No. 25-1279

IN THE UNITED STATES COURT OF APPEALS
FOR THE FOURTH CIRCUIT

PFLAG, INC., ET AL.,
Plaintiff-Appellees,

v.

DONALD J. TRUMP, IN HIS OFFICIAL CAPACITY AS PRESIDENT OF THE UNITED STATES, ET AL.,
Defendant-Appellants.

On Appeal from the United States District Court
for the District of Maryland (Case No. 25-cv-337-BAH)

BRIEF OF *AMICI CURIAE* CLINICAL PRACTICE GUIDELINE EXPERTS IN SUPPORT OF APPELLEES

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INTEREST OF *AMICI CURIAE*[1]

Amici are clinicians, professors, and researchers with decades of experience at institutions across the country, ranging from Yale University School of Medicine to Stanford Medicine Children's Health. They have expertise in the development and use of clinical practice guidelines across medical specialties in the United States. *Amici* include:

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[1] Pursuant to Fed. R. App. P. 29(a), all parties have consented to the filing of this brief. In addition, pursuant to Fed. R. App. P. 29(a)(4)(E), *amici* represent that no party's counsel authored this brief in whole or in part, no party or party's counsel contributed money that was intended to fund preparing or submitting this brief, and no one other than *Amici Curiae*, their members, or their counsel contributed money intended to fund preparing or submitting this brief.

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Amici submit this brief to address the widely accepted and evidence-based guidelines for the treatment of gender dysphoria, namely the Standards of Care 8 (SOC8).[3] SOC8 is the eighth edition of the Standards of Care, a set of clinical practice guidelines first published in 1979 that aims to promote the highest standards of healthcare for transgender people.[4] The development of SOC8 was sponsored by WPATH, "an international, multidisciplinary, professional association whose mission is to promote evidence-based care, education, research, public policy, and respect in transgender health."[5]

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[2] *Amici* join this brief as individuals; institutional affiliation is noted for informational purposes and does not indicate institutional endorsement.
[3] *See* Eli Coleman, et al., *Standards of Care for the Health of Transgender and Gender Diverse People*, *Version 8*, 23 Int. J. Transgend. Health S1 (2022) ("SOC8").
[4] *Id.* at S3.
[5] *Id.* at S5.

Amici share a significant interest in ensuring that clinical practice guidelines like SOC8 are reliable and evidence-based, and they submit this brief to outline the methodological rigor of SOC8's development process. *Amici* also wish to highlight their concerns about governments disregarding trustworthy guidelines. They are especially troubled by political actors' attempts to discredit SOC8 by citing isolated internal communications made by individuals involved in the development process, often without regard for the overall context, methodology, evidence, and substance of the final guidelines. These unscientific attacks could chill experts from participating in guideline development, especially for highly stigmatized medical interventions. The predictable result is more politicized medicine, less reliable guidelines, less effective clinical practice, and less healthy patients.

SUMMARY OF ARGUMENT

This case concerns two Executive Orders issued by President Trump directing federal agencies to "end the Federal funding of gender ideology"[6] and to "defund[]" the use of puberty blockers and hormones to treat transgender adolescents and young adults with gender dysphoria.[7] In evaluating the lawfulness of the President's orders, the district court recognized that these medical treatments

[6] *Defending Women from Gender Ideology Extremism and Restoring Biological Truth to the Federal Government*, Exec. Order No. 14168 § 3(e), 90 Fed. Reg. 8615 (Jan. 20, 2025) ("EO 14168"); *see also id.* § 3(g).
[7] *Protecting Children from Chemical and Surgical Mutilation*, Exec. Order No. 14187 § 4, 90 Fed. Reg. 8771 (Jan. 28, 2025) ("EO 14187"); *see also id.* §§ 1, 2(c).

are supported by "decades" of clinical experience and scientific research.[8] SOC8 reliably summarizes this evidence, considers relevant clinical factors, and sets forth targeted recommendations for individualized care.[9]

Political actors, including some State *amici* here, have attempted to rationalize banning essential healthcare for transgender adolescents by looking outside the scientific evidence and attacking the process used to develop SOC8.[10] Their critiques lack merit. The process for developing SOC8 was iterative, methodologically sound, and met or exceeded the developmental rigor of clinical practice guidelines produced in the United States. The process included a multidisciplinary committee of 119 leading clinicians and academics, an independent guideline methodologist, systematic evidence reviews conducted by an independent team from Johns Hopkins University, an evaluation of dozens of preexisting systematic evidence reviews on a wide range of issues, and a structured process for achieving consensus on treatment recommendations. The SOC8 chapter dedicated exclusively to adolescents flowed from this rigorous process and made

[8] *PFLAG, Inc. v. Trump*, 769 F. Supp. 3d 405, 448 (D. Md. 2025) (quoting *Washington v. Trump*, 768 F. Supp. 3d 1239, 1274 (W.D. Wa. 2025)).
[9] *See generally* SOC8 at S43–66 (adolescent chapter), S110–27 (hormone therapy chapter).
[10] Brief of the States of Alabama et al. as *Amici Curiae*, *PFLAG, Inc. v. Trump*, No. 25-1279 (4th Cir.), ECF No. 40 (Aug. 1, 2025).

targeted recommendations based on data that, "as a whole," consistently show "early medical intervention . . . can be effective and helpful for many."[11]

The critiques of SOC8 made by some State *amici* misunderstand fundamental principles of evidence-based medicine. Accepting those critiques could undermine thousands of clinical guidelines on all kinds of medical interventions—from vaccines to pediatric critical care and more. The result: an increased politicization of medical guidelines, as illustrated by a recent report issued by the U.S. Department of Health & Human Services at the direction of the President; less evidence-based clinical practice; and lower-quality patient care.

