

July 5, 2024

Dear Drs [REDACTED]

We are writing in response to the World Health Organization's (WHO) [most recent request](#) for comment on updated plans for the guidelines on the health of trans and gender diverse (TGD) people. The mission of the Society for Evidence-Based Gender Medicine (SEGM) is to foster scientific discourse and apply the rigor of evidence-based medicine (EBM) to the field of youth gender medicine. Young TGD people are within the scope of the upcoming guidelines, and we remain concerned about WHO's guideline development process, which, if continued as planned, is poised to produce guidelines that are not trustworthy.

To date, we have submitted two letters of concern to WHO (8 January and 2 February 2024) in which we outlined two major sets of problems in the TGD guideline development process. Our January letter discussed the conflicts of interest (COI) in the Guideline Development Group (GDG), which biased the GDG towards the view that cross-sex hormones should be widely accessible to all those who want them. Our February letter questioned the process by which WHO had arrived at its decision not to review the evidence for benefits and harms of cross-sex hormones, instead choosing to focus on how to best promote widespread access and availability of hormones. Our concerns were supported by over 100 clinicians and researchers from 19 countries, all of whom focus on questions of transgender health, and many of whom are renowned experts in this contentious area of medicine.

In this letter, we briefly revisit our prior concerns, which remain unaddressed, and we also bring to your attention a new development. A series of recent lawsuits in the U.S. revealed that the World Professional Association for Transgender Health (WPATH) engaged in deeply problematic suppression of evidence related to medical care for TGD people in their own guideline development process for "Standards of Care 8" (SOC8).<sup>1</sup> The fact that two senior WPATH officials, directly implicated in this scientific scandal, are also part of the WHO Guideline Development Group

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<sup>1</sup> Research into Trans Medicine Has Been Manipulated. (2024, June 27). *The Economist*.  
<https://www.economist.com/united-states/2024/06/27/research-into-trans-medicine-has-been-manipulated>.



(GDG) tasked with decision-making about the evidence for TGD populations<sup>2</sup> is very disturbing. The fact that at least ten of the GDG members are WPATH members, and most others are vocal supporters of WPATH's biased positions, makes the current GDG, and the entire process excessively rooted in political activism rather than science and medicine. It is hard to see how proceeding as planned could result in a guideline that would be considered credible by clinical practice guideline (CPG) users worldwide.

We call on WHO to disband the current GDG and revisit the guideline scope and methods, ensuring that WHO adheres to the processes and procedures outlined in the [WHO handbook for guideline development](#) and produces a high quality, trustworthy CPG.

## 1. Profound conflicts of interest (restating of prior concerns)

In the January 2024 letter we wrote about the profound and unmanaged COIs in the WHO Guideline Development Group (GDG), observing that the majority of the GDG members have significant financial and non-financial COIs that biased them towards promoting widespread access to hormones.

These concerns came to a head last month, when lawsuits in the United States led to a disclosure of documents showing that WPATH, including two of its senior leaders who currently serve as WHO GDG members, engaged in deeply problematic suppression of evidence related to the practice of medical transgender interventions as part of its Standards of Care 8 (SOC8) development. The court documents demonstrate that WPATH, led by these two prominent individuals, focused on creating the appearance of an evidence-based CPG helpful to physicians and patients—while all along crafting a document to be used as a weapon in political and legal battles in the US. We expand on this in section 3.

## 2. Problematic decision not to review the evidence for endocrine interventions (restating of prior concerns)

In our February letter, we evaluated the basis for WHO's decision not to conduct systematic reviews of evidence for benefits and harms of endocrine interventions, but instead to focused on

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<sup>2</sup> Boe v. Marshall, 2:22-cv-00184, (M.D. Ala. Dec 04, 2023) ECF No. 523-1: Exhibit 1. Letter to JHU co-signed by Dr Knudson and Dr Bouman, both of whom serve on the WHO GDG.



recommendations about how best to promote the widespread availability of hormones. We explained that the notion that hormones should be widely available to all those who want them first appeared in the [WHO Self-Care Guideline published in June 2022](#) as a “key consideration” (a vague category with no established meaning in EBM) and was not supported by any evidence. Instead, it referenced a systematic review that itself referenced the WHO Self-Care Guideline, creating a circular reference.

