Commentary on “Medical treatment of minors with gender dysphoria. Ethical and legal considerations” by NEK-CNE

Dr. Jilles Smids,[1] 1-2-2025

[1] The author has written this commentary upon request by the Swiss parent organization AMQG (https://www.amqg.ch/). While it may be somewhat unusual for international scholars to get involved in the national debate of another country, ethics as a discipline is not bound to national borders. Moreover, all Western countries, including the Netherlands, are wrestling with largely the same questions. The commentary is based on a machine-translation of the NEK-CNE Position Paper, as provided by AMQG, which based on a brief comparison with the original German text seemed to the author to be of sufficient quality.

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1 Introduction

Ethical reflection on the difficult questions in pediatric gender care is indispensable. Therefore, it is commendable that national ethics committees such as NEK-CNE aim to inform the scholarly and societal discussion on the best possible care for minors with gender dysphoria (GD) by offering ethical analysis. The need for this type of analysis and advice is apparent from the fact that recently, the Italian bioethics committee has also issued advice.[2] And in the Netherlands, the Health Council is about to start a similar advisory trajectory.

There are many valuable observations and recommendations throughout NEK-CNE's Position Paper. In particular, it takes fully seriously the weight of an adolescent's decision to start medical treatment, also given its invasiveness, harmful side-effects, and increasingly irreversible character. Accordingly, the Position Paper emphasizes the importance of fully informed consent, by sufficiently mature minors themselves, who have decision-making capacity. Given the fundamental and highly personal nature of the decision to start medical transition, this view has much to be said for. At several places, the clear rationale for a watchful waiting approach that postpones medical interventions until children have further matured and developed decision-making capacity is recognized, even though ultimately, the Position Paper judges that the arguments against waiting should be decisive. Nevertheless, it rightly states that "the search for reliable predictors of permanent gender incongruence in particular must be intensified in order to prevent the potential damage caused by a misdiagnosis." For, the predictive value of gender dysphoria (GD) diagnoses in adolescence is too low indeed (Cass Review 2024; Byrne 2024; Bachmann et al. 2024).[3] Another welcome characteristic is the Position Paper's extensive attention to the role of psycho-social context (but see this commentary's section 3 on the changed patient profile). Finally, throughout the report there is a frank acknowledgment of the lack of good quality scientific evidence on potential harms, risks, and potential benefits, accompanied by a recommendation to close the many research gaps.

Despite these strong characteristics, in the opinion of the author of this commentary, the NEK-CNE Position Paper also has several fundamental weaknesses which make it unfit in its current form to help inform and guide Swiss decision-making with respect to adoption of the new German guideline. These can be summarized as follows, each corresponding to one of this commentary's sections. First, the Position Paper places very substantive argumentative weight on the supposed reversibility of puberty suppression, which is, however, far from certain (see section 2). Second, it does not discuss the change in the patient profile to in majority natal females whose GD emerged not in early

[2] For the relevant links, see: https://segm.org/Italy-Puberty-Blockers-Therapy-Bioethics
[3] For a helpful discussion of the German paper by Bachman et al., see: https://segm.org/gender-dysphoria-diagnosis-desistance-germany

childhood but after the onset of puberty, and who often have one or more psychiatric co-morbidities (see section 3). Third, the Position Paper's discussion of the medical information on harms, risks, and benefits is at various places incomplete, imbalanced, or even incorrect (see section 4). Finally, its ethical analysis in terms of the four principles of medical ethics is incomplete and imbalanced (see section 5). This commentary will end with some overall concluding remarks (see section 6).