[11] SOC8 at S47; *see also id.* at S112, S126 (reviewing additional consistent evidence).

ARGUMENT

I. Reliable clinical practice guidelines are essential to high-quality healthcare.

Every day, clinicians make complex decisions about the best treatments for their patients. In weighing treatment options, they must assess the evidence along with recommendations from subject-matter experts. And they must apply their individual clinical experience in light of that evidence.[12] This requires determining the likely risks and benefits of treatment for a particular patient, given the evidence and the patient's overall health, co-occurring conditions, values, preferences, and life circumstances.[13]

But clinicians cannot analyze every new development in the scientific literature. Every year, more than 30,000 scientific journals publish about 2 million biomedical research papers.[14] "An internist would have to read 33 articles 365 days a year to stay up to date."[15] Given the need to also critically analyze each individual article, clinicians are "at an increasing risk of drowning in doubtful data."[16] Thus, "[c]ritically appraised, synthesized information such as systematic

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[12] Institute of Medicine, *Clinical Practice Guidelines We Can Trust* 15 (Robin Graham et al. eds., 2011) ("Institute of Medicine Guidelines").
[13] *Id.* at ix.
[14] Jeffrey S. Flier, *Publishing Biomedical Research: A Rapidly Evolving Ecosystem*, 66 Perspect. Biol. & Med. 358, 363 (2023).
[15] Institute of Medicine Guidelines at 34 (citing D.L. Sackett, *Clinical Epidemiology: What, Who, and Whither,* 55 J. Clin. Epidemiol. 1163 (2002)).
[16] *Id.* (quoting Sackett, *Clinical Epidemiology*, *supra* note 15, at 1164).

reviews and [clinical practice guidelines]" have become "necessary tools for clinicians."[17]

Clinical practice guidelines evaluate and synthesize the best available evidence for treating certain medical conditions, incorporate practical knowledge provided by subject-matter experts, and weigh other factors likely to affect patient care to formulate recommendations for treatment.[18] This gives clinicians access to current, evidence-based, practical guidance they can explain to patients and apply in conjunction with their own clinical expertise.[19]

Clinical practice guidelines also reduce unnecessary variability and uncertainty in medical decision-making, which improves individual patient outcomes as well as overall healthcare quality.[20] These guidelines can be used as tools for evaluating the performance of healthcare providers, improving healthcare systems, and educating the public.[21] Given their potential to enhance patient care and public health, clinical practice guidelines have become "ubiquitous in our healthcare system."[22]

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[17] *Id*.
[18] *Id*. at 1–2.
[19] *Id*. at 15.
[20] *Id*. at xi, 65.
[21] *Id*. at 26–27.
[22] *Id*. at 2.

II. WPATH's Standards of Care 8 are reliable clinical practice guidelines.

A. SOC8 complies with best practices for guideline development.

In 2011, the Institute of Medicine of the National Academies, now known as the National Academy of Medicine, "published recommendations for trustworthy guidelines, effectively setting the 'gold standard' for what constitutes a high-quality guideline."[23] Although there are several ways to develop reliable guidelines,[24] the most trustworthy ones share the following characteristics:

a) They transparently disclose funding sources and explain the development process;[25]

b) They are developed by a multidisciplinary team including patient representatives, clinicians, subject-matter experts, and one or more methodological experts;[26]

c) They require members to disclose conflicts of interest and, if necessary, take steps to manage significant conflicts;[27]

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[23] Colin R. Cooke, et al., *Advancing Clinical Practice and Policy Through Guidelines: The Role of the American Thoracic Society*, 182 Am. J. Respir. Crit. Care Med. 910, 910 (2013).
[24] Institute of Medicine Guidelines at 68.
[25] *Id.* at 76–78.
[26] *Id.* at 93.
[27] *Id.* at 82–83.

d) Their recommendations are informed by systematic reviews of scientific literature and clinical experience;[28]

e) Their recommendations are approved by a consensus of members;[29]

f) They indicate the strength of their recommendations;[30]

g) They summarize the nature, quality, quantity, and consistency of the evidence concerning recommended treatments;[31]

h) They explain the risks and benefits of recommended treatments and specify the role played by patient preferences, values (including human rights and healthcare inequities), expert opinion, and clinical experience in developing each recommendation;[32] and

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[28] *Id.* at 97. "A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimizing bias, thus providing more reliable findings from which conclusion can be drawn and decisions made." Toby J. Lasserson, et al., *Chapter 1: Starting a Review*, *in* Cochrane Handbook for Systematic Reviews of Interventions (Julian Higgins, et al., eds., 2023), https://www.cochrane.org/authors/handbooks-and-manuals/handbook/current/chapter-01; *see also* Institute of Medicine Guidelines at 96.