We detailed how, within a month, this vague guidance was elevated to a much more authoritative “existing guidance statement” in the [WHO HIV guidelines published in July 2022](#). No new evidence had emerged in the month between the two guidelines’ publication to justify the change from a non-committal “consideration” to the authoritative “guidance statement.” We expressed our opinion, which we continue to hold, that it is unacceptable for WHO to be engaged in a guideline exhorting *expanding access* to hormones, when the benefits and harms of these interventions have not been systematically assessed.

Further, as the new U.S. court documents reveal, at least two members of the WHO GDG had been previously involved evaluating the evidence for as part of WPATH’s own evidence review of transgender interventions. When the evidence did not support the notion that hormones should be widely available to all those who wish to take them, these two individuals were directly involved in blocking the evidence evaluation team from publishing the research results.<sup>3</sup>

### **3. Problematic enmeshment with WPATH, which is at the center of the evidence manipulation scandal (new information)**

Last month, the United States District Court Middle District of Alabama Northern Division put on the docket documents regarding evidence evaluation for WPATH SOC8. While not all the official court documents have been unsealed as of this writing, the documents that are already in the public domain show a concerted effort by WPATH to manipulate and suppress evidence that does not support the premise that TGD endocrine and surgical interventions should be widely available to all those who want them. Should WHO continue to be enmeshed with WPATH members and senior

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<sup>3</sup> Boe v. Marshall, 2:22-cv-00184, (M.D. Ala. Dec 04, 2023) ECF No. 523-1: Exhibit 1.



leaders, which are heavily represented in the current GDG, these U.S. court findings will have direct negative implications for the credibility of WHO's own process.

The following facts have emerged from the documents unsealed to date:

- **WPATH Standards of Care 8 (SOC8), and the evidence evaluation strategy that underpinned the SOC8 recommendations, were crafted and phrased to be used primary as a tool in a court of law.** WPATH's evidence evaluation strategy was shaped by the advice of the "social justice attorneys," who instructed the WPATH GDG that commissioning a systematic review that "reveals little or no evidence and puts us in an untenable position in terms of affecting policy or winning lawsuits."<sup>4</sup> Specific to the medical necessity statement relating to hormones and surgery, the WPATH GDG stated that "it is important that such a statement is part of the actual SOC" because "we needed a tool for our attorneys to use in defending access to care here. I have long wanted this (and many of our other policy statements) to become part of the SOC because that gives them greater force."<sup>5</sup>

As the court documents show, WPATH was focusing on commissioning reviews where it expected at least somewhat favorable conclusions, while avoiding reviews that could result in questions about whether endocrine and surgical interventions should be widely available. WPATH's desire to restrict evidence reviews to avoid unfavorable findings has a troubling parallel to the WHO GDG's own decision not to evaluate the evidence for the risks, benefits, and harms of endocrine interventions. This is particularly alarming given the significant overrepresentation of WPATH members and leaders on the WHO GDG.

- **When the evidence reviews commissioned by WPATH came to unfavorable conclusions about treatments promoted by WPATH, it suppressed publication of the results.**<sup>6</sup> Court documents reveal a contentious exchange between researchers on Johns

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<sup>4</sup> Boe v. Marshall, 2:22-cv-00184, (M.D. Ala. May 27, 2024) ECF No. 560-24: Exhibit 174, p. 3 of 131. A heavily redacted document from WPATH Standards of Care 8 planning process, which justifies not conducting certain systematic reviews for fear it would negatively affect political and legal battles.

<sup>5</sup> Boe v. Marshall, 2:22-cv-00184, (M.D. Ala. May 27, 2024) ECF No. 560-31: Exhibit 181, pp. 33–34 of 86.

<sup>6</sup> Boe v. Marshall, 2:22-cv-00184, (M.D. Ala. Dec 04, 2023) ECF No. 523-1: Exhibit 1 (henceforth Boe v. Marshall: No. 523-1). The main exhibit showing WPATH exerted undue influence on JHU and the results of the evidence reviews.