2 Can puberty blockers protect adolescent's right to an open future?

The most central argument in the NEK-CNE Position Paper is based on the idea of puberty suppression as a reversible treatment that safeguards the adolescents right to an open future. The Position Paper firmly states that starting medical gender transition, or gender affirming medical treatment, is such a far-reaching and personal decision that only the person involved has the right to make it. This stance is justified with reference to the importance of autonomy and self-determination. On one hand, doubt is expressed regarding the capacity of young adolescents whose puberty has just begun, to give informed consent for this decision. On the other hand, waiting until their capacity is developed further, would 'force' them through unwanted puberty of their natal sex. The Position Paper presents puberty suppression as a reversible step that enables the adolescents to further develop their decision-making capacity and that provide time for further reflection. This Position Paper presents puberty blockade as a solution to this dilemma:

> While the right to a completely open future is practically impossible to fulfill, the respect for the self-determination of minors requires that groundbreaking life decisions be made by them whenever possible. However, puberty begins at an age at which it is not immediately clear whether the person concerned is already capable of making decisions regarding a possible medical transition. Only if they are able to assess the long-term personal, health and social consequences of their decision is their self-determination safeguarded. At the same time, a wait-and-see approach in the case of a desire to transition means that the minor has to live through puberty in the undesired gender against their will and that a later transition would be made more difficult by the physical changes that have already taken place, which from the perspective of self-determination is not a good thing. determination is also problematic. The use of puberty blockade in minors gender incongruence can therefore also be understood as an attempt to solve this dilemma by delaying the commitment to a specific gender future caused by puberty. This also explains the great relevance, from an ethical point of view, of the distinction between reversible and irreversible physical developments and medical interventions in this context. The less the person concerned is able to correct the decision at a later date (i.e. after attaining capacity), the more the open future is restricted (p 16; other places whether the same argument is made more briefly are p11 "Treatment goal" and p27 "treatment recommendation c")

If puberty blockers indeed could fulfill this role without significant harm, this solution could work. However, there are at least three problems with the Position Paper's proposed way out of the dilemma. First of all, evidence has mounted that puberty suppression is likely not reversible but rather that it, for the overwhelming majority, constitutes the first step on an irreversible treatment pathway (for extensive discussion, see (Jorgensen, Athéa, and Masson 2024; Baron and Dierckxsens 2022b). Second, it may very well be the case that puberty blockers have harmful side effects that foreclose options that can be regarded as central to an open future, such as unknown effects on brain development and impaired sexual function (Baxendale 2024; Women's Voices [@WomenReadWomen] 2022). And third, this way of framing the decision-making situation places too much weight on respect for autonomy, undervaluing other medical ethical principles, most notably beneficence and non-maleficence (this third problem will be discussed in section 5.)

The first problem, that puberty suppression (PS) might not be reversable at all, was already recognized by the Dutch clinicians of the Amsterdam gender clinic from the very beginning (Cohen-Kettenis and van Goozen 1998). They explained that adolescents might see PS as the first treatment step, a concern echoed by others (Wren 2000; Korte et al. 2008). Subsequent studies have consistently shown that nearly all, that is, more than 95 % of the children starting on PS continue to cross-sex hormones (CSHs) (Brik et al. 2020; Wiepjes et al. 2018; Carmichael et al. 2021). These numbers suggest that children may not engage in extended reflection on their (gender) identity and wishes for treatment or alternatives. For, as stated by Anna Hutchinson, who worked at the English Tavistock clinic, how likely would it be that given "time to think", virtually all would come to the same conclusion (Barnes 2023)? In any case, these high numbers are in need of explanation.

One explanation could be that the gender clinicians are very good at singling out those with a stable transgender identity, whose GD is very unlikely to resolve. This explanation is favoured by a number of prominent gender clinicians (de Vries et al. 2021). However, the alternative explanation is that pubertal suppression (PS) has an iatrogenic effect by *causing* the persistence of GD in adolescents who are on PS. This is not a mere possibility, because a plausible mechanism is suggested by Hillary Cass, most clearly in her interim report:

> The most difficult question is whether puberty blockers do indeed provide valuable time for children and young people to consider their options, or whether they effectively 'lock in' children and young people to a treatment pathway which culminates in progression to feminising/masculinising hormones by impeding the usual process of sexual orientation and gender identity development. (Cass 2022, 38).

