No. 23-477

IN THE

Supreme Court of the United States

UNITED STATES OF AMERICA,

Petitioner,

v.

JONATHAN SKRMETTI, ATTORNEY GENERAL AND REPORTER FOR TENNESSEE, *et al.*,

Respondents.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT

BRIEF OF PROFESSORS OF LAW, MEDICINE, AND PUBLIC HEALTH AS *AMICI CURIAE* IN SUPPORT OF PETITIONER

ELIZABETH REINHARDT
COOLEY LLP
1299 Pennsylvania Avenue, NW
Washington, DC 20004

CELENE CHEN
COOLEY LLP
500 Boylston Street
Boston, Massachusetts

KATHLEEN R. HARTNETT
Counsel of Record
ZOË HELSTROM
COOLEY LLP
3 Embarcadero Center
San Francisco, California 94111
(415) 693-2000
khartnett@cooley.com

KATELYN KANG
VALERIA M. PELET DEL TORO
COOLEY LLP
55 Hudson Yards
New York, New York 10001

Counsel for Amici Curiae

332095

COUNSEL PRESS

(800) 274-3321 • (800) 359-6859

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INTEREST OF *AMICI CURIAE*[1]

Amici curiae listed in the Appendix are professors of law, medicine, and public health who teach and write about biomedical ethics and health-related rights and discrimination. Biomedical ethics, sometimes referred to as bioethics, is "the discipline of ethics dealing with moral problems arising in the practice of medicine and the pursuit of biomedical research." J. R. Vevaina et al., *Issues in biomedical ethics*, 39 Disease-a-Month 869 (1993), https://pubmed.ncbi.nlm.nih.gov/8243220. *Amici* have a strong interest in ensuring that principles of biomedical ethics are accurately described and properly applied. They submit this brief to explain how Tennessee Senate Bill 1, codified at Tennessee Code § 68-33-101, is inconsistent with foundational principles of biomedical ethics.

INTRODUCTION AND SUMMARY OF ARGUMENT

From flu shots to cancer treatments, medical providers regularly support patients (and their parents, when the patients are minors) in deciding whether a given medical treatment is necessary and appropriate for them, without any undue interference from the government.

The Tennessee law at issue in this appeal, Senate Bill 1, codified at Tennessee Code § 68-33-101 ("SB1"), upends that normal operation of medical practice for a specific,

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1. No counsel for a party authored this brief in whole or in part. No person or entity other than *Amici curiae*, its members, or its counsel made a monetary contribution to the preparation or submission of this brief.

targeted group of patients: transgender minors seeking gender-affirming medical care for gender dysphoria. SB1 outlaws the normal course of medical decision-making for these individuals, under which patients, their parents, and their medical providers carefully deliberate to make informed, individualized decisions about whether gender-affirming medical care is medically appropriate and in the best interest of the particular patient. Tennessee imposed this sweeping law even though every major medical organization in the United States has concluded that gender-affirming medical care, including for minors, is not only safe and effective, but is the *only* evidence-based treatment for gender dysphoria.

Categorically barring patients from accessing evidence-based treatment is irreconcilable with foundational precepts of biomedical ethics. That is particularly so where, as here, that treatment is the *only* evidence-based treatment available for a given medical need and the prohibition applies *only* to a group of patients singled out by their identity.

As explained further below, core principles of biomedical ethics include respect for autonomy, beneficence, and justice. SB1 deprives transgender patients of medically necessary and appropriate treatment to which they have given informed consent (autonomy). It forces providers to deny their patients care that is known to alleviate suffering, and thus to abandon their patients to serious physical and mental harm (beneficence). And it compels providers to deny necessary care to patients who are transgender, while leaving that care available to non-transgender patients, thereby exacerbating stigma and inequity and damaging trust in the medical profession (justice).

Tennessee attempts to justify these harms by claiming that gender-affirming medical care lacks a sound evidentiary base. That position, which badly misunderstands how medical knowledge is credibly generated, is in fact unfounded. Randomized controlled trials are not, and have never been, requisite for medical care to be considered appropriate, and in fact are ill-suited for many types of treatment. Nor must longitudinal studies always be of a particular duration to be reliable. And off-label use is legal, commonplace, and often necessary to serve a patient's best interest. SB1 prohibits gender-affirming medical care that has been developed through rigorous and appropriate methods and rests on a strong evidentiary basis.

Further, even if gender-affirming medical care were, as defined by Tennessee, "experimental," SB1 still violates each of the three core principles of biomedical ethics. Although Tennessee permits (and in some cases, protects) many treatments that would qualify as "experimental" under Tennessee's use of that term, it is only gender-affirming medical care sought by transgender adolescents that is singled out by SB1 and prohibited.

In sum, SB1 effectively bans gender-affirming medical care for adolescent transgender patients based on false notions of science, public health, and biomedical ethics, without considering the grave harm that will come from denying vulnerable patients critical healthcare. This Court should reverse the Sixth Circuit's judgment.

ARGUMENT

I. GENDER-AFFIRMING MEDICAL CARE TO TREAT GENDER DYSPHORIA, INCLUDING IN MINORS, IS SUPPORTED BY A SUBSTANTIAL BODY OF EVIDENCE AND IS NOT "EXPERIMENTAL."

The gender-affirming medical care prohibited by SB1 was developed through rigorous and appropriate methods and is recommended by every major medical association in the United States. Kellan Baker, *The Future of Transgender Coverage*, 376 New Eng. J. Med. 1801 (May 2017); Ayden I. Scheim et al., *Health and Health Care Among Transgender Adults in the United States*, 43 Annual Rev. of Pub. Health 503, 510 (2021); *see also* Gesine Meyer et al., *Safety and rapid efficacy of guideline-based gender-affirming hormone therapy: an analysis of 388 individuals diagnosed with gender dysphoria*, 182 European J. of Endocrinology 149, 155 (2020). Despite this reality, Tennessee characterizes gender-affirming medical care as "experimental" and questionable, pointing to the lack of randomized controlled trials supporting the efficacy of hormone therapy, the duration of the longitudinal studies completed to date, and what Tennessee labels "low quality" or "very low quality" evidence on gender-affirming medical care. *See* State Br. in Opp. 3, 9-10, 33-34, 36. Likewise, Tennessee emphasizes that using puberty blockers and hormone therapy to treat gender dysphoria is not approved by the U.S. Food and Drug Administration (the "FDA"), suggesting that the FDA's silence on this particular use implies that the care is experimental or harmful. *Id.* at 7-8.

