopausal symptoms: estrogen diethylstilbestrol ("DES") in 1941 and conjugated equine estrogens ("Premarin®") in 1942.[38]

Over the next half century, FDA approved various formulations of estrogens, progestins, and combinations of them for various other conditions. Today, they are FDA-approved for (among other things) treatment of vasomotor symptoms due to menopause, treatment of vulvar and vaginal atrophy due to menopause, prevention of postmenopausal osteoporosis, treatment of androgen-dependent prostate cancer, pregnancy prevention, and "[h]ypo[-]estrogenism [(estrogen deficiency)] due to [h]ypogonadism, [c]astration, or [p]rimary [o]varian [f]ailure."[39] FDA has not approved any estrogen or progestin drug product for treatment of gender dysphoria in patients of any age.

Testosterone therapy also has a long history. For centuries, doctors prescribed preparations made from animal testes to treat the symptoms of male hypogonadism, including impotence.[40] Some researchers even performed transplants of human testicles.[41] In 1935, European scientists first isolated and extracted a hormone they called "testosterone" from bull testes,[42] and later

36. *Id.* at 417.

37. Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717, 52 Stat. 1040 (codified as amended at 21 U.S.C. §§ 301–399i (2018)). The drug application and approval provisions were codified at 21 U.S.C. § 355.

38. Marcia L. Stefanick, *Estrogens and Progestins: Background and History, Trends in Use, and Guidelines and Regimens Approved by the US Food and Drug Administration*, 118 AM. J. MED. (SUPP. ISSUE 2) 64S, 65S (2005). Until 1962, FDA did not "approve" NDAs but rather let them become effective if it had no objections, and, as a formal matter, it reviewed the drugs for safety but not for effectiveness. This changed with the 1962 Drug Amendments. *See* Drug Amendments of 1962, Pub. L. No. 87-781, § 102, 76 Stat. 780, 781 (1962).

39. *See, e.g.*, FDA, PREMARIN® PRESCRIBING INFORMATION 1, 19, 28 (2024), https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/004782s181lbl.pdf [https://perma.cc/SUT8-XG55] (also noting that "estrogen therapy has been used for the induction of puberty in adolescents with some forms of pubertal delay" and discussing clinical studies of "delayed puberty due to female hypogonadism"); FDA, YAZ® PRESCRIBING INFORMATION 1 (2012), https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/021676s020lbl.pdf [https://perma.cc/8CFU-TE56]; Stefanick, *supra* note 38, at 66S.

40. Eberhard Nieschlag & Susan Nieschlag, *Testosterone Deficiency: A Historical Perspective*, 16 ASIAN J. ANDROLOGY 161, 163 (2014). As late as 1947, the Reed & Carnrick company sold "Ampacoids Testicle," an injectable "purified . . . extract . . . of desiccated, defatted, whole fresh testicle" for treatment of "[s]exual neurasthenia," "prostatitis, and the male climeractic" (a condition later commonly referred to as "male menopause"). PHYSICIANS' DESK REFERENCE 321 (1st ed. 1947).

41. Mary Rostom, Ranjith Ramasamy & Taylor P. Kohn, *History of Testosterone Therapy Through the Ages*, 34 INT. J. IMPOTENCE RSCH. 623, 624 (2022).

42. Nieschlag & Nieschlag, *supra* note 40, at 165.

that year other scientists learned to synthesize testosterone in the laboratory.[43] From that point on, drug companies focused on developing the synthesized version of the hormone, first in the form of subdermal pellets and then in injectable form.[44] Schering started selling injectable synthesized testosterone propionate under the brand name Oreton® in about 1938.[45] In its early years, Oreton's label declared: "Oreton stimulates the development of male sex characteristics and is consequently of value in the treatment of male hypogonadism. In the male climeractic and prostatism, both the physical and mental status is improved."[46] (The "male climeractic" is an obsolete term for what is now sometimes called "male menopause.")

Today, testosterone drugs are available in multiple formulations (including transdermal patches) and are approved for "primary hypogonadism (congenital or acquired)"[47] and "hypogonadotropic hypogonadism (congenital or acquired)."[48] In 2015, FDA began requiring all prescription testosterone products to declare that their "safety and efficacy . . . in men with age-related hypogonadism have not been established."[49] The only pediatric use for which a testosterone product has been approved is delayed puberty.[50] Nevertheless, testosterone is routinely used off-label for treatment of other disorders of sexual development ("DSDs") in children, such as micropenis in infants and Klinefelter syndrome.[51] Testosterone is not approved for treatment of gender dysphoria.

Despite the lack of FDA approval, health professionals have been prescribing estrogen and testosterone for gender-affirming care in adults since the middle

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43. *Id.*

44. *Id.*; Rostom et al., *supra* note 41, at 625.

45. B.P. Lewis & R.V. Castle, *Grandfathered Drugs of 1938*, 18 AM. PHARM. 36, 38 (1978).

46. PHYSICIANS' DESK REFERENCE, *supra* note 40, at 325. The drug was also indicated for use in "check[ing]" various conditions in women, including "postpartum pains, lactation, breast engorgement, functional uterine bleeding, dysmenorrhea, and endometriosis." *Id.*

47. FDA, ANDROGEL® PRESCRIBING INFORMATION 1 (2019), https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022309s020lbl.pdf [https://perma.cc/3CNL-V2DU].

48. FDA, DELATESTRYL® PRESCRIBING INFORMATION 2 (2016), https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/009165s034lbl.pdf [https://perma.cc/7RCH-5293].

49. *E.g.*, *id.*; *FDA Drug Safety Communication: FDA Cautions About Using Testosterone Products for Low Testosterone Due to Aging; Requires Labeling Change to Inform of Possible Increased Risk of Heart Attack and Stroke with Use*, FDA, [hereinafter *FDA Drug Safety Communication*] https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-cautions-about-usl,ing-testosterone-products-low-testosterone-due [https://perma.cc/K6Y7-FFTC].

50. FDA, *supra* note 48, at 2–3. The "Indications and Usage" section for testosterone drugs not approved for delayed puberty specifically states that "[s]afety and efficacy . . . in males less than [eighteen] years old have not been established." *See* FDA, *supra* note 47, at 1.

51. *Clinical Guidelines for the Management of Disorders of Sex Development in Childhood*, DSD GUIDELINES (2006), https://dsdguidelines.org/htdocs/clinical [https://perma.cc/EV8W-WUCT]; Ganka Douglas et al., *Consensus in Guidelines for Evaluation of DSD by the Texas Children's Hospital Multidisciplinary Gender Medicine Team*, INT'L J. PEDIATRIC ENDOCRINOLOGY, 2010, at 1; Simon Chang, Anne Skakkebæk & Claus Højbjerg Gravholt, *Klinefelter Syndrome and Medical Treatment: Hypogonadism and Beyond*, 14 HORMONES 531, 534 (2015) ("Although studies on the effect of testosterone treatment in KS are few, the general consensus dictates that most men with KS should have testosterone treatment offered to them sometime around puberty.").

of the twentieth century.[52] Today, they and puberty blockers are part of standard-of-care treatment for gender dysphoria in adolescents.[53] In accordance with the WPATH Standards of Care and Endocrine Society Clinical Practice Guideline, physicians may—following a comprehensive, multidisciplinary physical and mental health evaluation—commence the use of a puberty blocker in patients showing the first signs of puberty. This drug delays development while patients, parents, and physicians together decide whether to proceed to the use of cross-sex hormones, a step with more permanent implications. If gender dysphoria persists, doctors may (after a comprehensive assessment of the patient and robust communication about risks and implications) prescribe estrogenic drugs to transgender females or testosterone to transgender males. Physicians ordinarily wait until the patient is sixteen years old before commencing hormone treatments, although occasionally, under compelling circumstances, they will initiate them in younger post-pubertal patients.[54]

An abundance of published research provides evidence of these drugs' safety and effectiveness for treatment of gender dysphoria in minors.[55] A recent report commissioned by the United Kingdom's National Health Service ("NHS"), the *Cass Review*, recommended that the NHS severely restrict this use of puberty blockers and cross-sex hormones because of the dearth of "high quality" research supporting their effectiveness for improving mental health in transgender youth.[56] But a primary characteristic of "high quality" studies is the double-blinded use of randomized controls, preferably placebo controls,[57] and this type of research is challenging, if not impossible, for drugs with such obvious physical manifestations, as well as arguably unethical in the

52. Eknes-Tucker v. Marshall, 603 F. Supp. 3d 1131, 1141 n.12 (M.D. Ala. 2022), *vacated sub nom.* Eknes-Tucker v. Governor of Ala., 80 F.4th 1205 (11th Cir. 2023).

53. Coleman et al., *supra* note 2, at S110–27, S254.

54. *Endocrine Society Clinical Practice Guideline*, *supra* note 2, at 3870; Coleman et al., *supra* note 2, at S43–66.

55. Brief for Am. Acad. of Pediatrics et al. as Amici Curiae Supporting Petitioner at 17–18 nn.55–56, Koe v. Noggle, 688 F. Supp. 3d 1321 (N.D. Ga. 2023) (No. 23-cv-02904) (citing eighteen studies finding positive mental health outcomes for adolescents receiving puberty blockers or hormone therapy); *id.* at 18 ("These studies find positive mental health outcomes . . . including statistically significant reductions in anxiety, depression, and suicidal ideation.").

56. HILARY CASS, THE CASS REVIEW, INDEPENDENT REVIEW OF GENDER IDENTITY SERVICES FOR CHILDREN AND YOUNG PEOPLE 33, 184 (2024). For early critiques of the *Cass Review*, see generally Cal Horton, The Cass Review*: Cis-Supremacy in the UK's Approach to Healthcare for Trans Children*, INT'L J. TRANSGENDER HEALTH (Mar. 14, 2024), https://www.tandfonline.com/doi/epdf/10.1080/26895269.2024.2328249 [https://perma.cc/L7D3-7CM2]; D.M. Grijseels, *Biological and Psychosocial Evidence in the* Cass Review*: A Critical Commentary*, INT'L J. TRANSGENDER HEALTH (June 6, 2024), https://www.tandfonline.com/doi/full/10.1080/26895269.2024.2362304 [https://perma.cc/JE9G-FP5P]; MEREDITHE MCNAMARA ET AL., AN EVIDENCE-BASED CRITIQUE OF "THE CASS REVIEW" ON GENDER-AFFIRMING CARE FOR ADOLESCENT GENDER DYSPHORIA (July 1, 2024), https://law.yale.edu/sites/default/files/documents/integrity-project_cass-response.pdf [https://perma.cc/3C5Z-8YAA].

57. *See* Adrian Baker et al., *A Review of Grading Systems for Evidence-Based Guidelines Produced by Medical Specialties*, 10 CLINICAL MED. 358, 358 (2010); *Grading Quality of Evidence and Strength of Recommendations*, 328 BRIT. MED. J. 1490, 1490–93 (2004).

context of treatment of gender dysphoria.[58] Thus, pharmaceutical treatment of gender dysphoria will likely remain an area in which the standard of care is determined by the best available evidence, but not necessarily "high quality" evidence. This is a common situation in many areas of medicine, notably including pediatrics.[59] As a group of scientists and legal scholars observes in its critique of the *Cass Review*: "If high-quality evidence were a prerequisite for medical care, we would all be worse off. Moderate, low, and very low-quality evidence . . . informs necessary, valued care at every stage of life."[60]

Although the use of sex hormones in the treatment of gender dysphoria is off-label, efforts are underway to gain FDA approval. In 2023, a nonprofit called the Research Institute for Gender Therapeutics ("RIGT") was founded expressly for the purpose of pursuing this goal.[61] Its first major action was to propose a Phase 3 (late-stage) clinical trial of the use of estradiol, an estrogenic drug, as a treatment for "gender incongruence."[62] Although RIGT proposed "a double-blind placebo-controlled study," FDA responded by suggesting that other designs might be more appropriate, in view of ethical and practical concerns about using a placebo in such a trial.[63] The agency also suggested including individuals as young as thirteen years old in the study.[64] RIGT intends to commence its research following a study re-design.[65] It plans eventually to seek FDA approval of puberty blockers and testosterone in gender-affirming care, as well.[66] If FDA approves these products for treatment of gender dysphoria in minors, a strong argument could then be advanced that federal law preempts the state bans.[67]

Like most pharmaceuticals, these drugs present risks as well as benefits. Puberty blockers pose the risk of loss of bone mineral density.[68] Estrogenic

58. Horton, *supra* note 56, at 12–16; McNamara et al., *supra* note 56, at 12–13.

59. McNamara et al., supra note 56, at 11–13.

60. *Id.* at 11.

61. Theresa Gaffney, *The Push to Get Estrogen FDA-Approved for Gender-Affirming Care*, STAT (Nov. 28, 2023), https://www.statnews.com/2023/11/28/fda-gender-affirming-care-estrogen-approval [https://perma.cc/T3ZT-QFQ2].

62. *Id.* "This signals support for the categorization of transgender and gender-diverse identities as related to sexual health rather than mental health, as the Diagnostic and Statistical Manual of Mental Disorders term 'gender dysphoria' indicates." *Id.*

63. *Id.*

64. *Id.*

65. *Id.*

66. *Id.*; Maya Goldman, *How the FDA Could Boost Gender-Affirming Care*, AXIOS (Dec. 15, 2023), https://www.axios.com/2023/12/15/fda-transgender-hormone-therapy-gender-affirming-care [https://perma.cc/ZAN9-JNTY].

67. *See* Zogenix, Inc. v. Patrick, No. 14-11689, 2014 WL 1454696, at *3 (D. Mass. Apr. 15, 2024) (granting preliminary injunction against state ban on FDA-approved drug on obstacle preemption grounds). For analysis of the preemptive force of FDA drug approvals, see Lars Noah, *State Affronts to Federal Primacy in the Licensure of Pharmaceutical Products*, 2016 MICH. ST. L. REV. 1, 27–35; and Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845, 861–69, 872–75 (2017).

68. LUPRON DEPOT PRESCRIBING INFORMATION, *supra* note 34; Coleman et al., *supra* note 2, at S114 (observing that "the long-term effects on bone mass" in adolescent patients "have not

drugs are associated with endometrial cancer, cardiovascular disorders, breast cancer, and dementia, among other diseases.[69] Testosterone drugs are associated with various conditions, including benign prostatic hyperplasia, prostate cancer, and thromboembolism.[70]

For adolescents commencing cross-hormone therapy, a particularly concerning risk is permanently diminished fertility. In individuals assigned male at birth, estrogens and progestins impair sperm production, with an unknown effect on long-term fertility if treatment is discontinued.[71] Individuals assigned female at birth who are prescribed testosterone similarly face the risk of diminished future fertility, even following termination of treatment, although little research has been performed on this question, either.[72] The WPATH Standards of Care and the Endocrine Society Clinical Practice Guideline stress the importance of informing and counseling adolescents requesting gender-affirming medical treatments about the potential loss of fertility and advising them about available options to preserve fertility.[73] Fertility preservation techniques, such as cryopreservation of oocytes and ovarian tissue, are available and improving for individuals assigned female at birth.[74] Individuals assigned male at birth can cryopreserve their sperm, although the sperm production of those still in early puberty is insufficient for cryopreservation.[75]

B. THE STANDARD OF CARE QUESTION

The parties in the ongoing litigation are clashing over the question of whether the WPATH Standards and Endocrine Society Guidelines constitute the standard of care for treatment of gender dysphoria in adolescents. In Alabama, for example, the plaintiffs challenging the PB/CSH ban emphasized that "[WPATH] developed the standard of care, which represents an expert

been well established"). On September 1, 2023, a group of physicians and organizations submitted a citizen petition to FDA requesting that the agency take steps to study and suppress the off-label use of puberty blockers to treat gender dysphoria in minors. *See generally* Citizen Petition from Nancy Sade, et al., to FDA (Sept. 1, 2023), https://www.regulations.gov/document/FDA-2023-P-3767-0029 [https://perma.cc/64AF-WTGA]. The petitioners contended that the drugs pose risks to bone health, fertility, and neurocognitive development and that their benefit to minors with gender dysphoria has not been demonstrated. *Id.* at 3–6.

69. *See, e.g.*, PREMARIN® PRESCRIBING INFORMATION, *supra* note 39.

70. *See, e.g.*, FDA, *supra* note 47.

71. Coleman et al., *supra* note 2, at S158.

72. *Id.* at S157.

73. *Id.* at S48, S57; *Endocrine Society Clinical Practice Guideline*, *supra* note 2, at 3879–80.

74. *Endocrine Society Clinical Practice Guideline*, *supra* note 2, at 3880; Coleman et al., *supra* note 2, at S103.

75. *Endocrine Society Clinical Practice Guideline*, *supra* note 2, at 3879; Coleman et al., *supra* note 2, at S102–03. Researchers are currently investigating the possibility of using direct testicular extraction of sperm and cryopreservation of immature testicular tissue to preserve the fertility of such younger adolescents. Coleman et al., *supra* note 2, at S103.

consensus based on the best available science, [sic] on transgender healthcare."[76] They highlighted the fact that numerous medical associations embrace these standards, including the American Medical Association ("AMA"), the American Academy of Pediatrics, the American Psychiatric Association, and the Endocrine Society.[77] The plaintiffs also stressed that "decades of substantial scientific evidence show that treatment dramatically improves mental health outcomes for transgender youth, including reducing rates of suicidal ideation and suicide attempts."[78]

Alabama responded: "The evidence is distressingly thin. But contrary to Plaintiffs' claims, the best evidence available does not show that the interventions improve mental health or reduce suicides in the long term."[79] The state pointed to multiple European nations that have recently restricted minors' access to gender-affirming care based on reviews of the literature.[80] Alabama asserted:

> Though Plaintiffs and their experts rely on the WPATH Standards and the Endocrine Society Guidelines as establishing "gender affirming care" as the accepted "standard of care," in fact these proposed treatment guidelines from various professional societies and interest groups simply reflect "increasingly divergent views" for "how to approach the management of gender dysphoria in youth." They are not "standards of care" in the traditional sense.[81]

It is unnecessary to resolve the dispute about exactly what practices constitute the standard of care to conclude that the state PB/CSH bans prohibit at least some necessary standard-of-care treatment.[82] No credible American medical

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76. Memorandum in Support of Plaintiffs' Motion for Temporary Restraining Order & Preliminary Injunction at 16, Eckes-Tucker v. Marshall, 603 F. Supp. 3d 1131 (M.D. Ala. 2022) (No. 22-cv-00184).

77. *Id.*

78. *Id.* at 27–28.

79. Defendants' Response in Opposition to Plaintiffs' Motion for Preliminary Injunction at 3, Eknes-Tucker v. Marshall, 603 F. Supp. 3d 1131 (M.D. Ala. 2022) (No. 22-cv-00184).

80. *Id.* at 3, 58–64.

81. *Id.* at 26 (citations omitted); *see also* Defendants' Combined Brief in Opposition to Plaintiffs' Motion for Preliminary Injunction: and Reply in Support of Defendants' Motion to Dismiss at 12, 84 n.148, Brandt v. Rutledge, 2023 WL 4073727 (E.D. Ark. 2023) (No. 21-cv-00450) ("[T]he WPATH and Endocrine Society documents are merely 'treatment guidelines'—not 'standards of care.'" (quoting AM. PSYCH. ASS'N, *Guidelines for Psychological Practice with Transgender and Gender Nonconforming People*, 70 AM. PSYCH. 832, 833 (2015))).

82. The board of medicine of at least one state (Florida) has taken steps to declare the provision of gender-affirming treatments to minors a violation of the standard of care. *See, e.g.*, Azeen Ghorayshi, *Florida Restricts Doctors from Providing Gender Treatments to Minors*, N.Y. TIMES (Nov. 5, 2022), https://www.nytimes.com/2022/11/04/health/florida-gender-care-minors-medical-board.html (on file with the *Iowa Law Review*); Christine Jordan Sexton, *Ron DeSantis Is Reshaping Florida's Medical Boards*, FLA. POL. (Dec. 30, 2022), https://floridapolitics.com/archives/578266-gov-desantis-is-reshaping-floridas-medical-boards [https://perma.cc/N2WR-SPQ8]. However, when I use the phrase "standard of care" in this Article, I am referring to the standards established by the actual practices of reasonably prudent healthcare providers under similar

authority asserts that it is *never* appropriate to prescribe puberty blockers and sex hormones to treat gender dysphoria in youth. And the foreign nations Alabama cites in its brief do not prohibit this use of these drugs in all cases. France, for example, urges "great medical caution."[83] Finland's policy allows for hormonal interventions "under certain conditions."[84] Sweden allows it in "strictly controlled research settings or in very 'exceptional cases.'"[85] In March 2024, NHS—in response to an interim version of the *Cass Review*—adopted a new, more conservative policy regarding the use of pharmaceuticals in the treatment of gender-dysphoric youth, but even under this revised policy, puberty blockers may be used in the context of a research protocol and cross-sex hormones may be prescribed if approved by an independent multidisciplinary team of clinicians.[86] In short, the United States is the only western nation with laws that completely ban physicians from using pharmaceutical treatments for gender dysphoria in minors.

Even the lawyers representing the plaintiffs in the recently proliferating "detransitioner" malpractice lawsuits generally do not allege that PB/CSH treatments for minors always violate the standard of care. In 2023, approximately a dozen people who received gender-affirming care in their teenage years and later regretted doing so brought lawsuits against their healthcare providers

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circumstances, as attested to by qualified experts, not to standards that state legislatures or potentially politicized state medical boards establish by fiat. Moreover, standards of care for specialty areas, including pediatrics, are established by practitioners within that specialty, not by state boards of medicine composed of physicians mostly or entirely from outside the specialty area in question. FED'N OF STATE MED. BDS, CONSIDERATIONS FOR IDENTIFYING STANDARDS OF CARE 5–6 (2023), https://www.fsmb.org/siteassets/advocacy/policies/standards-of-care-policy.pdf [https://perma.cc/S9GZ-5GDU].

83. Opening Brief of State Defendants at 24, Eknes-Tucker v. Governor of Ala., 80 F.4th 1205 (11th Cir. June 27, 2022), ECF No. 31 (quoting Press Release, Académie Nationale de Médicine, Medicine and Gender Transidentity in Children and Adolescents 1 (Feb. 25, 2022), https://www.academie-medecine.fr/wp-content/uploads/2022/03/22.2.25-Communique-PCRA-19-Gender-identity-ENG.pdf [https://perma.cc/3RBQ-ELSB]).

84. *Id.* at 23 (citing PALKO/COHERE FIN., PALVELUVALIKOIMANEUVOSTON SUOSITUS: ALAIKÄISTEN SUKUPUOLI-IDENTITEETIN VARIAATIOIHIN LIITTYVÄN DYSFORIAN LÄÄKETIETEELLISET HOITOMENETELMÄT 7 (2020), https://palveluvalikoima.fi/documents/1237350/22895008/Alaik%C3%A4iset_suositus.pdf [https://perma.cc/2L8X-ANVR], *translated in One Year Since Finland Broke with WPATH "Standards of Care"*, SOC'Y FOR EVIDENCE BASED GENDER MED. (July 2, 2021), https://segm.org/Finland_deviates_from_WPATH_prioritizing_psychotherapy_no_surgery_for_minors [https://perma.cc/5QF4-EETZ]).

85. *Id.* (quoting SOCIALSTYRELSEN: THE NAT'L BD. OF HEALTH & WELFARE, GOV'T OFFS. SWED., ART. NR 2022-3-7799, CARE OF CHILDREN AND ADOLESCENTS WITH GENDER DYSPHORIA 3 (2022), https://web.archive.org/web/20230314183837/https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/kunskapsstod/2022-3-7799.pdf [https://perma.cc/G6G5-4MUA]).

86. *NHS England Stops Prescribing Puberty Blockers and Updates Its Cross-Sex Hormones Policy for Minors*, SOC'Y EVIDENCE BASED GENDER MED. (Mar. 29, 2024), https://segm.org/England-UK-Puberty-Blockers-Cross-Sex-Hormones-Policy-March-2024 [https://perma.cc/DE9W-SKBZ]. Following issuance of the *Cass Review,* Dr. Cass herself clarified: "There are young people who absolutely benefit from a medical pathway, and *we need to make sure that those young people have access*—under a research protocol, because we need to improve the research." Azeen Ghorayshi, *Hilary Cass Says U.S. Doctors Are 'Out of Date' on Youth Gender Medicine*, N.Y. TIMES (May 13, 2024) (emphasis added), https://www.nytimes.com/2024/05/13/health/hilary-cass-transgender-youth-puberty-blockers.html (on file with the *Iowa Law Review*).

alleging malpractice and fraud.[87] If their attorneys thought they could credibly contend that the provision of puberty blockers and sex hormones to a minor for gender-affirming care constitutes medical malpractice in and of itself, they surely would have done so. Most have not, however.