[29] Institute of Medicine Guidelines at 86–87.

[30] *See id.* at 5.

[31] *Id.* at 124-125.

[32] *Id.* at 67.

i) They are updated periodically or when new evidence suggests a need for revision.[33]

SOC8 meets these criteria, as set forth below.[34]

Funding, Methodology, Membership, and Conflicts of Interest: SOC8 provides a detailed description of its development process[35] and discloses funders in the text of the document.[36] It was developed by a diverse team of 119 subject-matter experts, healthcare professionals, researchers, and stakeholders, each of whom applied to participate and completed conflict of interest declarations.[37]

Guideline Methodologist, Evidence Review Team, and Systematic Reviews: A guideline methodologist and Evidence Review Team from Johns Hopkins University—one of the top medical research universities in the United States—assisted with planning and executing systematic reviews for SOC8.[38] The Evidence Review Team collaborated with SOC8 members to develop review questions,[39] conducted systematic reviews, and presented the results, including evidence tables, to the members of each relevant chapter.[40] In addition to these

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[33] *Id.* at 6–9, 26.
[34] This analysis is based on SOC8's description of its methodology. *See* SOC8 at S247–51. *Amici* did not participate in developing SOC8.
[35] *Id.*
[36] *Id.* at S177.
[37] *Id.* at S249.
[38] *Id.* at S247, 49.
[39] *Id.* at S249–50.
[40] *Id.* at S248.

systematic reviews, the final version of SOC8 relied on evidence from dozens of prior systematic reviews on a huge range of topics.[41]

Development and Grading of Recommendations: The recommendations in SOC8 were based on newly-conducted systematic reviews in addition to existing evidence reviews, expert opinion, and clinical experience.[42] Consensus on recommendations was achieved through a widely used tool known as the Delphi process, which encouraged rigorous debate through three rounds of structured feedback and required approval of at least 75 percent of voting members for each recommendation.[43]

Once recommendation statements passed the Delphi process, chapter members rated the strength of each statement using a process adapted from GRADE.[44] SOC8 used the phrase "we recommend" for a strong recommendation

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[41] *See, e.g.*, *id.* at S120–21, S123–24, S126, S148, S153, S182, S190, S193, S201, S215, S218, S220, S229–30, S233, S242–43.
[42] *Id.* at S250.
[43] *Id.*
[44] *Id.* GRADE stands for "Grades of Recommendation, Assessment, Development, and Evaluation." Its evidence rating framework assesses the statistical degree of certainty that a particular treatment will have its intended effect. *See* World Health Organization, *Handbook for Guideline Development* 110 (2d ed. 2014) ("WHO Handbook"). Guideline developers are not required to strictly adhere to GRADE and may exercise discretion in establishing systems for evaluating the strength of recommendations. *See* Institute of Medicine Guidelines at 116 (recommending only that guideline developers "adopt[] systematic methods for rating quality of evidence and strength of recommendations").

and "we suggest" for a weak recommendation.[45] The recommendation strength considered the "balance of potential benefits and harms," "confidence in that balance or quality of evidence," "values and preferences of providers and patients," and "resource use and feasibility."[46] Scientific literature and expert clinical experience were considered in determining the strength of each recommendation.[47]

Strong recommendations were made where one or more of several conditions were met: "the evidence is of high quality"; "estimates of the effect of an intervention/therapy/strategy (i.e., there is a high degree of certainty effects will be achieved in practice)"; "there are few downsides of therapy/intervention/strategy"; and "there is a high degree of acceptance among providers and patients or those for whom the recommendation applies."[48]

Explanation of Evidence and Recommendations: In explanatory text validated by independent reviewers,[49] SOC8 details potential risks and benefits associated with recommended interventions, explaining the available evidence as well as gaps in the literature and areas of uncertainty. In addition, the explanatory text provides guidance for implementing recommendations and acknowledges the

[45] SOC8 at S250.
[46] *Id.*
[47] *Id.*
[48] *Id.*
[49] *Id.* at S251.

values, human rights perspectives, patient preferences, and practical considerations that influenced the recommendations.[50]

For example, in evaluating the evidence supporting puberty blockers and hormone therapy for transgender adolescents, SOC8 walks through the relevant research, including at least one systematic review and numerous primary studies, which consistently demonstrate that puberty blockers and hormones are associated with improved psychological functioning and quality of life,[51] reduced depression and anxiety,[52] and reduced suicidal ideation and suicide risk.[53] This evidence provides ample support for SOC8's conclusion that the "emerging evidence base indicates a general improvement in the lives of transgender adolescents who, following careful assessment, receive medically necessary gender-affirming medical treatment."[54] SOC8 also addresses potential risks of treatment, including the possibility of regret and potential effects on fertility and sexual health outcomes.[55]

