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USPATH and WPATH Respond to NY Times Article "They Paused Puberty, But Is There a Cost?" published on November 14, 2022

The recent *New York Times* article, "They Paused Puberty, But Is There a Cost?", furthers the atmosphere of misinformation and subjectivity that has grown to surround the area of gender affirming medical interventions for transgender youth. The methods of the authors of this piece come up short in their interpretation and application of available data; the article supports inaccurate narratives that puberty blocking medicines are conclusively harmful to long-term bone density or other health outcomes, and that transition reversal/regret is a common outcome for these treatments. Additionally lacking in the article is an explicit statement that any harms which may exist are outweighed by the substantial benefits these treatments confer to transgender youth, and we wish to respond below to certain specific statements and references made in this article.

The cited bone expert from Mayo Clinic, Dr. Sundeep Khosla, MD, is an adult endocrinologist who does not work clinically with transgender youth and has only a single publication on transgender health. This <u>publication</u> is not a research study, but a brief review commentary on the issue of bone density in adult transgender people. Transgender youth are not addressed in the commentary. In this paper, data are reviewed and discussed, and it is concluded that in the context of hormone therapy, "bone mineral density is generally preserved in both trans women and trans men".

The anecdote provided of an adolescent who began, and then stopped pubertal suppression due to bone density loss lacks important details, including age and pubertal stage at initiation of puberty blockers, length of time on blockers, baseline bone density ("Z-score"), and whether the bone density comparison was made to identified gender or birth-assigned sex. Additional important information not provided includes calcium intake, and vitamin D intake and level, as well as level of physical activity, all of which play a substantial role in maintenance of bone mineral density.

The single expert who performed the literature review, Dr. Farid Foroutan, PhD, is an epidemiologist with no experience in clinical medicine, child and identity development, bone density, or any aspect of the field of transgender health. Nearly the entirety of his professional experience lies in population health studies of heart disease. The interpretation of clinical studies, especially those with findings that are nuanced, inconclusive, or have a small effect size, require interpretation through a clinical lens, with clinician-scientists experienced in the

translation of research data into clinical practice. In fact, Dr. Foroutan recently co-authored a <u>paper</u> which highlighted this very concern, so it is unclear why he did not advocate for a more nuanced and clinically grounded analysis, and an expanded roster of expertise on the review team.

We were surprised to see reference to a subjective statement from Dr. Catherine Gordon, MD regarding "getting behind" on bone density, and we question whether this comment was taken out of context. Dr. Gordon is a long-standing advocate for trans youth care, and in her June 2022 single-author commentary published in *Pediatrics*, she stated that, "The duration of pubertal suppression with gonadotropin hormone releasing hormone agonists varies, but can extend up to 4 years for younger patients who are not able to provide consent until age 16 for receipt of gender-affirming therapy. Puberty blockers represent an invaluable intervention for these children and adolescents, to reduce anxiety and 'buy time' until final decisions can be made about gender assignment." A subsequent commentary co-authored by Dr. Gordon and published in November 2022 in JAMA Open Access stated, "Concerns about skeletal losses become less significant in an adolescent with active suicidal ideations. Although the significance of the risks may be unclear, there is strong evidence regarding the benefits of GnRHa in transgender youth: it can be a life-changing and lifesaving treatment for a vulnerable population who is at high risk for anxiety, depression, and suicide."

Anecdotes are provided about two teens who were found to have severe osteoporosis after 1 and 3 years of blocker treatment. In both cases, a baseline bone density test was not done. It is unlikely that such a degree of severe osteoporosis would develop after these short courses of treatment, and there were likely other pre-existing factors at play. The 2017 Endocrine Society Guidelines, co-sponsored by WPATH, as well as the SOC8 recommend baseline bone density assessment prior to initiating blocker therapy, as well as ongoing reassessments, and optimization of calcium and vitamin D.

The blockers themselves do not impact bone density. Bone density is impacted by the fact that sex steroid production is temporarily halted when puberty blockers are initiated. The adolescent in this anecdote was already using estrogen, which promotes bone health. Therefore, the point about stopping blockers due to bone density loss is moot. Many types of blockers are routinely used in combination with estrogen well through adulthood without deleterious effects on bone density. This has been the common practice for treatment of adult transgender individuals for decades. Bone density loss is generally not a concern once hormone therapy has begun. In fact, Dr. Khosla's paper states that, "the skeleton should be relatively well protected, assuming adequate compliance with hormone therapy".

Experts in the field are indeed concerned regarding bone density among youth using puberty blockers. The WPATH SOC8 cautions that, "for adolescents older than 14 years, there are currently no data to inform HCPs whether GnRHas (puberty blocking medication) can be administered as monotherapy (and for what duration) without posing a significant risk to skeletal health." The SOC8 also states that, "When deciding on the duration of GnRHa monotherapy, all contributing factors should be considered, including factors such as pretreatment bone mass..." and, "The clinical course of the treatment, e.g., the development of bone mass during GnRHa treatment and the adolescent's response to treatment, can help to determine the length of GnRHa monotherapy."

The spotlighting of three youth, one of whom continues on treatment, one of whom stopped due to bone density loss under unclear circumstances, and one of whom reversed their transition, is

not a proportionate representation of the actual population. Transition reversal, especially when unrelated to external factors such as discrimination or rejection by family, is rare. In fact, more study is needed on the reasons youth are kept on blockers for extended reasons; what percentage of cases are due to the youth continuing to explore goals, and what percentage involves parental hesitance to support moving forward with hormone therapy?

The findings of the seven citations provided at the end of the paper require a nuanced interpretation by clinician-scientists familiar with this population and subject matter. Many of the studies used sex assigned at birth, rather than identified gender, as the comparitor. Many of the differences found failed to reach statistical significance, and of those that did, many are of questionable clinical significance. Any such risk must also be taken into context with the substantial benefits of treatment, and harms of not accessing such treatment, including high rates of mental health disorders and suicidality.

Finally, the authors of this article suggest that "England's National Health Service last month proposed restricting use of the drugs for trans youths to research settings." In fact, the pivot that the National Health Service took was to enroll ALL youth initiating puberty blockers for treatment of gender dysphoria into a prospective research protocol so that more comprehensive data might be collected.

We agree that "less vitriol, more science", as stated in conclusion by the authors, is needed in this area. This includes responsible reporting that takes into consideration realistic estimates of the prevalence of transition reversal, a nuanced and transparent discussion of all bone health factors, and an overall risk-benefit analysis that includes the substantial risks of delayed or denied treatment. Misinformation about the science behind the care of trans youth, such as presented in this article, can be and has been used to justify political actions or even violence against the trans and gender diverse community. With growing efforts to ban medically necessary gender affirming care for trans youth, and attacks rise such as was recently seen in the mass murder at Club Q in Colorado Springs, CO, measured and responsible journalism is ever the more essential. With the recent release of the WPATH SOC8, USPATH is working to explore quality assurance and fidelity in the provision of this life-saving care in the US, and will report the findings and recommendations of our group once the process is completed.

Signed:

USPATH Board WPATH Executive Committee