Hopkins University's (JHU) evidence evaluation team and WPATH leadership, with JHU researchers objecting to WPATH's attempts to interfere with the independence of the JHU evidence appraisal team's work.<sup>7</sup> Eventually, however, WPATH prevailed in suppressing publication of several completed evidence reviews.<sup>8</sup> This evidence suppression was later confirmed by the leading JHU researcher in an exchange with the U.S. Department of Health and Human Services.<sup>9</sup>

- **WPATH also instituted a policy that effectively controlled all future evidence review publications and their content related to SOC8.** Upon seeing two JHU manuscripts that contained conclusions that WPATH considered unfavorable, WPATH not only disallowed the manuscripts' publication, but also instituted a new approval policy requiring that all future research, either by JHU, or any SOC8 GDG members, must receive WPATH's explicit approval. First, the research conclusions had to be approved by WPATH before the researchers could even begin drafting the manuscript for publication.<sup>10</sup> The second level of review required approval of the final manuscript, with WPATH retaining the ability to amend the content.

The goal of the two-step WPATH approval policy was to ensure that “any publication based on the WPATH SOC8 data is thoroughly scrutinized and reviewed to ensure that publication does not negatively affect the provision of transgender healthcare in the broadest sense.”<sup>11</sup> The WPATH policy also stated and should any manuscript surviving the extensive

<sup>7</sup> *Boe v. Marshall*, 2:22-cv-00184, (M.D. Ala. May 27, 2024) ECF No. 560-17: Exhibit 167, p. 27 of 93. Email from Dr Robertson at JHU objecting to WPATH's attempts to exert influence on the JHU research results; *Boe v. Marshall*, No. 523-1, pp. 12–13 of 15. Email from Dr Robinson at JHU objecting to suppression of the review of two completed manuscripts and objecting to the post-factum implementation of the new WPATH approval policy.

<sup>8</sup> *Boe v. Marshall*, No. 523-1, pp. 2–3 of 15. Email from WPATH leadership, co-signed by two of the current WHO GDG members, notifying JHU that the two manuscripts should not be published because they are in violation of the newly-minted, post-factum approval policy that WPATH implemented.

<sup>9</sup> *Voe v. Mansfield* 1:23-cv-00864: 100-1 (M.D.N.C. May 27, 2024), p. 1. Email between AHRQ (a division of the US Health and Human Services) and the lead researcher at JHU working on systematic reviews, wherein JHU states: “we have been having issues with this sponsor [WPATH] trying to restrict our ability to publish”.

<sup>10</sup> *Boe v. Marshall*, No. 523-1, pp. 4–11 of 15. New approval policy instituted by WPATH for any future publications by JHU regarding evidence reviews and their findings.

<sup>11</sup> *Boe v. Marshall*, No. 523-1, pp. 14–15 of 15. “Dear SOC8 Working Group Members” letter from WPATH leadership to the WPATH GDG, informing them of the two systematic reviews by JHU that



WPATH “scrutiny” and securing the final approval be submitted for publication in a peer-reviewed journal, the authors’ COI disclosures must attest to their independence from WPATH, with the false implication that WPATH had no influence on the manuscript’s content.<sup>12</sup>

Only one systematic review of evidence was published after the new WPATH “approval” policy had been introduced.<sup>13</sup> This systematic review, Baker et al., 2021 (hereafter, the Baker review), bears all the markings of WPATH interference. The following problems are apparent in the Baker review:

- **The Baker review’s conclusion asserts the benefits of endocrine interventions, but this conclusion is not supported by the review’s actual findings.** The Baker conclusion states, “Despite the limitation of the available evidence, our review indicates that gender-affirming hormone therapy is likely associated with improvements in QOL, depression, and anxiety. No studies showed that hormone therapy harms mental health or quality of life among transgender people. These benefits make hormone therapy an essential component of care that promotes the health and well-being of transgender people.” However, the body of the review found only “low quality” and “uncertain” evidence, so the stated conclusion is totally unjustified.