Weighing the best available evidence regarding risks and benefits, SOC8 recommends that physicians only prescribe puberty blockers or hormones to a

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[50] *See, e.g.*, *id.* at S43–66 (adolescent chapter).
[51] *Id.* at S46, S112, S126.
[52] *Id.* at S46.
[53] *Id.* at S126.
[54] *Id.* at S47.
[55] *Id.* at S47, S57, S61, 64, S118–19, S156–60.

transgender adolescent when, among other things, the adolescent has reached puberty; they have undergone a careful assessment that confirms their persistent gender dysphoria; they have the emotional and cognitive maturity necessary to assent; and their parents give informed consent.[56] Given "the emerging nature of knowledge regarding adolescent gender identity development," SOC8 emphasizes that "an individualized approach to clinical care is both ethical and necessary."[57] As in all areas of medicine, "each study has methodological limitations, and conclusions drawn from research cannot and should not be universally applied to all adolescents."[58]

SOC8 also specifies that "adolescents, their parents, and care providers should be informed about the nature of the evidence base,"[59] consistent with the Institute of Medicine's recommendations on informed consent: "Rather than dictating a one-size-fits-all approach to patient care," guidelines "should aid clinician and patient decision making by clearly describing and appraising the evidence and reasoning regarding the likely benefits and harms related to specific clinical recommendations."[60]

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[56] *Id.* at S48–49, S56, S59–64.
[57] *Id.* at S45.
[58] *Id.*
[59] *Id.* at S46.
[60] Institute of Medicine Guidelines at 16.

Comment Period, Revisions, Publication, and Plan for Updating: After consensus was reached on recommendations and explanatory text was approved, an international advisory committee and the public were given opportunities to provide feedback,[61] which led to a second Delphi process and another round of reference checks.[62] After these steps were completed, SOC8 was published, along with a plan to issue a new edition when new evidence or other changes in the field made revisions necessary.[63]

In sum, the process for developing SOC8 was transparent, rigorous, and methodologically sound. Its findings regarding transgender adolescent healthcare are consistent with those of other clinical practice guidelines in the field.[64] The reliability of these consistent findings was recently confirmed by an independent systematic review ordered by the Utah State Legislature in connection with a bill banning medical treatments for transgender adolescents.[65] The resulting report, prepared by independent pharmacy and medical experts at the University of Utah,

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[61] To understand the benefits of public comment on draft guidelines, see *id.* at 91.
[62] SOC8 at S251.
[63] *Id*.
[64] *See* Wylie C. Hembree, et al., *Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline*, 102 J. Clin. Endocrinol. Metab. 3869 (2017).
[65] Transgender Medical Treatments and Procedures, S.B. 16, 65th Leg., Gen. Sess. § 1(4) (Utah 2023). The bill contained a narrow continued-care exception. *Id.* § 3(2)(b).

was exhaustive, totaling over 1,000 pages.[66] The report concluded based on the evidence that puberty blockers and hormones are safe and effective treatments for gender dysphoria in adolescents[67] that are associated with a reduced risk of suicide;[68] and that there is "virtually no regret associated with receiving the treatments, even in the very small percentages of patients who ultimately discontinued them."[69] It also found that the evidence supporting these treatments "exceeds the amount of evidence that often serves as the basis of FDA approval for many high-risk, new drugs approved in pediatric populations."[70] These objective findings independently validate SOC8's assessment that medical treatments for gender dysphoria are beneficial for transgender adolescents in appropriate cases.

B. Methodological critiques of SOC8 are misplaced and, if accepted, could undermine many other guidelines.

States that ban transgender adolescent healthcare have tried to discredit SOC8 by pointing to alleged methodological flaws. These attacks lack scientific validity and ignore practical realities of guideline development. SOC8's development process was at least as rigorous as the process typical for clinical

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[66] Joanne LaFleur, et al., *Gender-Affirming Medical Treatment for Pediatric Patients with Gender Dysphoria*, University of Utah College of Pharmacy (Aug. 6, 2024), https://le.utah.gov/AgencyRP/reportingDetail.jsp?rid=636 ("Utah Report").
[67] *Id.* at 90.
[68] *Id.* at 914.
[69] *Id.* at 91. Reasons for the rare instances of discontinuation were varied, with a change in gender identity being a "very minor proportion." *Id.*
[70] *Id.* at 4.

practice guidelines in the United States. Giving credence to these kinds of critiques would cast doubt on most guidelines used every day nationwide. We address their criticisms in turn.