Consider the complaint Kayla Lovdahl filed in California state court. It never asserts that it is a breach of the standard of care to administer gender affirming drugs to a teenager. Instead, the complaint alleges:

> Defendants breached the standard of care . . . by, among other things: (1) failing to properly evaluate, assess, diagnose, discover, and treat Plaintiff's medical and mental health conditions . . . that presented prior to and concurrent with her gender dysphoria symptoms; (2) failing to recognize and provide or refer Kayla to a qualified mental health care provider who could evaluate and treat her on a regular basis over an extended period of time; (3) grossly overemphasizing Plaintiff's gender dysphoria symptoms . . . ; (4) failing to provide Plaintiff with competent informed consent regarding the treatment options available and the relevant risks and benefits of treatment; and (5) manipulating Plaintiff and her parents into a false decision-making matrix by deliberately obscuring relevant information, by presenting false and misleading information, and by . . . grossly exaggerating the suicide risk when no such risk existed for Kayla.[88]

The complaints of most other "detransitioner" plaintiffs frame their malpractice claims similarly.[89]

In contending that the administration of puberty blockers and sex hormones to transgender minors violates the standard of care, the states with PB/CSH bans stress the uncertainty regarding the proper treatment protocol

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87. Molly Hennessy-Fiske, *'Detransitioners' Wield Influence in Shaping Conservative Transgender Laws*, WASH. POST (Jan. 3, 2024), https://www.washingtonpost.com/nation/2023/12/06/detransitioners-transgender-care-laws (on file with the *Iowa Law Review*).

88. Complaint at 29, Lovdahl v. Kaiser Found. Hosps., Inc., No. STK-CV-UMM-2023-0006100 (Cal. Super. Ct. June 14, 2023).

89. *See, e.g.*, Petition at 19–20, Aldaco v. Perry, No. 067-343803 (Tex. Dist. Ct. July 21, 2023) (alleging that doctors failed to thoroughly "assess, consider, and rule out [the plaintiff's] other, diagnosed psychological comorbidities and neurodivergences" before providing gender-affirming care); Complaint and Jury Demand at 14, Mosley v. Emerson, No. 23 CVS 2375 (N.C. Sup. Ct. July 17, 2023) (alleging that defendant doctors "guided [the plaintiff] into medicalized gender transition through deception and negligence" and "conceal[ed] certain material facts, such as that [the plaintiff's] psychological problems stemmed from other causes"); Complaint at 33–35, Ayala v. Am. Acad. of Pediatrics, No. PC-2023-05428 (R.I. Sup. Ct. Oct. 23, 2023) (alleging that doctors "fail[ed] to properly investigate [the plaintiff's] history" before starting treatment and "misrepresent[ed] that no other treatment options existed treating [plaintiff's] symptoms of depression, anxiety, and suicidality"); Verified Complaint for Damages at 13–15, Carlan v. Fenway Cmty. Health Ctr., No. 23-cv-12361 (D. Mass. Oct. 12, 2023) (alleging insufficient consideration of alternatives and consent). *But see* First Amended Complaint for Damages at 6, Anumene v. Permanente Med. Grp., No. CGC-22-598800 (Cal. Sup. Ct. May 10, 2022) (alleging defendants failed to comply with the standards of care by, among other actions, "performing gender transition techniques . . . on plaintiff without data and/or peer reviewed studies objectively proving the effectiveness of any gender affirming techniques . . . in relieving the mental stress otherwise known as 'gender dysphoria'").

for adolescent gender dysphoria.[90] In this respect, it is interesting to contrast how some of these same states addressed the recent question of whether doctors violated the standard of care when they prescribed the antiparasitic drug ivermectin for COVID-19 treatment—a truly experimental off-label use with almost no significant scientific support.[91] The Indiana Attorney General opined:

> The SARS-CoV-2 virus, and thus COVID-19 and the medical field's knowledge of both, is rapidly evolving. Furthermore, studies on the safety and efficacy of potential treatments and preventative medications conflict in outcomes and results . . . [M]edical judgments . . . should be left to the [health care providers] who are trained and skilled in the knowledge to know what is best for their patients. If scientists and public health experts cannot come to a consensus on the safety and efficacy of certain medications, such as ivermectin, then it is reasonable to believe that prescribing them off-label would likely fall within the standard of care.[92]

In the same context, the Nebraska Attorney General advised: "[P]hysicians may utilize reasonable 'investigative or unproven therapies' that reflect a reasonable approach to medicine so long as physicians obtain 'written informed patient consent.'"[93]

These statements are strikingly inconsistent with the states' (almost contemporaneously) expressed reason for passing the PB/CSH bans—to protect children from "experimental" treatments.[94]

II. THE LEGAL STRUGGLE OVER THE STATE BANS

A. EMERGENCE OF THE BANS

In March 2021, the Arkansas legislature passed House Bill 1570, titled "To Create the Arkansas Save Adolescents from Experimentation (SAFE) Act."[95] Governor Asa Hutchinson vetoed the bill, but the legislature overrode the veto, and the law took effect on April 6, 2021.[96] Thus, Arkansas became the

90. *See, e.g.*, Defendants' Response in Opposition to Plaintiffs' Motion for Preliminary Injunction, *supra* note 79, at 26.

91. Kirsten Bibbins-Domingo & Preeti N. Malani, *At a Higher Dose and Longer Duration, Ivermectin Still Not Effective Against COVID-19*, 329 JAMA 897, 897–98 (2023).

92. Off-Label Prescription of Medications for Treatment and Prevention of COVID-19, 2022 Op. Ind. Att'y Gen. No. 1, at 7, 2022 WL 2812523.

93. Prescription of Ivermectin or Hydroxychloroquine as Off-Label Medicines for the Prevention or Treatment of Covid-19, 2021 Op. Neb. Att'y Gen. No. 17, at 7, 2021 WL 5183144 .

94. *Infra* Section II.A.

95. *See generally* H.B. 1570, 93d Gen. Assemb., Reg. Sess. (Ark. 2021) (codified at ARK. CODE ANN. §§ 20-9-1501 to -1504 (2023)). The full history of the bill is available at HB1570—To Create the Arkansas Save Adolescents from Experimentation ("SAFE") Act, ARK. STATE LEG. (Apr. 6, 2021) [hereinafter H.B. 1570 Bill History], https://www.arkleg.state.ar.us/Bills/Detail?id=HB1570&ddBienniumSession=2021%2F2021R [https://perma.cc/B8K3-ZTP6].

96. H.B. 1570 Bill History, *supra* note 95.

first state in the nation to ban the provision of gender-affirming care for minors.

The SAFE Act prohibits a physician or other health care professional from providing "gender transition procedures" to people under eighteen years of age.[97] The statute defines "gender transition procedures" as:

> [A]ny medical or surgical service, including without limitation physician's services, inpatient and outpatient hospital services, or prescribed drugs related to gender transition that seeks to:
>
> (i) Alter or remove physical or anatomical characteristics or features that are typical for the individual's biological sex; or
>
> (ii) Instill or create physiological or anatomical characteristics that resemble a sex different from the individual's biological sex, including without limitation medical services that provide puberty-blocking drugs, cross-sex hormones, or other mechanisms to promote the development of feminizing or masculinizing features in the opposite biological sex, or genital or nongenital gender reassignment surgery performed for the purpose of assisting an individual with a gender transition.[98]

With respect to pharmaceutical treatments in particular, the Arkansas legislature's findings declare: "The prescribing of puberty-blocking drugs is being done despite the lack of any long-term longitudinal studies evaluating the risks and benefits of using these drugs for the treatment of . . . distress [at identifying with one's biological sex] or gender transition."[99] These findings also state:

> Healthcare providers are . . . prescribing cross-sex hormones for children who experience distress at identifying with their biological sex, despite the fact that no randomized clinical trials have been conducted on the efficacy or safety of the use of cross-sex hormones in adults or children for the purpose of treating such distress or gender transition . . . .[100]

The findings then identify a list of "serious known risks" associated with the use of "cross-sex hormones."[101] Finally, the law establishes a variety of mechanisms for enforcing the ban. First, it declares: "Any referral for or provision of gender transition procedures to an individual under eighteen (18) years of age is unprofessional conduct and is subject to discipline by the appropriate licensing entity or disciplinary review board with competent jurisdiction in this state."[102] Second, the law provides: "A person may assert an actual or threatened violation of this subchapter as a claim or defense in a

97. ARK. CODE ANN. § 20-9-1502(a) (2023).
98. *Id.* § 20-9-1501(6)(A).
99. Ark. H.B. 1570 § 2(6)(A)–(B).
100. *Id.* § 2(7).
101. *Id.* § 2(8).
102. ARK. CODE ANN. § 20-9-1504(a) (2023).

judicial or administrative proceeding and obtain compensatory damages, injunctive relief, [or] declaratory relief . . . ."[103] Third, the law gives the attorney general authority to bring an action to enforce compliance with the law.[104] Finally, HB 1570 prohibits insurers from reimbursing gender transition procedures for minors.[105]

In August 2021, a U.S. district court preliminarily enjoined enforcement of the Arkansas law as likely violative of both the Equal Protection Clause and Due Process Clause of the Fourteenth Amendment of the U.S. Constitution.[106] The Eighth Circuit upheld this preliminary injunction in August 2022.[107] In June 2023, the district court made the injunction permanent.[108] Thus, the first state ban on medical treatment for adolescent gender dysphoria is not currently in force. But Arkansas inspired an astonishing surge of similar statutes around the country. Since the enactment of HB 1570, twenty-three additional states have passed similarly broad prohibitions on gender-affirming care for adolescents—twenty-one in 2023 alone.[109] Much of the language of these statutes closely echoes that of the Arkansas statute. Five states, however, go further than Arkansas by making violation of these bans a crime—in four of these states, a *felony*.[110]

Today, thirty-six percent of American transgender youth live in states that prohibit both medication and surgery for treatment of gender dysphoria in minors.[111]

B. CONSTITUTIONAL CHALLENGES

Transgender minors and their parents have brought constitutional challenges to most or all of these state bans in court, on both equal protection and due process grounds.[112] They have had significant success obtaining preliminary injunctions in U.S. district courts.[113] The results in federal courts

103. *Id.* § 20-9-1504(b).

104. *Id.* § 20-9-1504(f)(1).

105. Ark. H.B. 1570 § 6 (codified at ARK. CODE ANN. § 23-79-166(b) (Supp. 2023)).

106. *See* Brandt v. Rutledge, 551 F. Supp. 3d 882, 889–94 (E.D. Ark. 2021), *aff'd*, 47 F.4th 661, 672 (8th Cir. 2022). The court also based the injunction on likely violations of the First Amendment. *Id.* at 893–94.

107. *Brandt*, 47 F.4th 661, 672.

108. Brandt v. Rutledge, 677 F. Supp. 3d 877, 925 (E.D. Ark. 2023).

109. *See supra* note 8 and accompanying text.

110. ALA. CODE § 26-26-4(c) (LexisNexis Supp. 2023) (Class C felony); FLA. STAT. ANN. § 456.52(5)(b) (2023) (third degree felony); IDAHO CODE § 18-1506C(5) (Supp. 2023) (felony with mandatory imprisonment); N.D. CENT. CODE § 12.1-36.1-02(2)(b) (Supp. 2023) (Class A misdemeanor); OKLA. STAT. ANN. tit. 63 § 2607.1(D) (West 2024) (felony).

111. *Bans on Best Practice Medical Care for Transgender Youth*, *supra* note 7.

112. *See supra* notes 12–14 and accompanying text.

113. Brandt v. Rutledge, 551 F. Supp. 3d 882, 894 (E.D. Ark. 2021), *aff'd*, 47 F.4th 661 (8th Cir. 2022); Eknes-Tucker v. Marshall, 603 F. Supp. 3d 1131, 1151 (M.D. Ala. 2022), *vacated sub nom.* Eknes-Tucker v. Governor of Ala., 80 F.4th 1205 (11th Cir. 2023); Doe v. Ladapo, No. 23-cv-144, 2024 WL 2947123, at *39 (N.D. Fla. June 11, 2024); Doe v. Ladapo, 676 F. Supp. 3d

of appeals have been mixed, however. As noted above, in August 2022, the Eighth Circuit upheld the Arkansas preliminary injunction, which is now permanent.[114] But in 2023, in *L.W. v. Skrmetti*, the Sixth Circuit reversed the preliminary injunctions issued with respect to the Tennessee ban and the Kentucky ban.[115] Also in 2023, the Eleventh Circuit, in *Eknes-Tucker v. Governor of Alabama*, vacated a district court's preliminary injunction against the enforcement of Alabama's ban.[116] The discussion below will focus on the substantive due process claims in the litigation challenging the Tennessee, Kentucky, and Alabama bans. In June 2024, as this Article was being edited for publication, the U.S. Supreme Court granted certiorari on the equal protection issue in *Skrmetti*, with argument expected to be heard in fall 2024.[117]

In issuing preliminary injunctions, the federal district courts in Tennessee, Kentucky, and Alabama all found that the PB/CSH bans under review violated the parents' substantive due process rights to direct the medical care of their children. A Supreme Court case concerning visitation rights, *Troxel v. Granville*, held that parents have the right "to make decisions concerning the care, custody, and control of their children" and described this right as "the oldest of the fundamental liberty interests" recognized by the Court.[118] The three district courts all cited cases from their respective circuits holding that *Troxel* protected parents' right to direct their children's medical care.[119]

To say that parents have the right to direct their children's medical care raises a second question, however: Can they demand *any* treatment for

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1205, 1226 (N.D. Fla. 2023); K.C. v. Individual Members of Licensing Bd. of Ind., 677 F. Supp. 3d 802, 820–21 (S.D. Ind. 2023) (based on equal protection only); Doe 1 v. Thornbury, 679 F. Supp. 3d 576, 587 (W.D. Ky. 2023), *rev'd and remanded*, L.W. *ex rel.* Williams v. Skrmetti, 83 F.4th 460 (6th Cir. 2023); L.W. v. *ex rel.* Williams v. Skrmetti, 679 F. Supp. 3d 668 (M.D. Tenn.), *rev'd and remanded*, 83 F.4th 460 (6th Cir. 2023); Koe v. Noggle, 688 F. Supp. 3d 1321, 1363–64 (N.D. Ga. 2023) (based on equal protection only); Poe *ex rel.* Poe v. Labrador, 709 F. Supp. 3d 1169, 1190–200 (D. Idaho 2023). *But see* Poe v. Drummond, 697 F. Supp. 3d 1238, 1264–65 (N.D. Okla. Oct. 5, 2023) (denying request for preliminary injunction). In *van Garderen v. Montana*, the plaintiffs won a preliminary injunction in state district court based on the Equal Protection and Privacy Clauses of the Montana Constitution. *See* Order Granting Plaintiff's Motion for Preliminary Injunction at 45–48, van Garderen v. Montana, No. DV-23-541 (Mont. 4th Jud. Dist. Sept. 27, 2023) (on file with the *Iowa Law Review*).

114. *Brandt*, 47 F.4th at 672.

115. *Skrmetti*, 83 F.4th at 491 (overturning *Skrmetti*, 679 F. Supp. 3d 668 (M.D. Tenn. 2023); Doe 1 v. Thornbury, 679 F. Supp. 3d 576 (W.D. Ky. 2023)).

116. *Eknes-Tucker*, 80 F.4th at 1231.

117. United States v. Skrmetti, 144 S. Ct. 2679 (2024) (mem.) (granting certiorari); Howe, *supra* note 19.

118. Troxel v. Granville, 530 U.S. 57, 65–66 (2000).

119. The district court in Alabama cited Bendiburg v. Dempsey, 909 F.2d 463, 470 (11th Cir. 1990) (holding that a father has the right to refuse risky method of administering antibiotics to his son). Eknes-Tucker v. Marshall, 603 F. Supp. 3d 1131, 1144 (M.D. Ala. 2022), *vacated sub nom.* Eknes-Tucker v. Governor of Ala., 80 F.4th 1205 (11th Cir. 2023). The district courts in Kentucky and Tennessee cited Kanuszewski v. Mich. Dep't of Health & Hum. Servs., 927 F.3d 396, 419 (6th Cir. 2019) (holding parents have the right to refuse collection of blood sample from newborn to test for diseases and retention of these samples). *See Thornbury*, 679 F. Supp. 3d at 586; *Skrmetti*, 679 F. Supp. 3d at 683.

their children, regardless of its regulatory status, its scientific support, and its acceptance in the medical community? Such a reading would give minors a greater constitutional right to access medical treatments than adults, because courts have consistently held that people do not have a substantive due process right to obtain investigational drugs that FDA has not approved for any use.[120] In defending its statute, Kentucky asserted that the plaintiffs were asserting "a fundamental right to obtain whatever drugs they want for their children, without restriction."[121] Alabama suggested that the plaintiffs were claiming "a substantive due process fundamental right to access experimental gender-transition procedures."[122] Framed as such, the plaintiffs' claims have little support in the case law.

In fact, however, the parent plaintiffs in these cases limited the range of treatments they claimed they were constitutionally entitled to provide to their children. They did so in various ways: "medical treatments that are recognized to be safe, effective, and medically necessary,"[123] "established medical treatments,"[124] "appropriate medical care,"[125] and "well-accepted medical treatment."[126] The district court in *Skrmetti* was vague in its pronouncement of the fundamental right, calling it "the right of parents to request certain medical treatments on behalf of their children."[127] The other courts were more careful, however. In *Thornbury* (the Kentucky case), the district court explained:

> [T]he puberty-blockers and hormones barred by [the Kentucky law] are established medical treatments essential to the well-being of many transgender children: every major medical organization in the United States agrees that these treatments are safe, effective, and appropriate when used in accordance with clinical guidelines. This case is therefore distinguishable from those . . . in which plaintiffs claimed

120. Abigail All. for Better Access to Developmental Drugs v. von Eschenbach, 495 F.3d 695, 703 (D.C. Cir. 2007); Rutherford v. United States, 616 F.2d 455, 457 (10th Cir. 1980).

121. *Thornbury*, 679 F. Supp. 3d at 585 (W.D. Ky. 2023), *rev'd and remanded*, L.W. *ex rel.* Williams v. Skrmetti, 83 F.4th 460 (6th Cir. 2023) (quoting Kentucky's brief).

122. Defendants' Response in Opposition to Plaintiffs' Motion for Preliminary Injunction, *supra* note 79, at 103.

123. Complaint for Declaratory and Injunctive Relief at 28, Eknes-Tucker v. Marshall, 603 F. Supp. 3d 1131 (M.D. Ala. 2022) (No. 22-cv-184).

124. Complaint at 20, Doe 1 v. Thornbury, No. 23-cv-230, 679 F. Supp. 3d 576 (W.D. Ky. May 3, 2023).

125. Complaint for Declaratory and Injunctive Relief at 34, L.W. *ex rel.* Williams v. Skrmetti, 679 F. Supp. 3d 668 (M.D. Tenn. 2023) (No. 23-cv-00376), *rev'd and remanded*, 83 F.4th 460 (6th Cir. 2023).

126. *Id.* at 38; *cf.* Poe *ex rel.* Poe v. Labrador, 709 F. Supp. 3d 1169, 1195 (D. Idaho 2023) ("[T]he appropriately precise way to frame the issue is to ask whether parents' fundamental right to care for their children includes the right to choose a particular medical treatment, in consultation with their healthcare provider, that is generally available and accepted in the medical community.").

127. *Skrmetti*, 679 F. Supp. 3d 668, 684, *rev'd and remanded*, 83 F.4th 460 (6th Cir. 2023).

> a right to access treatment for themselves that was not already available or accepted.[128]

The *Eknes-Tucker* court (reviewing the Alabama ban) found that the parents had a "fundamental right to treat their children with transitioning medications subject to *medically accepted standards*."[129] It emphasized, "Defendants produce no credible evidence to show that transitioning medications are 'experimental.'"[130]

In reversing the Tennessee and Kentucky injunctions, the Sixth Circuit maintained that the use of puberty blockers and hormones to treat gender dysphoria in minors is, in fact, "experimental." In an initial opinion temporarily staying the preliminary injunction in Tennessee, Chief Judge Sutton observed that no Supreme Court case extends parents' right to make decisions concerning the care of their children "to a general right to receive *new medical or experimental treatments*."[131] In drawing the line between drugs within the zone of substantive due process protection and those without, Sutton placed great emphasis on FDA approval. He remarked: "There is no constitutional right to use a new drug that the FDA has determined is unsafe or ineffective." Here, Judge Sutton manifested a misunderstanding of the drug approval process. FDA has *not* determined that puberty blockers and sex hormones are "unsafe" or "ineffective" for gender-affirming care in adolescents. Because nobody has submitted a supplemental NDA to the agency seeking approval of any of these drugs for this indication, FDA has reached no conclusions at all.

Judge Sutton continued:

> Gender-affirming procedures often employ FDA-approved drugs for non-approved, "off-label" uses. . . . But the Constitution does not require Tennessee to view these treatments the same way as the majority of experts or to allow drugs for all uses simply because the FDA has approved them for some . . . . It is well within a State's police power to ban off-label uses of certain drugs. At the same time, it is difficult to maintain that the medical community is of one mind about the use of hormone therapy for gender dysphoria when the FDA is not prepared to put its credibility and careful testing protocols behind the use.[132]

This passage evinces a further misconception about the FDA drug approval system. FDA itself does not research drugs for approval; drug manufacturers do. And, as explained below,[133] manufacturers frequently opt not to submit a

128. Doe 1 v. Thornbury, 679 F. Supp. 3d 576, 585 (W.D. Ky. 2023) (citation omitted), *rev'd and remanded*, L.W. *ex rel.* Williams v. Skrmetti, 83 F.4th 460 (6th Cir. 2023).

129. Eknes-Tucker v. Marshall, 603 F. Supp. 3d 1131, 1145 (M.D. Ala. 2022), *vacated sub nom.* Eknes-Tucker v. Governor of Ala., 80 F.4th 1205 (11th Cir. 2023) (emphasis added).

130. *Id.*

131. L.W. *ex rel.* Williams v. Skrmetti, 73 F.4th 408, 417 (6th Cir. 2023) (emphasis added).

132. *Id.* at 418.

133. *See infra* text accompanying note 151.

supplemental NDA for a new indication for reasons totally unrelated to the level of scientific evidence or medical consensus supporting the use.[134]

In his decision finally overturning both the Tennessee and Kentucky injunctions, Judge Sutton continues to impart too much significance to FDA approval and to misapprehend FDA's role. Once again, he asserts: "Neither doctors, adults, nor their children have a constitutional right to use a drug that FDA deems unsafe or ineffective,"[135] without recognizing that the agency only makes such a determination when reviewing an NDA.[136] The opinion then wrongly states that it is not "unusual for the FDA to permit drugs to be used for some purposes but not for others, or to allow some drugs to be used by adults but not by children."[137] In fact, as also explained below,[138] FDA almost never restricts off-label uses in this manner; indeed, it generally lacks the power to do so.[139]

By contrast, in *Eknes-Tucker*, the Eleventh Circuit decision reversing the Alabama injunction, Judge Lagoa does not dwell on the fact that FDA has not approved puberty blockers and sex hormones for gender-affirming care.[140] This fact is largely irrelevant to the court; it intimates that parents might not even have a right to obtain a drug for an FDA-*approved* use.[141] Moreover, the court sees no need to decide whether the use of these drugs to treat gender dysphoria meets the professional standard of care, because there is no "fundamental right to treat one's children with transitioning medications subject to medically accepted standards."[142] *Eknes-Tucker* reaches this conclusion

134. *See infra* text accompanying note 151.

135. L.W. *ex rel.* Williams v. Skrmetti, 83 F.4th 460, 473 (6th Cir. 2023).

136. Indeed, even when it denies an NDA, FDA often does not conclude that a drug is ineffective for the relevant use, but merely that the sponsor has not provided sufficient proof ("substantial evidence") that the drug is effective. 21 U.S.C. § 355(d)(5).

137. *Skrmetti*, 83 F.4th at 473.

138. *See infra* notes 152–74 and accompanying text.

139. The opinion's citations to regulations requiring pediatric studies for some drugs and mandating labeling information for approved pediatric and geriatric indications are entirely unrelated to the legality of off-label prescribing, as is its citation to a case concerning a manufacturer's *promotion* of an off-label use. *Skrmetti*, 83 F.4th at 473–74 (citing 21 C.F.R. §§ 201.23(a), 201.57(c)(9)(iv)–(v); *In re* Celexa & Lexapro Mktg. & Sales Pracs. Litig., 915 F.3d 1, 8–9 (1st Cir. 2019)). The only authority FDA may have to influence the indications for which drugs are prescribed is through imposition of Elements to Assure Safe Use ("ETASU") as components of Risk Evaluation and Mitigation Strategies ("REMS") for particularly risky drugs. 21 U.S.C. § 355-1(f). However, the REMS provisions of the FDCA envision that ETASU will have an indirect impact—at most—on prescribing drugs for unapproved indications. *See* 21 U.S.C. § 355-1(f)(3) (listing permissible components of ETASU); Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 SAN DIEGO L. REV. 427, 498 n.410 (2015) ("FDA has not exercised its REMS authority to prohibit off-label prescribing of drugs . . . .").

140. When analyzing why the Alabama ban survives rational basis scrutiny, the court observes that "FDA has not approved [the drugs] for this purpose although it has for others." Eknes-Tucker v. Governor of Ala., 80 F.4th 1205, 1234 (Brasher, J., concurring).

141. In this regard, Judge Lagoa may have written the opinion with an eye to current and future disputes regarding federal preemption of state prohibitions on the FDA-approved use of the drug mifepristone for abortion. *See, e.g.*, GenBioPro, Inc. v. Sorsaia, No. 23-0058, 2023 WL 5490179, at *5–13 (S.D. W. Va. Aug. 24, 2023).