The notion that gender-affirming medical care, including for minors, lacks a sufficient evidentiary foundation is wrong. As the District Court found, the medical care targeted by SB1 is supported by a strong evidentiary base. Pet. App. 194a-198. Tennessee's attempts to justify SB1 reflect a fundamental misunderstanding of medical practice and the ways medical knowledge and treatment guidelines are generated, particularly in the context of pediatric care. Medical providers are not and have never been restricted to providing only those treatments that have been generated via randomized controlled trial and received FDA approval for the particular indication. *Cf.* State Br. in Opp. at 7-8, 36 (suggesting that without FDA approval for the particular indication, or randomized controlled trial studies, certain gender-affirming treatment poses risk to minors). Indeed, as explained herein, such restrictions would be impractical and unethical. In short, the medical care targeted by SB1 is based on appropriate, ethical study and medical knowledge, and Tennessee's claim that it is "experimental" is misleading at best.

A. Tennessee Ignores the Difference Between Clinical Care and Clinical Research, and Thus Misconstrues How Medical Knowledge is Generated.

To start, Tennessee conflates clinical care with clinical research and fails to engage with the ethical standards attendant to each, presuming—incorrectly—that any gender-affirming medical care is and should be treated as research. Medical care delivered by a clinician to a patient, on the one hand, and clinical research, on the other, have distinct purposes and processes. *See, e.g.*,

Nat'l Comm'n for the Protection of Hum. Subjects of Biomedical and Behavioral Rsch., *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (1979) (discussing the importance of distinguishing between research and clinical practice); U.S. Food & Drug Admin., *Clinical Research Versus Medical Treatment* (Mar. 22, 2018), https://www.fda.gov/patients/clinical-trials-what-patients-need-know/clinical-research-versus-medical-treatment (describing differences between clinical research and medical treatment in terms of intent, intended benefit, funding, timeframe, and other factors). In the clinical care setting, the provider's aim is to improve a patient's health, and the provider is duty bound to act in that patient's best interest. By contrast, the aim of a research study is to generate knowledge useful for *future* patients. *See* José A. Sacristán, *Clinical Research and Medical Care: Towards Effective and Complete Integration*, 15 BMC Med. Res. Methodol. (2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4323129/. Accordingly, a research study's protocols must be ethically designed and administered, but there is no obligation to do what is in each participant's best interest. Importantly, receiving gender-affirming medical care for gender dysphoria does not automatically render a patient a subject of a research study—and certainly not a subject of experimentation unmoored from ethical standards. To the contrary, gender-affirming medical care can advance individual patients' best interests and is provided as clinical care for that purpose. Tennessee's use of the label "experimental" in this context is thus misleading.

Further, Tennessee's arguments misconceive how medical knowledge is credibly and rigorously generated,

and so, among other things, wrongly suggest that the lack of randomized controlled trials means the care has not been appropriately vetted. *See, e.g.*, *Eknes-Tucker v. Governor of Alabama*, 80 F.4th 1205, 1217 (11th Cir. 2023) (citing witness emphasizing lack of randomized studies). But there is no one method used to generate medical knowledge in all contexts, and no one method is considered requisite to a treatment being deemed medically appropriate. Rather, medical knowledge and practice are informed by a range of research and clinical inputs that are often dependent on the type of care, context, and state of development.

A randomized controlled trial—where some participants are randomly assigned to a treatment group and others are randomly assigned to a control group—is one of many types of credible research designs used to evaluate a medical intervention. Medical interventions also can be and often are evaluated through observational studies, which include cross-sectional studies (based on data collected from a single point in time), and longitudinal studies (based on data collected from particular individuals over time). *See, e.g.*, Edward L. Hannan, *Randomized Clinical Trials and Observational Studies: Guidelines for Assessing Respective Strengths and Limitations*, 1(3) JACC: Cardiovascular Interventions 211 (2008), https://www.sciencedirect.com/science/article/pii/S1936879808001702. In addition, randomized clinical trials, which compare different established interventions to one another, may be used to inform medical treatment.[2] For example, a randomized clinical trial has been used to

2. "Randomized controlled trials" and "randomized clinical trials" are often used synonymously.

evaluate sex hormone treatment for gender dysphoria, comparing different, established pharmacological treatments to one another. *See* Carla Pelusi et al., *Effects of Three Different Testosterone Formulations in Female-to-Male Transsexual Persons*, 11 J. Sex Med. 3002–11 (2014), https://www.jsm.jsexmed.org/article/S1743-6095(15)30626-3/fulltext.

Study methods other than randomized controlled trials and extended longitudinal studies also may be preferable in some circumstances, given that randomized controlled trials and extended longitudinal studies are not always feasible, appropriate, or the most reliable way to evaluate a medical intervention. For instance, randomized controlled trials are rarely used for interventions focused on children or pregnant people, or for surgical interventions. *See, e.g.*, Denise Thomson et al., *Controlled Trials in Children: Quantity, Methodological Quality and Descriptive Characteristics of Pediatric Controlled Trials Published 1948–2006*, 5 PLoS One (2010), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2948021/; Katrien Oude Rengerink et al., *Pregnant women's concerns when invited to a randomized trial: A qualitative case control study*, 15 BMC Pregnancy and Childbirth 207 (2015), https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-015-0641-x; Natalie S. Blencowe et al., *Interventions in randomised controlled trials in surgery: issues to consider during trial design*, 16 Trials 392 (2015), https://doi.org/10.1186/s13063-015-0918-4. Randomized controlled trials also are only ethical when there is clinical "equipoise," meaning that there is genuine uncertainty about whether the intervention will be more effective than the control. *See* Benjamin Freedman, *Equipoise and the Ethics of Clinical*