Use of Systematic Reviews: Some states have criticized SOC8 for failing to conduct additional systematic reviews, suggesting a separate review was necessary to support every recommendation.[71] But SOC8 undertook a "separate detailed systematic review protocol . . . for each review question or topic, as appropriate."[72] The guideline methodologist and Evidence Review Team guided SOC8 members in determining which questions were eligible for systematic review.[73] In addition, SOC8 considered dozens of preexisting systematic reviews on a huge range of topics, including the effects of puberty blockers and hormones on cardiovascular function, bone health, anxiety, depression, and psychosocial functioning.[74]

SOC8 acknowledges that some questions were not selected for systematic review. For example, the chapter on adolescent care explicitly relies on a narrative review of evidence rather than a systematic review.[75] While noting the limitations of the evidence base, the chapter found that "as a whole," the data show that

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[71] *See, e.g.*, Brief of Alabama as *Amicus Curiae* Supporting Respondents, *United States v. Skrmetti*, Nos. 23-466, 23-477, 23-492 (U.S. Feb. 2, 2024), at 11.
[72] SOC8 at S249.
[73] *See id.*
[74] *See* note 41.
[75] *Id.* at S46.

puberty blockers and hormone therapy can be "effective and helpful for many transgender adolescents."[76] That chapter then offers targeted recommendations supported by the literature and approved by a consensus of experts through a rigorous Delphi process.[77] Those recommendations also find support in a later chapter devoted to hormone therapy, which found based on a "thorough review of evidence" that puberty blockers and hormones benefit adolescents with gender dysphoria.[78]

The degree of evidence underlying SOC8's recommendations for adolescent care is typical of many clinical practice guidelines. While in theory it might be ideal for every aspect of a guideline to be directly supported by a systematic review, in practice this is extraordinarily rare if not impossible.[79] If courts permit political actors to target transgender healthcare simply because SOC8 lacks a

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[76] *Id.* at S47.
[77] *Id.* at S49-66. Experts participating in a Delphi process may rely on various sources of information and evidence, including their own clinical expertise, systematic reviews, observational studies, and any other relevant evidence.
[78] *See* SOC8 at S112, S126.
[79] *See, e.g.,* Benjamin A. Lipsky, et al., *2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections*, 54 Clin. Infect. Dis. e132, e160 (describing why reliance on clinical experience is necessary for some recommendations related to wound care); Shiveindra Jeyamchan, et al., *Athletes returning to play after cervical spine or neurobrachial injury*, 1 Curr. Rev. Musculoskelet. Med. 175, 177 (2008) (recognizing "the difficulty in accruing a sound body of evidence" on some topics).

systematic review for every single recommendation, that will cast doubt on countless medical treatments that are similarly situated.

Evidence quality: Some State *amici* criticize SOC8 for relying on so-called "low quality" evidence for some recommendations. But almost all clinical practice guidelines use this common and scientifically valid practice. In the medical research context, "low quality" is a technical term referring to a rating under a methodological framework known as GRADE. Evidence ratings under GRADE assess the statistical degree of certainty that a particular treatment will have its intended effect.[80] In general, GRADE categorizes randomized controlled trials as "high quality" evidence and nonrandomized trials and observational studies as "low quality."[81]

In many clinical domains, including pediatrics, "there is little or no high-quality evidence."[82] Further, in many settings, observational studies may be more

[80] WHO Handbook at 110.
[81] *Id.* at 112.
[82] Institute of Medicine Guidelines at 26; *see also* WHO Handbook at 112-13; Meredithe McNamara, et al., *An Evidence-Based Critique of "The Cass Review" on Gender-Affirming Care for Adolescent Gender Dysphoria*, at 11-14 (2024) (estimating that less than one in seven systematic reviews across numerous medical specialties reported high-quality evidence for a primary outcome); Michael L. Groff, et al., *Publication Trends of Pediatric and Adult Randomized Controlled Trials in General Medical Journals, 2005-2018: A Citation Analysis*, 7 Children (Basel) 293 (2020) (noting a persistent "paucity" of randomized controlled trials in pediatrics).

valuable than randomized controlled trials[83] as indicators of "effectiveness in real-world practice."[84] Thus, GRADE's emphasis on randomized controlled trials "often results in . . . inappropriately low grades" for recommendations.[85]

Ethical constraints on randomized controlled trials also impose an important practical limit on the availability of "high quality" evidence. Randomized controlled trials are ethical only if there is "clinical equipoise," or "a state of genuine uncertainty . . . regarding the comparative therapeutic merits of each arm in a trial."[86] Clinical equipoise does not exist in the context of transgender adolescent healthcare. As outlined above, the evidence consistently shows medical treatment is beneficial for adolescents with gender dysphoria. It would be unethical to withhold these treatments from patients for the sake of maintaining a control or placebo group.[87] Accordingly, these treatments may never be supported by "high quality" evidence from randomized controlled trials.

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[83] Jizzo R. Bosdriesz, et al., *Evidence-based medicine—When observational studies are better than randomized controlled trials*, Nephrology (Carlton), 25, at 737–43 (2020).
[84] Cooke, *supra* note 23, at 910–14.
[85] Adrian Baker, et al., *A review of grading systems for evidence based guidelines produced by medical specialties*, 10 Clin. Med. (Lond.), at 358 (2010).
[86] Benjamin Freedman, *Equipoise and the Ethics of Clinical Research*, 317 N. Engl. J. Med. 3 (1987).
[87] Florence Ashley, et al., *Randomized-controlled trials are methodologically inappropriate in adolescent transgender healthcare*, 25 Int. J. Transgend. Health No. 3, 407–18 (2024).