142. *Eknes-Tucker*, 80 F.4th at 1225 (internal quotation marks omitted).

by narrowly applying the *Dobbs* "deeply rooted in our history and tradition" test to puberty blockers and sex hormones in particular, noting that the use of these drugs to treat gender dysphoria did not emerge "until well into the twentieth century."[143]

The same, of course, could be said for most uses of modern pharmaceuticals. While acknowledging "that parents retain 'plenary authority' as well as 'a substantial, if not the dominant, role' in deciding to pursue *lawfully available* treatment for their children," the Eleventh Circuit denies that parents have "a fundamental right to direct a particular medical treatment for their child that is prohibited by *state law*."[144] The Eleventh Circuit thus seems to grant states the plenary authority to restrict the use of any drugs for any purpose, FDA-approved or not, subject only to rational basis review.[145]

The remainder of this Article seeks to undermine the reasoning of both circuit courts and to explain why American parents possess a fundamental right to obtain necessary standard-of-care medical treatment for their children, including when that treatment is an off-label use of an FDA-approved drug.

III. FDA (NON)REGULATION OFF-LABEL PRESCRIBING AND THE PREVALENCE OF OFF-LABEL USE

A. FDA POWER AND POLICY

As mentioned earlier, states defending their bans in the ongoing litigation rely heavily on the argument that the use of puberty blockers and hormones for gender-affirming care in adolescents is "experimental" because FDA has not approved these drugs for this purpose.[146] This contention misunderstands, or misrepresents, a fundamental aspect of FDA drug regulation: In most instances, the mere fact that the agency has not approved a particular additional use of a drug that it has approved for one or more other indications tells us nothing about the amount of scientific support for that additional use. To equate "off-label" and "experimental" is simply inaccurate.[147]

Since enactment of the 1962 Drug Amendments, FDA has formally reviewed new drugs for effectiveness as well as safety.[148] The agency does not

143. *Id.* at 1220–21.

144. *Id.* at 1223 (emphasis added) (quoting Parham v. J. R., 442 U.S. 584, 604 (1979)).

145. *Id.* (emphasis added).

146. *See supra* Section II.B.

147. Katrina Furey & Kirsten Wilkins, *Prescribing "Off-Label": What Should a Physician Disclose?*, 18 AMA J. ETHICS 587, 588 (2016) ("Contrary to what patients might assume, off-label drug use is not the same as experimental or research use.").

148. Drug Amendments of 1962, Pub. L. 87-781, 76 Stat. 780, 781 (codified at 21 U.S.C. § 355). I use the word "formally" because even before 1962, FDA drug reviewers were considering the effectiveness of drugs for the labeled indications in some situations. Most obviously, if a drug under review was labeled as effective for a critical or imminently fatal disease or condition (such as a heart attack), the safety of that product could not be divorced from its effectiveness. *Drug Safety: Hearings Before a Subcomm. of the H. Comm. on Govt. Operations*, 88th Cong. 150 (1964) (statement of George Larrick, Comm'r of Food and Drugs) ("Of course, [before 1962] the question of benefit was an integral part of the safety question in dealing with a product to be used

review and approve drug *substances*, but rather drug substances labeled for specific indications. The applicant chooses what uses to study for purposes of preparing an NDA. When FDA approves an NDA, it approves not only the drug substance, but also the required labeling.[149] This labeling, the specific wording of which is laboriously negotiated between the agency and sponsor, sets forth the particular indication or indications for which the drug is approved (along with much additional information).[150]

If after initial approval, the manufacturer wants to seek approval for an additional indication, it can perform additional studies trying to demonstrate that the product is safe and effective for that indication and (if these studies are successful) file a supplemental NDA.[151] The absence of a particular indication from a drug's labeling does not ordinarily mean that the manufacturer has filed a supplemental NDA that the FDA rejected because of safety or effectiveness concerns. Rather, in the vast majority of instances, it simply reflects the fact that the sponsor has not sought approval for that indication and thus has not presented FDA with any relevant data. In other words, an unapproved use of a drug is usually not one that FDA has *disapproved*, but rather one that the agency has not *considered*.

FDA has long embraced the view that once a drug is approved for one use, the agency will not interfere with physicians' decisions to prescribe it for other indications.[152] In 1972, the agency issued a proposed rule in which it declared: "Once the new drug is in a local pharmacy after interstate commerce, the physician may, as part of the practice of medicine, lawfully . . . vary the conditions of use from those approved in the package insert, without informing or obtaining the approval of the Food and Drug Administration."[153] FDA thought this approach was consistent with Congress's intent when it enacted the 1938 Food, Drug, and Cosmetic Act and the 1962 Drug Amendments. "Throughout the debate leading to enactment, there were repeated statements that Congress did not intend [FDA] to interfere with medical practice and references to the understanding that the bill did not purport to regulate the practice of medicine as between the physician and the patient."[154] FDA emphasized: "The labeling is not intended either to preclude

in a life-threatening disease . . . ."). Moreover, as Daniel Carpenter has shown, FDA reviewers were, without explicit statutory authority to do so, beginning to take account of efficacy data even in other situations before 1962. DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA 118–227 (Ira Katznelson et al. eds., 2010).

149. *New Drug Application*, FDA (Jan. 21, 2022), https://www.fda.gov/drugs/types-applications/new-drug-application-nda [https://perma.cc/U3BW-Y39C].

150. *Id.*; 21 U.S.C. §§ 321(p)(1), 355(b)(1)(A), (d); PETER BARTON HUTT ET AL., FOOD AND DRUG LAW: CASES AND MATERIALS 918–19, 949, 1076–77 (5th ed. 2022).

151. 21 C.F.R. §§ 314.70(b)(2)(v)(A), 314.71(b) (2024).

152. Although states also authorize various other categories of health care providers to prescribe prescription drugs, this Article will, for simplicity's sake, refer only to "physicians" or "doctors."

153. Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration, 37 Fed. Reg. 16503, 16503 (Aug. 15, 1972) (to be codified at 21 C.F.R. pt. 130).

154. *Id.*

the physician from using his best judgment in the interest of the patient, or to impose liability if he does not follow the package insert."[155] Although the agency never finalized this rule, it has referred to it as established policy[156] and has articulated the principle of noninterference in the practice of medicine in additional contexts.[157] FDA's regulations on investigational new drug applications (that is, requests for NDA exemptions for unapproved drugs used in clinical research) incorporate this policy by exempting the off-label use of an approved drug in the practice of medicine from FDA review.[158]

When FDA enunciated this noninterference policy in the 1972 proposed rule, it observed that it nonetheless was "obligated . . . to take whatever action is warranted to protect the public" when an "unapproved use of an approved new drug becomes widespread or endangers the public health."[159] Soon thereafter, however, a federal court severely cabined the agency's power to address even such situations. The case, *United States v. Evers*, concerned an off-label practice addressed in detail later in this Article: the intravenous administration of Calcium EDTA, a "chelation" drug approved only for treatment of lead poisoning, to treat cardiovascular disease—a use with little scientific support.[160] The United States, at FDA's behest, brought a misbranding action against an Alabama doctor who promoted and ran a chelation clinic, seeking to enjoin him from continuing the practice.[161]

The district court ruled in Dr. Evers' favor, explaining, "It is well-recognized that a package insert may not contain the most up-to-date information about a drug and the physician must be free to use the drug for an indication not in the package insert when such usage is part of the practice of medicine and for the benefit of the patient.[162] The district court held that an FDA prohibition of a physician's off-label use of an approved drug would be *unconstitutional*. The court observed that it would "exceed the powers of Congress" to "interfere with medical practice as between the physician and

155. *Id.* at 16504.

156. *E.g.*, *Use of Approved Drugs for Unlabeled Indications*, FDA DRUG. BULL. (Dep't of Health & Hum. Servs., Rockville, Md.), Apr. 1982, at 4, 4; Labeling for Prescription-Drug Advertisements, 40 Fed. Reg. 15392, 15393–94 (Apr. 7, 1975) (to be codified at 21 C.F.R. pt. 1, 3).

157. FDA, "OFF-LABEL" AND INVESTIGATIONAL USE OF MARKETED DRUGS, BIOLOGICS, AND MEDICAL DEVICES 1 (Jan. 1998) ("Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgement. If physicians use a product for an indication not in the approved labeling . . . when the intent is the 'practice of medicine' [the use] does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE) or review by an Institutional Review Board (IRB)."(emphasis removed)).

158. New Drug, Antibiotic, and Biologic Drug Product Regulations, 52 Fed. Reg. 8798, 8832 (Mar. 19, 1987) (to be codified at 21 C.F.R. § 312.2(d)) ("This part does not apply to the use in the practice of medicine for an unlabeled indication of a new drug . . . .").

159. Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration, 37 Fed. Reg. 16503, 16504 (Aug. 15, 1972) (to be codified at 21 C.F.R. pt. 130).

160. *See infra* notes 228–36.

161. United States v. Evers, 453 F. Supp. 1141, 1144 (M.D. Ala. 1978).

162. *Id.* at 1149.

the patient."[163] Furthermore, citing recently decided Supreme Court abortion decisions, the district court observed: "The courts have rather uniformly recognized the patients' rights to receive medical care in accordance with their licensed physician's best judgment and the physician's rights to administer it as may be derived therefrom."[164]

The U.S. Court of Appeals for the Fifth Circuit upheld the district court.[165] The reviewing court found it unnecessary to reach the constitutional issues, however, because it held, as a statutory matter, that Evers' conduct did not violate the Food, Drug, and Cosmetic Act.[166] The government contended that the defendant's off-label prescribing violated a provision of the Act that prohibits the performance of any act "done while [a drug] is held for sale (whether or not the first sale) after shipment in interstate commerce and results in such article being [adulterated or] misbranded."[167] The particular misbranding provision the government alleged Dr. Evers had violated deems a drug to be misbranded "unless its labeling bears . . . adequate directions for use."[168] By regulation, FDA defines "adequate directions for use" to mean adequate directions for the "layman."[169] In another rule, however, the agency states that directions for a layman are not required for a prescription drug that, among other requirements, provides "adequate information for use" by a practitioner.[170] Despite the undeniable absence of such "information for use" against cardiovascular disease in the chelation drug's labeling, the court concluded that this requirement could not rationally be applied to Dr. Evers's off-label prescribing:

> The requirement which the FDA seeks to impose is nonsensical. Since Calcium EDTA is a prescription drug, the misbranding provision under which Dr. Evers was charged requires him to provide adequate information for use by prescribing physicians. However, Dr. Evers was the only physician who used the Calcium EDTA in question. The government's application of the statute may therefore be reduced to the following proposition: Dr. Evers did not provide adequate information to himself. It is doubtful at best that this interpretation was intended by the drafters of the statute.[171]

163. *Id.* at 1149–50 (citing Linder v. United States, 268 U.S. 5, 45 (1925)).

164. *Id.* at 1150 (citing Doe v. Bolton, 410 U.S. 179, 197 (1973); Whalen v. Roe, 429 U.S. 589, 597 (1977)); *see also* State Bd. of Med. Exam'rs v. Rogers, 387 So. 2d 937, 939 (Fla. 1980) (holding that a state medical board's requirement that a physician discontinue chelation therapy "unreasonably interferes with [his] right to practice medicine by curtailing the exercise of his professional judgment").

165. United States v. Evers, 643 F.2d 1043, 1054 (5th Cir. 1981).

166. *Id.* at 1044.

167. *Id.* at 1047 (quoting 21 U.S.C. § 331(k)).

168. *Id.* (quoting 21 U.S.C. § 352(f)(1)).

169. 21 C.F.R. § 201.5 (2023).

170. 21 C.F.R. § 201.100(c)(1) (2023).

171. *Evers*, 643 F.2d at 1053.

Later decisions have confirmed that FDA does not have authority under the FDCA to prohibit physicians from prescribing approved drugs for off-label uses. The Second Circuit has declared: "Once FDA-approved, prescription drugs can be prescribed by doctors for both FDA-approved and -unapproved uses; the FDA generally does not regulate how physicians use approved drugs."[172] The Third Circuit has observed: "Because the FDCA does not regulate the practice of medicine, physicians may lawfully prescribe drugs for off-label uses."[173] In the related context of medical device regulation, the U.S. Supreme Court has asserted that off-label use "is an accepted and necessary corollary of the FDA's mission to regulate in this area without directly interfering with the practice of medicine."[174]

B. THE PREVALENCE OF OFF-LABEL PRESCRIBING

In part because FDA has almost no power over off-label prescribing,[175] it is extremely common in American medicine.[176] A study of office-based physicians' prescribing patterns for 160 commonly used drugs found that twenty-one percent of the prescriptions were off-label.[177] Recent estimates of the percentage of prescriptions overall that are off-label range as high fifty percent.[178] The frequency of off-label prescribing varies significantly by drug type and therapeutic area. For example, psychiatric drugs—especially antipsychotics—are particularly likely to be prescribed off-label.[179] So are

172. United States v. Caronia, 703 F.2d 149, 153, 160–69 (2d. Cir. 2012) (analyzing First Amendment protection of the promotion of off-label uses).

173. *In re* Schering Plough Corp. Intron/Temodar Consumer Class Action, 678 F.3d 235, 240 (3d Cir. 2012); *see also* Planned Parenthood Ariz., Inc. v. Humble, 753 F.3d 905, 909 (9th Cir. 2014) ("FDA has consistently maintained [the] position" that the FDCA "does not . . . limit the manner in which a physician may use an approved drug" (quoting *Use of Approved Drugs for Unlabeled Indications*, *supra* note 156, at 5)); Chaney v. Heckler, 718 F.2d 1174, 1180 (D.C. Cir. 1983) ("FDCA's legislative history expresses a specific intent to prohibit FDA from regulating physicians' practice of medicine . . . . Congress would have created havoc in the practice of medicine had it required physicians to . . . obtain[] FDA approval before putting drugs to new uses.").

174. Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 350 (2001) (analyzing federal preemption of state medical device regulations). The FDCA contains a provision explicitly disclaiming any intention "to interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship." 21 U.S.C. § 396. No similar provision exists for drugs.

175. As noted previously, *supra* note 139 and accompanying text, since 2007 FDA has had power to limit off-label prescribing of some particularly risky drugs by imposing REMS containing ETASU. 21 U.S.C. § 355-1(a)(1). ETASU may control the distribution and use of a drug in ways that, in practice, inhibit off-label use. For example, ETASU can require that a drug be prescribed only by health care providers with particular training or experience or that it be prescribed only in certain health care settings. *Id.* § 355-1(f)(3)(A), (C).

176. Randall S. Stafford, *Regulating Off-Label Drug Use — Rethinking the Role of the FDA*, 358 NEW ENG. J. MED. 1427, 1427 (2008).

177. David C. Radley, Stan N. Finkelstein & Randall S. Stafford, *Off-Label Prescribing Among Office-Based Physicians*, 166 ARCHIVES INTERNAL MED. 1021, 1021 (2006).

178. James M. Beck, *Off-Label Use in the Twenty-First Century: Most Myths and Misconceptions Mitigated*, 54 U. ILL. CHI. L. REV. 1, 25 (2021).

179. Stafford, *supra* note 176, at 1427–28.

cardiovascular medications.[180] Off-label prescribing of oncology drugs is especially prominent, with one estimate as high as seventy-five percent of uses.[181]

Notably for purposes of this Article, pediatrics is another area in which the prevalence of off-label uses is extremely high.[182] Clinical data regarding the use of drugs in children (and thus FDA approvals for these uses) are relatively sparse for various reasons, "including unfamiliarity with age-related developmental pharmacology in pediatric patients, ethical considerations with conducting pediatric research, and a lack of financial incentive for the pharmaceutical industry."[183] Congressional efforts to incentivize and (in many instances) mandate pediatric research[184] have mitigated but not solved the problem.[185] According to one study, almost forty percent of pediatric prescriptions are off-label.[186] Moreover, about eighty percent of off-label prescriptions to children in the outpatient setting are off-label by *indication*, not merely because the drugs have been approved for use in adults but not children.[187]

None of this is to deny that much off-label use lacks robust scientific support. One study of off-label prescriptions of commonly used medications for adults found that seventy-three percent of them were for indications with

180. Gail A. Van Norman, *Off-Label Use vs Off-Label Marketing of Drugs*, 8 JACC BASIC TRANSL. SCI. 224, 225 (2023).

181. Michael Soares, *"Off-Label" Indications for Oncology Drug Use and Drug Compendia: History and Current Status*, 1 J. ONCOLOGY PRAC. 102, 104 (2005); Beck, *supra* note 178, at 25.

182. Soares, *supra* note 181, at 104.

183. H. Christine Allen et al., *Off-Label Medication Use in Children, More Common than We Think: A Systematic Review of the Literature*, 111 J. OKLA. ST. MED. ASS'N 776, 777 (2018). *See generally* Aysha Muthanna Shanshal & Saad Abdulrahman Hussain, *Off-Label Prescribing Practice in Pediatric Settings: Pros and Cons*, 12 SYSTEMATIC REVS. PHARMACY 1267 (2021) (ascribing the dearth of pediatric data to "the complexity of the clinical trials, lack of attention of the added value, and inconvenient return on financial resources for pediatric medicine development").

184. In 1997, Congress incentivized pediatric testing by providing six months of "pediatric exclusivity" for innovator drugs (that is, a half-year delay on generic entry) when the NDA sponsor performs pediatric testing at FDA's request. FDA Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (codified as amended at 21 U.S.C. § 355(a)). In 2003, Congress added another section to the FDCA requiring every NDA for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration to include a "pediatric assessment" (absent an agency waiver or deferral) and authorizing FDA to mandate pediatric testing of approved drugs in some circumstances. Pediatric Research Equity Act of 2003 ("PREA"), Pub. L. No. 108-155, 117 Stat. 1936 (codified as amended at 21 U.S.C. § 355(c)). Congress and FDA have also taken other steps to encourage pediatric testing. HUTT ET AL., *supra* note 150, at 896–99.

185. Allen et al., *supra* note 183, at 2; Katelyn Yackey et al., *Off-Label Medication Prescribing Patterns in Pediatrics: An Update*, 9 HOSP. PEDIATRICS 186, 192 (2019).

186. Allen et al., *supra* note 183, at 5. A 2014 study showed that the frequency of pediatric inpatient off-label prescriptions was declining but that they still represented about one quarter of the total. Yackey et al., *supra* note 185, at 192.

187. Divya Hoon et al., *Trends in Off-Label Drug Use in Ambulatory Settings: 2006–2015*, 144 PEDIATRICS 1, 5 (2019) ("74.6 % were off-label by indication, 17.6% were off-label by age, 0.6% were off-label by weight, and 4.7% were off-label based on the combination of age, indication, and [where applicable] weight.").

little or no scientific support,[188] and another (conducted in the Netherlands) found that only fourteen percent of off-label prescriptions for children were supported by high-quality evidence.[189] Researchers have also found that off-label drug uses lacking strong scientific evidence are associated with a much higher incidence of adverse drug events in both adults and children.[190]

Conversely, however, many off-label drug uses—including the use of puberty-blockers and sex hormones for treatment of gender dysphoria—have significant scientific support. As FDA has explained:

> "[U]napproved" or, more precisely, "unlabeled" uses may be appropriate and rational in certain circumstances, and may, in fact, reflect approaches to drug therapy that have been extensively reported in medical literature. Valid new uses for drugs already on the market are often . . . confirmed by well-planned and executed clinical investigations. Before such advances can be added to the approved labeling, however, data substantiating the effectiveness of a new use or regimen must be submitted by the manufacturer to [the] FDA for evaluation. This may take time and, without the initiative of the drug manufacturer whose product is involved, may never occur. For that reason, accepted medical practice often includes drug use that is not reflected in approved drug labeling.[191]

In other words, even when strong clinical evidence in support of an off-label use is available, manufacturers may not invest the resources necessary to persuade FDA to make the use "on-label" because they conclude that such an effort, even if successful, would not increase profits enough to offset its costs. After all, when an off-label use of a drug is widely known, a manufacturer can make substantial revenues from sales of the drug for that use without pursuing approval. Although the manufacturer cannot advertise an unapproved use, it can—under the protection of the First Amendment—disseminate truthful and nonmisleading scientific information about it.[192] Moreover, scientists,

188. Radley et al., *supra* note 177, at 1021, 1022 (explaining scientific support of an effective use as "effectiveness shown in controlled trials or observed in clinical settings").

189. *See generally* Tjitske M. van der Zanden et al., *Off-Label, but on-Evidence? A Review of the Level of Evidence for Pediatric Pharmacotherapy*, 112 CLINICAL PHARMACOLOGY & THERAPEUTICS 1243 (2022) (defining "high quality evidence" as meta-analysis, systematic reviews, and high-quality randomized controlled trials).

190. Tewodros Eguale et al., *Association of Off-Label Drug Use and Adverse Drug Events in an Adult Population*, 176 JAMA INTERNAL MED. 55, 55 (2016) (finding an ADE rate of 21.7 per 10,000 person-months for off-label use lacking strong scientific evidence versus 1.54% for on-label drug use); Benjamin Horen, Jean-Louis Montastruc & Maryse Lapeyre-Mestre, *Adverse Drug Reactions and Off-Label Drug Use in Paediatric Outpatients*, 54 BRIT. J. CLINICAL PHARMACOLOGY 665, 668 (2002) (finding higher incidence of adverse drug reactions for off-label uses in pediatric outpatients). Notably, the first study cited above also found that off-label uses with strong evidence were *not* associated with a higher risk of adverse drug events than on-label uses. Eguale et al., *supra*, at 59.

191. *Use of Approved Drugs for Unlabeled Indications*, *supra* note 156, at 5.

192. Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51, 66 (D.D.C. 1998), *vacated for lack of controversy sub. nom.* Wash. Legal Found. v. Henney, 202 F.3d 331 (D.C. Cir. 2000); FDA,

physicians, and journalists unassociated with the manufacturer can spread the word about a promising or firmly established off-label use with no limitations whatsoever. Drug manufacturers thus often decide that seeking FDA approval is not a worthwhile investment.[193] This calculation not only inhibits manufacturers from submitting supplemental NDAs; it often dissuades them from funding the costly trials necessary to develop data regarding the off-label use in the first place.

Nevertheless, sometimes—as with puberty blockers and sex hormones for treatment of gender dysphoria in adolescents[194]—the safety and efficacy of an off-label use are so well established that it constitutes the standard of care.[195] FDA itself recognizes this phenomenon.[196] In such situations, a doctor is effectively *obligated* to prescribe the drug off-label to avoid the possibility of medical malpractice liability or board discipline.[197] In pediatrics, off-label use constitutes the standard of care so frequently that the National Institute of Child Health and Human Development ("NICHD") is sponsoring an ongoing study of medicines prescribed off-label for about sixty different diseases and

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COMMUNICATIONS FROM FIRMS TO HEALTH CARE PROVIDERS REGARDING SCIENTIFIC INFORMATION ON UNAPPROVED USES OF APPROVED/CLEARED MEDICAL PRODUCTS: QUESTIONS AND ANSWERS 12 (2023); United States v. Caronia, 703 F.3d 149, 166–68 (2d Cir. 2012). Precisely when true and nonmisleading promotional communications by manufacturers about off-label uses are protected by the First Amendment remains uncertain. David A. Simon, *Off-Label Innovation*, 56 GA. L. REV. 701, 739 n.158 (2022).

193. Pearson Bownas & Mark Herrmann, *Keeping the Label Out of the Case*, 103 NW. U. L. REV. COLLOQUY 477, 483–85 (2009). Bownas and Herrmann list some additional reasons why manufacturers do not seek FDA approval for well-supported off-label uses, including the ethical and practical difficulty of performing placebo-controlled studies on an off-label use that is already the standard of care. *Id.* at 484–85.

194. *See supra* Section I.A.

195. Beck, *supra* note 178, at 28; Stephanie Greene, *False Claims Act Liability for Off-Label Promotion of Pharmaceutical Products*, 110 PENN ST. L. REV. 41, 46 (2005); George Horvath, *Off-Label Drug Risks: Toward a New FDA Regulatory Approach*, 29 ANNALS HEALTH L. & LIFE SCIS. 101, 102 (2020); Simon, *supra* note 192, at 721–22; Veronica Henry, *Off-Label Prescribing: Legal Implications*, 20 J. LEGAL MED. 365, 380 (1999); Valentina Petkova, Dilyana Georgieva, Milen Dimitrov & Irina Nikolova, *Off-Label Prescribing in Pediatric Population—Literature Review for 2012–2022*, 15 PHARMACEUTICS 2652, 2653 (2023); Bownas & Herrmann, *supra* note 193, at 486; Philip M. Rosoff & Doriane Lambelet Coleman, *The Case for Legal Regulation of Physicians' Off-Label Prescribing*, 86 NOTRE DAME L. REV. 649, 656 (2011) (asserting that "many" off-label uses are "evidence-based" and thus "appropriately established as the standard of care").

196. FDA, GUIDANCE FOR INDUSTRY: RESPONDING TO UNSOLICITED REQUESTS FOR OFF-LABEL INFORMATION ABOUT PRESCRIPTION DRUGS AND MEDICAL DEVICES 2 (2011) ("FDA recognizes that . . . off-label uses . . . may be important therapeutic options and may even constitute a medically recognized standard of care."); *see also Wash. Legal Found.*, 13 F. Supp. 2d at 71 ("[E]ven by FDA's own admissions, off-label treatments may constitute the standard of care for some conditions.").