Research, 317 N. Engl. J. Med. 141–45 (1987), https://www.nejm.org/doi/full/10.1056/NEJM198707163170304. That is because it is unethical to knowingly expose participants to an inferior intervention or control. For example, in acknowledging limitations to its analysis, a 2023 open-label randomized clinical trial assessing the effect on gender dysphoria, depression, and suicidality of testosterone therapy compared with no hormone treatment explained that the trial was limited to three months in order to ensure that "participants would not be disadvantaged by waiting longer than standard of care waiting times of 3 months for an initial consultation." Brendan J. Nolan et al., *Early Access to Testosterone Therapy in Transgender and Gender-Diverse Adults Seeking Masculinization: A Randomized Clinical Trial*, JAMA Network Open (2023), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2809058. This principle plainly applies to the treatments for gender dysphoria subject to SB1: performing randomized, placebo-controlled trials on the efficacy of that treatment would be unethical, because the prevailing view among the medical community based on the existing evidence is that for patients who need it, hormone therapy is superior to a lack of pharmacological treatment. *See id.*

B. Gender-Affirming Medical Care Is Safe and Effective.

Tennessee is also wrong in claiming that research regarding the "long-term" safety and efficacy of gender-affirming medical care is lacking. State Br. in Opp. 9-10. In reality, there are many long-term studies supporting the provision of gender-affirming medical care to treat gender

dysphoria, including for minors.[3] Moreover, the underlying premise of Tennessee's argument—that long-term studies are necessary to prove a treatment's efficacy and safety—is mistaken. Longitudinal studies need not last for some unspecified "long-term" period to be reliable, nor are such studies always the most ethically and legally appropriate. Often, other reliable and trustworthy methods are preferable. For example, before conducting longitudinal studies involving children, researchers must consider a child's privacy and autonomy, all while maintaining data integrity—a sometimes difficult balancing act that can be avoided by using an alternative study design. *See, e.g.*, Gert Helgesson, *Children, Longitudinal Studies, and Informed Consent*, 8 Med., Health Care & Philos. 307 (2005), https://doi.org/10.1007/s11019-005-0978-4.

Tennessee also betrays an erroneous understanding of what it means for evidence to be graded as "low-quality." State Br. in Opp. 9-10. Under the GRADE system, which is

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3. *See, e.g.*, Jack L. Turban et al., *Access to gender-affirming hormones during adolescence and mental health outcomes among transgender adults*, 17(1) PLoS ONE, e0261039, 2 (2022), https://doi.org/10.1371/journal.pone.0261039 (collecting studies); Katherine L. Kraschel et al., *Legislation restricting gender-affirming care for transgender youth: Politics eclipse healthcare*, 3(8) Cell Reports Medicine 4 (2022), https://doi.org/10.1016/j.xcrm.2022.100719 (reviewing numerous studies that have linked gender-affirming medical care to improvements in depression, anxiety, and suicidality); *see also Brandt v. Rutledge*, 47 F.4th 661, 671 (8th Cir. 2022) ("According to surveys of the research on hormone treatment for adolescents done by the British National Institute for Health & Care Excellence, several studies have shown statistically significant positive effects of hormone treatment on the mental health, suicidality, and quality of life of adolescents with gender dysphoria. None has shown negative effects.").

often used for presenting summaries of scientific evidence and making clinical practice recommendations, the level of quality ascribed to evidence is based on the type of research methodology used, with evidence generated via a randomized controlled trial typically labeled "high quality" and evidence generated via an observational study typically labeled "low quality." Howard Balshem et al., *GRADE guidelines: 3. Rating the quality of evidence*, 64(4) J. Clinical Epidemiol. 401 (2011), https://medicinna.net/wp-content/uploads/2023/08/—evidence.pdf; Holger Schünemann et al. (eds.), *Grading of Recommend., Assess., Dev. & Eval. Handbook* 14 (2013) ("GRADE Handbook"). Randomized trials with limitations (such as inconsistent results or publication bias) will go down in quality, and observational studies with a particular relationship between a stimulus and a response or a large magnitude of effect will go up in quality. GRADE Handbook at 13.

These "high quality" and "low quality" labels under GRADE thus are descriptive of the underlying method, but they do not necessarily reflect the reliability of the evidence generated. As noted, observational studies are sometimes favored for both ethical and practical reasons. For example, despite their "low quality" technical category, observational studies have been used in forming the Cholesterol Guidelines of the American College of Cardiology and the American Heart Association. *See* Meredithe McNamara et al., *A Critical Review of the June 2022 Florida Medicaid Report on the Medical Treatment of Gender Dysphoria*, Yale Sch. of Med. 1, 16 (2022), https://medicine.yale.edu/lgbtqi/clinicalcare/gender-affirming-care/florida%20report%20final%20july%208%202022%20accessible_443048_284_55174_v3.pdf. The same is true for a range of other treatments, from

gallbladder surgery to the determination that aspirin is not appropriate to treat fevers in children. *See id.* at 14, 16. Because randomized controlled trials are often inappropriate or infeasible, research that falls in the technical category of "low quality" as that term is used in the GRADE system can still be reliable and valuable when it comes to clinical practice. *See* McNamara at 15.

Furthermore, "low-quality" evidence may be and often is sufficient to justify a strong recommendation for clinical care under that same grading system. *See* GRADE Handbook at 5; Balshem at 402–04 ("A particular level of quality does not imply a particular strength of recommendation. Sometimes, low or very low quality evidence can lead to a strong recommendation."). Indeed, if the "low-quality" label were enough to render care suspect, whole swaths of modern care for which randomized controlled trials are inappropriate for ethical and/or practical reasons would be called into question. *See* Robert J. Ligthelm et al., *Importance of observational studies in clinical practice*, 29(6) Clinical Therapeutics 1284 (2007), https://pubmed.ncbi.nlm.nih.gov/18036390/ (noting that observational evidence is sometimes favored for both ethical and practical reasons); *see also infra* Section II. Accordingly, the treatment for many other conditions, such as drugs for cancer and hematologic disorders, are widely recommended and used based on similarly "low-quality" evidence, without having been studied through randomized, controlled clinical trials. *See* Anthony J. Hatswell et al., *Regulatory approval of pharmaceuticals without a randomised controlled study: analysis of EMA and FDA approvals 1999-2014*, BMJ Open (June 30, 2016), https://pubmed.ncbi.nlm.nih.gov/27363818/.