Further, clinical practice guidelines can, and often do, make strong treatment recommendations based on so-called "low quality" evidence.[88] For example, about 55.4 percent of strong recommendations issued by the World Health Organization from 2007 to 2012 were supported by "low quality" evidence.[89] That is because, as the GRADE system makes clear, the evidence rating is only one factor affecting the strength of a recommendation.[90] Other factors include the quantity and consistency of available evidence, the degree and strength of expert consensus, patient preferences, and value judgments regarding the relative importance of different effects of treatment.[91] These factors are considered at the recommendation stage to account for the different purposes of medical research and clinical medicine.[92]

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[88] *See, e.g.*, Lipsky et al., *supra* note 79, at e139–140.

[89] Paul E. Alexander, et al., *World Health Organization recommendations are often strong based on low confidence in effect estimates*, 67 J. Clin. Epidemiol. No. 6, at 629–34, n.120 (2014).

[90] Institute of Medicine Guidelines at 110; *see also* Holger J. Schünemann, et al., *Improving the use of research evidence in guideline development: 1. Guidelines for guidelines*, 4 Health Rsch. Pol'y and Sys. 21 (2006). Thus, many guidelines do not show the GRADE evidence ratings for each recommendation; SOC8 is not an outlier for choosing not to publish these ratings. *See, e.g.*, Jeyamchan et al., *supra* note 79, at 175; Lipsky et al., *supra* note 79, at 54.

[91] Institute of Medicine Guidelines at 110 (quantity and consistency of evidence, value judgments); *id.* at 111 (patient preferences and value judgments); *id.* at 113 (guidelines can make a strong recommendation on low quality evidence if the guideline development group reaches expert consensus that benefits outweigh harms).

[92] While the goal of research is to "contribute to generalizable knowledge" by making objective findings that can be replicated, clinical practice is intended

Rejecting SOC8's recommendations simply because they do not rely on "high quality" evidence would severely undermine other clinical practice guidelines and lead to less effective patient care across specialties. "If high-quality evidence were a prerequisite for medical care, we would all become worse off."[93] That is especially true in pediatrics, where clinicians often "begin with a dearth of evidence and yet must deliver care to a heterogeneous population in need."[94] Although "[t]he quest for longer and more data is never-ending," when high-certainty evidence is not available, patients are not required to "wait for a cure."[95]

Dr. Gordon Guyatt, a professor and evidence-based medicine expert who played a key role in developing GRADE, recently issued a statement with colleagues reaffirming the importance of providing competent medical care to transgender adolescents and emphasizing that the absence of "high quality" evidence does not justify banning medical treatment for gender dysphoria:

> Following fundamental principles of humane medical practice, clinicians have an obligation to care for those in need, often in the context of shared decision making. **It is unconscionable to forbid clinicians from delivering gender-affirming care**. . . .

"solely to enhance the well-being of an individual patient," which requires a thorough assessment of the patient's circumstances and a careful consideration of subjective factors. *See* U.S. Dep't of Health & Hum. Servs., *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* 3 (1979).

[93] McNamara, *supra* note 82, at 11.

[94] *Id.* at 14.

[95] *Id.* at 15.

> **It is profoundly misguided to cast health care based on low-certainty evidence as bad care or as care driven by ideology, and low-certainty evidence as bad science.** Many of the interventions we offer are based on low certainty evidence, and enlightened individuals often legitimately and wisely choose such interventions.
>
> Thus, **forbidding delivery of gender-affirming care and limiting medical management options on the basis of low certainty evidence is a clear violation of the principles of evidence-based shared decision-making and is unconscionable.** The appropriate use of our work is in ensuring patients receive needed care and in helping [transgender] patients and their clinicians in decision making.[96]

Conflicts of Interest: Contrary to the contentions of some State *amici*, SOC8 also adhered to established standards in identifying and managing conflicts of interest. Everyone involved in developing SOC8 was required to declare conflicts of interest.[97] No conflicts were found to be significant or consequential.[98] Critics erroneously argue that SOC8 members were conflicted and should have been excluded because they were already WPATH members and because a substantial proportion of their income was derived from providing gender transition care. These contentions do not hold water.

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[96] Gordon Guyatt et al., *Systematic reviews related to gender-affirming care*, McMaster Univ. Dep't of Health Rsch. Methods, Evidence, and Impact (Aug. 14, 2025), https://hei.healthsci.mcmaster.ca/systematic-reviews-related-to-gender-affirming-care/ (emphasis added).
[97] SOC8 at S249.
[98] *Id*. at S177.