197. Beck, *supra* note 178, at 28–29; Sandra H. Johnson, *Polluting Medical Judgment? False Assumptions in the Pursuit of False Claims Regarding Off-Label Prescribing*, 9 MINN. J.L. SCI. & TECH. 61, 68 (2008); John Berlau, *Dr. Kessler, Remove the Gag*, WALL ST. J., Dec. 5, 1995, at A20 (quoting AMA Vice President Roy Schwarz as saying: "In some cases, if you didn't use drugs in the off-label way, you'd be guilty of malpractice"); *Off-Label Prescribing? Know Evidence Base!*, RELIAS MEDIA (Mar. 1, 2013), https://www.reliasmedia.com/articles/62949-off-label-prescribing-know-evidence-base [https://perma.cc/KYY8-55LJ] (quoting attorney Samantha L. Prokop as saying, "In fact, failure to use a drug or product off-label could also be considered malpractice, if the standard of care required off-label use").

conditions entitled "Pharmacokinetics of Understudied Drugs Administered to Children Per Standard of Care" ("POPS").[198]

IV. STATE (NON)REGULATION OF OFF-LABEL PRESCRIBING CONSISTENT WITH THE STANDARD OF CARE

As discussed above, FDA does not prohibit off-label prescribing because it does not have authority to interfere with the "practice of medicine."[199] A corollary to this principle is that the states—which indisputably have regulatory power over the practice of medicine[200]—*can* regulate or prohibit off-label uses of approved drugs.

It is astonishing how rarely they have done so, however. This Section examines state limitations on off-label use of drugs and reveals that the states are almost as *laissez-faire* with respect to off-label prescribing as FDA is. As the review below will show, states have, in rare instances, banned specific off-label uses of particular drugs. But an examination of these scarce examples reveals another notable fact: Outside the context of gender-affirming drugs and abortion medication, no state has *ever* prohibited—let alone criminalized—off-label prescribing of an FDA-approved drug for a use that constituted the medical standard of care.

A. *MEDICAL BOARD DISCIPLINE*

States *could* regulate off-label prescribing through their disciplinary systems for physicians administered by state medical boards. The most longstanding form of state regulation of the "practice of medicine" is the medical licensing schemes controlling who is permitted to be a physician.[201]

The U.S. Supreme Court explicitly confirmed the states' power to exclude unqualified people from the practice of medicine in 1889.[202] Furthermore, as the Court later acknowledged, "a state's legitimate concern for maintaining high standards of professional conduct extends beyond initial licensing."[203] Thus, legitimate state regulation of the practice of medicine extends to discipline (license suspension or revocation, probation, reprimands, monetary

198. Daniel Benjamin, *Pharmacokinetics of Understudied Drugs Administered to Children Per Standard of Care*, NAT'L LIB. MED. (June 9, 2023), https://clinicaltrials.gov/study/NCT01431326 [https://perma.cc/87LU-UGSV].

199. *See supra* notes 164–68 and accompanying text.

200. McNaughton v. Johnson, 242 U.S. 344, 356 (1917) ("It is established that a State may regulate the practice of medicine, using this word in its most general sense."); Lambert v. Yellowly, 272 U.S. 581, 594 ("[T]here is no right to practice medicine which is not subordinate to the police power of the States."); Gonzales v. Oregon, 546 U.S. 243, 270 (2006) (referring to "the States' general regulation of medical practice").

201. *See* GROSSMAN, *supra* note 28, at 14–18, 24–74 (discussing state medical licensing in the late eighteenth century and the nineteenth century).

202. Dent v. West Virginia, 129 U.S. 114, 122–23 (1889).

203. Barsky v. Bd. of Regents, 347 U.S. 442, 451 (1954).

fines, and censures) imposed by state boards on already-licensed physician for "unprofessional, immoral, dishonorable, or gross misconduct."[204]

Because "unprofessional conduct" and "gross misconduct" both encompass situations in which a physician fails to comply with the standard of care,[205] a board may discipline a doctor for off-label prescribing that violates this standard. Indeed, doctors have occasionally been disciplined for off-label prescriptions below the standard of care.[206] It is important to emphasize, however, that this discipline was based on the violation of the standard of care, not on off-label prescribing in and of itself.

Medical licensing boards rarely intervene in off-label prescribing, however. They do not have the resources or motivation to routinely examine the prescribing practices of individual doctors.

> [T]he medical licensing boards are not well placed either to regulate or even investigate anything other than the most grievous violations of medical standards, generally brought to their attention by disgruntled or poorly served patients, or occasionally by law enforcement authorities . . . . [T]hey tend to grant great leeway to physicians in the way they care for their patients and prescribe medicines . . . . [S]crutiny of off-label use is generally off limits.[207]

B. MALPRACTICE LAW

State malpractice law is another way states regulate the practice of medicine. State courts do not frequently interfere with physicians' off-label prescribing practices, however. Reported cases that explicitly hold a doctor accountable simply for straying from the approved labeling are sparse to nonexistent.[208]

This dearth of decisions reflects the fact that prescribing a drug off-label does *not* automatically—or even presumptively—violate the standard of care.[209]

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204. S. Sandy Sanbar, *Medical Practice: Education and Licensure*, *in* LEGAL MEDICINE 7, 12 (S. Sandy Sanbar et al. eds., 7th ed. 2007).

205. *Id.*; *see, e.g.*, 22 TEX. ADMIN. CODE § 190.8(1) (2024) (in a rule implementing section 164.052 of the Texas Occupations Code, a Texas statutory provision allowing the Board of Medical Examiners to take disciplinary action against a person who "fails to practice medicine in an acceptable professional manner consistent with public health and welfare," the board defines "[f]ailure to practice medicine in an acceptable professional manner consistent with public health and welfare" in the administrative code to include "failure to treat a patient according to the generally accepted standard of care"). A state court upheld this interpretation of the Code in *Chalifoux v. Texas State Board of Medical Examiners*, No. 03-05-00320-cv, 2006 WL 3196461, at *15–17 (Tex. App. Nov. 1, 2006).

206. *See generally* Tex. Med. Bd. v. McClellan, SOAH Docket No. 503-14-0243, 2015 TX SOAH LEXIS 521 (Tex. St. Off. of Admin. Hearings Nov. 19, 2015); *In re* Sapp, 20A-30780, 2020 WL 5512486 (Ariz. Med. Bd. Sept. 4, 2020).

207. Rosoff & Coleman, *supra* note 195, at 665.

208. My searches for such cases on Lexis turned up no examples. *Id.* at 666–67 (reporting, based on their own Westlaw search, "the dearth of published cases . . . in which off-label use by a medical provider was a focus of the plaintiff's case" and that these cases "evidence strong deference to the professional judgment of individual physicians").

209. 124 AM. JUR. TRIALS 487 § 13 (2012) (Aug. 2024 update); Beck, *supra* note 178, at 12.

As explained earlier,[210] many off-label uses are supported by extensive evidence. Moreover, the sheer frequency of off-label prescribing undermines malpractice claims against doctors for harm allegedly caused by this practice. The traditional standard of care that doctors owe their patients in malpractice cases is measured by the "customary practice among physicians" as shown by expert testimony.[211] As Professor Philip G. Peters explains, "Under a custom-based standard of care, the relevant inquiry is not whether the defendant behaved like a reasonable person or even whether she behaved as a reasonable physician, but instead whether the defendant conformed with customary practices."[212] In 2000, Peters identified a "quiet and persistent shift" away from this standard, as many states—starting with Washington in the seminal case of *Helling v. Cary*[213]—embraced a "reasonable physician" approach and either explicitly or implicitly ceased to defer to physician custom in malpractice cases.[214] A quarter of a century later, however, the customary standard maintains a strong hold on American malpractice law. A recent article observes that although "some commentators ascertain an overall trend towards replacing the custom standard with that of a 'reasonable physician,' . . . this continues to remain a minority approach amongst the states."[215]

In states that still use the customary standard of care in malpractice cases, the very prevalence of off-label prescribing compels courts to assign minimal, if any, probative value to the fact that a physician has strayed from the FDA-approved label.[216] Some state courts require physicians merely to "take account" of the information in the FDA-approved physician package insert.[217] In these states, the labeling may serve as evidence of the standard of care, but

210. *See supra* Section III.B.

211. Theodore Silver, *One Hundred Years of Harmful Error: The Historical Jurisprudence of Medical Malpractice*, 1992 WIS. L. REV. 1194, 1194; Philip G. Peters, Jr., *The Quiet Demise of Deference to Custom: Malpractice Law at the Millenium*, 57 WASH. & LEE L. REV. 163, 164–70 (2000); *see also* RESTATEMENT (SECOND) OF TORTS § 299A (AM. L. INST. 1965) (physicians are required "to exercise the skill and knowledge *normally* possessed by members of [their] . . . profession . . . in good standing in similar communities" (emphasis added)). In many jurisdictions, specialists' standard of care is derived from nationwide standards rather than those of a particular community or type of community. Jay M. Zitter, Annotation, *Standard of Care Owed to Patient by Medical Specialists as Determined by Local, "Like Community," State, National, or Other Standards*, 18 A.L.R. 4th 603 §6 (2024).

212. Peters, *supra* note 211, at 165.

213. Helling v. Carey, 519 P.2d 981, 983–85 (Wash. 1974) (rejecting reliance on custom and instead embracing a reasonableness test).

214. Peters, *supra* note 211, at 204.

215. Edward K. Cheng, Elodie O. Currier & Payton B. Hampton, *Embracing Deference*, 67 VILL. L. REV. 855, 864 (2022).

216. Rosoff & Coleman, *supra* note 195, at 666 (the state judiciaries' deference to physician's off-label prescribing decisions "is not surprising, as medical malpractice law in general reflects the standard of care as set by the medical profession, not by the judiciary or juries"); James R. Bird, *Package Inserts for Prescription Drugs as Evidence in Medical Malpractice Suits*, 44 U. CHI. L. REV. 398, 399 (1976). On the limited probative force of the fact that a prescription was off-label, see, for example, Richardson v. Miller, 44 S.W.3d 1, 22 (Tenn. Ct. App. 2000) ("[T]he fact that terbutaline was put to an off-label use is simply one piece of information along with everything else for the fact-finders to sort out and consider.").

217. Rosoff & Coleman, *supra* note 195, at 670.

only if accompanied by expert testimony supporting the assertion.[218] Other states reject the use of FDA-approved labeling as evidence of the standard of care altogether.[219]

In sum, states rarely use malpractice law to rein in off-label prescribing precisely because off-label prescribing is such a common practice in the medical community. With respect to off-label prescribing, state malpractice law thus effectively defers to the expert judgment of the medical profession.[220] Yet some of the very same states whose malpractice law is most deferential to the medical community's judgment (including in the off-label context[221]) are today banning the use of puberty blockers and hormones for gender dysphoria in adolescents, thus outlawing a treatment approach widely embraced and used by the same professionals they defer to in other contexts.[222]

C. General State Affirmations of Noninterference with Off-Label Prescribing

Some state legislatures have explicitly articulated their states' policies of not interfering with off-label prescribing. An Arizona statute prohibits any organ of the state from punishing a health care provider "for offering, providing or making available lawful health care services, including the off-label use of health care services for which there is a reasonable basis that is allowed under state law."[223] Montana recently enacted a similar provision.[224]

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218. *Id.*

219. *Id.* at 670–71; *see* Bownas & Herrmann, *supra* note 193 ("[I]n medical malpractice cases involving an off-label use, the product's label should not be admitted as evidence of either the standard of care or the physician's alleged breach of that standard.").

220. Cheng et al., *supra* note 215, at 864.

221. *See, e.g.*, Arnold v. Lee, No. 05–0651, 2006 WL 1410161, at *6 (Iowa Ct. App. May 24, 2006) (upholding trial court's refusal to admit the FDA approved drug labeling into evidence because of the "risk for unfair prejudice").

222. *See, e.g.*, NEB. REV. STAT. § 44-2810 (2021) (defining the general standard of care in medical malpractice cases as "the ordinary and reasonable care, skill, and knowledge ordinarily possessed and used under like circumstances by members of his profession engaged in a similar practice in his or in similar localities"); IDAHO CODE § 6-1012 (2023) (requiring plaintiff in malpractice suit to "affirmatively prove by direct expert testimony . . . that [the] defendant . . . negligently failed to meet the applicable standard of health care practice of the community in which such care allegedly was or should have been provided, as such standard existed at the time and place of the alleged negligence of such physician"); TENN. CODE ANN. § 29-26-115(a)(1) (2012) (malpractice plaintiff has burden of proving that defendant failed to act in accordance with "[t]he recognized standard of acceptable professional practice in the profession . . . in the community in which the defendant practices or in a similar community at the time the alleged injury or wrongful action occurred").

223. ARIZ. REV. STAT. ANN. § 32-3221(A) (Supp. 2023). The statute defines "off-label use" to mean: "any use if the intent is the practice of medicine and the use is not specified in the labeling or indications for use for prescription drugs, biologics, approved medical devices and dietary supplements approved by the United States food and drug administration." *Id.*

224. Medical Practice Protection Act § 3(1)(c), 2023 Mont. Laws 533 ("A health care provider may . . . offer, provide, or make available health care services, including the off-label use of health care services as allowed under state law."). In addition, many states have laws prohibiting insurance companies from denying drug coverage based solely on the fact that the drug was prescribed for

Such policies have also been articulated by state attorneys general. For example, in 1978, the California Attorney General issued an opinion interpreting that state's Sherman Food, Drug, and Cosmetic Law not to restrict off-label prescribing. As explained by the opinion, although California "has the power to regulate, through the exercise of its police power, the practice of medicine . . . and . . . may regulate the administration of drugs," the Sherman Law nonetheless protects "the right of the practitioner to exercise his professional discretion when providing drugs in a therapeutic setting."[225]

Recent controversies regarding off-label prescribing of the antimalarial drug hydroxychloroquine and the antiparasitic drug ivermectin for treatment COVID-19 (a topic discussed in more detail below[226]) generated a spurt of similar pronouncements by the attorneys general of some of the very same states that would, shortly thereafter, ban off-label uses of puberty blockers and sex hormones. For example, the Nebraska Attorney General opined that "governing law allows physicians to use FDA-approved medicines that are unproven for a particular off-label use so long as (1) reasonable medical evidence supports that use and (2) a patient's written informed consent is obtained."[227] The Indiana Attorney General stated: "Off-label prescribing of medications is a generally accepted and widespread practice. Therefore, it is often within the standard of care absent other circumstances that would make such action medical malpractice or otherwise negligent in some way."[228]

These attorney general opinions, which authorized the use of hydroxychloroquine and ivermectin against COVID-19 under the principles they laid out, embraced an extremely capacious vision of appropriate prescribing that is markedly inconsistent with the same states' bans on pharmaceutical treatments for adolescent gender dysphoria.

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an unapproved use. These laws variously apply to specific off-label uses (such as for cancer and AIDS); off-label uses for some combination of "chronic," "serious," "disabling," and "life-threatening" illnesses; or, in numerous jurisdictions, to all off-label uses. *See* Beck, *supra* note 178, at 11–12 n.49 (collecting statutes). The jurisdictions with the most expansive coverage protections for off-label uses include Maryland, New Hampshire, North Dakota, Ohio, Oregon, Puerto Rico, Tennessee, Virginia, and Washington. *Id.* Tennessee's Code section providing the broadest type of coverage guarantee includes the following legislative finding: "Off-label use of an FDA-approved drug is legal when prescribed in a medically appropriate way and is often necessary to provide needed care." TENN. CODE ANN. § 56-7-2352(a)(6) (2016).

225. Laws Regulating Prescription and Dispensation of New Drugs, 61 Op. Cal. Att'y. Gen. 192, 194, 209 (1978).

226. *See infra* Section VI.B.

227. Prescription of Ivermectin or Hydroxychloroquine as Off-Label Medicines for the Prevention or Treatment of Covid-19, *supra* note 93, at 6.

228. Off-Label Prescription of Medications For Treatment and Prevention of COVID-19, *supra* note 92, at 9–10; *see also* COVID-19 Response and Reopening for Business Liability Act, 2022 Op. Kan. Att'y Gen. No. 4, at 2, 2022 WL 1051357 (off-label prescribing is legal under Kansas law "if the physician or other authorized prescriber under the appropriate licensing statute meets the standard of care and conduct obligations to the patient").

D. State Authorization of Off-Label Use of Puberty Blockers and Hormones for Other Conditions

Notably, the very same state laws that prohibit the use of puberty blockers and sex hormones to treat gender dysphoria in minors explicitly authorize off-label use of these drugs in minors for other conditions. For instance, the West Virginia statute (in language echoed in every other state's law) expressly exempts from the ban the provision of any service (including medication) to a minor "when a physician has . . . diagnosed a disorder of sexual development and . . . the physician has determined through genetic or biochemical testing that the individual does not have normal sex chromosome structure, sex steroid hormone production, or sex steroid hormone action."[229] As discussed above,[230] although puberty blockers and sex hormones are FDA-approved for some sexual development disorders, they are frequently prescribed off-label for others.

Consider, for example, the typical treatment of Klinefelter syndrome, a condition in which boys are born with an extra X chromosome. Klinefelter syndrome is the most common cause of congenital primary hypogonadism, affecting about one in every 600 males.[231] Doctors routinely prescribe testosterone to minors with Klinefelter syndrome on a long-term basis, starting around puberty, even though it is not approved for this use or for any other long-term use in adolescents.[232] Moreover, the only completed studies regarding the long-term use of testosterone for Klinefelter syndrome are observational, not controlled.[233] Nevertheless, all the states that have banned the use of testosterone for gender-affirming care in minors explicitly permit its use for Klinefelter syndrome.

Moreover, none of these states have ever intervened in the commonplace long-term, off-label prescription of testosterone and estrogen to adults for another type of "gender-affirming" use—the preservation of desired female and male secondary characteristics into middle age and beyond. Estrogen is approved for specific menopausal symptoms (vasomotor symptoms and vulvar and vaginal atrophy) "at the lowest effective dose and for the shortest duration consistent with treatment goals and risks for the individual women."[234] Nevertheless, despite the risks (including endometrial cancer, cardiovascular disorders, dementia, and breast cancer), untold numbers of women take hormone replacement therapy in an effort to remain—in the words of the

229. W. VA. CODE § 30-14-17(c)(2) (2023).

230. *See supra* Section I.A.

231. Chang et al., *supra* note 51, at 532.

232. *Id.* at 534; Maria Vogiatzi, James P. Tursi, Jonathan S. Jaffe, Sue Hobson & Alan D. Rogol, *Testosterone Use in Adolescent Males: Current Practice and Unmet Needs*, J. ENDOCRINE SOC. 2 (Dec. 1, 2020), https://academic.oup.com/jes/article/5/1/bvaa161/5943483 [https://perma.cc/JQ2H-6Y46].

233. Vogiatzi et al., *supra* note 232, at 7; Chang et al., *supra* note 51, at 534–35.

234. *E.g.*, PREMARIN® PRESCRIBING INFORMATION, *supra* note 39, at 3.

title of a 1960s bestseller promoting the use—"Feminine Forever."[235] And although the labeling of all testosterone products now states that their "safety and efficacy . . . in men with 'age-related hypogonadism' has not been established,"[236] American men frequently shrug at the potential heart disease risks and use these drugs as a "fountain of youth" to "recapture their vitality, decrease body fat, and enhance libido."[237] The same states that are banning PB/CSH treatment for adolescents in severe crisis have nothing to say about these risky, nonessential off-label uses of the same drugs in adults.

V. STATE AUTHORIZATION OF PHYSICIAN PRESCRIBING *OUTSIDE* THE STANDARD OF CARE

The previous Section alone does not fully capture the states' broad acceptance of off-label prescribing. Many of the same states that have enacted PB/CSH bans on the grounds that they are protecting children from "experimental" treatments have also, in other contexts, passed laws explicitly protecting doctors who prescribe unproven treatments that clearly do *not* represent the standard of care. This Section reviews these instances, which illustrate not only the depth of these states' commitment to noninterference with physicians' prescribing practices, but also their hypocrisy in banning well-established gender-affirming care—an arbitrariness that, as explained later, causes the bans to fail strict scrutiny (and perhaps even rational basis scrutiny).

A. CHELATION THERAPY FOR CARDIOVASCULAR DISEASE

The drug Calcium EDTA, also known as disodium edetate and calcium disodium versenate, is FDA-approved for treatment of lead poisoning.[238] The use of this and other drugs that bind to metals in the blood is called "chelation therapy." FDA approved Calcium EDTA in 1953 as an injection for treatment of lead poisoning.[239] Although FDA deemed the drug to be safe at the relevant dose, subsequent studies showed that high doses of the drug could lead to kidney disorders.[240] In 1970 (eight years after Congress required FDA to assess drugs' effectiveness as well as safety), the agency found injectable Calcium EDTA to be effective for lead poisoning and lead encephalopathy.[241]

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235. *See generally* ROBERT A. WILSON, FEMININE FOREVER (1966) (coining the phrase). On historical usage patterns, see Kohn et al., *supra* note 35, at 5–7.

236. *See, e.g.*, FDA, *supra* note 47; *FDA Drug Safety Communication*, *supra* note 49.

237. *Hormone Therapy No Cure-All for "Low T" in Aging Men*, HEART.ORG (June 17, 2020), https://www.heart.org/en/news/2020/06/17/hormone-therapy-no-cure-all-for-low-t-in-aging-men [https://perma.cc/S84D-T6TB].

238. FDA, CALCIUM DISODIUM VERSENATE PRESCRIBING INFORMATION (2023), https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/008922s022lbl.pdf [https://perma.cc/9GPY-QHHU].

239. PM Wax, *The Use and Hazards of EDTA as an Alternative Medicine*, 45 CLINICAL TOXICOLOGY 354, 354 (2007).

240. Matteo Paolieri, *Ferdinand Münz: EDTA and 40 Years of Inventions*, 42 BULL. FOR HIST. CHEMISTRY 133, 138 (2017).

241. Calcium Disodium Edetate and Disodium Edetate, 35 Fed. Reg. 437 (Jan. 13, 1970). The agency also found calcium disodium edetate injection "probably effective in the treatment

Since the 1950s, Calcium EDTA has also acquired an alternative, unproven use for treatment of cardiovascular disease ("CVD").[242] Early on, some conventional practitioners embraced this use based on published observational studies.[243] During the 1960s, however, as further research yielded uneven results, conventional practitioners largely stopped prescribing Calcium EDTA for treatment of CVD.[244] In the early 1970s, the use of EDTA injections as a treatment for heart disease reemerged among a small group of "integrative" physicians (some with sketchy professional backgrounds[245]) who combined orthodox and alternative therapies in their practices.[246] The rise of chelation therapy as an alternative treatment was part of a broader surge of interest in "holistic" medicine in the 1970s.[247] Chelation therapy differed in an important way from most other alternative medicine modalities, however: It was the off-label use of a drug approved by FDA for another indication.

What chelation therapy for heart disease shared with most other alternative treatments was a lack of scientifically rigorous evidence of effectiveness—namely, successful well-controlled randomized clinical trials. Although some case reports published in alternative medicine journals in the 1980s and 1990s declared spectacular results, the few, small controlled clinical trials performed during this period failed to show Calcium EDTA to be an effective treatment for CVD.[248] In the mid-1980s, the AMA, the American College of Cardiology,

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of other heavy metal poisoning and in the removal of radioactive and nuclear fission products, such as plutonium and yttrium." *Id.* However, they reclassified it as lacking substantial effectiveness for these other purposes in 1976, after nobody submitted data in support of them. Drugs for Human Use; Drug Efficacy Study Implementation; Followup Notice and Opportunity for Hearing, 41 Fed. Reg. 40206 (Sept. 17, 1976).

242. Robin Rowbury, *Miracle Molecules of Our Age: Ethylenediaminetetraacetic Acid*, 94 SCI. PROGRESS 232, 237 (2011); Heidi Braun Grebe & Philip J. Gregory, *Inhibition of Warfarin Anticoagulation Associated with Chelation Therapy*, 22 PHARMACOTHERAPY 1067, 1067 (2002); Jeanne A. Drisko, *Chelation Therapy*, *in* INTEGRATIVE MEDICINE 1004, 1004 (David Rakel ed., 4th ed. 2018).

243. *See generally* Filippo Ravalli et al., *Chelation Therapy in Patients with Cardiovascular Disease: A Systematic Review*, J. AM. HEART ASS'N (Mar. 1, 2022), https://www.ahajournals.org/doi/full/10.1161/JAHA.121.024648 [https://perma.cc/S3BA-EVLN]; Gervasio A. Lamas, Ana Navas-Acien, Daniel B. Mark & Kerry L. Lee, *Heavy Metals, Cardiovascular Disease, and the Unexpected Benefits of Chelation Therapy*, 67 J. AM. COLL. CARDIOLOGY 2411, 2412 (2016).

244. Drisko, *supra* note 242, at 1005; *Home*, INTRAVENOUS DISODIUM EDETATE ("CHELATION"), https://chelation.me [https://perma.cc/UL4C-NTKJ]; Lamas et al., *supra* note 243, at 2412.

245. Allan Parachini, *Chelation Advocates Face Legal and Image Problems*, L.A. TIMES (Apr. 14, 1985), https://www.latimes.com/archives/la-xpm-1985-04-14-vw-8384-story.html (on file with the *Iowa Law Review*).

246. A search of the phrase "chelation therapy" in the Newspapers.com database shows mentions starting to appear in about 1974, climbing throughout the remainder of the decade, peaking in about 1983, settling into a pre-peak level of usage for about ten years, and then surging again starting in about 1994.