C. Off-Label Drug Use is Common and Widely Accepted.

Finally, and contrary to the Sixth Circuit's suggestion, a medication need not be approved by the FDA for a particular indication to be safe and effective treatment for that indication. Off-label drug use is legal, accepted, and, when medically indicated, safe and in service of a patient's best interest. *See Planned Parenthood Cincinnati Region v. Taft*, 444 F.3d 502, 505 (6th Cir. 2006) (observing that off-label use is "a widely employed practice").

An understanding of the FDA approval process makes clear why Tennessee's "FDA approval" argument is wrong. Garnering the FDA's approval of a drug requires showing that it is both safe and effective—*i.e.*, the benefits outweigh the potential risks—for its intended use. *See* U.S. Food & Drug Admin., *The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective* (Nov. 24, 2017), https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective. It is well-established practice that once a drug has been approved by the FDA, health care providers may then prescribe it for other medically appropriate uses and in other dosages at their discretion without pharmaceutical companies first having to return to the FDA and seek approval for each indication. *See Taft*, 444 F.3d at 505. Such off-label use occurs because medical knowledge about how a drug might be beneficial in a different context or a different dosage continues to develop after FDA approval, but it is often too costly and impractical for drug makers to put each possible use of a drug through the FDA's "formal, lengthy, and expensive" approval process. Am. Cancer Soc'y,

Off-Label Drug Use (Mar. 17, 2015), https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/off-label-drug-use.html (noting that off-label drug use is "well-documented and very common in" oncology, "pediatrics and HIV/AIDS care"). In addition, providers often prefer that drug makers *not* seek approval for every off-label use, given that it could increase the cost of the drug and limit the scope of its clinical application, all of which would make it less available to their patients. *See id.*; Cong. Rsch. Serv., *Off-Label Use of Prescription Drugs* 4 (Feb. 23, 2021), https://sgp.fas.org/crs/misc/R45792.pdf.

Off-label use of medication is common and "generally accepted." *Buckman Co. v. Pls.' Legal Comm.*, 531 U.S. 341, 351 (2001); Christopher M. Wittich et al., *Ten common questions (and their answers) about off-label drug use*, 87 Mayo Clinic Proc. 982, 983 (2012), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3538391/ (discussing off-label drug uses that have "become widely entrenched in clinical practice and become predominant treatments for a given clinical condition" and citing studies showing that in a group of commonly used medications, 21% of prescriptions were for off-label use). For example, about half of drugs used to treat cancer are prescribed off-label. *See* Am. Soc'y of Clinical Oncology, *Reimbursement for cancer treatment: Coverage of off-label drug indications*, 24 J. Clinical Oncology 3206 (2006), https://ascopubs.org/doi/10.1200/JCO.2006.06.8940.

Off-label use is legal because FDA approval only limits how a drug can be marketed—*i.e.*, a drug cannot be marketed for a use different from its FDA-approved use—but not how a physician can prescribe it. *See Buckman*, 531 U.S. at 350, 351 & n.5 (explaining that "[o]ff-label usage . . . is an accepted and necessary corollary of the FDA's mission

to regulate in this area without directly interfering with the practice of medicine"); Daniel G. Aaron, *The Fall of FDA Review*, 22 Yale J. Health Pol'y & Ethics 95, 135 (2023) ("After approval, physicians may prescribe the drug for so-called 'off-label use,' a long-accepted and important part of the practice of medicine").

In fact, multiple federal and state laws have been enacted in recent years to promote and protect off-label prescriptions. *See, e.g.*, Tennessee Code § 63-6-301 (2015) (allowing patients to take investigational drugs, biological products, or devices under Tennessee's "Right to Try Act"); Am. Soc'y of Clinical Oncology, *Recent Developments in Medicare Coverage of Off-Label Cancer Therapies*, 5 J. Oncology Practice 18 (2009), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2790627/ (discussing 1993 legislation requiring Medicare to cover off-label uses of anti-cancer drugs and an expansion of Medicare's off-label coverage in 2008). Indeed, Tennessee recently passed a law expressly protecting the right to promote off-label uses and forbidding state regulatory boards from prosecuting medical providers for truthfully promoting such usage. Tennessee Code § 53-10-113 (2023).

Off-label use is especially common and important in treating minors. As noted above, minors are often excluded from clinical drug studies, including for ethical reasons. *See* Wittich at 983 (citing study finding that nearly 80% of children discharged from pediatric hospitals were taking at least one off-label medication and discussing range of widely practiced off-label drug uses in pediatric population); 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 State Med. Assoc. 776 (2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6677268 (surveying ten years of literature and finding that "[t]he use of off-label medications in children remains a common practice for pediatric providers").

Finally, and critically, off-label use is often essential for delivering the best care. James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions*, 53 Food & Drug L.J. 71, 72 (1998), https://pubmed.ncbi.nlm.nih.gov/11795338/ ("Off-label use is widespread in the medical community and often is essential to giving patients optimal medical care, both of which medical ethics, FDA, and most courts recognize."); William Janssen, *A Historical Perspective on Off-Label Medicine: From Regulation, Promotion, and the First Amendment to the Next Frontiers*, SSRN Elec. J. (2014), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2519223 (explaining that in some circumstances, "a physician's *failure* to prescribe the medical product for such an unapproved use can constitute medical malpractice").

Thus, off-label use is legal, common, and often essential for delivering medically necessary care. Any suggestion otherwise—including the Sixth Circuit's contention that off-label use signals that "the FDA is not prepared to put its credibility and testing protocols behind the [drug's] use," Pet. App. 27a—greatly misunderstands and misstates how the FDA works.