Of note, the research community unsuccessfully queried the lead author and the journal itself about this discrepancy between the review’s findings and its conclusion. Now that the court documents reveal that WPATH required that the conclusion of any published research must be approved prior to granting the research team permission to draft the manuscript, and that the research conclusions must “not negatively affect the provision of transgender

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would not be allowed to be published due to their findings’ failure to “promote transgender health in the broadest sense”.

<sup>12</sup> *Boe v. Marshall*, No. 523-1, p. 8 of 15. The requirement that after submitting to two rounds of approval with WPATH approving conclusions and retaining the ability to alter content, the researchers then had to attest to the publishing journal that the research maintained independence from WPATH. The specific required language had to state: “the authors are solely responsible for the content of the manuscript, and the manuscript does not necessarily reflect the view of WPATH in the publication”.

<sup>13</sup> Baker, K. E., Wilson, L. M., Sharma, R., Dukhanin, V., McArthur, K., & Robinson, K. A. (2021). Hormone Therapy, Mental Health, and Quality of Life Among Transgender People: A Systematic Review. *Journal of the Endocrine Society*, 5(4), 1–16, <https://doi.org/10.1210/jendso/bvab011>.



healthcare in the broadest sense,”<sup>14</sup> the divergence between the conclusion and the actual findings is now entirely explained by WPATH’s interference.

- **The Baker review inappropriately conflated puberty blocker and cross-sex hormone interventions, likely to avoid negative conclusions about puberty blockers, which would have rendered the manuscript unpublishable per WPATH approval policy.** Puberty blockers and cross-sex hormones are targeting two markedly different populations (adolescents and adults) and have markedly different mechanisms of action. These interventions were to be appropriately addressed in the protocol as two different questions (KQ10 and KQ11).<sup>15</sup> However, the Baker review treated both populations and both sets of interventions as though they were one and the same.

At this point, several systematic reviews of evidence completed by other teams revealed that while the evidence for both interventions is low quality, the evidence for puberty blockers is particularly poor, given profound problems in the underlying studies and the lack of clinically meaningful psychological improvements.<sup>16-17</sup> By combining the two different PICOs (population, intervention, comparator, outcome)—one for puberty blockers, and the other for cross-sex hormones—into a single research question with a single answer, the Baker research avoided having to publish an unfavorable conclusion about puberty blockers, which would have rendered the research unpublishable according to the WPATH approval policy. Of course, other explanations are also possible, but there is no reasonable explanation for conclusion conflating puberty blockers for early-pubertal youth, and cross-

<sup>14</sup> Boe v. Marshall, No. 523-1, pp. 14–15 of 15. “Dear SOC8 Working Group Members” letter from WPATH leadership to the WPATH GDG, informing them of the two systematic reviews by JHU that would not be allowed to be published due to their findings’ failure to “promote transgender health in the broadest sense”.

<sup>15</sup> Sharma R, Robinson K, Wilson LM, Baker KE. 2018. *Effects of Hormone Therapy in Transgender People* [protocol] [https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD42018115379](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42018115379).

<sup>16</sup> Wiseman J. *Evidence Review: Gonadotrophin Releasing Hormone Analogues for Children and Adolescents with Gender Dysphoria.*; 2020:131. [https://cass.independent-review.uk/wp-content/uploads/2022/09/20220726\\_Evidence-review\\_GnRH-analogues\\_For-upload\\_Final.pdf](https://cass.independent-review.uk/wp-content/uploads/2022/09/20220726_Evidence-review_GnRH-analogues_For-upload_Final.pdf);

<sup>17</sup> Taylor J, Mitchell A, Hall R, et al. Interventions to suppress puberty in adolescents experiencing gender dysphoria or incongruence: a systematic review. *Archives of Disease in Childhood*. Published online 2024. doi:[10.1136/archdischild-2023-326669](https://doi.org/10.1136/archdischild-2023-326669);



sex hormones for older adolescents and mature adults, into a singular undifferentiated conclusion about “hormone therapy.”