247. Jeanne Drisko, *The Role of Chelation Therapy in Cardiovascular Disease, Diabetes Mellitus, and Heavy Metal Detoxification: The TACT Trials*, THORACIC KEY (Feb. 27, 2020), https://thoracickey.com/the-role-of-chelation-therapy-in-cardiovascular-disease-diabetes-mellitus-and-heavy-metal-detoxification-the-tact-trials [https://perma.cc/X9TH-UP82]; GROSSMAN, *supra* note 28, at 143–44.

248. Maria Vanessa Villarruz-Sulit, Rachel Forster, Antonio L. Dans, Flordeliza N. Tan & Dennis V. Sulit, *Chelation Therapy for Atherosclerotic Cardiovascular Disease (Review)*, COCHRANE

and the American Heart Association all issued statements advising against chelation therapy for CVD.[249] In 1994, the AMA issued another position statement on chelation therapy, asserting that "chelation therapy for atherosclerosis is an experimental process without proven efficacy."[250] In 1998, a chelationist organization called the American College for the Advancement in Medicine was forced to acknowledge—in a settlement with the Federal Trade Commission—that science did not support its claims that EDTA chelation therapy was effective in treating atherosclerosis.[251] Today, chelation therapy's effectiveness for treatment of CVD has still not been established.[252]

Earlier, this Article discussed how FDA's efforts to shut down Dr. Evers' Alabama chelation clinic in the early 1970s culminated in a court decision that restricts the agency's authority to regulate off-label prescribing in general.[253] Around that time, some state medical boards also took steps to prevent doctors from using chelation therapy for CVD. In 1977, the Florida Board of Medical Examiners disciplined chelationist Dr. Robert Rogers,[254] but in a remarkable 1980 opinion, the Supreme Court of Florida quashed this order, holding that "the Board's action unreasonably interferes with Dr.

DATABASE SYS. REV. 15 (May 5, 2020), https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002785.pub2/full [https://perma.cc/M5TN-8HDK; Lamas et al., *supra* note 243, at 2412.

249. Matthew R. Lewin, *Chelation Therapy for Cardiovascular Disease: Review and Commentary*, 24 TEX. HEART INST. J. 81, 81 n.* (1997).

250. AMA, *Health Fraud: Chelation Therapy H–175.997*, *in* AMA POLICY COMPENDIUM (1994).

251. Press Release, Fed. Trade Comm'n, Medical Association Settles False Advertising Charges Over Promotion of "Chelation Therapy" (Dec. 8, 1998), https://www.ftc.gov/news-events/news/press-releases/1998/12/medical-association-settles-false-advertising-charges-over-promotion-chelation-therapy [https://perma.cc/BPV9-TAV9].

252. In 2012, the results of an NIH-sponsored placebo-controlled trial left open the possibility that chelation might be effective for CVD, but the authors emphasized that the results were not, by themselves, "sufficient to support the routine use of chelation therapy for treatment of post-MI patients." Gervasio A. Lamas et al., *Effect of Disodium EDTA Chelation Regimen on Cardiovascular Events in Patients with Previous Myocardial Infarction: The TACT Randomized Trial*, 309 JAMA 1241, 1249 (2013). Following the completion of TACT, a task force of the American Heart Association and American College of Cardiology acknowledged the trial's modestly positive findings but remained convinced that "the usefulness of chelation therapy in cardiac disease is highly questionable." Stephan D. Fihn et al., *2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients with Stable Ischemic Heart Disease*, 64 J. AM. COLL. CARDIOLOGY 1749, 1757 (2014). Recent meta-analyses of all evidence to date found insufficient evidence to conclude that chelation therapy is effective for treatment of CVD. Villarruz-Sulit et al., *supra* note 248, at 15; Ravalli et al., *supra* note 243, at 1, 20.

253. *See generally* United States v. Evers, 453 F. Supp. 1141 (M.D. Ala. 1978); *supra* note 171 and accompanying text.

254. Howard Wolinsky, *Therapy Decision Delayed*, FLA. TODAY, Mar. 5, 1977, at 2B (on file with the *Iowa Law Review*); Rogers v. State Bd. of Med. Exam'rs of Fla., 371 So.2d 1037, 1038 (Fla. Dist. Ct. App. 1979).

Rogers' right to practice medicine by curtailing the exercise of his professional judgment to administer chelation therapy."[255]

Perhaps inspired by this decision, in 1983, the Oklahoma Legislature protected chelationists with what seems to have been the very first state law authorizing physicians to prescribe a drug for a specific off-label use. The governor vetoed a provision that would have required insurance companies to cover chelation therapy, but he allowed the following language to become law: "Nothing in the [act defining the standard of care for the healing arts] shall be construed to prohibit the use of chelation therapy . . . ."[256] This provision shielding doctors from discipline for prescribing an unproven remedy often dismissed as "quackery"[257] remains in effect today.

Two other states subsequently also passed chelation shield laws. In 1993, after the South Dakota medical board ordered a physician to stop providing chelation therapy to treat blocked arteries, the legislature enacted an amendment to the medical licensing law stating that "the board may not base a finding of unprofessional or dishonorable conduct solely on the basis that a licensee . . . practices chelation therapy."[258] A supporter of the bill in the state legislature explained, "I believe the people . . . should have the freedom of choice on this issue."[259] Louisiana followed suit in 1999, passing a law providing that "it shall be lawful . . . for a licensed physician to prescribe, dispense, [or] administer . . . to any person, any chelating agent or chelation therapy for the treatment or prevention of any medical condition when the physician, in his professional judgment, deems it in the best interest of a patient."[260] Soon afterward, the Tennessee and Missouri medical boards decided to not interfere with chelation therapy in their states.[261]

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255. State Bd. of Med. Exam'rs of Fla. v. Rogers, 387 So.2d 937, 939 (Fla. 1980). The court did not question the Board's conclusion that "chelation therapy can best be classified as investigational." *Id.* But after emphasizing the absence of allegations that Dr. Rogers had either harmed his patients or defrauded them, the court opined: "Although the state has the power to regulate the practice of medicine . . . [t]he regulations imposed must be reasonably related to the public health and welfare and must not amount to an arbitrary or unreasonable interference with the right to practice one's profession . . . ." *Id.* (citing Doe v. Bolton, 410 U.S. 179, 199–200 (1973)).

256. OKLA. STAT. tit. 76, § 20.2 (2011).

257. For example, the Oklahoma State Medical Association condemned the bill mandating health insurance coverage of chelation therapy as "pure and simple quackery." Editorial, *Prime Target for Nigh*, OKLAHOMAN, May 19, 1983, at 1 (on file with the *Iowa Law Review*).

258. 1993 S.D. Sess. Laws ch. 272, 422 (codified at S.D. CODIFIED LAWS § 36-4-29); *see House Approves Legislation Allowing Chelation Therapy*, ARGUS LEADER, Feb. 27, 1993, at 3A (on file with the *Iowa Law Review*) (describing medical board action).

259. *Chelation Treatment Bill Passes Senate Hurdle 6-1*, ARGUS LEADER, Feb. 11, 1983, at 3A (on file with the *Iowa Law Review*) (statement of Rep. Ed Olson, R-Mitchell).

260. 1999 La. Acts 2711–12. By its terms, this statute sunsetted on February 1, 2001. *Id.*

261. In 2000, the Tennessee medical board—in response to a public outcry—unanimously rejected proposed regulations that would have restricted chelation therapy for conditions other than heavy metal poisoning to clinical trials in academic institutions. Bill Snyder, *Outcry Stops Vote to Restrict Chelation*, TENNESSEAN, Nov. 16, 2000, at 1B (on file with the *Iowa Law Review*). The following year, the Missouri Board of Registration for the Healing Arts adopted a rule that

Every one of these states that protects doctors who prescribe Calcium EDTA for CVD, a truly experimental off-label use, are now outlawing scientifically supported, standard-of-care off-label use of puberty blockers and hormones.

B. HYDROXYCHLOROQUINE AND IVERMECTIN FOR COVID-19

The chelation statutes discussed above, though now decades old, cannot be dismissed as an artifact of the past. During the past few years, some states have taken similar actions to authorize the off-label, unproven use of drugs to treat COVID-19.

As discussed above,[262] during the pandemic, some state attorneys general authorized the off-label prescription of hydroxychloroquine and ivermectin for COVID-19, even though these were entirely unproven remedies for the virus. The Indiana Attorney General concluded his opinion: "Experts disagree and studies conflict on prevention and treatment methods for COVID-19, so it is not unreasonable for [health care providers] to prescribe medications off-label and it be considered within the standard of care."[263] Only an extremely expansive vision of "standard of care" would include this use of either hydroxychloroquine or ivermectin.[264] By authorizing the use of these drugs for COVID-19, these states were protecting off-label treatments that were far more "experimental" than the use of puberty blockers and sex hormones for treatment of adolescent gender dysphoria.

Some state legislatures explicitly protected the off-label use of ivermectin by *statute*. In 2021, North Dakota enacted a law declaring: "The [medical] board may not take disciplinary action against a licensee based solely on the

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declared EDTA chelation therapy "of no medical or osteopathic value except for those uses approved by the [FDA]" but nonetheless also provided that "[t]he board shall not seek disciplinary action against a licensee based solely upon a non-approved use of EDTA chelation if the licensee has the patient sign the Informed Consent for EDTA Chelation Therapy form, included herein." MO. CODE REGS. ANN. tit. 20, § 2150-2.165 (2001). In multiple other states, including North Carolina, physicians practicing chelation therapy claimed protection under more general Medical Freedom Acts enacted during the 1990s, which will be described below, *infra* Section V.C. *See Cardiovascular Disease: Is the Government Doing More Harm than Good? EDTA Chelation Therapy: Hearing Before the H. Comm. on Gov't Reform*, 106th Cong. 42 (1999) (Chelationist Ted Rozema testifying in Congress that his home state of North Carolina was "one of eight States that have legislation protecting the physician doing alternative medicine, including chelation therapy.").

262. *See supra* Section IV.C.

263. Off-Label Prescription of Medications For Treatment and Prevention of COVID-19, *supra* note 92, at 10.

264. As one author observed in April 2020, early in the pandemic, there was "no evidence-based literature supporting a standard-of-care for coronavirus infections." Joseph M. Geskey, *Off-Label Prescribing in the Era of COVID-19*, MED. ECON. (Apr. 14, 2020), https://www.medicaleconomics.com/view/label-prescribing-era-covid-19 [https://perma.cc/7LQX-S6TU]. As time went on, neither remedy developed significant scientific support. *See, e.g.*, Demarco v. Christiana Care Health Servs., Inc., 263 A.3d 423, 425 (Del. Ch. 2021) (noting ivermectin "is not part of the standard of care for the COVID-19 virus"); Ilan S. Schwartz, David R. Boulware & Todd C. Lee, Comment, *Hydroxychloroquine for COVID19: The Curtains Close on a Comedy of Errors*, LANCET REG'L HEALTH – AMS. 1–2 (Mar. 31, 2022), https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(22)00085-0/fulltext [https://perma.cc/2MWD-4RLK].

licensee prescribing or dispensing ivermectin for the off-label treatment or prevention of [COVID-19]."[265] Missouri and Tennessee passed similar measures.[266] All three of these states shortly afterward outlawed the prescription of puberty blockers and sex hormones to transgender teens on the grounds of protecting them from "experimental" treatments.

C. STATE PROTECTIONS OF DOCTORS PRESCRIBING DRUGS NOT APPROVED FOR ANY USE

Numerous states—including many with PB/CSH bans—have enacted two types of statutes that protect doctors' use of entirely unapproved treatments that they deem appropriate for their patients: "right to try" laws designed to give terminally ill patients access to early-stage investigational drugs and "medical freedom" acts that authorize physicians to prescribe alternative and complementary therapies. These laws further demonstrate the states' widespread commitment to not interfering with the practice of medicine and to ensuring that patients can exercise freedom of therapeutic choice in consultation with their physicians.[267]

Since 2014, forty-one states (including all but one of the states that has enacted a PB/CSH ban) have passed "right-to-try" laws based on a model bill disseminated by the libertarian Goldwater Institute.[268] These statutes allow patients with terminal diseases to access investigational medical products that have "successfully completed Phase One clinical trials"—a phase comprising small, uncontrolled safety studies not designed to assess efficacy.[269] The model statute and the state laws based on it apply to minor patients as well as adults.[270]

These statutes all explicitly protect physicians from legal consequences for prescribing unapproved drugs pursuant to the "right to try" schemes. The model statute states: "No medical licensing board shall revoke a license, fail

265. N.D. CENT. CODE § 43-17-31.2 (Supp. 2023).

266. MO. REV. STAT. § 334.100(8) (Supp. 2023); TENN. CODE ANN. § 63-10-224(e) (2023).

267. GROSSMAN, *supra* note 28, at 197–98, 213–14.

268. *Id.* at 197. Goldwater's Model Right to Try Act is available at CHRISTINA CORIERI, EVERYONE DESERVES THE RIGHT TO TRY: EMPOWERING THE TERMINALLY ILL TO TAKE CONTROL OF THEIR TREATMENT, GOLDWATER INST. 2–3 (2014), https://www.goldwaterinstitute.org/wp-content/uploads/cms_page_media/2015/1/28/Right%20To%20Try.pdf [https://perma.cc/XP8Z-2D6B]. Kansas is the only state with a ban against pharmaceutical treatment of adolescent gender dysphoria that has not also enacted a right to try statute. *See Right to Try in Your State*, RIGHT TO TRY, https://righttotry.org/in-your-state [https://perma.cc/U6RU-3LKR].

269. CORIERI, *supra* note 268, at 2. This aspect of the laws is "mostly symbolic, for [the right to access provisions] are almost certainly preempted by [the federal Food, Drug, and Cosmetic Act]." GROSSMAN, *supra* note 28, at 198. In any event, the FDCA itself was amended in 2018 to include a new section that basically provides the same path to access at a federal level. *See generally* Right to Try Act of 2017, Pub. L. No. 115-176, 132 Stat. 1372 (2018) (codified in part at 21 U.S.C. § 360bbb-0a).

270. *See, e.g.*, CORIERI, *supra* note 268, at 3 ("In the case that the patient is a minor or lacks the mental capacity to provide informed consent, a parent or legal guardian may provide informed consent on the patient's behalf."); N.C. GEN. STAT. § 90-325.1(d) (2023) (defining an eligible patient, in part, as an individual who "[h]as given informed consent in writing," or "if the individual is a minor or is otherwise incapable of providing informed consent, the parent or legal guardian has given informed consent in writing").

to renew a license, or take any other action against a license solely based on a medical professional's recommendation, prescription, or treatment with an investigational drug, biological product, or device."[271] Some of the parallel state law provisions are relatively modest; they protect physicians only if the prescription is consistent with the standard of care.[272] Others, however, are astonishingly broad. Consider, for example, this provision from the Utah right to try law:

> *Standard of care–Medical practitioners not liable–No private right of action*
>
> (1) It is not a breach of the applicable standard of care for a physician, other licensed health care provider, or hospital to treat an eligible patient with an investigational drug or investigational device under this chapter.
>
> (2) A physician, other licensed health care provider, or hospital that treats an eligible patient with an investigational drug or investigational device under this chapter may not, for any harm done to the eligible patient by the investigational drug or device, be subject to:
>
> (a) civil liability;
>
> (b) criminal liability; or
>
> (c) licensure sanctions . . . .[273]

It is important to emphasize that these "right to try" laws protect doctors who prescribe not only approved drugs for unapproved uses but also *entirely unapproved* drugs.[274]

The second common type of state statute protecting doctors who prescribe unapproved drugs are "medical freedom acts." These laws shield physicians from disciplinary action for practicing complementary and alternative medicine ("CAM").[275] Alaska passed the first such law in 1990, amending its medical practice act to declare that "the board may not base a finding of professional incompetence solely on the basis that a licensee's practice is unconventional or experimental in the absence of demonstrable physical

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271. CORIERI, *supra* note 268, at 3.

272. *See, e.g.*, W. VA. CODE ANN. § 16-51-5 (LexisNexis 2021) ("Notwithstanding any other law, a licensing board may not revoke, fail to renew, suspend or take any action against a health care provider's license . . . based solely on the health care provider's recommendations to an eligible patient regarding access to or treatment with an investigational drug, biological product or device *as long as the recommendations are consistent with medical standards of care*." (emphasis added)).

273. UTAH CODE ANN. § 58-85-104 (LexisNexis 2020 & Supp. 2024); *cf.* GA. CODE. ANN. § 31-52-10 (2019) (immunizing health care providers using investigational products pursuant to the right to try act from civil liability so long as they obtain written informed consent). Some other states immunize health care providers without any requirement they follow the standard of care or exercise reasonable care, but only with respect to licensing board sanctions. *See, e.g.*, N.C. GEN. STAT. § 90-325.4 (2023).

274. Peter Loftus & Dan Frosch, *States Open to Drug Options*, WALL ST. J. (May 18, 2014, 10:22 PM), https://www.wsj.com/articles/states-open-to-drug-options-1400466099 (on file with the *Iowa Law Review*).

275. GROSSMAN, *supra* note 28, 213–14.

harm to the patient."[276] Since then, about sixteen additional states have enacted such measures, including seven of the states that have recently passed bans on pharmaceutical treatment of adolescent gender dysphoria.[277]

Although the medical freedom acts vary in the degree of protection they provide to physicians, they are all motivated by the goal of ensuring (in the words of the Florida law's "legislative intent" statement) "that citizens be able to choose from all health care options, including the prevailing or conventional treatment methods as well as other treatments designed to complement or substitute for the prevailing or conventional treatment methods."[278]

Extremely few CAM treatments have been demonstrated to be safe and effective in scientific studies.[279] With these medical freedom acts, states are thus encouraging physicians to administer drugs that have much less scientific support or professional acceptance than pharmaceutical treatments for adolescent gender dysphoria.

VI. PREVIOUS STATE BANS ON SPECIFIC OFF-LABEL PRESCRIBING

Before now, have states ever *banned* particular off-label uses of drugs? On rare occasions, state legislatures have enacted statutes prohibiting specific off-label uses, and state medical boards have issued policies declaring an off-label use to violate state practice standards. This Section contains the first-ever systematic examination of the entire body of state restrictions on off-label prescribing.[280] Most of these restrictions concern one of four off-label uses: chelation therapy for cardiovascular disease, anabolic steroids for enhancing athletic performance, abortion medication for terminating pregnancy beyond a certain gestation period, and hydroxychloroquine for treatment of COVID-19. As will be made clear below, all these restrictions vary in significant ways from the current state criminal bans on the off-label use of puberty blockers and sex hormones for treatment of adolescent gender dysphoria.

A. CHELATION THERAPY FOR CARDIOVASCULAR DISEASE

Over the years, as some states have enacted laws permitting physicians to prescribe chelation therapy for treatment of cardiovascular disease,[281] the

276. *Id.* at 213; ALASKA STAT. § 08.64.326(a)(8)(A) (2023). Eleven states have enacted a different type of statute known as "safe harbor legislation." These laws exempt CAM providers from the states' medical licensing requirements. GROSSMAN, *supra* note 28, at 213–16.

277. For lists of the states, see Michael Ruggio & Lauren DeSantis-Then, *Complementary and Alternative Medicine: Longstanding Legal Obstacles to Cutting Edge Treatment*, 2 J. HEALTH LIFE SCI. L. 137, 159 nn.119–30 (2009); John Lunstroth, *Voluntary Self-Regulation of Complementary and Alternative Medicine Practitioners*, 70 ALB. L. REV. 209, 222 n.86 (2006). The seven states that have enacted both medical freedom acts and bans on pharmaceutical treatment of adolescent gender dysphoria are Oklahoma, Florida, Georgia, Texas, Indiana, Louisiana, and South Dakota. *Compare* Lunstroth, *supra*, at 222 n.86, *with* statutes cited *supra* note 8.

278. FLA. STAT. ANN. § 456.41(1) (2023).

279. GROSSMAN, *supra* note 28, at 204.

280. Others have provided examples of such prohibitory measures. *See, e.g.*, Beck, *supra* note 178, at 10–11 nn.47–48 (collecting case citations for such bans on off-label drug uses).

281. *See supra* notes 254–61 and accompanying text.

medical boards in a number of other states have declared this practice to be misconduct subject to discipline. For example, in 2001, the Iowa Medical Examiners Board adopted a rule prohibiting physicians from prescribing Calcium EDTA for indications other than heavy metal poisoning except in "carefully controlled clinical investigation[s] of its effectiveness."[282] The next year, Mississippi's board issued a rule allowing off-label use of EDTA only in approved research protocols or if the use is supported by "substantial, high-quality research" and the physician obtains informed consent.[283]

Though these regulations severely limited an off-label use of an FDA-approved drug, they differed dramatically from the current PB/CSH bans, both because they were directed at an unproven use roundly rejected by the medical establishment and because they continued to allow the use under restricted circumstances.

B. HYDROXYCHLOROQUINE FOR COVID-19

In March and April 2020, as the COVID-19 pandemic ravaged the nation, the internet was replete with assertions that various medicines approved for other uses might be effective against the new virus. The first drug to capture the web by storm was hydroxychloroquine, an off-patent product approved for uncomplicated malaria and for the autoimmune disorders lupus and rheumatoid arthritis.[284] Even though the evidence in support of using hydroxychloroquine as a COVID-19 treatment was anecdotal, President Donald Trump began touting hydroxychloroquine in late March, and Fox News started featuring it regularly.[285] By mid-April 2020, forty-six percent of voters supported using hydroxychloroquine for COVID-19 before the completion of full testing.[286] Runs on pharmacies and widespread hoarding led to shortages of the medicine, risking the health of lupus and arthritis patients.[287]

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282. 23 Iowa Admin. Bull. 1409 (Mar. 7, 2001) (codified at IOWA ADMIN. CODE r. 653-13.5 (2024)).

283. 30-4 MISS. CODE R. § 30-2635-4.1 (LexisNexis 2002) (supportive research must be "peer-reviewed and published in recognized journals such as those cited in PubMed or in the National Library of Medicine").

284. Press Release, FDA, Coronavirus (COVID-19) Update: FDA Reiterates Importance of Close Patient Supervision for 'Off-Label' Use of Antimalarial Drugs to Mitigate Known Risks, Including Heart Rhythm Problems (Apr. 24, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-reiterates-importance-close-patient-supervision-label-use [https://perma.cc/X86X-WSYT]; Philip Bump, *The Rise and Fall of Trump's Obsession with Hydroxychloroquine: Forty Days of Promotion, Hype—and Eventual Retreat*, WASH. POST (Apr. 24, 2020, 2:17 PM), https://www.washingtonpost.com/politics/2020/04/24/rise-fall-trumps-obsession-with-hydroxychloroquine (on file with the *Iowa Law Review*) (reviewing the emergence of the idea of treating COVID-19 with the drug in mid-March).

285. Bump, *supra* note 284.

286. MORNING CONSULT & POLITICO, NATIONAL TRACKING POLL #200436, at 253 tbl.POL10 (2020), https://www.politico.com/f/?id=00000171-7b49-d92d-a5ff-fb6b10400000 [https://perma.cc/5MYX-39TD].

287. Denise Grady, *Malaria Drug Helps Virus Patients Improve, in Small Study*, N.Y. TIMES (June 30, 2021), https://www.nytimes.com/2020/04/01/health/hydroxychloroquine-coronavirus-malaria.html (on file with the *Iowa Law Review*).

During the hydroxychloroquine craze (which started to die down in late April 2020 because of emerging information about its risks and ineffectiveness against COVID-19[288]), a few states took steps to limit off-label prescribing of the drug to preserve its availability to patients with lupus and arthritis.[289] These restrictions took the form of either executive orders by governors or administrative rules by health agencies. For example, New York Governor Andrew Cuomo ordered: "No pharmacist shall dispense hydroxychloroquine or chloroquine except when written as prescribed for an FDA-approved indication; or as part of a state approved clinical trial related to COVID-19 . . . . No other experimental or prophylactic use shall be permitted."[290] The Georgia Board of Pharmacy issued an emergency rule restricting the dispensing of hydroxychloroquine unless the prescription included a "diagnosis . . . consistent with the evidence for its use."[291]

These state actions bore no resemblance to the state PB/CSH bans. Firstly, the off-label use of hydroxychloroquine they were designed to suppress—the prevention or treatment of COVID-19—lacked any significant evidence of effectiveness or safety. In addition, these were time-limited measures designed for the specific purpose of ensuring, during a public health emergency, that the drug would remain available to patients using it for its FDA-approved uses.

C. ANABOLIC STEROIDS FOR ATHLETIC PERFORMANCE

At the 1988 Seoul Olympics, Canadian sprinter Ben Johnson was stripped of his gold medal for illegal doping.[292] This event occurred during a period in which Americans were becoming aware of an anabolic steroid and human growth hormone "abuse explosion" among not only high-level athletes, but also high school students and younger children trying to boost their strength and performance.[293] American lawmakers, concerned about the integrity of

288. Denise Grady, *New U.S. Treatment Guidelines for Covid-19 Don't See Much Progress*, N.Y. TIMES (Apr. 21, 2020), https://www.nytimes.com/2020/04/21/health/nih-covid-19-treatment.html (on file with the *Iowa Law Review*); Christopher Rowland, *Anti-Malarial Drug Trump Touted Is Linked to Higher Rates of Death in VA Coronavirus Patients, Study Says*, WASH. POST (Apr. 21, 2020, 4:14 PM), https://www.washingtonpost.com/business/2020/04/21/anti-malarial-drug-trump-touted-is-linked-higher-rates-death-va-coronavirus-patients-study-says (on file with the *Iowa Law Review*); *FDA Cautions Against Use of Hydroxychloroquine or Chloroquine for COVID-19 Outside of the Hospital Setting or a Clinical Trial Due to Risk of Heart Rhythm Problems*, FDA: FDA DRUG SAFETY PODCASTS (Apr. 24, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-reiterates-importance-close-patient-supervision-label-use [https://perma.cc/S3SV-KRH5].