* * *

Contrary to Tennessee's claims, the health care outlawed by SB1 is not "experimental"; treatments are

regularly provided in a wide range of contexts without randomized controlled trials, observational studies of a specific length, or exclusively "high quality" evidence; and off-label use is safe, effective, and common practice. At bottom, Tennessee's arguments are based on a fundamental misunderstanding of both how scientific knowledge is generated and how the FDA approval process works.

II. WERE THE GOVERNMENT ALLOWED TO BAN MEDICAL CARE ON THE BASES ADVANCED BY TENNESSEE, A WIDE SWATH OF COMMON AND NECESSARY CARE COULD BE BANNED.

Tennessee's claimed justifications for SB1, including the "experimental" label as used by Tennessee, apply not only to gender-affirming medical care for minors but also to a range of other treatments that are widely used and accepted. *See supra* Section I (discussing lack of randomized controlled studies and longitudinal studies for certain cancer treatments and surgical interventions). Thus, were Tennessee's rationales for SB1 accepted in this case, the clear implication would be that the government could also ban all sorts of other common and necessary care. And that Tennessee has not done so—but instead has singled out gender-affirming medical care for minors for differential treatment—only underscores why Tennessee's claimed justifications for SB1 do not hold up.

Indeed, under the State's justifications for SB1, numerous treatments for a wide swath of indications would be vulnerable to an outright ban because they are supported by "low-quality" evidence, constitute off-label use, and/or have the potential for life-long side effects,

including certain treatments for anxiety disorders,[4] infertility,[5] bariatric conditions,[6] rare or uncommon diseases,[7] and in the intensive care context.[8]

Notably, Tennessee expressly protects patient access to "experimental" treatments in other contexts. For example, Tennessee has enacted a "Right to Try Act," which allows a terminally ill patient, in consultation with their physician, to give "informed consent" to use non-FDA approved drugs and medical products in order to treat their illness. Tennessee Code § 63-6-301

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4. Kimberly J. Stone et al., *Off-Label Applications for SSRIs*, 68 Am. Fam. Physician 498 (2003), https://www.aafp.org/pubs/afp/issues/2003/0801/p498.pdf.

5. Mahmoud Chehab et al., *On-label and off-label drugs used in the treatment of male infertility*, 103 Fertility and Sterility 595 (2015), https://www.sciencedirect.com/science/article/pii/S0015028214025539.

6. Valentina Martinelli et al., *Ethics of Bariatric Surgery in Adolescence and Its Implications for Clinical Practice*, 20 Children 1232 (2023), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9859476/ (discussing benefits of bariatric weight loss surgery for minors despite potential for life-long side effects).

7. Hans-Georg Eichler et al., *Randomized Controlled Trials Versus Real World Evidence: Neither Magic Nor Myth*, 109 Clinical Pharmacology & Therapeutics 1212 (2021), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8246742/ (discussing how an increased usage in specialized drug treatments for rarer diseases may warrant changes in how treatments are evaluated for approved use).

8. Jean-Louis Vincent, *We should abandon randomized controlled trials in the intensive care unit*, 38 Crit. Care Med. (2010).

(2015). Under these Right to Try laws, patients are given access to experimental treatments for which there is little information available regarding that treatment's benefits and risks. *See* Jennifer Piel, *Informed Consent in Right-to-Try Cases*, 44 J. Am. Acad. Psychiatry Law 290 (2016), https://web.archive.org/web/20200319213334id_/http://jaapl.org/content/jaapl/44/3/290.full.pdf. In these contexts, it is more difficult for physicians to weigh the risks and benefits of a treatment in order to advise their patients, and more difficult for patients to make an informed decision regarding their care. *Id.* Additionally, many Right to Try laws, including Tennessee's Right to Try law, do not require a physician to oversee a patient's usage of the experimental care, to facilitate the treatment's administration, or to assist in managing side effects. Tennessee Code § 63-6-301 (2015); *see* Lisa Kearns & Alison Bateman-House, *Who Stands to Benefit? Right to Try Law Provisions and Implications*, 51 Therapeutic Innovation & Regulatory Science 170 (2017), https://www.researchgate.net/publication/314289043_Who_Stands_to_Benefit_Right_to_Try_Law_Provisions_and_Implications. Nonetheless, Tennessee's Right to Try Act protects access to these experimental treatments, notwithstanding the potential risks, lack of FDA approval, and lack of randomized or longitudinal studies.

By contrast, under SB1, medical providers are *prohibited* from providing gender-affirming medical care to transgender adolescent patients, even though (as in Right to Try cases) the patient, provider, and parent (if the patient is a minor) have evaluated the risks and benefits of the care and have consented to that care. Furthermore, unlike the investigational treatments that are made available under Right to Try laws, gender-

affirming medical care is provided under the supervision of trained medical providers, who can assist in evaluating the appropriateness of treatment, oversee the treatment's administration, and assist in managing any side effects that may occur. Claire A. Coyne et. al., *Gender Dysphoria: Optimizing Healthcare for Transgender and Gender Diverse Youth with a Multidisciplinary Approach*, 19 Neuropsychiatric Dis. & Treat. 479 (2023), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9985385/. This disparity between Tennessee's treatment of gender-affirming medical care compared to other so-called "experimental" treatments underscores SB1's irrationality and disregard for biomedical ethics.

III. SB1 CONTRAVENES KEY TENETS OF BIOMEDICAL ETHICS.

By eliminating minor patients' ability to decide, together with their medical providers and parents, about whether accessing a safe and effective form of treatment is in their best interest, SB1 is directly at odds with key tenets of biomedical ethics: respect for autonomy, beneficence, and justice. Tom L. Beauchamp & James F. Childress, *Principles of Biomedical Ethics*, 13 (8th ed. 2019). These universal principles, which are the cornerstones of modern-day healthcare standards, guide providers' treatment decisions regardless of the type of medical care they are providing, and they provide "meaningful guidance" to courts assessing wholesale bans on and/or exclusions of coverage for care. *Contra* Pet. App. 28a. To be clear, *amici* do not invoke these principles to suggest that they provide the legal test pursuant to which judges should "assess the validity of [SB1]." *Id.* Rather, *amici* discuss how SB1 compromises these

principles rather than protecting them, thus undermining Tennessee's claimed rationales for SB1. *Amici* have a strong interest in ensuring that courts and policymakers alike have an accurate understanding of bioethics to the extent Tennessee seeks to justify SB1 as aligned with the ethical treatment of patients and practice of medicine.