- **The Baker review’s conflict of interest (COI) disclosure falsely asserts that the review was free from WPATH influence (apart from funding).** The official court documents reveal that the Baker review was explicitly subjected to WPATH’s approval policy (including a checklist showing that the final Baker et al. manuscript checked all the required boxes).<sup>18</sup> However, the COI disclosure printed by the journal asserted the publication’s independence from WPATH. Ironically, the wording of the disclosure matches, word-for-word, the WPATH-mandated language outlined in its approval policy.

Stepping back from the Baker review, it is apparent that of the 13 research questions registered by the JHU team in relation to the evaluation of endocrine interventions for SOCS, the majority do not appear in any peer-reviewed publications. The Baker review appears to have answered two of the 13 questions registered in the protocol (KQ10 and KQ11 relating to the psychological benefit of endocrine interventions), while another published review that predated the Baker review addressed another question (KQ3, relating to the use of antiandrogens on prolactin levels)<sup>19</sup>.

This suggests that as many as 10 questions outlined in the protocol remain unanswered in any published research, including important questions about the risks of estrogen in relation to pulmonary embolism, deep-vein thrombosis, stroke, and myocardial infarction (KQ5); the risk of polycythemia in transgender men on gender-affirming therapy with testosterone (KQ6); the effect of testosterone therapy on uterine, ovarian, cervical, vaginal, and breast pathology in transgender men who have not had hysterectomy or oophorectomy (KQ7); and a number of other questions.<sup>20</sup>

The court documents reveal that all 13 questions indeed had been addressed by the JHU evidence evaluation team, whose lead researcher stated in her response to the U.S. Health and Human Services AHRQ division, “we addressed 13 questions regarding hormone therapy.” This same email

<sup>18</sup> Boe v. Marshall, 2:22-cv-00184, (M.D. Ala. May 27, 2024) ECF No. 560-17: Exhibit 167, p. 41 of 93. The WPATH approval “checklist” for the Baker et al.’s 2021 review.

<sup>19</sup> Wilson, L. M., Baker, K. E., Sharma, R., Dukhanin, V., McArthur, K., & Robinson, K. A. (2020). Effects of antiandrogens on prolactin levels among transgender women on estrogen therapy: A systematic review. *International Journal of Transgender Health*, 21(4), 391–402. <https://doi.org/10.1080/15532739.2020.1819505>.

<sup>20</sup> See Appendix A.





exchange shows that the JHU team is frustrated with the “sponsor” (WPATH) who preventing JHU from publishing the research findings. These exchanges strongly suggest that these evidence reviews exist, yet their conclusions likely were not compatible with WPATH’s mission to promote widespread access to hormones, which is likely the reason they have never been published.

In light of these troubling revelations, the lead author of WPATH SOC8, Dr. Coleman, recently stated that the pressure exerted by WPATH on JHU “was not because WPATH had any interest in suppressing John Hopkins’ research,” but merely “to ensure that its release of SOC8 would be the first publication of the research.”<sup>21</sup> However, the veracity of this explanation questionable. Not only are the answers to as many as 10 specific questions relating to hormone use outlined in the protocol as yet unpublished, but also, as court documents reveal, at least six WPATH SOC8 chapters had completed systematic reviews of evidence as of June 2020, including Assessment, Primary Care, Endocrinology, Surgery, Reproductive Medicine, and Voice Therapy.<sup>22</sup> Four years later the research was completed (and more than two years after the SOC8 publication) , only two WPATH-commissioned reviews have ever been published: the very limited Baker review of psychological effects of endocrine interventions discussed earlier, and the review of the effects of androgen suppression on prolactin levels.<sup>23</sup>

The unknown fate of the two suppressed reviews referenced in the court documents, and the lack of any other published reviews beside the two already discussed at length, raises questions about the sincerity of WPATH’s claim that its decision to disallow the publication of the reviews by JHU was merely to allow WPATH SOC8 to “go first.” Instead, it is evident that the unpublished reviews remained unpublished because their conclusions did not meet the WPATH approval policy which stipulated that only favorable reviews could be submitted for publication.