289. *State Action on Hydroxychloroquine and Chloroquine Access*, LUPUS FOUND. AM. (July 30, 2020), https://www.lupus.org/advocate/state-action-on-hydroxychloroquine-and-chloroquine-access [https://perma.cc/N64Z-ZS3H].

290. N.Y. COMP. CODES R. & REGS. tit. 9, § 8.202.10 (2021).

291. GA. COMP. R. & REGS. 480-10-0.38-.22 (2020).

292. Michael Janofsky, *The Seoul Olympics: Johnson Loses Gold to Lewis After Drug Test*, N.Y. TIMES (Sept. 27, 1988), https://www.nytimes.com/1988/09/27/sports/the-seoul-olympics-johnson-loses-gold-to-lewis-after-drug-test.html (on file with the *Iowa Law Review*).

293. JON R. MAY, FDA, STATE LAWS/REGULATIONS PERTAINING TO THE CONTROL OF ANABOLIC STEROIDS 2 (1991); Charles E. Yesalis, *Views of Sport; Steroid Use Is Not Just an Adult Problem*, N.Y. TIMES (Dec. 4, 1988), https://www.nytimes.com/1988/12/04/sports/views-of-sport-steroid-use-is-not-just-an-adult-problem.html (on file with the *Iowa Law Review*).

sport and the health of youth, turned their attention to the problem of performance-enhancing drugs.[294]

Anabolic steroids "are synthetic substances similar to the male sex hormone testosterone" that "promote the growth of skeletal muscle (anabolic effects) and the development of male sexual characteristics (androgenic effects)."[295] As discussed earlier, FDA has approved these synthetic testosterone products for a variety of medical uses, and doctors prescribe them off-label for others—including gender-affirming care.[296] Human growth hormone ("HGH"), a different type of synthetic hormone, is FDA-approved for various medical conditions in children and adults.[297]

Between 1988 and 1990, Congress held three hearings on the abuse of anabolic steroids and HGH by athletes.[298] It enacted a law making it a felony to "distribute any anabolic steroid for any use in humans other than the treatment of disease pursuant to the order of a physician."[299] It added anabolic steroids to the list of Schedule III controlled substances under the Controlled Substances Act ("CSA"), thus effectively barring doctors from prescribing them for nonmedical purposes.[300] Congress also added a provision to the FDCA prohibiting the distribution of HGH "for any use in humans other than the treatment of disease or other recognized medical condition, where such use has been [approved by FDA] and pursuant to the order of a physician."[301] This provision remains the FDCA's only explicit restriction of an off-label drug use.

During this period, most state legislatures also took steps to suppress nonmedical uses of anabolic steroids and, in some states, nonmedical uses of HGH.[302] In many states, these steps included making it unprofessional conduct for a physician to prescribe these drugs for body building or enhancement of athletic performance. Colorado law, for example, makes it unprofessional

294. Yesalis, *supra* note 293.

295. *Anabolic Steroids and Other Appearance and Performance Enhancing Drugs (APEDs)*, NIH: NAT'L INST. ON DRUG ABUSE (May 2023), https://nida.nih.gov/research-topics/anabolic-steroids [https://perma.cc/JLD3-3UPL] (under the "What are anabolic steroids and other appearance and performance enhancing drugs (APEDs)?" section).

296. *See supra* notes 40–54 and accompanying text.

297. *See, e.g.*, FDA. HUMATROPE® PRESCRIBING INFORMATION (2023), https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/019640s108lbl.pdf [https://perma.cc/3U74-7CJ9].

298. Maxwell J. Mehlman, Elizabeth Banger & Matthew M. Wright, *Doping in Sports and the Use of State Power*, 50 ST. LOUIS U. L.J. 15, 15 (2005); Ryan J. McGrew, *Raising the Bar: Why the Anabolic Steroid Control Acts Should Be Repealed and Replaced*, 15 HOUS. J. HEALTH L. & POL'Y 233, 236–37 (2015).

299. Anti-Drug Abuse Act of 1988, Pub. L. No. 100-690 § 2403, 102 Stat. 4181, 4230–31 (1988).

300. Anabolic Steroids Control Act of 1990, Pub. L. No. 101-647 § 1902, 104 Stat. 4789, 4851-52 (codified at 21 U.S.C. §§ 802(41)(A), 812 Sch. III(e)). A Drug Enforcement Administration ("DEA") regulation criminalizes prescribing any controlled substance unless the prescription is "issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice." 21 C.F.R. § 1306.04(a) (2024).

301. § 1904, 104 Stat. at 4853 (codified at 21 U.S.C. § 333(e)).

302. MAY, *supra* note 293, at app. I; Jeffrey A. Black, Comment, *The Anabolic Steroids Control Act of 1990: A Need for Change*, 97 DICK. L. REV. 131, 136 (1992).

conduct to prescribe an anabolic steroid "for the purpose of the [sic] hormonal manipulation that is intended to increase muscle mass, strength, or weight without a medical necessity to do so or for the intended purpose of improving performance in any form of exercise, sport, or game."[303] Delaware's legislature went further; in that state, it is a *felony* to "prescribe . . . any anabolic steroid . . . for the purposes of increasing human muscle weight or improving human performance in any form of exercise, sport, or game."[304]

Such laws represent another rare example of state prohibitions on off-label prescribing. Nonetheless, they differ in a critical way from the PB/CSH bans currently being litigated. They prohibit the *nonmedical* use of controlled substances.[305] They have no effect on legitimate medical practice.

D. CONTROLLED SUBSTANCES FOR OBESITY

For many decades, before the recent emergence of Ozempic® and Wegovy®, amphetamines were popular treatments for obesity.[306] But these stimulants are addictive, commonly abused, produce psychosis and violent and erratic behavior in chronic users, and contribute to social ills like crime and unemployment.[307] They are thus "scheduled" substances under the federal CSA. Amphetamines with no currently accepted medical use are in Schedule I. Those with an FDA-approved indication but a high potential for abuse and a high risk of dependence (such as Aderall® for attention-deficit/hyperactivity disorder[308]) are in Schedule II. Others are in Schedule III or Schedule IV, depending on their potential for abuse and risk of dependence.[309] Two Schedule III amphetamines and two Schedule IV amphetamines are currently approved as short-term treatments for obesity; no Schedule II amphetamine is approved for this purpose.[310]

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303. S.B. 81, 1987 Reg. Sess. (Colo. 1987) (codified at COLO. REV. STAT. § 12-240-121(1)(o) (1987)).

304. H.B. 311, 135th Gen. Assemb. (Del. 1990) (codified at DEL. CODE ANN. tit. 16, § 4757(a)(7) (1990)).

305. *Id.*

306. Ann A. Coulter, Candida J. Rebello & Frank L. Greenway, *Centrally Acting Agents for Obesity: Past, Present, and Future*, 78 DRUGS 1113, 1115 (2018).

307. *Methamphetamine Research Report: Overview*, NAT'L INST. ON DRUG ABUSE (Aug. 2011), https://nida.nih.gov/publications/research-reports/methamphetamine/overview [https://perma.cc/L99Q-AV7Q]; *Drug Fact Sheet: Amphetamines*, DRUG ENF'T AGENCY (Apr. 2020), https://www.dea.gov/sites/default/files/2023-02/Amphetamines%202022%20Drug%20Fact%20Sheet_0.pdf [https://perma.cc/8D6K-EYLU]; *see also* Dani Blum, *What Is Ozempic and Why Is It Getting So Much Attention?*, N.Y. TIMES (Nov. 13, 2023), https://www.nytimes.com/2022/11/22/well/ozempic-diabetes-weight-loss.html (on file with the *Iowa Law Review*).

308. FDA, ADDERALL® XR CAPSULES PRESCRIBING INFORMATION (2001), https://www.accessdata.fda.gov/drugsatfda_docs/label/2001/21303lbl.pdf [https://perma.cc/MFF7-T6HQ].

309. 21 U.S.C. § 812.

310. Coulter et al., *supra* note 306, at 1115; *see, e.g.*, FDA, FENDIQUE® ER PRESCRIBING INFORMATION 2–3 (2021), https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/018074Orig1s037lbl.pdf [https://perma.cc/M573-2LXW].

Several states have enacted statutes prohibiting physicians from prescribing Schedule II amphetamines for treatment of obesity.[311] Two state medical boards have done the same by regulation.[312] Ohio's medical board goes further, with a rule providing: "A prescriber may utilize a schedule III or IV controlled substance for the treatment of obesity only if it has an F.D.A. approved indication for this purpose . . . ."[313] Finally, the medical boards of Kansas and Louisiana have taken even more restrictive actions, issuing regulations prohibiting the prescription of *any* amphetamines for treatment of obesity (and thus banning on-label as well as off-label uses).[314]

For the most part, these statutes and rules are distinguishable in important ways from the PB/CSH bans. First of all, obesity was not recognized as a disease by the scientific community until 1985 and by the medical community until 2013,[315] so the older provisions were arguably enacted to prohibit *nonmedical* uses of amphetamines. Second, the statutes and rules banning the use of Schedule II amphetamines for treatment of obesity are not prohibiting standard of care treatment; doctors rarely prescribe even Schedule III drugs for weight control, let alone Schedule II drugs.[316]

Finally, it is important to emphasize that these statutes and rules are directed at *controlled substances*. Indeed, many of them appear in the controlled substance portions of their state's statutory or administrative codes.[317] Controlled substances raise public health issues beyond their safety and effectiveness for the patients taking them for legitimate medical purposes in accordance with prescriptions. Like the federal CSA, state-controlled substances acts are intended to protect society at large by preventing *abuse* of addictive drugs by people to

311. ALA. CODE §§ 20-2-54, 34-24-360(21) (LexisNexis 2015 & 2019); MISS. CODE ANN. § 41-29-139(e) (2018 & Supp. 2022); N.Y. PUB. HEALTH LAW § 3304(b) (McKinney 2023).

312. 201 KY. ADMIN. REGS. 9:016, § 3(3) (2007); N.J. ADMIN. CODE § 13:35–7.8(a) (2023).

313. OHIO ADMIN. CODE 4731-11-04 (2023).

314. KAN. ADMIN. REGS. § 100-23-1(a) (2022); LA. ADMIN. CODE tit. 46, § 6905(A) (2020) (prohibiting the prescription "for the purpose of weight control or weight reduction in the treatment of obesity any amphetamine, dextroamphetamine, methamphetamine, or phenmetrazine drug or compound; any Schedule II controlled substance; human chorionic gonadotropin (HCG); thyroid hormones; diuretic medications; or any drug, medication, compound, or substance which is not indicated for use in the treatment of exogenous obesity by express approval of the U.S. Food and Drug Administration"). It is an open question whether a state can completely ban an FDA-approved use for an approved drug. *See* Lars Noah, *State Affronts to Federal Primacy in the Licensure of Pharmaceutical Products*, 2016 MICH. ST. L. REV. 1, 2; Jared C. Huber, Note, *Preemption Exemption: FDA-Approved Abortion Drugs After* Dobbs, 98 NOTRE DAME L. REV. 2217, 2218 (2022); Thomas A. Costello, Note, *Quitting Cold Turkey: Federal Preemption Doctrine and State Bans on FDA-Approved Drugs*, 26 WM. & MARY BILL RTS. J. 839, 840 (2017); *cf.* Zogenix, Inc. v. Patrick, No. 14-11689-RWZ, 2014 WL 4373251, at *3 (D. Mass. Aug. 28, 2014) (striking down a state ban on any use of an FDA-approved opioid).

315. Coulter et al., *supra* note 306, at 1114.

316. *Id.* at 1115.

317. For example, the Alabama, Mississippi, and New York provisions all appear in the portions of their respective codes regulating controlled substances.

whom they are inappropriately prescribed or illegally diverted.[318] Thus, the state lawmakers passing these prohibitions were not motivated by a particular medical interest in amphetamines' safety and efficacy for treatment of obesity; rather, they wanted to limit these drugs' availability for nontherapeutic uses. For example, the New Jersey Board of Medical Examiners justified its regulation forbidding physicians to prescribe Schedule II amphetamines for obesity as follows: "The expected benefits should include a severe reduction in the black-market availability of these Controlled Dangerous Substances, with fewer people abusing and addicted to these drugs."[319]

Puberty blockers, estrogen, and progesterone are not controlled substances, so the states banning their use in treating gender dysphoria in adolescents cannot have been similarly motivated. And although testosterone is a controlled substance, the legislatures that have banned its use for treatment of gender dysphoria have not justified these prohibitions with reference to the risks of diversion, addiction, or abuse. The PB/CSH bans are, unlike the amphetamine restrictions, direct intrusions into medical practice based merely on clinical disagreement with the medical profession.

E. ABORTION MEDICATION

The abortion context provides the only prior example in which multiple states have completely banned an off-label use that clearly accords with the standard of care.

In 2000, FDA approved an oral regimen of two drugs, mifepristone and misoprostol, for use in medication abortion.[320] The original labeling described the indication as "medical termination of intrauterine pregnancy through [forty-nine] days' pregnancy."[321] It set the dose of mifepristone at 600 mg, followed in two days by .4 mg of misoprostol.[322] But within a year of the approval, ninety-six percent of medication abortions did not follow this

318. JOANNA R. LAMPE, CONG. RSCH. SERV., R45948, THE CONTROLLED SUBSTANCES ACT (CSA): A LEGAL OVERVIEW FOR THE 118TH CONGRESS, at i (2023) ("The CSA simultaneously aims to protect public health from the dangers of controlled substances diverted into the illicit market while also seeking to ensure that patients have access to pharmaceutical controlled substances for legitimate medical purposes."). Most state-controlled substances acts are modeled on the Uniform Controlled Substances Act drafted by the U.S. Department of Justice. *See* Grinspoon v. DEA, 828 F.2d 881, 887 n.9 (1st Cir. 1987) ("To date, [forty-eight] states, the District of Columbia, Guam, and the Virgin Islands have adopted the Uniform CSA."); RUFUS KING, THE DRUG HANG-UP: AMERICA'S FIFTY-YEAR FOLLY 319–22 (1972).

319. Lemmon Co. v. N.J. State Bd. of Med. Exam'rs, 417 A.2d 568, 570–71 (N.J. Super. Ct. App. Div. 1980) (quoting communication from the Board president to the New Jersey Attorney General).

320. Letter from the FDA Center for Drug Evaluation and Research, to Sandra P. Arnold, Population Council (Sept. 28, 2000), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2000/20687appltr.pdf [https://perma.cc/HAY7-Y99L].

321. FDA, MIFEPREX PRESCRIBING INFORMATION (2000), https://www.accessdata.fda.gov/drugsatfda_docs/label/2000/20687lbl.pdf [https://perma.cc/UZW9-RDAB]. The entire two-drug regimen was included in the mifepristone labeling. The labeling for misoprostol, already approved for ulcer prevention in certain patients, was not revised to mention abortion. *Id.*

322. *Id.* FDA also imposed a restricted distribution regime requiring, among other things, in-person administration of both drugs and a follow-up visit. *Id.*

protocol.[323] Instead, they followed a new protocol based on clinical trials that was embraced by the American College of Obstetricians and Gynecologists ("ACOG"), the AMA, and other leading authorities.[324] This protocol—deemed to be safer and more effective than the labeled regimen—used 200 mg of mifepristone and .8 mg of misoprostol, the latter administered vaginally instead of orally.[325] It was used through sixty-three days of pregnancy.[326]

Despite the emergence of this new protocol, over the next few years, at least six states enacted bans (in some instances *criminal* bans) on off-label prescribing of mifepristone.[327] Although the legislatures of these states were purportedly motivated by concerns about women's safety,[328] this explanation was clearly a pretext for the true goal of limiting medication abortion beyond forty-nine days of pregnancy and thus reducing the number of abortions overall.[329] In a decision striking down that state's law, the Oklahoma Supreme Court emphatically declared it to be "so completely at odds with the standard that governs the practice of medicine that it can serve no purpose other than to prevent women from obtaining abortions and to punish and discriminate against those who do."[330] The court reached this conclusion in part because of the utter inconsistency between the off-label ban for abortion medication and "the deference physicians receive regarding treatment decisions in almost all other areas of medicine."[331] This deference, the court pointed out, was reflected in other Oklahoma laws "recogniz[ing] the importance of allowing physicians to prescribe medications based on science and their medical judgment rather than dogmatic adherence to FDA labeling."[332]

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323. Okla. Coal. for Reproductive Just. v. Cline, 368 P.3d 1278, 1284 (Okla. 2016).

324. Planned Parenthood Ark. & E. Okla. v. Jegley, No. 15-cv-00784, 2016 WL 6211310, at *23 (E.D. Ark. 2016), *vacated and remanded*, 864 F.3d 953 (8th Cir. 2017); Planned Parenthood of Cincinnati Region v. Taft, 444 F.3d 502, 505–06 (6th Cir. 2005).

325. *Planned Parenthood of Cincinnati Region*, 444 F.3d at 505–06.

326. *Id.* at 506.

327. H.B. 126, 125th Gen. Assemb., Reg. Sess. (Ohio 2004) (codified at OHIO REV. CODE ANN. § 2919.123(A) (2004)); OKLA. STAT. tit. 63 § 1-729a (2011) (amended by 2014 Okla. Sess. Law Serv. Ch. 121 (West)); 2011 N.D. Laws ch. 109, § 6 (1)–(2); ARIZ. REV. STAT. ANN. § 36-449.03(E)(6) (2012); TEX. HEALTH & SAFETY CODE ANN. § 171.063 (2013); ARK. CODE ANN. § 20-16-1504 (West 2015).

328. OKLA. STAT. tit. 63 § 1-729a(A) (legislative findings); Planned Parenthood Ariz., Inc. v. Humble, 753 F.3d 905, 910 (9th Cir. 2014).

329. *See Planned Parenthood Arizona*, 753 F.3d at 915 (plaintiffs introduced evidence that "the law will effectively ban medication abortions outright because many women do not discover they are pregnant before 49 days").

330. Cline v. Okla. Coal. for Reproductive Just., 313 P.3d 253, 262 (Okla. 2013) (endorsing and bolding this language from state district court opinion Okla. Coal. for Reproductive Just. v. Cline, No. cv–2011–1722, slip op. ¶ 7 (Dist. Ct. Okla. Cnty. May 11, 2012)).

331. *Id.*

332. *Id.* at 261. Oklahoma's true motives were clearly exposed after FDA updated the mifepristone labeling in 2016, largely to reflect the ACOG protocol that most physicians were already following. *See* FDA, MIFEPREX PRESCRIBING INFORMATION (2016), https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf [https://perma.cc/V873-VUGK]. After the update, the unrevised Oklahoma statute no longer gave special status to current FDA

As will be discussed below, a majority of courts that considered state laws prohibiting the off-label use of mifepristone agreed with the Oklahoma Supreme Court that they were unconstitutional under the heightened scrutiny that *Planned Parenthood v. Casey* required before *Dobbs* overruled it in 2022.[333] For now, the main lesson to be drawn from such laws is that a legislature's stated objective of protecting the health of patients receiving a drug may be a mere pretext for another policy. And as will be addressed further below, whereas the Supreme Court has recognized the true goal of these mifepristone statutes (whether it be described as protecting "potential life" or "the life of an unborn human being") as legitimate,[334] the Court has also stated that "animus" toward a class affected by a law (for example, transgender individuals) is *not* a legitimate state interest.[335]

F. SUMMARY

This Section has demonstrated that the rare instances in which states have interfered with off-label prescribing are distinguishable from current state bans on the off-label use of puberty blockers and sex hormones for treatment of adolescent gender dysphoria. The restrictions on chelation therapy for treatment of cardiovascular disease were directed at a use rejected by mainstream doctors and thus violative of the standard of care, whereas the use of pharmaceutical treatments for gender dysphoria accords with the standard of care. The state bans on off-label prescribing of hydroxychloroquine for COVID-19 were intended to preserve a sufficient supply of that drug for patients taking it for its approved uses; no such shortage concerns exist for puberty blockers or sex hormones. States prohibited only *nonmedical* uses of anabolic steroids; by contrast, the administration of PB/CSH drugs to treat gender dysphoria is indisputably a medical use. The state prohibitions on prescribing certain amphetamines for treatment of obesity were motivated by addiction, abuse, and diversion concerns inapplicable to PB/CSHs. None of these measures were based on lawmakers' disagreement with the medical profession regarding a drug's safety and efficacy in treating a medical condition—the purported impetus for the PB/CSH bans.

The state prohibitions on off-label use of abortion medication represent the closest parallel to the PB/CSH bans, in that they similarly outlawed standard-of-care medical practice and purportedly did so to protect patients. But the actual goal of the abortion medication laws was to reduce the number of abortions and thus protect "potential life"—a goal the Supreme Court has confirmed to be legitimate. By contrast, the actual motivation of the PB/CSH

labeling; instead, it continued to require physicians to comply with the outdated, obsolete 2000 labeling. Okla. Coal. for Reproductive Just. v. Cline, 441 P.3d 1145, 1150 (Okla. 2019). The Oklahoma Supreme Court declared this mandate to be unconstitutional under the Due Process Clause of the Fourteenth Amendment. *Id.* at 1153–60.

333. *See infra* Section VIII.B.

334. Dobbs v. Jackson Women's Health Org., 597 U.S. 215, 222, 256 (2022).

335. Romer v. Evans, 517 U.S. 620, 632 (1996); *see infra* Section VIII.C.

bans is animus, which the Supreme Court has declared to be an illegitimate legislative purpose.[336] In any event, as discussed below, a majority of courts that considered the constitutionality of state bans on standard-of-care off-label prescribing of abortion pills deemed them to be unconstitutional under the heightened scrutiny then required by *Casey*.[337] In the following sections, this Article argues that people have a fundamental right to receive standard-of-care treatment and that the PB/CSH bans should thus similarly fall under heightened scrutiny.

VII. A FUNDAMENTAL RIGHT TO RECEIVE STANDARD-OF-CARE OFF-LABEL TREATMENT

A. REVIEW OF THE RELEVANT CASE LAW

This Article contends that Americans have a fundamental right to access drugs for off-label uses that meet the standard of care, and thus that the state bans on PB/CSH treatment of gender dysphoria in adolescents violate the Due Process Clause of the Fourteenth Amendment. This Section explains why this assertion is consistent with the existing case law.

Under the Supreme Court's decision in *Washington v. Glucksberg*, "the Due Process Clause specially protects those fundamental rights and liberties which are, objectively, 'deeply rooted in this Nation's history and tradition' and 'implicit in the concept of ordered liberty' such that 'neither liberty nor justice would exist if they were sacrificed.'"[338] The second element of the *Glucksberg* test is easily met in this situation; laws that prevent people from obtaining standard-of-care treatment from licensed physicians violate the most basic notions of self-protection and bodily autonomy (especially when it is a treatment for a life-threatening condition).

The two courts that have upheld state PB/CSH bans have instead decided that these laws violate no rights that are "deeply rooted in this Nation's history and tradition." The Eleventh Circuit observed,

> [T]he use of these medications in general—let alone for children—almost certainly is not "deeply rooted" in our nation's history and tradition. . . . [T]he earliest-recorded uses of puberty blocking medication and cross-sex hormone treatment for purposes of treating the discordance between an individual's biological sex and sense of gender identity did not occur until well into the twentieth century.[339]

This inappropriately narrow approach to framing the asserted right would, in our quickly evolving and highly technological society, entirely immunize many laws from strict scrutiny no matter how severely they violated people's

336. *See infra* Section VIII.C.

337. *See infra* Section VIII.B.

338. Washington v. Glucksberg, 521 U.S. 702, 720–21 (1997) (quoting Snyder v. Massachusetts, 291 U.S. 97, 105 (1934) and Palko v. Connecticut, 302 U.S. 319, 325, 326 (1937)); *see also Dobbs*, 597 U.S. at 237–38 (embracing this standard).

339. Eknes-Tucker v. Governor of Ala., 80 F.4th 1205, 1220–21 (11th Cir. 2023).

liberties. As observed by the authors of the seminal article on the appropriate level of generality in defining fundamental rights, "[d]escribing a claimed right in very specific terms . . . disconnects it from previously established rights."[340] A judicial approach requiring such specificity, they argue, would "all but abidcat[e] the judicial responsibility to protect individual rights."[341]

The Sixth Circuit, describing the asserted right more broadly, concluded: "This country does not have a "deeply rooted" tradition of preventing governments from regulating the medical profession in general or certain treatments in particular, whether for adults or their children."[342] This assertion may be true with respect to prohibitions against the administration of never-marketed investigational drugs that FDA has not reviewed at all. But puberty blockers and sex hormones have been thoroughly investigated for other conditions, reviewed by FDA for these uses, prescribed by physicians for many decades, and are part of the standard-of-care treatment regimen for gender dysphoria, including in minors. *Abigail Alliance v. von Eschenbach* (cited and discussed by the Sixth Circuit[343]) is thus clearly distinguishable. In that case, the D.C. Circuit held that terminally-ill patients did not have a fundamental right to access innovative, entirely unapproved drugs that had never been subjected to controlled clinical trials and had never been available for use by physicians.[344] Such drugs *could not* be standard-of-care treatment.[345]

If we define the right as one to access standard-of-care treatment, the "history and tradition" is met. As shown above, the state bans on the use of puberty blockers and sex hormones for treatment of gender dysphoria apparently represent the first instances ever, outside the abortion context, of either the federal government or a state government *banning* the standard-of-care off-label use of a drug—or indeed, any standard-of-care treatment—based exclusively on a purported disagreement with the medical profession about the treatment's safety and efficacy for patients.