A. SB1 Forces Providers to Disregard Patients' Autonomy.

As a general matter, Tennessee has repeatedly acknowledged the importance of obtaining informed consent and respecting the decision-making of the patient (and in the context of minors, the decision-making of their legal guardian), reflecting the core biomedical ethical principle of respect for autonomy. *See supra* Section II (discussing Tennessee's "Right to Try" laws). That principle requires that patients have the ability to decide whether to receive appropriate medical care within the framework of informed consent. Beauchamp & Childress at 105. For example, Tennessee has rendered the failure to adequately obtain informed consent tortious and has created a standard jury instruction on how to evaluate the negligent failure to obtain informed consent. Tennessee Code §§ 29-26-115–118; Tennessee Civil Pattern Jury Instr. 6.25 (discussing standard for finding liability for lack of informed consent). SB1 attacks autonomy by preventing individuals from pursuing, and health care professionals from providing, beneficial medical treatment with due regard for a patient's interests.

Empowering a patient's autonomy is essential to the integrity of the provider-patient relationship, as well as the patient's individual liberty and ability to determine

the course of their life. In keeping with that bioethical principle, "the physician's professional role [is] to make recommendations on the basis of the best available medical evidence and to pursue options that comport with the patient's unique health needs, values, and preferences." Lois Snyder Sulmasy & Thomas A. Bledsoe, *American College of Physicians Ethics Manual*, 170 Annals of Internal Medicine 86 (7th ed. 2019) ("ACP *Ethics Manual*"), https://www.acpjournals.org/doi/10.7326/m18-2160; *see also* Beauchamp & Childress at 105 (respect for autonomy requires health care professionals "to disclose information, to probe for and ensure understanding and voluntariness, and to foster adequate decision making"). Informed consent is a crucial mechanism for ensuring respect for autonomy. In all non-emergency encounters, the provider is obligated to offer the patient material information and guidance, but the patient must be trusted and empowered to make the informed and voluntary decision that best advances their interests. *See* Parth Shah et al., *Informed Consent*, StatPearls (2023), https://www.ncbi.nlm.nih.gov/books/NBK430827/. After the patient makes their decision, the provider's duty is to "protect and foster [the] patient's free, uncoerced choices." ACP *Ethics Manual* at 74.

Where, as here, the patients at issue include minors, the informed consent process usually involves the provider, the minor patient, and the minor's parents. When that is so, each actor has an important role to play: the provider offers medical instruction, the parents provide stewardship and consent, and the minor—assisted by that medical instruction and parental stewardship—provides assent. *See* Am. Med. Ass'n ("AMA"), *Code of Medical Ethics Opinion 2.2.1*, *Pediatric Decision Making*, https://

www.ama-assn.org/delivering-care/ethics/pediatric-decision-making (discussing the importance of "[r]espect and shared decision making" between parents and minors "in the context of decisions for minors"); Beth A. Clark, *Ethics in Child & Youth Care Practice with Transgender Youth*, 8 Int'l J. of Child, Youth & Fam. Studies 74 (2017), http://dx.doi.org/10.18357/ijcyfs82201716754 (discussing relational ethics).

The process of informed consent (which, for minors, also frequently includes their parents) involves five core elements: 1) patient competence, 2) disclosure, 3) comprehension, 4) voluntariness, and 5) consent. Beauchamp & Childress at 122. As to the first element, parents generally have competence to participate in the informed consent process on behalf of their minor children, and many adolescent patients also have the competence to participate in the informed consent process, including in the context of gender-affirming medical care. *See* Jessica Kremen et al., *Addressing Legislation That Restricts Access to Care for Transgender Youth*, 147 Pediatric Perspectives (2021), https://pubmed.ncbi.nlm.nih.gov/33883246/ (minor patients who are transgender "possess decisional capacity, and with guardian consent and the support of a multidisciplinary team, [] are able to contribute to decisions in their own best interests about [Gonadotropin Releasing Hormones] and gender-affirming hormones"); Beth A. Clark & Alice Virani, *This Wasn't a Split-Second Decision: An Empirical Ethical Analysis of Transgender Youth Capacity, Rights, and Authority to Consent to Hormone Therapy*, 18 J. Bioethical Inquiry 151 (2021), https://pubmed.ncbi.nlm.nih.gov/33502682/ (concluding, based on qualitative empirical analysis, that "trans[gender] youth demonstrated the understandings

and abilities characteristic of the capacity to consent to hormone therapy and that they did consent to hormone therapy with positive outcomes"); Richard E. Redding, *Children's Competence to Provide Informed Consent for Mental Health Treatment*, 50 Wash. & Lee L. Rev. 695, 707 (1993), https://scholarlycommons.law.wlu.edu/cgi/viewcontent.cgi?article=1759&context=wlulr ("Research . . . indicates that children often are capable of making important life decisions in a rational manner, including decisions about medical and psychological treatment.").

Once competence has been established, the elements of disclosure and comprehension require the provider to accurately and sensitively present relevant information about any diagnosis; the nature and purpose of recommended interventions; the burdens, risks, and expected benefits of all options, including forgoing treatment; and any limitations to the medical community's knowledge regarding burdens, risks, and expected benefits. AMA, *Code of Medical Ethics Opinion 2.1.1*, *Informed Consent*, https://www.ama-assn.org/delivering-care/ethics/informed-consent; Aníbal Torres Bernal & Deborah Coolhart, *Treatment and Ethical Considerations with Transgender Children and Youth in Family Therapy*, 23 J. of Fam. Psychotherapy 287, 296 (2012), http://dx.doi.org/10.1080/08975353.2012.735594.