#### 4. Implications for the WHO TGD guideline

The U.S. court documents referenced in our letter are in the public domain and are independently verifiable. They set a troubling context for WHO’s current effort, given the strong overlap between

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<sup>21</sup> *Boe v. Marshall*, 2:22-cv-00184, (M.D. Ala. Jul 01, 2024) ECF No. 629-20.

<sup>22</sup> *Boe v. Marshall*, 2:22-cv-00184, (M.D. Ala. May 27, 2024) ECF No. 560-17: Exhibit 167, p. 59 of 93.

<sup>23</sup> Wilson, L. M., Baker, K. E., Sharma, R., Dukhanin, V., McArthur, K., & Robinson, K. A. (2020). Effects of antiandrogens on prolactin levels among transgender women on estrogen therapy: A systematic review. *International Journal of Transgender Health*, 21(4), 391–402. <https://doi.org/10.1080/15532739.2020.1819505>.



the WHO GDG and WPATH membership (ten of 26 members are WPATH members). Of the four WPATH leaders who made the decision to suppress the systematic reviews of evidence and to institute a new policy to unduly influence JHU's findings, two serve on the current WHO GDG for the TGD guidelines.<sup>24</sup> The conduct of these individuals appears to have breached the [WHO Values Charter](#).

**The most troubling aspect of the current plan is the decision by WHO not to evaluate the evidence for the benefits and harms of cross-sex hormones, but instead to proceed with recommendations that expand access to these interventions.** The decision to bypass the evidence review was justified by the fact that there was already an “existing guidance statement” from WHO that cross-sex hormones should be widely available. However, as we wrote in our February 2024 analysis, the “existing guidance,” has itself deviated from the proper process outlined in the [WHO handbook for guideline development](#). Further, the apparent existence of multiple evidence reviews relating to the potential harms of endocrine interventions, which have been suppressed by WPATH, requires that WHO engage in its own, independent evidence review.

Currently, over 7% of US college-aged females, and over 4% of college-aged males consider themselves transgender.<sup>25</sup> These numbers likely mirror trends in many other countries. With the rapidly growing numbers of young adults questioning their gender and reporting gender-related distress — a finding underscored by the Cass Report<sup>26</sup> — we strongly recommend that WHO reconsider the scope of the current guideline. To respect their right to health, this vulnerable population of youth deserves high quality care informed by evidence-based clinical practice guidelines.

WPATH has demonstrated that it approaches the question of access to hormones as a civil right, misusing its treatment guidelines as a political weapon. This makes it more urgent than ever that WHO evaluates this intervention like any other medical intervention with the potential to help and to harm. To produce a trustworthy guideline in this contentious arena, WHO must compose an

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<sup>24</sup> Boe v. Marshall, No. 523-1. Letter to JHU co-signed by Dr Knudson and Dr Bouman, both of whom serve on the WHO GDG.

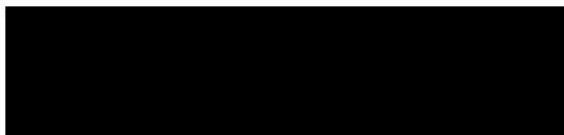
<sup>25</sup> American College Health Association, National College Health Assessment III. Undergraduate Student Reference Group. Data Report. Fall 2023. [https://www.acha.org/documents/ncha/NCHA-IIIb\\_FALL\\_2023\\_UNDERGRADUATE\\_REFERENCE\\_GROUP\\_DATA\\_REPORT.pdf](https://www.acha.org/documents/ncha/NCHA-IIIb_FALL_2023_UNDERGRADUATE_REFERENCE_GROUP_DATA_REPORT.pdf).

<sup>26</sup> Cass, H. (2024). Independent review of gender identity services for children and young people: Final report. [https://cass.independent-review.uk/wp-content/uploads/2024/04/CassReview\\_Final.pdf](https://cass.independent-review.uk/wp-content/uploads/2024/04/CassReview_Final.pdf), p. 19.



unbiased and representative GDG and change the scope, starting with systematically evaluating the evidence of benefits and harms of hormones, as well as alternative treatments. SEGM remains available to assist WHO in this important effort.