Supporters of the PB/CSH bans try to draw support from the Supreme Court's 1926 decision in *Lambert v. Yellowley*. This case, decided shortly after the 1917 ratification of the Eighteenth Amendment establishing prohibition, upheld provisions of two federal criminal statutes that limited the amount of liquor a physician could prescribe for medical purposes.[346] Two features of

340. Laurence H. Tribe & Michael C. Dorf, *Levels of Generality in the Definition of Rights*, 57 U. CHI. L. REV. 1057, 1066 (1990).

341. *Id.* at 1086.

342. L.W. *ex rel.* Williams v. Skrmetti, 83 F.4th 460, 473 (6th Cir. 2023).

343. *Id.* at 474–75.

344. *See generally* Abigail All. for Better Access to Developmental Drugs v. Eschenbach, 495 F.3d 695 (D.C. Cir. 2007).

345. Similarly distinguishable is *Rutherford v. United States*, 616 F.2d 455 (10th Cir. 1980), in which the court denied a substantive due process right to obtain an unapproved, unorthodox remedy never subjected to successful controlled clinical testing and never accepted by the medical profession. *See supra* note 120 and accompanying text (rejecting due process right to access Laetrile, an alternative cancer remedy derived from apricot pits).

346. *See generally* Lambert v. Yellowley, 272 U.S. 581 (1926). These statutes were the Volstead Act, Pub. L. 66-66, 41 Stat. 305 (1919) and the Willis–Campbell Act, Pub. L. 67-96, 42 Stat. 222 (1921).

Yellowley distinguish it from the dispute over PB/CSH bans, however. First, although the medical profession once widely embraced the medicinal use of alcoholic beverages, it was no longer the standard of care by the 1920s.[347] *Yellowley* observed: "[P]hysicians differ about the value of malt, vinous, and spiritous liquors for medicinal purposes, but . . . the preponderating opinion is against their use for such purpose . . . ."[348] Moreover, when Congress limited the volume of alcoholic beverages that doctors could prescribe, it was acting not to protect patients from dangerous or ineffective medical treatment, but rather to inhibit liquor's diversion to beverage use. As the Supreme Court recognized, Congress was thus promoting the purpose of the Eighteenth Amendment itself—the suppression of social and moral evils stemming from the consumption of alcoholic beverages.[349]

Importantly, in the context of medical care in prison, multiple courts have already held that a total ban on the use of drugs to treat gender dysphoria violates inmates' constitutional rights. Prisoners' right to access medical treatment is protected, not by the Due Process Clause, but by the Cruel and Unusual Punishments Clause of the Eighth Amendment. Writing for the majority in *Estelle v. Gamble*,[350] Justice Thurgood Marshall opined that the Eighth Amendment embodies "broad and idealistic concepts of dignity, civilized standards, humanity, and decency" that "establish the government's obligation to provide medical care for those whom it is punishing by incarceration."[351] An incarcerated person advancing a claim of inadequate medical care must show first, a serious medical need, and second, "deliberate indifference" by the prison officials responding to the need.[352] The high burden of "deliberate indifference" reflects inmates' diminished expectation of a right to care as compared to, for example, people involuntarily confined to mental institutions, who are protected by the Due Process Clause.[353]

Nevertheless, even under the "deliberate indifference" standard, "[n]umerous courts have concluded that categorical bans on hormone therapy, and so-called 'freeze-frame' policies that prohibit hormone therapy for those who were not receiving it prior to incarceration, violate the Eighth

347. In 1917, the AMA passed a resolution stating that alcohol's "use in therapeutics . . . has no scientific value." *American Medical Association and Prohibition*, 176 BOS. MED. & SURGICAL J. 884, 885 (1917). For a historical review of the use of medical alcohol and its regulation, see GROSSMAN, *supra* note 28, at 228–31; Jacob M. Appel, *"Physicians Are Not Bootleggers": The Short, Peculiar Life of the Medicinal Alcohol Movement*, 82 BULL. HIST. MED. 355, 367–70 (2008).

348. *Yellowley*, 272 U.S. at 590.

349. *Id.* at 589–90.

350. *See generally* Estelle v. Gamble, 429 U.S. 97 (1976).

351. *Id.* at 102–03.

352. *Id.* at 105; Jennifer Levi & Kevin M. Barry, *Transgender Rights & the Eighth Amendment*, 95 S. CAL. L. REV. 109, 128–29 (2021).

353. Youngberg v. Romeo, 457 U.S. 307, 321–22 (1982) ("Persons who have been involuntarily committed are entitled to more considerate treatment and conditions of confinement than criminals whose conditions of confinement are designed to punish."); *see* Rose Carmen Goldberg, Note, *The Antidotes to the Double Standard: Protecting the Healthcare Rights of Mentally Ill Inmates by Blurring the Line Between* Estelle *and* Youngberg, 16 YALE J. HEALTH POL'Y L. & ETHICS 111, 119–25 (2016) (challenging this differential treatment of mentally ill people in state custody).

Amendment because such policies are deliberately indifferent to the individual medical needs of incarcerated people."[354] For instance, in *Fields v. Smith*,[355] the Seventh Circuit held that a Wisconsin ban on providing hormone therapy to inmates with gender dysphoria (then called "gender identity disorder" or "GID") violated the Eighth Amendment. In their defense, the corrections officials invoked *Gonzalez v. Carhart*, the Supreme Court case upholding a ban on "partial birth abortion."[356] They asserted that *Carhart* stood for the proposition that a legislature may "constitutionally limit the discretion of physicians by outlawing a particular medical procedure."[357] The court rejected this argument:

> *Carhart* is not helpful to defendants in this case because they did not present any medical evidence that alternative treatments for GID are effective. As defendants point out, some medical uncertainty remains as to the causes of GID, but there was no evidence of uncertainty about the efficacy of hormone therapy as a treatment. Just as the legislature cannot outlaw all effective cancer treatments for prison inmates, it cannot outlaw the only effective treatment for a serious condition like GID.[358]

In *Keohane v. Florida Department of Corrections Secretary*, the Eleventh Circuit similarly struck down, on Eight Amendment grounds, the department's policy of refusing to start inmates on hormone therapy during the first two years of their sentence. The court explained, "It seems to us that responding to an inmate's acknowledged medical need with what amounts to a shoulder-shrugging refusal even to consider whether a particular course of treatment is appropriate is the very definition of 'deliberate indifference'—anti-medicine, if you will."[359] If a ban on hormone treatments for prisoners with gender dysphoria violates the Eighth Amendment, it certainly also violates the more robust due process rights of people, including adolescents, who are not in state custody.

B. RESPONSES TO LIKELY OBJECTIONS

Finally, it is important to address two likely objections to this Article's assertion that people have a fundamental right to access standard-of-care off-label drug treatment. One is that this right cannot be "deeply rooted" in American history and tradition because the very notion of "off-label prescribing" is largely a creation of the authority that FDA received in 1962 to comprehensively regulate the effectiveness claims made in drug labeling. In fact, however, if we pull the lens back a bit from the specific question of "off-label prescription" of drugs, the right to access standard-of-care treatment extends back to the country's origins.

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354. Levi & Barry, *supra* note 352, at 130.
355. Fields v. Smith, 653 F.3d 550, 559 (7th Cir. 2011).
356. Gonzales v. Carhart, 550 U.S. 124, 140, 168 (2007). Carhart is discussed *infra* Section VIII.B.
357. *Fields*, 653 F.3d at 557.
358. *Id.*
359. Keohane v. Fla. Dep't Corr. Sec'y, 952 F.3d 1257, 1266–67 (11th Cir. 2020) (dictum).

As I show in my book *Choose Your Medicine: Freedom of Therapeutic Choice in America*, efforts to limit people's access to drugs and other treatments—and disputes over those efforts—are as old as the country.[360] In that book, I show that "throughout most of American history, a broad swath of the population has believed that people have a right to choose their preferred medical treatments without government interference."[361] In the book, I concede that the history I relate "does not necessarily demonstrate that a right to try potentially life-saving treatments—let alone treatments for less severe conditions—is so 'rooted' in American history and tradition that it is entitled to special constitutional protection in court."[362] But *none* of the contested restrictions that I examine in *Choose Your Medicine* were prohibitions on what we would now call standard-of-care medicine. To the contrary, the book's episodes concern struggles over government limitations (generally supported by the medical establishment) on *unorthodox* remedies or, in modern times, on drugs that FDA has not approved for any use.

There is a simple reason why one cannot find declarations from throughout the country's history that people have a fundamental right to access treatments endorsed by the medical profession: Outside abortion restrictions and the PB/CSH bans, American lawmakers have virtually never *tried* to prohibit such treatments.[363] The presumption that people have a right to obtain standard-of-care medical treatments is so deeply rooted in America's history and traditions that it has almost never even been tested. Still, it is possible to find compelling evidence that the very notion of prohibiting a physician from prescribing a drug—even a potentially harmful drug—for a use recognized by the medical profession is utterly foreign to Anglo-American jurisprudence.

Most of the "great [English] common law authorities" cited by *Dobbs* to support that holding also made statements suggesting that the law should not second-guess physicians' standard-of-care prescriptions, particularly through the imposition of criminal penalties.[364] In 1644, Sir Edward Coke pronounced: "If one that is in the myster[y] of a physician take a man in cure and give[] him such physic as within three day[]s he d[i]e thereof, without any felonious intent, and against his will, it is no homicide."[365] About a century later, Sir Matthew Hale stated: "If a physician gives a person a potion without any intent of doing him any bodily hurt, but with an intent to cure or prevent a disease, and contrary to the expectation of the physician it kills him, this is no homicide . . . ."[366] On the eve of the American Revolution, Sir William Blackstone agreed with both of his predecessors that "[i]f a physician or

360. GROSSMAN, *supra* note 28, at 5.

361. *Id.*

362. *Id.* at 7.

363. The one possible exception to this statement is the state prohibitions on the FDA-approved use of amphetamines to treat obesity. *See supra* notes 311–19 and accompanying text.

364. Dobbs v. Jackson Women's Health Org., 597 U.S. 215, 242–45 (2022) (citing Coke, Hale, and Blackstone).

365. EDWARD COKE, 4 INSTITUTES OF THE LAW OF ENGLAND 251 (London, 1644).

366. MATTHEW HALE, 1 THE HISTORY OF THE PLEAS OF THE CROWN 429 (London, 1736).

surgeon gives his patient a potion or plaster to cure him, which, contrary to expectation kills him, this is neither murder, nor manslaughter, but misadventure; and he shall not be punished criminally . . . ."[367]

Before independence, American colonial governments sporadically took steps to defend their citizens from *irregular* medicine, but they never sought to interfere with the provision of care in accordance with orthodox medical professional standards. A 1649 Massachusetts statute—intended to protect the colony's inhabitants from quacks—prohibited people employed as physicians or surgeons from "exercis[ing] or put[ting] forth any act contrary to the known, *approved rules of the art* in each . . . occupation . . . without the advice and consent of such as are skilful [sic] in the same art . . . and consent of the patient or patients."[368] The colonies of New York and New Jersey enacted medical licensing laws in 1760 and 1772, respectively. These largely unenforced measures were designed to exclude, through examination, unorthodox practitioners as well as ignorant ones, while leaving the field open to qualified "regulars."[369]

After independence, although state governments did not directly regulate drugs' safety or effectiveness, they increasingly did so indirectly through licensing regimes. Organized medicine advocated for these regimes in part to suppress irregular sects with different armamentariums. These sects included Thomsonianism (a botanical approach based on lobelia and cayenne pepper) and homeopathy (a system based on extremely diluted preparations of substances that, in much greater amounts, produced symptoms like those of the disease being treated). As I observed in *Choose Your Medicine*, "[These sects] were so firmly identified with the particular types of drugs they administered that state licensing laws were effectively a form of drug regulation."[370] These licensing regimes, though not always effective, were extremely controversial. Indeed, state legislatures revoked almost all of them by the time of the Civil War in response to populist activism.[371]

The important point here, however, is that when licensing was in effect, it invariably privileged orthodox medicine—the type of care provided by practitioners who were members of local and state medical societies and graduates of foreign and domestic medical schools.[372] By putting the state's stamp on regular medicine, these antebellum licensing laws implicitly endorsed the types of drugs used by regular physicians. Notably, orthodox drug treatments were potent and potentially dangerous. In the early nineteenth century, regular doctors widely practiced what is now referred to as "heroic" medicine, a methodology centered on copious bleeding and the administration of depleting drugs such as blistering plasters and mineral-based purgatives

367. 4 WILLIAM BLACKSTONE, COMMENTARIES *197.
368. Commonwealth v. Thompson, 6 Mass. (5 Tyng) 134, 140 n.† (1809) (emphasis added).
369. GROSSMAN, *supra* note 28, at 15.
370. *Id.* at 5.
371. *Id.* at 24–44.
372. *Id.* at 13, 25.

and emetics.[373] Medical dissidents condemned these drugs as dangerous "poisons."[374] The licensing laws, by limiting the medical field to regular doctors, effectively authorized their use.

Early American medical malpractice law similarly protected the use of orthodox remedies in accordance with regular standards of care. The first American treatise focused on medical malpractice observed: "The standard of ordinary skill, which is required of every physician and surgeon . . . is that degree and amount of knowledge and science, which the *leading authorities* have pronounced as the result of their researches and experience . . . ."[375] An 1853 Pennsylvania Supreme Court decision articulated the standard of care as "reasonable skill and diligence; by which we mean such as thoroughly educated surgeons ordinarily employ."[376]

Under these principles, a physician was not liable if a drug he prescribed in accordance with professional standards injured a patient. Although there seem to be no reported cases that articulate this precise rule (perhaps because of an absence of relevant claims), it is implicit in the holding of a prominent case involving Samuel Thomson, the famously *unorthodox* founder of the Thomsonian school. One of Thomson's patients died after Thomson repeatedly induced violent "puking" in him with lobelia, a botanical emetic. The Supreme Judicial Court of Massachusetts—citing Lord Hale—acquitted Thomson of criminal malpractice. The court's decision hinged on the fact that the state legislature did not, at the time, restrict the practice of such "itinerant quacks" through licensing or otherwise. The court explained:

> [T]here is no law which prohibits any man from prescribing for a sick person with his consent, if he honestly intends to cure him by his prescription. And it is not felony, if, through his ignorance of the quality of the medicine prescribed, or of the nature of the disease, or of both, the patient, contrary to his expectation, should die.[377]

The same principle obviously applied to a licensed regular physician prescribing drugs in accordance with professional standards.

The fact that American law traditionally privileges standard-of-care medicine and protects physicians who provide it does not, in and of itself, demonstrate that *patients* have a fundamental right to access this type of care. As observed earlier,[378] however, judges have rarely had an opportunity to articulate this

373. *Id.* at 12–13.

374. *Id.* at 32–33.

375. JOHN J. ELWELL, A MEDICO-LEGAL TREATISE ON MALPRACTICE AND MEDICAL EVIDENCE, COMPROMISING THE ELEMENTS OF MEDICAL JURISPRUDENCE 55 (New York, Alfred Elwell & Co. 1860) (emphasis added).

376. McCandless v. McWha, 22 Pa. 261, 268 (1853).

377. Commonwealth v. Thompson , 6 Mass. (5 Tyng) 134, 140 (1809); *see also* Bowman v. Woods, 1 Greene 441, 442, 444 (Iowa 1848) (in states where the licensing regime did not regard "the regular system" with "partiality or distinguishing favor," irregular practitioners did not commit malpractice if they provided care consistent with the "ordinary diligence and skill in their respective systems of treating diseases").

378. *See supra* Section II.B.

right precisely because of the dearth of laws prohibiting such care—a dearth itself explained by Americans' deep commitment to bodily autonomy and the right of self-preservation. Nevertheless, a few courts have recognized a right to obtain standard-of-care medical treatment in other contexts. Consider, for example, *State v. Housekeeper*, an 1889 case in which a man brought a malpractice suit against a surgeon who operated on his wife against his wishes.[379] Maryland's highest court ruled that a "husband had no power to withhold from his wife the medical assistance which her case might require."[380] It explained: "The consent of the wife, not that of the husband, was necessary . . . . The professional men whom she had called in and consulted, being possessed of skill and scientific knowledge, were the proper persons to determine what ought to be done."[381] A contrary result, the court declared, would be "cruel."[382]

Still, the strongest evidence of a fundamental right to obtain standard-of-care medical treatment is the lack of statutes invading this right. The only early examples I can find of American laws banning treatments routinely prescribed by regular physicians are nineteenth-century statutes forbidding all provision of alcoholic beverages, with no exception for medical purposes.[383] (At the time, orthodox doctors commonly prescribed liquor and wine to their patients, and brandy, whisky, sherry, and port appeared in the United States Pharmacopoiea.[384]) But these state laws were motivated not by a legislative rejection of liquor's value as a drug, but rather by concerns that "ill-behaved druggists or pretended pharmacists [would] debauch the public morals by dealing out intoxicating liquors and nostrums as beverages."[385] In any event, many state courts read a medical exception into these prohibitory statutes, holding that the measures were otherwise absurd and unjust, or even unconstitutional.[386]

In sum, an examination of the historical record reveals no instances in which a state prohibited physicians from providing a standard-of-care pharmaceutical treatment based on the government's independent assessment of the drug's safety and efficacy. The absence of such laws is powerful evidence of a right deeply rooted in the nation's history and traditions. When the U.S. Supreme Court, in *New York State Rifle & Pistol Association v. Bruen*, performed a "history and tradition" test to determine that a "public carry" firearm licensing law violated New Yorkers' Second Amendment rights, it assigned apparently dispositive importance to the fact that "[a]part from a few late-19th-century outlier jurisdictions, American governments simply have not broadly

379. State v. Housekeeper, 16 A. 382, 383 (Md. 1889).
380. *Id.* at 384.
381. *Id.*
382. *Id.* (quoting Carstens v. Hanselman, 28 N.W. 159, 159 (Mich. 1886)).
383. GROSSMAN, *supra* note 28, at 229.
384. *Id.*
385. Commonwealth v. Fowler, 28 S.W. 786, 787 (Ky. 1894).
386. GROSSMAN, *supra* note 28, at 229.

prohibited the public carry of commonly used firearms for personal defense."[387] Moreover, the absence of inconsistent statutes is not the only evidence of a "deeply rooted" American right to obtain standard-of-care treatments prescribed by one's physician; this lack of regulation must be viewed in light of a long, robust tradition of statements and actions favoring a broader right to therapeutic choice extending even to *unorthodox* therapies.[388]

A second argument likely to be advanced against this Article's assertion of a substantive due process right to obtain standard-of-care treatment is that because the medical "standard of care" changes over time and can differ from state to state,[389] it is too unstable and variable a concept upon which to base a constitutional right. One simple response to this objection is that American courts already determine people's rights by reference to the standard of care all the time—namely, the rights of plaintiffs to recover damages in medical malpractice cases. Furthermore, even if constitutional law raises unique concerns, there is already a type of constitutional litigation in which courts routinely determine the contours of a fundamental right by reference to evolving and variegated "community standards"—obscenity cases.

In the 1973 case *Miller v. California*, the Supreme Court defined the line between speech protected by the First Amendment and unprotected "obscenity" by asking whether "the average person, applying *contemporary community standards*, would find that the work, taken as a whole, appeals to the prurient interest."[390] The Court specifically rejected the argument that application of a national constitutional right cannot vary with local standards:

> Under a National Constitution, fundamental First Amendment limitations on the powers of the States do not vary from community to community, but this does not mean that there are, or should or can be, fixed, uniform national standards of precisely what appeals to the "prurient interest" or is "patently offensive." These are essentially questions of fact, and our Nation is simply too big and too diverse for this Court to reasonably expect that such standards could be

387. N.Y. State Rifle & Pistol Ass'n, Inc. v. Bruen, 597 U.S. 1, 70 (2022). In *Bruen*, the Court was examining the historical record to determine whether there was a tradition of firearms regulation that constituted a limit on the enumerated Second Amendment right to bear arms, rather than to determine whether a fundamental substantive due process right existed in the first place. *Id.* at 18–31. Nevertheless, the law at issue in *Bruen* was a state law, and the Second Amendment thus applied only because it was incorporated via the Due Process Clause of the Fourteenth Amendment, the same provision at issue here. *Id.* at 8–11. Moreover, the Supreme Court has not suggested that the history and tradition test should be applied differently in these two different contexts. For a critique of the use of the absence of legislation to demonstrate a Second Amendment right, see Jacob D. Charles, *The Dead Hand of a Silent Past:* Bruen*, Gun Rights, and the Shackles of History*, 73 DUKE L.J. 67, 113–16 (2023).

388. *See generally* GROSSMAN, *supra* note 28.

389. Some jurisdictions apply a national or nongeographic standard of care for medical specialists. *See generally* Zitter, *supra* note 211.

390. Miller v. California, 413 U.S. 15, 24 (1973) (emphasis added).

> articulated for all [fifty] States in a single formulation, even assuming the prerequisite consensus exists.[391]

Although, as the Court has acknowledged, "contemporary community standards . . . change a great deal between communities and over time,"[392] the *Miller* standard remains the test for obscenity, and many hundreds of federal and state courts have applied it over the years to delineate the scope of parties' fundamental First Amendment rights.[393]

VIII. SCRUTINIZING THE BANS

In the wave of litigation concerning the bans on pharmaceutical treatment of adolescent gender dysphoria, different courts have subjected the bans to different levels of scrutiny. Some have applied strict scrutiny because they, like this Article, have deemed the laws to violate a fundamental right.[394] Other courts have determined that the bans are unconstitutional sex-based classifications under the Equal Protection Clause, struck down the bans using the intermediate scrutiny required for such claims, and then deemed it unnecessary to apply the more stringent strict scrutiny applicable to violations of fundamental rights under the Due Process Clause.[395] Finally, some courts—most notably the Sixth and Eleventh Circuits—have held that the bans are not subject to heightened scrutiny under either the Due Process Clause or the Equal Protection Clause and have thus applied the rational basis test.[396] This Section will show how the bans almost certainly cannot survive any form of heightened scrutiny and may even be vulnerable under a rational basis analysis.

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391. *Id.* at 30.

392. Counterman v. Colorado, 143 S. Ct. 2106, 2130 (2023) (Sotomayor, J., concurring); *see also* Sable Commc'ns of Cal. v. Fed. Commc'n Comm'n, 492 U.S. 115, 124 (1989) ("There is no constitutional barrier under *Miller* to prohibiting communications that are obscene in some communities under local standards even though they are not obscene in others.").

393. A Westlaw search on March 7, 2023, of all federal and state cases for "obscenity" & "contemporary community standards" produced 1,608 results. Even if some of these are cases in which courts do not directly apply the "contemporary community standards" test, many hundreds certainly are such cases.

394. Doe 1 v. Thornbury, 679 F. Supp. 3d 576 (W.D. Ky. 2023), *rev'd and remanded*, L.W. *ex rel.* Williams v. Skrmetti, 83 F.4th 460 (6th Cir. 2023); Brandt v. Rutledge, 551 F. Supp. 3d 882, 892 (E.D. Ark. 2021), *aff'd*, 47 F.4th 661 (8th Cir. 2022) (applying intermediate scrutiny); Eknes-Tucker v. Marshall, 603 F. Supp. 3d 1131 (M.D. Ala. 2022), *vacated sub nom.* Eknes-Tucker v. Governor of Ala., 80 F.4th 1205 (11th Cir. 2023).

395. *See generally Brandt*, 47 F.4th 661; L.W. *ex rel.* Williams v. Skrmetti, 679 F. Supp. 3d 668 (M.D. Tenn. 2023), *rev'd and remanded*, 83 F.4th 460 (6th Cir. 2023); Koe v. Noggle, 688 F. Supp. 3d 1321 (N.D. Ga. 2023); K.C. v. Individual Members Med. Licensing Bd., 677 F. Supp. 3d 802 (S.D. Ind. 2023); Poe *ex rel.* Poe v. Labrador, 709 F. Supp. 3d 1169 (D. Idaho 2023). Some of these cases also found the bans to be unconstitutional classifications based on *transgender status*. *See, e.g.*, *Brandt*, 679 F. Supp. 3d at 698.

396. *See generally Skrmetti*, 83 F.4th 460; *Eknes-Tucker*, 80 F.4th 1205; Doe v. Ladapo, 676 F. Supp. 3d 1205 (N.D. Fla. 2023).