For the fourth element, voluntariness, the provider must then assess the patient's (and, if not a mature minor, the parents') ability to understand relevant medical information and the implications of treatment alternatives and to make an independent, voluntary decision. AMA *Informed Consent*. Fifth, and finally, the patient—and,

where the patient is a minor, usually the parents as well—decides how to proceed.

From the perspective of biomedical ethics, a decision that is made by a patient (and, when a minor, jointly with a parent/guardian) through a process of informed consent and that aligns with a provider's recommendations should be fully respected. Indeed, medical professionals and patients are regularly entrusted to together decide the best course of treatment, including when the treatment has significant risks or permanent effects. Pediatric chemotherapy or radiation, for example, are subject to principles of informed consent, despite the potential lasting effects on growth development and reproductive capabilities. *See, e.g.*, Am. Cancer Soc'y, *Late Effects of Childhood Cancer Treatment* (Sept. 18, 2017), https://www.cancer.org/treatment/children-and-cancer/when-your-child-has-cancer/late-effects-of-cancer-treatment.html. Pediatric breast reduction performed to address excess breast tissue, back pain, or social anxiety; pediatric rhinoplasty; and orthopedic surgery on minors following sports injuries likewise can have enduring impacts. There is nothing unique about gender-affirming medical care that justifies denying coverage when the provider, and the patient (and the patient's parents, when a minor) all agree about the best course of action.

By prohibiting health care providers from offering medically necessary and appropriate treatment to patients with gender dysphoria and denying patients the ability to access such care when they have given informed consent, SB1 disregards autonomy and undermines the provider-patient relationship.

B. SB1 Forces Providers to Violate Their Duty of Beneficence.

The duty to act in the best interest of the patient is called beneficence, which is best understood as "a group of norms pertaining to relieving, lessening, or preventing harm and providing benefits and balancing benefits against risks and costs." Beauchamp & Childress at 13; *see also id.* at 217 ("[M]orality requires that we treat persons autonomously and refrain from harming them, but morality also requires that we contribute to their welfare.").[9] Medical professionals in the United States and around the world take oaths and are held to duties that encompass beneficence. The World Medical Association's "Modern Hippocratic Oath" requires physicians to attest upon admission to the medical profession that the "health and well-being of [their] patient[s] will be [their] first consideration." World Medical Association, *Declaration of Geneva* (1948). Likewise, the United Kingdom's General Medical Council *requires medical professionals to "make the care of your patients your first concern." Good medical practice: Duties of medical professionals registered with the [General Medical Council], Gen. Med. Council, at 7 (2024), https://www.gmc-uk.org/-/media/documents/good-medical-practice-2024---english-102607294.pdf.* And the AMA recognizes that "[t]he practice of medicine, and its embodiment in the clinical encounter between a patient and a physician, is fundamentally a moral activity that arises from the imperative to care for patients and to alleviate suffering." AMA, *Code of Medical Ethics*

9. A related principle, nonmaleficence, concerns avoiding the causation of harm. Nonmaleficence thus prohibits action while beneficence requires it. SB1 contravenes both principles.

Opinion 1.1.1, *Patient-Physician Relationships*, https://www.ama-assn.org/system/files/code-of-medical-ethics-chapter-1.pdf.

Applying the principle of beneficence to the treatment of patients with gender dysphoria is straightforward. When untreated, gender dysphoria has serious mental and physical consequences, including anxiety, depression, self-harm, and suicidality. *See, e.g.*, Norman P. Spack et al., *Children and adolescents with gender identity disorder referred to a pediatric medical center*, 129 Pediatrics 418 (2012), https://pubmed.ncbi.nlm.nih.gov/22351896; Kristina R. Olson et al., *Mental health of transgender children who are supported in their identities*, 137 Pediatrics (2016), https://www.transgendertrend.com/wp-content/uploads/2017/10/Olson-2016_gender-affirmation.x45051.pdf; Pet. App. 206a-208a (order finding minor petitioners would suffer "emotional and psychological harms as well as unwanted physical changes if they are deprived [of] access to treatment[.]").

By contrast, evidence from both research and clinical experience makes clear that gender-affirming medical care improves patients' health and alleviates their suffering. *See, e.g.*, *Brandt*, 47 F.4th at 671; *Brandt v. Rutledge*, 551 F. Supp. 3d 882, 891 (E.D. Ark. 2021); Kraschel at 4; Arjee Javellana Restar, *Gender-affirming care is preventative care*, 24 The Lancet Regional Health – Americas (2023) https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(23)00118-7/fulltext. In order to practice beneficence, practitioners must act for the benefit of the patient and promote their welfare. This is not possible when Tennessee denies care to transgender patients. SB1 prohibits providers from administering care

that would relieve their patients' suffering. *See* Pranav Gupta et al., *Exploring the Impact of Legislation Aiming to Ban Gender-Affirming Care on Pediatric Endocrine Providers: A Mixed-Methods Analysis*, 7 Journal of the Endocrine Society 1 (2023), https://doi.org/10.1210/jendso/bvad111 (finding that laws like SB1 may negatively impact the provisioning of pediatric care overall). Withholding care for gender dysphoria thus can result in serious harm to patients, contrary to the core principle of beneficence. Recent articles have highlighted the impact of laws such as SB1 on the wellbeing of transgender adolescents. *See, e.g.*, Roberto L. Abreu et al., *Impact of Gender-Affirming Care Bans on Transgender and Gender Diverse Youth: Parental Figures' Perspective*, 36 J. Family Psychol. 643 (2022), https://pubmed.ncbi.nlm.nih.gov/35324250/ (parents of transgender youth indicating children have experienced "increased negative mental health concerns as a result of passing or introducing" laws such as SB1); Jessie Melina Garcia Gutiérrez et al., *A Narrative Synthesis Review of Legislation Banning Gender-Affirming Care*, 12 Current Pediatrics Reports (2024) (summarizing literature on gender-affirming care bans and adverse impacts of such legislation).

In sum, the principle of beneficence obligates providers to remove conditions that will cause harm to others. Beauchamp & Childress at 219. By mandating that providers deny care to their patients with gender dysphoria when the patient seeks that care and the provider deems it medically indicated, SB1 forces providers to cause harm to their patients and, thus, to violate their core duty of beneficence.