Best regards,



William Malone, MD (on behalf of the SEGM Board)



**Appendix 1: List of research questions relating to hormone interventions registered by the Johns Hopkins University's evidence appraisal team for SOC8<sup>27</sup>—and their current status:<sup>28</sup>**

- KQ1. For transgender women, what are the safety and efficacy of androgen lowering medications compared to Spironolactone vs cyproterone vs GnRH agonists in terms of surrogate outcomes, clinical outcomes, and harms? (*does not appear to have been published*).
- KQ2. For transgender adolescent, what are the long term effect of GnRH agonists compared to no treatment, in terms of surrogate outcomes, clinical outcomes, and harms? (*does not appear to have been published*).
- KQ3. For transfeminine people on gender-affirming hormone therapy with estrogen, what are the comparative risks of prolactinomas and hyperprolactinemia between spironolactone, cyproterone, and GnRH agonists, in terms of prolactin levels and presence of prolactinomas confirmed by imaging? (*addressed in the only other published review, Wilson et al., which predated the WPATH approval policy and the Baker review*).<sup>29</sup>
- KQ4. For transgender people, what are the effect of progesterones (cyproterone) compared to Medroxyprogesterone and other progesterones in terms of breast growth (adults), delay of puberty (children), and side effects? (*does not appear to have been published*).
- KQ5. For transgender women, what are the comparative risks of different regimens of gender-affirming hormone therapy with estrogens (conjugated estrogen, estradiol, ethinyl estradiol) in terms of pulmonary embolism, deep-vein thrombosis, stroke, and myocardial infarction? (*does not appear to have been published*).
- KQ6. For transgender men, what is the risk of polycythemia among transgender men on gender-affirming therapy with testosterone, as measured by hematocrit and hemoglobin levels? (*does not appear to have been published*).

<sup>27</sup> Sharma R, Robinson K, Wilson LM, Baker KE. *Effects of Hormone Therapy in Transgender People (PROSPERO 2018)*; 2018. [https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD42018115379](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42018115379).

<sup>28</sup> We invite others to verify the accuracy of our assertions regarding which questions have been addressed in published manuscripts, and correct us if we are wrong in our assessment.

<sup>29</sup> Wilson, L. M., Baker, K. E., Sharma, R., Dukhanin, V., McArthur, K., & Robinson, K. A. (2020). Effects of antiandrogens on prolactin levels among transgender women on estrogen therapy: A systematic review. *International Journal of Transgender Health*, 21(4), 391–402. <https://doi.org/10.1080/15532739.2020.1819505>



- KQ7. For transgender men, what is the effect of testosterone therapy on uterine, ovarian, cervical, vaginal, and breast pathology in transgender men who have not had a hysterectomy or oophorectomy? (*does not appear to have been published*).
- KQ8. For transgender women what is the effect of estrogen therapy on breast, testicular, prostate and penile tissue in transgender women who have not had a gonectomy? [sic] (*does not appear to have been published*).
- KQ9. For transgender women, what is the safety of different routes of administration for estrogen (oral, cutaneous, intramuscular) in terms of myocardial infarction, stroke, deep-vein thrombosis, and pulmonary embolism? (*does not appear to have been published*).
- KQ10. For transgender adolescent, what are the effects of suppressing puberty with GnRH agonists on quality of life? (*addressed in the Baker review but combined adolescents and adults and did not separately evaluate GnRHAs and cross-sex hormone therapy, instead combining the two*).
- KQ11. For transgender people, what are the psychological effects (including quality of life) associated with hormone therapy (*addressed in the Baker review but combined adolescents and adults and did not separately evaluate GnRHAs and cross-sex hormone therapy, instead combining the two*).
- KQ12. For transgender people, what are the effects of hormone therapy on metabolic syndrome? (*does not appear to have been published*).
- KQ13. For transgender people, what are the effects of hormone therapy on fertility? (*does not appear to have been published*).