First, medical societies routinely restrict guideline development group membership to their own members,[99] and any potential conflict of interest in SOC8 was appropriately managed through public disclosure.[100] *Second*, concerns about financial conflicts typically arise from members' ties to commercial sectors such as the pharmaceutical industry, not from clinical practice.[101] Guideline development groups are often comprised of practicing clinicians who are involved in providing the treatment in question. Excluding their perspectives would severely undercut or even negate the utility of the guideline. Clinicians bring essential insight into how treatments function in practice, helping to ensure that clinical guidelines reflect both the evidence base and the practical realities of patient care. Without their input, research findings risk being misinterpreted in ways that overlook important clinical context. Thus, potential financial conflicts based on clinical income are unavoidable and insignificant.[102] And, in any event, such potential conflicts were

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[99] Institute of Medicine Guidelines at 38.
[100] SOC8 at S249.
[101] Institute of Medicine Guidelines at 61–62.
[102] "Individuals selected for their technical expertise in a guideline's subject area are critically important" and should be included along with other members with "a range of expertise and institutional and professional affiliations." WHO Handbook at 26; *see also id.* at 67 ("conflicts of interest represent a spectrum; they are not absolute situations"); *id.* at 67–69 (listing substantial ties to industry—and not clinical practice—as conflicts of interest that must be managed "at the individual level" through exclusion or other means, indicating that potential financial conflicts from clinical practice do not require exclusion and can be managed at the group level); Institute of Medicine Guidelines at 80 (focusing on concerns raised by financial ties to commercial entities, including "pharmaceutical and medical

adequately managed here through the selection of a multidisciplinary guideline development group and the disclosure of all SOC8 members' names and affiliations.[103]

Internal Communications: Some State *amici* have also sought to undermine SOC8 by highlighting certain internal deliberations relating to some aspects of the SOC8 development process. Of course, deliberations are not scientific evidence, and there is nothing remarkable about SOC8 members communicating about the relevant literature and their clinical experience.

Any objective evaluation of SOC8's trustworthiness must begin with its 190 pages of text and 68 pages of references and must end well short of any speculation

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device companies," while noting that clinicians "may provide valuable insight" and "may simply be without substitutes").

[103] *See* SOC8 at S1–S2 (names and affiliations of all members); World Pro. Ass'n for Transgender Health, *SOC8 Contributors* (July 26, 2021), https://wpath.org/wp-content/uploads/2024/11/SOC8-Full-Contributor-List-FINAL-UPDATED-09232021.pdf (last visited Sept. 18, 2025) (biographies of all members); WHO Handbook at 70 (physician groups "tend to recommend procedures that they personally deliver, whereas multidisciplinary groups tend to be more conservative in their recommendations"). To the extent critics suggest some SOC8 members should have been disqualified due to non-financial or intellectual conflicts of interest, those potential conflicts were also adequately managed through the selection of a diverse multidisciplinary team and the use of an independent methodologist and Evidence Review Team to conduct literature reviews. *See* SOC8 at S247, S249; *see also* WHO Handbook at 72 (a methodologist "help[s] to mitigate the effects of intellectual conflicts of interest"); *id.* at 65 (subject-matter experts with intellectual conflicts may be "deemed essential," and these conflicts can be managed if "members with diverse perspectives and experiences" are included in the guideline development group).

about SOC8 members' states of mind. To help users "determine the level of confidence they should have in any individual recommendation," guidelines should include an "explicit statement of how evidence, expertise, and values were weighed."[104] SOC8 meets or exceeds this standard. It describes SOC8's rigorous and iterative weighing process in detail. Scrutinizing what a few SOC8 members wrote in emails says nothing about the reliability of the final guidelines. Indeed, statements cherry-picked from thousands of pages of correspondence are irrelevant given that the medical literature consistently supports SOC8's recommendations on adolescent care.

Inspecting internal communications for evidence of bias is also unwise for another reason. Understanding the meaning and context of each communication often requires medical expertise, intimate familiarity with the guideline development process, and a comprehensive understanding of the timing, nature, and purpose of the communication as related to that process. To evaluate the significance of a communication, courts would also have to consider other communications expressing different perspectives; attempt to determine the relative weight each perspective was given at each stage of the process; and extrapolate whether and how the communication influenced the final guideline recommendations. The diversity of perspectives represented in SOC8's

[104] Institute of Medicine Guidelines at 77.

membership and the sheer volume of communications exchanged during its development make this next to impossible. Assessments of guideline development processes are better left to scientific experts using objective measures.

Relying on internal communications is also contrary to a fundamental assumption built into guideline development processes: experts and clinicians must be free to advocate for access to medically necessary, evidence-backed healthcare without fear that their written communications will be taken out of context and misused in court to harm the patients they have dedicated their careers to serving. The Institute of Medicine Guidelines recognize that excessive transparency may be counterproductive: "The desire to have public access to [guideline development group] deliberations and documents must be balanced with resource and time constraints as well as the need for [group] members to engage in frank discussion."[105] If SOC8 members' internal communications are used to justify laws banning or restricting access to recommended treatments, members of guideline development groups across medical specialties may be fearful of engaging in the candid, uninhibited dialogue that is necessary to produce reliable guidelines. They will likely communicate less, and less freely—especially if they are involved in studying or providing a highly stigmatized form of healthcare. Subject-matter

[105] *Id.* at 76.

experts could even be deterred from volunteering to develop future clinical practice guidelines altogether.