A. *HEIGHTENED SCRUTINY*

The strict scrutiny standard requires a court to strike down a law as unconstitutional if it is not "narrowly drawn" (or "the least restrictive means") to advance a "compelling government interest."[397] Predictably, the few U.S. district courts that have performed the exercise of applying strict scrutiny to the state PB/CSH bans have found these laws to be unconstitutional. None of them has questioned whether the state has a compelling interest in protecting the health and safety of children.[398] But they have easily concluded that a total ban on the use of puberty blockers and hormones for treatment of gender dysphoria in minors is not narrowly tailored to advance this interest.[399]

In supporting their conclusion that the bans are more restrictive than necessary, these courts have cogently emphasized that none of the European nations that have restricted PB/CSH treatment for gender dysphoria in adolescents have entirely *prohibited* the use of these drugs for this purpose.[400] As one of these courts pointed out: "The [Alabama] Act, unlike the cited European regulations, does not even permit minors to take transitioning medications for research purposes, even though Defendants adamantly maintain that more research is needed."[401]

In short, because these state laws prohibit the use of puberty blockers and sex hormones for treatment of gender dysphoria in adolescents under any circumstances, they are extremely unlikely to survive strict scrutiny.[402] Indeed, none of the PB/CSH bans has yet survived even intermediate

397. *E.g.*, Carey v. Population Servs. Int'l, 431 U.S. 678, 686 (1977) ("[R]egulations imposing a burden on [a fundamental right] may be justified only by compelling state interests, and must be narrowly drawn to express only those interests."); Roman Cath. Diocese v. Cuomo, 592 U.S. 14, 21 (2020) (Gorsuch, J., concurring) (explaining that government officials' actions subject to strict scrutiny are unconstitutional "unless they are pursuing a compelling interest and using the least restrictive means available").

398. *Brandt*, 47 F.4th at 670 ("The state has a compelling interest in 'safeguarding the physical and psychological well-being of a minor.'" (quoting Globe Newspaper Co. v. Superior Ct. for Norfolk Cnty., 457 U.S. 596, 607 (1982))); *Eknes-Tucker*, 603 F. Supp. 3d at 1145 (quoting same language from *Globe Newspaper Co.*); *Thornbury*, 679 F. Supp. 3d at 586 (assuming sub silentio that state has a compelling interest).

399. *Brandt*, 47 F.4th at 670; *Eknes-Tucker*, 603 F. Supp. 3d at 1146; *cf. Thornbury*, 679 F. Supp. 3d at 586–87 (finding the ban is not designed to serve the state's interest in protecting children because it allows the same treatments for cisgender minors, and the Commonwealth does not "even attempt to show" that it "employs the 'least restrictive means' necessary to achieve its purpose" (quoting *Eknes-Tucker*, 603 F. Supp. 3d at 1146)).

400. *Brandt*, 47 F.4th at 670; *Eknes-Tucker*, 603 F. Supp. 3d at 1146. For a discussion of these other countries' restrictions, see *supra* notes 80–86 and accompanying text.

401. *Eknes-Tucker*, 603 F. Supp. 3d at 1146.

402. Applying strict scrutiny to laws regulating standard-of-care pharmaceutical treatment of gender dysphoria in minors—or laws regulating any other standard-of-care treatment—would not necessarily result in courts overturning narrowly tailored restrictions short of complete bans. As one scholar who performed an empirical analysis of the application of strict scrutiny concluded: "Courts routinely uphold laws when applying strict scrutiny, and they do so in every major area of law in which they use the test. Overall, [thirty] percent of all applications of strict scrutiny . . . result in the challenged law being upheld." Adam Winkler, *Fatal in Theory and Strict in Fact: An Empirical Analysis of Strict Scrutiny in the Federal Courts*, 59 VAND. L. REV. 793, 795–96 (2006).

scrutiny, which requires a court to strike down a law unless it serves "important governmental objectives" and is "substantially related to the achievement of those objectives."[403] The states obviously have an "important" interest in protecting children.[404] Nonetheless, the judges applying intermediate scrutiny have found that the bans are not "substantially related" to that interest, a test the Supreme Court has said requires a "close means-end fit."[405]

In denying that such a fit exists, these courts, like the courts that have applied strict scrutiny, have emphasized that the states "opted to ban—rather than otherwise regulate—gender transition procedures for minors."[406] As a U.S. district court observed in striking down the Florida ban:

> [T]he treatments are available in appropriate circumstances in all the countries cited by the defendants, including Finland, Sweden, Norway, Great Britain, France, Australia, and New Zealand. Some or all of these insist on appropriate preconditions and allow care only in approved facilities—just as the Endocrine Society and WPATH standards insist on appropriate preconditions, and just as care in the United States is ordinarily provided through capable facilities. Had Florida truly joined the international consensus—making these treatments available in appropriate circumstances or in approved facilities—these plaintiffs would qualify, and the instant motions would not be necessary.[407]

Courts applying intermediate scrutiny have also found a lack of a substantial relationship between the PB/CSH bans and the states' goal of protecting children's health because the scientific evidence does not support such a relationship. As one court stressed, the available evidence clearly demonstrates that the pharmaceutical treatments for gender dysphoria "are safe, effective, and medically necessary for some adolescents."[408] The U.S.

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403. Craig v. Boren, 429 U.S. 190, 190 (1976).

404. Koe v. Noggle, 688 F. Supp. 3d 1321, 1349 (N.D. Ga. 2023) ("[T]he state's asserted interest in protecting children through regulation of the medical profession is, of course, and important one."); K.C. v. Individual Members Med. Licensing Bd., 677 F. Supp. 3d 802, 806, 815 (S.D. Ind. 2023) (concluding that "the State's interest in protecting the wellbeing of minors and regulating the medical profession" are sufficient to survive intermediate scrutiny). One court considering a PB/CSH ban confusingly held that the state did *not* demonstrate an important interest; it reached this conclusion by narrowly (and tautologically) identifying that interest as an "interest in banning these treatments." L.W. *ex rel.* Williams v. Skrmetti, 679 F. Supp. 3d 668, 709 (M.D. Tenn. 2023).

405. Sessions v. Morales-Santana, 582 U.S. 47, 68 (2017).

406. *K.C.*, 677 F. Supp. 3d at 816; *see also* Poe *ex rel.* Poe v. Labrador, 709 F. Supp. 3d 1169, 1194 (D. Idaho 2023) (ruling that the ban fails heightened scrutiny "because the means (a total prohibition on gender-affirming medical care) is not closely fitted with the ends (protecting children)"); *Noggle*, 688 F. Supp. 3d at 1353 (stressing that the state's scheme "prohibits clinicians and parents from determining the correct course of treatment on an individualized basis").

407. Doe v. Ladapo, 676 F. Supp. 3d 1205, 1224 (N.D. Fla. 2023).

408. *Labrador*, 709 F. Supp. 3d at 1182; *see also Noggle*, 688 F. Supp. 3d at 1350 ("[T]he preliminary record evidence of the medical risks and benefits of hormone therapy shows that a broad ban on the treatment is not substantially likely to serve the state's interest in protecting children.").

district court in Florida found, in light of the scientific record, that the state's ban would not survive even *rational basis* scrutiny."[409]

B. PRECEDENTS FROM THE ABORTION CONTEXT

Courts have subjected government bans on standard-of-care abortion services to a different form of heightened scrutiny, namely, the "undue burden" test of *Planned Parenthood v. Casey*.[410] The mixed results of these cases offer lessons to litigants challenging the state PB/CSH bans. Overall, they suggest that these laws should not survive any form of heightened scrutiny.

In 1992, the U.S. Supreme Court, in *Planned Parenthood v. Casey*, modified the approach to reviewing abortion rights established nineteen years earlier by *Roe v. Wade*.[411] (*Dobbs* overturned both of these decisions in 2022.)[412] *Casey* replaced the strict scrutiny standard of *Roe*[413] with a more forgiving—but still heightened—standard asking whether the challenged regulation imposes an "undue burden" on a woman's ability to obtain an abortion.[414] Subsequently, courts confronted some situations in which they had to decide whether prohibitions against standard-of-care abortion services violated this test. These cases provide insight into whether any law prohibiting standard-of-care treatment could ever survive heightened scrutiny.[415]

In *Gonzalez v. Carhart*,[416] decided in 2007, the Supreme Court upheld the constitutionality of Congress's ban on "partial birth abortion" (intact dilation and evacuation), a method for ending a second-trimester pregnancy. The plaintiffs contended that the Partial Birth Abortion Ban imposed an unconstitutional burden on the abortion right because it prohibited the procedure even when it was "necessary, in appropriate medical judgment, for the preservation of the . . . health of the mother."[417] The Court rejected this argument. While acknowledging that some abortion doctors believed intact dilation and evacuation ("D&E") was sometimes the safest method of abortion, the Court stressed that other physicians disagreed and thus that "[t]here is documented medical disagreement whether the Act's prohibition would ever

409. *Ladapo*, 676 F. Supp. 3d at 1214 ("There is no rational basis for a state to categorically ban these treatments.").

410. Planned Parenthood of Se. Pa. v. Casey, 505 U.S. 833, 876 (1992).

411. Roe v. Wade, 410 U.S. 113, 166 (1973). *See generally Casey*, 505 U.S. 383.

412. Dobbs v. Jackson Women's Health Org., 597 U.S. 215, 231 (2022).

413. *See Roe*, 410 U.S. at 155.

414. *Casey*, 505 U.S. at 874.

415. Jonathan H. Adler, *Super Deference and Heightened Scrutiny*, 74 FLA. L. REV. 267, 298 n.194 (2022) (describing the "'undue burden' test [as] a *sui generis* form of heightened scrutiny, but a form of heightened scrutiny nonetheless"); David L. Faigman, Ashutosh A. Bhagwat & Kathryn M. Davis, *Amicus Brief of Constitutional Law Professors David L. Faigman and Ashutosh A. Bhagwat, et al. in the Case of* Gonzales v. Carhart, 34 HASTINGS CONST. L.Q. 69, 72–73 (2006) ("[T]he level of scrutiny applicable to abortion regulations, including that inherent in the 'undue burden' test . . . is heightened scrutiny.").

416. Gonzalez v. Carhart, 550 U.S. 124, 140, 147–48 (2007).

417. *Id.* at 161 (quoting Ayotte v. Planned Parenthood of N. New Eng., 546 U.S. 320, 327–28 (2005)).

impose significant health risks on women."[418] The opinion observed: "The Court has given state and federal legislatures wide discretion to pass legislation in areas where there is medical and scientific uncertainty."[419]

Though *Carhart*, on its face, might seem to weigh against an argument that state PB/CSH bans should fall under heightened scrutiny, there are some important distinctions. First, at least the way the Court presented the facts, a "substantial part" of the medical community thought that the intact D&E procedure was never necessary to preserve the mother's health.[420] Implicitly, the Court seemed to be conceding that a total ban on a medical procedure *would* be unconstitutional if almost the entire medical community deemed it to sometimes be necessary. And one could argue that there is no significant disagreement within the medical community regarding whether puberty blockers and sex hormones are sometimes necessary when treating minors for gender dysphoria.

Second, in upholding the ban on intact D&E, *Carhart* emphasized that there was "a commonly used and generally accepted [alternative] method."[421] No such "generally accepted" alternative treatment exists for adolescent gender dysphoria. Finally, and importantly, the *Carhart* court was not applying the strict scrutiny standard of *Roe*, but rather the less stringent "undue burden" test of *Casey*, an opinion that "confirms the State's interest in promoting respect for human life at all stages in the pregnancy."[422] This Article argues that the PB/CSH bans violate a fundamental right and are thus subject to *strict scrutiny* review.

Courts also applied *Casey*'s "undue burden" test to the state bans on off-label use of the abortion drug mifepristone discussed earlier in this Article. Notably, a slight majority of these courts concluded that these laws violated the Due Process Clause (or were likely to do so).[423] As explained earlier, both the ACOG and the AMA endorsed an off-label protocol for medication abortion. In striking down the Arkansas law, a U.S. district court emphasized:

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418. *Id.* at 162.

419. *Id.* at 163.

420. *But see* Neil S. Siegel, *The Virtue of Judicial Statesmanship*, 86 TEX. L. REV. 959, 1024 (2008) ("[A]s every lower court had found, the weight of credible evidence heavily favors the position of the American College of Obstetricians and Gynecologists that the banned procedure is safest for women in certain circumstances.").

421. *Carhart*, 550 U.S. at 163–65, 167.

422. *Id.* at 163.

423. Okla. Coal. for Reproductive Just. v. Cline, 441 P.3d 1145, 1160–61 (Okla. 2019); Cline v. Okla. Coal. for Reproductive Just., 313 P.3d 253, 262 (Okla. 2013); Planned Parenthood Ark. & E. Okla. v. Jegley, No. 15-cv-00784, 2016 WL 6211310, at *21 (E.D. Ark. Mar. 14, 2016); Planned Parenthood Ariz., Inc. v. Humble, 753 F.3d 905, 914 (9th Cir. 2014); *cf.* MKB Mgmt. Corp. v. Burdick, 855 N.W.2d 31, 89 (N.D. 2014) (finding, by a three-justice majority, the prohibition on off-label prescribing of mifepristone unconstitutional, but North Dakota requires concurrence of four justices to declare statute unconstitutional); Planned Parenthood of Greater Tex. Surgical Health Servs. v. Abbott, 748 F.3d 583, 604 (5th Cir. 2014) (rejecting a facial challenge, because "an as-applied challenge . . . is the proper means of challenging the lack of [a health and life of the mother] exception to the regulations at issue"). *Contra* Planned Parenthood S.W. Ohio Region v. DeWine, 696 F.3 490, 506–07 (6th Cir. 2012).

> Defendants offer no justification for why, in legislation, the State of Arkansas would reject the evidence-based protocols for medication abortion in the light of this evidence regarding the ACOG and the AMA. Further, in determining whether regulations actually further women's health, the Supreme Court has repeatedly looked at the generally accepted standards for medicine set by the nation's major health organizations. *See, e.g.*, *Simopoulos v. Virginia*, 462 U.S. 506, 517 (1983) (considering American College of Obstetricians and Gynecologists and other standards).[424]

In these cases, multiple courts thus decided that state prohibitions on off-label medication abortion protocols that constituted the standard of care violated *Casey*'s "undue burden test." The use of puberty blockers and sex hormones for treatment of gender dysphoria in adolescents similarly represents the standard of care embraced by major medical organizations. And because in the gender-affirming care context, the states have no countervailing interest in protecting potential life, courts should subject the PB/CSH bans to less forgiving strict scrutiny and strike them down as unconstitutional.

C. ARBITRARINESS

One court that struck down a PB/CSH ban using intermediate scrutiny appropriately called the law "arbitrary" in explaining why it was not substantially related to the state's interest in protecting the health of minors.[425] The utterly arbitrary nature of the state bans is perhaps their greatest constitutional weakness, regardless of what level of scrutiny is applied.

As shown earlier,[426] the states that have enacted PB/CSH bans maintain a commitment to noninterference in physicians' off-label prescribing practices in virtually every other situation that conforms to the standard of care. This is no less true when it comes to pediatrics—an area with a particularly high rate of off-label prescribing.[427] Moreover, as also shown earlier,[428] some of these states explicitly *permit* some off-label prescribing that does *not* conform to the standard of care, with no limitations on pediatric use. This fact alone puts a lie to these states' assertions that they are trying to protect children from "experimental" treatments. Finally, there is the bans' most arbitrary feature of all: The very same statutes that prohibit the use of puberty blockers and sex hormones for treatment of gender dysphoria in minors explicitly permit off-label prescribing of these same drugs for other conditions in minors.[429]

The states argue that these bans are nonetheless *not* arbitrary because they prohibit a type of care that is supported by particularly low-quality evidence. Lawyers defending the Arkansas ban, for example, stressed that

424. *Planned Parenthood Ark. & E. Okla.*, 2016 WL 6211310 at *23.
425. L.W. *ex rel.* Williams v. Skrmetti, 679 F. Supp. 3d 668, 710–11 (M.D. Tenn. 2023).
426. *See supra* Part IV.
427. *See supra* Section III.B.
428. *See supra* Part V.
429. *See supra* Section IV.D.

according to the Endocrine Society itself, the evidence supporting the use of puberty blockers and cross-sex hormones in minors is "'*very* low quality' or, at best, merely 'low quality.'"[430] But this assertion ignores the fact that only a small minority of medical treatments—perhaps as few as ten percent—are supported by high quality evidence.[431] With respect to off-label prescriptions in particular, one study found that only twenty-one percent were backed by strong scientific evidence.[432] Why, then, are state legislatures prohibiting—and even criminalizing—this *one* off-label use while leaving virtually all other off-label prescribing untouched?

Such arbitrariness can sometimes lead courts to declare state laws unconstitutional even under rational basis review.[433] For example, the Supreme Court has held that a zoning requirement not subject to heightened scrutiny can be declared unconstitutional under the Due Process Clause if it is "clearly arbitrary and unreasonable, having no substantial relation to the public health, safety, morals, or general welfare."[434] In *Moore v. City of East Cleveland*, Justice Stevens, concurring separately in a plurality judgement, applied this standard to strike down an ordinance arbitrarily limiting who counts as a family member for legal occupancy of a single family home.[435] In *City of Cleburne v. Cleburne Living Center*, an equal protection case, the Supreme Court struck down, for lack of a legitimate rational basis, an ordinance that "arbitrar[ily]" required group-care facilities for the intellectually disabled to obtain land use permits, but not other facilities with multiple occupants.[436]

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430. Defendants' Combined Brief in Opposition to Plaintiffs' Motion for Preliminary Injunction: and Reply in Support of Defendants' Motion to Dismiss, *supra* note 81, at 86 (quoting Endocrine Society Guidelines); *see also, e.g.*, Respondents' Brief in Opposition to Petitions for Certiorari at 9, L.W. *ex rel.* Williams v. Skrmetti, No. 23-466 (U.S. Feb. 2, 2024) (emphasizing "very low quality" of evidence in support of WPATH and Endocrine Society protocols).

431. Mark H. Ebell, Randi Sokol, Aaron Lee, Christopher Simons & Jessica Early, *How Good Is the Evidence to Support Primary Care Practice?*, 22 J. EVIDENCE-BASED MED. 88, 91 (2017) (finding that only eighteen percent of primary care treatments "are based on patient-oriented evidence from consistent, high-quality studies"); Jeremy Howick et al., *The Quality of Evidence for Medical Interventions Does Not Improve or Worsen: A Metaepidemiological Study of Cochrane Reviews*, 126 J. CLINICAL EPIDEMIOLOGY 154, 157 (2020) (finding that 9.9% of Cochrane reviews of treatments "had high-quality evidence supporting the first-listed primary outcome"). Acquisition of high-quality evidence is particularly challenging with respect to pediatric treatments. McNamara et al., *supra* note 56, at 13.

432. Tewodros Eguale et al., *Drug, Patient, and Physician Characteristics Associated with Off-Label Prescribing in Primary Care*, 172 ARCHIVES INTERNAL MED. 781, 784 (2012) (compiling data from primary care physicians).

433. Carolene Prods. Co. v. United States, 323 U.S. 18, 31–32 (1944) (holding that a law subject to rational basis review is unconstitutional if "it is an arbitrary fiat").

434. Village of Euclid v. Ambler Realty Co., 272 U.S. 365, 395 (1926).

435. *See* Moore v. City of East Cleveland, 431 U.S. 494, 513–20 (1977) (Stevens, J., concurring in judgment). The plurality also deemed the ordinance to be unconstitutionally arbitrary, but it did so under a heightened level of scrutiny that it applied because the ordinance infringed the "freedom of personal choice in matters of marriage and family life." *Id.* at 499 (majority opinion) (quoting Cleveland Bd. of Educ. v. LaFleur, 414 U.S. 632, 639–40 (1970)).

436. City of Cleburne v. Cleburne Living Ctr., 473 U.S. 432, 446–50 (1985); *see also* U.S. Dep't of Agric. v. Moreno, 413 U.S. 528, 538 (striking down, for lack of a legitimate rational basis, a statute denying food stamps to members of a household with unrelated members).

Even under the rational basis test, the state must be pursuing a "legitimate" interest by enacting the law under review.[437] In some decisions striking down arbitrary laws under rational basis review, courts have concluded that the state's purported motive for enacting the law was a mere pretext for an illegitimate purpose.[438] The Supreme Court used this reasoning in *Romer v. Evans*, a case of particular relevance to this Article.[439] *Romer* considered an equal protection challenge to a Colorado constitutional provision that prohibited any state action designed to protect homosexuals from discrimination.[440] The Court presumed that homosexuality was not a "suspect classification" subject to strict scrutiny, but it nonetheless struck down the amendment under rational basis review.[441] The Court explained that the amendment's "sheer breadth is so discontinuous with the reasons offered for it that the amendment seems inexplicable by anything but animus toward the class it affects; *it lacks a rational relationship to legitimate state interests*."[442]

Some of the decisions that have struck down PB/CSH bans have used similar reasoning. For example, a U.S. district court in Florida dismissed that state's justifications of its ban as "pretextual," maintained that "the state's disapproval of transgender status . . . was a substantial motivating factor in enactment of [the ban]," and held that "dissuading a person from conforming to the person's gender identity rather than to the person's natal sex is not a legitimate state interest."[443] The court concluded: "[T]here is no rational basis, let alone a basis that would survive heightened scrutiny, for prohibiting these treatments in appropriate circumstances."[444]

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437. Dobbs v. Jackson Women's Health Org., 597 U.S. 215, 301 (2022).

438. *See, e.g.*, Romer v. Evans, 517 U.S. 620, 623–26 (1996); Lazy Y Ranch LTD v. Behrens, 546 F.3d 580, 589–93 (9th Cir. 2008); One Barberry Real Est. Holding, LLC v. Maturo, No. 17-CV-985, 2023 WL 10511255, at *47 (D. Conn. Oct. 3, 2023); *cf.* Squaw Valley Dev. Co. v. Goldberg, 375 F.3d 936, 950 (9th Cir. 2004) (reversing lower court's summary judgment) (overruled on other grounds).

439. *Romer*, 517 U.S. at 635.

440. *Id.* at 624.

441. *Id.* at 632–36.

442. *Id.* at 632 (emphasis added). *See generally* William D. Araiza, *Animus and Its Discontents*, 71 FLA. L. REV. 155 (2019). When discussing the PB/CSH bans' arbitrariness, it is difficult to divorce the substantive due process analysis from the equal protection arguments also advanced in the ongoing litigation. After all, by prohibiting essential medical care to a particular disfavored group (transgender individuals), the bans raise both liberty and equality concerns. As Justice Anthony Kennedy observed in his opinion protecting the right of same-sex marriage:

> The Due Process Clause and the Equal Protection Clause are connected in a profound way, though they set forth independent principles. Rights implicit in liberty and rights secured by equal protection may rest on different precepts and are not always co-extensive, yet in some instances each may be instructive as to the meaning and reach of the other.

Obergefell v. Hodges, 576 U.S. 644, 672 (2015).

443. Doe v. Ladapo, 676 F. Supp. 3d 1205, 1220 (N.D. Fla. 2023); *see also* Poe *ex rel.* Poe v. Labrador, 709 F. Supp. 3d 1169, 1193 (D. Idaho 2023) ("[T]he Court finds that the asserted objective is pretextual, given that [the law] allows the same treatments for cisgender minors that are deemed unsafe and thus banned for transgender minors.").

444. *Ladapo*, 676 F. Supp. 3d at 1220.

Thus, the arbitrariness of the state PB/CSH bans arguably makes them unconstitutional even under highly deferential rational basis review. As this Article has shown, however, the bans should be subject to strict scrutiny because they violate the fundamental rights of adolescent patients and their parents. And if an arbitrary law cannot survive rational basis scrutiny, it stands to reason that it cannot survive strict scrutiny.

Indeed, the Supreme Court has held that a law that infringes on fundamental rights is unconstitutional if it attacks a problem only in one narrow situation while ignoring other manifestations of the same problem. For example, in *Church of the Lukumi Babalu Aye, Inc. v. City of Hialeah*, the Court observed, "All laws are selective to some extent, but categories of selection are of paramount concern when a law has the incidental effect of burdening religious practice."[445] The Court explained, "It is established in our strict scrutiny jurisprudence that 'a law cannot be regarded as protecting an interest of the highest order . . . when it leaves appreciable damage to that supposedly vital interest unprohibited.'"[446] Or, as Justice Alito similarly observed with respect to a state policy limiting large religious services during the COVID-19 pandemic, "Having allowed thousands to gather in casinos, the State cannot claim to have a compelling interest in limiting religious gatherings to [fifty] people."[447]

How then, can states that allow puberty blockers and sex hormones to be used off-label for any other condition in patients of any age have a compelling interest in prohibiting their use only for treatment of gender dysphoria in minors?

CONCLUSION

Although a majority of the current roster of U.S. Supreme Court justices is unlikely to embrace the arguments set forth in this Article, I offer them with the goal of nudging the Court back toward a more capacious view of fundamental rights that eventually embraces a right so basic as the right to obtain standard-of-care treatments prescribed by one's physician. Moreover, the state PB/CSH bans are also subject to *state* constitutional limitations, and state supreme courts need not embrace the U.S. Supreme Court's currently parsimonious approach to fundamental rights. In any event, throughout American history, the constitutional right of access to medical treatments has been forged much more frequently in legislatures, agencies, popular publications, and street demonstrations than in courthouses.[448] Perhaps this Article will assist advocates for transgender medical rights—and medical rights more broadly—in these other forums.

445. Church of the Lukumi Babalu Aye, Inc. v. City of Hialeah, 508 U.S. 520, 542 (1993).

446. *Id.* at 547 (quoting Fla. Star v. B.J.F., 491 U.S. 524, 541–42 (1989) (Scalia, J., concurring in part and concurring in judgment)).

447. Calvary Chapel Dayton Valley v. Sisolak, 140 S. Ct. 2603, 2608 (2020) (Alito, J., dissenting).

448. *See generally* GROSSMAN, *supra* note 28.