C. SB1 Forces Providers to Violate Their Duty of Justice.

A third core principle of bioethics—justice—requires providers to acknowledge inequalities in the delivery of medical care and to work toward fair, equitable, and appropriate treatment for all. Beauchamp & Childress at 267–68; Clark, *Ethics in Child & Youth Care Practice with Transgender Youth* at 79. SB1 undermines this ethical duty of providers by denying care to a targeted class of patients based on their identity: care is banned if it is for treatment of gender dysphoria, which is care that only transgender individuals seek, but remains available for non-transgender adolescents to treat a variety of other conditions.

For example, SB1, if allowed to go into effect, will force individuals who are transgender to consider moving out of state (leaving behind their schools, jobs, and/or families) or to endure the negative health effects from stopping hormone therapy and to fear for their ability to survive without treatment. *See* Pltfs. Pet. 16-17, 32. These potential costs are on top of the many socioeconomic and geographic barriers to gender-affirming medical care that transgender youth often already face. *See* Phillip E. Wagner et al., *Health (Trans)gressions: Identity and Stigma Management in Trans* Healthcare Support Seeking*, 39 Women & Language 49, 56 (2016), https://adriannekunkel.ku.edu/wp-content/uploads/2015/04/Wagner-Kunkel-Asbury-Soto-2016-1.pdf (noting "[t]he difficult decisions trans* individuals make in regard to their healthcare have been well documented" and include "[f]inancial barriers, insurance issues, and access to services"); Rishub K. Das & Brian C. Drolet, *The True Cost of Antitransgender Legislation*, 8 Trans Gender Health 405 (2023), https://pubmed.ncbi.nlm.nih.gov/37810936/

(discussing economic costs and loss to human capital as a result of antitransgender legislation like SB1). SB1 exacerbates and reinforces these already significant challenges by preventing transgender individuals from accessing the gender-affirming healthcare they require.

Medical practitioners must not cause patients to fear seeking care, nor deny them care that, by definition, only people who are transgender need. SB1 forces health care providers to violate the core biomedical ethics principle of justice by mandating discrimination against a vulnerable and stigmatized population. By prohibiting minors who are transgender from accessing treatment for gender dysphoria simply because they are transgender, SB1 deprives them of their autonomy and signals that they are not worthy of beneficence. Without autonomy and beneficence, only injustice can occur.

As explained above, gender-affirming medical care is rooted in a strong evidentiary base and has been demonstrated to generate positive outcomes for patients struggling with gender dysphoria. *See supra* Section I. But even accepting the State's premise that gender-affirming medical care is "experimental," Tennessee's disparate treatment of gender-affirming medical care compared to other kinds of care that is equally "experimental" under Tennessee's use of that term underscores that SB1 fails to comport with core principles of bioethics.

* * *

SB1 is unsupported by biomedical ethics or any of its core principles. To the contrary, SB1 commands their violation, for no legitimate purpose, resulting in physical and emotional suffering.

CONCLUSION

Gender-affirming medical care, including for minors, is evidence-based, and not experimental as Tennessee contends. Indeed, were this care "experimental" as Tennessee understands that term, it would open the door to unprecedented government intrusion into the practice of medicine and patients' rights across a wide range of common treatments. This Court should reverse the Sixth Circuit's judgment.

Respectfully submitted,

ELIZABETH REINHARDT
COOLEY LLP
1299 Pennsylvania Avenue, NW
Washington, DC 20004

CELENE CHEN
COOLEY LLP
500 Boylston Street
Boston, Massachusetts

KATHLEEN R. HARTNETT
Counsel of Record
ZOË HELSTROM
COOLEY LLP
3 Embarcadero Center
San Francisco, California 94111
(415) 693-2000
khartnett@cooley.com

KATELYN KANG
VALERIA M. PELET DEL TORO
COOLEY LLP
55 Hudson Yards
New York, New York 10001

Counsel for Amici Curiae

APPENDIX

TABLE OF APPENDICES

APPENDIX — LIST OF *AMICI CURIAE*

Daniel G. Aaron
Associate Professor of Law
S.J. Quinney College of Law, University of Utah

George J. Annas
Warren Professor and Director, Center for Health Law, Ethics & Human Rights
Boston University School of Public Health

Julia Zoe Beckerman, JD, MPH
Teaching Professor and Vice Chair, Health Policy and Management
George Washington University Milken Institute School of Public Health

Yael Cannon
Associate Professor of Law
Georgetown University Law Center

Carl H. Coleman
Professor of Law
Seton Hall Law School

David M. Frankford
Professor of Law
Rutgers Law School

Allegra Gordon
Assistant Professor of Community Health Sciences
Boston University School of Public Health

Appendix

Kathleen Hoke
Professor of Law
University of Maryland Carey School of Law

Dana Howard
Assistant Professor
The Ohio State University

Adnan Hyder
Senior Associate Dean for Research
& Professor of Global Health
George Washington University

Taimur Khan
Associate Medical Research Director
Fenway Health / The Fenway Institute

Jeffrey Levi
Professor Emeritus of Health Policy and Management
George Washington University

Sarah Lipson
Associate Professor
Boston University

Maya Manian
Professor of Law
American University Washington College of Law

Marsha Regenstein
Professor of Health Policy
George Washington University Milken
Institute School of Public Health

Appendix

Sara Rosenbaum
Professor Emerita, Health Law and Policy
Milken Institute School of Public Health,
George Washington University

Nadia N. Sawicki
Beazley Co-Chair in Health Law;
Georgia Reithal Professor of Law
Loyola University Chicago School of Law

Naomi Scheinerman
Assistant Professor of Bioethics
The Ohio State University

Michael S. Sinha, MD, JD, MPH
Assistant Professor of Law,
Center for Health Law Studies
Saint Louis University School of Law

Michael R. Ulrich, JD, MPH
Associate Professor of Health Law,
Ethics, & Human Rights
Boston University School of Public Health
& School of Law

Heather Walter-McCabe
Associate Professor
Saint Louis University School of Law