In sum, rejecting an otherwise valid guideline based on isolated internal communications would chill the development of reliable clinical practice guidelines, to the detriment of providers, patients, and our entire healthcare system.

III. The "Review of Evidence and Best Practices" by the U.S. Department of Health and Human Services represents a shift away from science and toward politicized medicine.

On May 1, 2025, at the direction of President Trump, the U.S. Department of Health and Human Services published a report entitled "Treatment for Pediatric Gender Dysphoria Review of Evidence and Best Practices." The HHS Report repudiates SOC8 and purports to "provide the most accurate and current information available regarding the evidence base for the treatment of gender dysphoria" in adolescents.[106] In truth, the HHS Report ignores SOC8's rigorous methodology, suffers from serious risks of bias, and cannot be considered reliable.

To start, the HHS Report explicitly disclaims that it is a clinical practice guideline and acknowledges that it was not developed according to recognized guideline development procedures.[107] By the report's own admission, it lacks the

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[106] U.S. Dep't of Health & Hum. Servs., *Treatment for Pediatric Gender Dysphoria: Review of Evidence and Best Practices*, at 10 (May 1, 2025), https://opa.hhs.gov/sites/default/files/2025-05/gender-dysphoria-report.pdf ("HHS Report").

[107] *Id*. at 261.

methodological rigor required to produce reliable clinical guidance.[108] For that reason alone, it should not be used to craft healthcare policy or to determine the appropriateness of treatment in individual cases.

Beyond this fundamental limitation, the HHS Report suffers from significant methodological deficiencies. Most alarming, the report was ordered by the President in connection with an executive order directing the Secretary of HHS to "take all appropriate actions to end" the use of medications to treat gender dysphoria in adolescents.[109] The report must be understood in the context of that order, along with the federal government's broader effort to restrict rights and healthcare access for transgender people.[110] The HHS Report was also completed in just a few months—an extraordinarily compressed period for publishing a systematic review on this topic.[111] And it was published without disclosing its authors, preventing any meaningful assessment of expertise, bias, or conflicts of

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[108] *Id.*

[109] EO 14187, § 3(ii) ("[W]ithin 90 days of the date of this order, the Secretary of Health and Human Services . . . shall publish a review of the existing literature on best practices for promoting the health of children who assert gender dysphoria, rapid-onset gender dysphoria, or other identity-based confusion.").

[110] *See, e.g.*, EO 14168 (stripping legal rights and healthcare funding for transgender people); Exec. Order No. 14183, 90 Fed. Reg. 8757 (Jan. 27, 2025) (banning transgender people from the military); Exec. Order No. 14201, 90 Fed. Reg. 9279 (Feb. 5, 2025) (banning transgender women and girls from sports).

[111] *See* EO 14187 (published on January 28, 2025); HHS Report (published on May 1, 2025). By contrast, the Utah Report took more than a year to develop, and SOC8 more than five years. *See* Utah Report at i (dated August 6, 2024, more than a year after the passage of S.B. 16 on January 28, 2023); SOC8 at S247.

interest.[112] All these factors, along with other methodological defects,[113] raise the possibility that the HHS Report's findings were predetermined by executive fiat.[114]

The HHS Report does not provide a reliable assessment of the evidence supporting medical treatments for transgender adolescents. Its publication signals a turn away from objective scientific inquiry and toward politicized medicine, which is likely to harm patients and compromise public health in the United States.

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[112] Institute of Medicine Guidelines at 76 (transparency is an indicator of reliability that, at a minimum, requires disclosure of information that allows users to "understand how recommendations were derived and *who developed them*" (emphasis added)).

[113] *See id.* at 342–45.

[114] *See* Nadia Dowshen et al., *A Critical Scientific Appraisal of the Health and Human Services Report on Pediatric Gender Dysphoria*, 77 J. Adolesc. Health 342, 343 (2025).

CONCLUSION

SOC8 is a set of reliable and evidence-based clinical practice guidelines that were developed through a rigorous process. The methodological critiques of SOC8 offered by some State *amici* are not grounded in science. Accepting those critiques would chill the development of reliable guidelines, which could mean less guidance for clinicians; worse patient outcomes; and diminished public health.

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limits in Fed. R. App. P. 29(a)(5) because it contains 6,478 words, according to the word count function of Microsoft Word for Office 365, excluding the parts of the document exempted by Fed. R. App. P. 32(f).

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/s/ Mary Rohmiller
Mary Rohmiller

CERTIFICATE OF SERVICE

I hereby certify that on September 26, 2025, I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the Fourth Circuit using the Court's CM/ECF system. I certify that all participants in the case are registered CM/ECF users and that service will be accomplished by the CM/ECF system.

/s/ Mary Rohmiller
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