Further evidence undermining the 'reversibility' and 'time to think' rationale comes from empirical ethics studies from researchers who themselves favor a gender-affirming approach. In a Dutch

interview study all eight participating adolescents who continued to CSHs stated that they did not regard PS as time to reflect, thereby confirming the very early Dutch concern cited above:

> …none of the eight interviewed adolescents who had proceeded with GAH [gender affirming hormones], and none of their parents, stated that more time to explore and decide whether or not to pursue GAMT [gender affirming medical treatment] was a function of PS for them. They mentioned that they were/their child was already certain that they wanted to proceed with GAMT when starting PS (Lieke J.J.J. Vrouenraets et al. 2022, 433).[4]

Importantly, also parents seemed to already have decided that a medical treatment pathway was the best for their children. Given the importance of parents and the further social context of children in decision-making on medical treatment for their GD, such attitude of parents may easily undermine the right to an open future and autonomous decision-making on the part of the child.

These findings and observation brought Amsterdam clinicians already years ago to recommend regarding the start with PS as the real decision-making moment, and therefore, to discuss all risks already at that point in time:

> In addition, from our clinical experience, most adolescents and parents experience puberty suppression as the first step in gender transitioning. It is therefore important to discuss the iatrogenic risks of possible future gender-affirming treatments (e.g., cross-sex hormones and gender-affirming surgeries), *although it may be several years before the adolescent is eligible for such treatments*. Such discussions might, for instance, include informing patients about genital sensitivity after genital surgery and about the possibility (in case of hormonal therapy) or certainty (in case of removal of the uterus and ovaries) of fertility loss [26]." (Steensma, Wensing-Kruger, and Klink 2017 emphasis added).

In summary, it is highly doubtful that PS is a truly reversible medical intervention that enables children to further mature until a stage that they have developed sufficient capacity to give informed consent for cross-sex hormones(CSHs). Rather, all evidence points to the conclusion that the real decision is being made at the point of starting PS. Hence, PS is not the desired solution to the dilemma; it does not ensure an open future, but rather closes off a non-medicalized future for children with GD at an age at which their capacity to give informed consent is very much in doubt (Baron and Dierckxsens 2022b; Levine, Abbruzzese, and Mason 2022; Lieke Josephina Jeanne Johanna Vrouenraets et al. 2015). An apt way to summarize the above discussion may be to say that

[4] The reader is referred to (Jorgensen, Athéa, and Masson 2024) for several other telling quotes from Dutch interview studies.

even tough adolescents *could* stop PS *if* they would want to, PS is very likely to be *psychologically* irreversible for the overwhelming majority.[5]

Adding to this is the second problem with the Position Paper's proposed solution: puberty blockers may have harmful side-effects, some of which directly concern capacities that arguably are important to a child's open future. One of the most important is the potential negative impact of PS on brain development and cognitive capacities. Again, the interim Cass report puts it very clearly, directly following the passage quoted above:

> A closely linked concern is the unknown impacts on development, maturation and cognition if a child or young person is not exposed to the physical, psychological, physiological, neurochemical and sexual changes that accompany adolescent hormone surges. It is known that adolescence is a period of significant changes in brain structure, function and connectivity.40 During this period, the brain strengthens some connections (myelination) and cuts back on others (synaptic pruning). There is maturation and development of frontal lobe functions which control decision making, emotional regulation, judgement and planning ability. Animal research suggests that this development is partially driven by the pubertal sex hormones, but it is unclear whether the same is true in humans.41 If pubertal sex hormones are essential to these brain maturation processes, this raises a secondary question of whether there is a critical time window for the processes to take place, or whether catch up is possible when oestrogen or testosterone is introduced later. (Cass 2022, 38)

In section 4, it will be explained why the Position Paper's reassuring take on this risk is based on an inadequate representation of the literature. Further medical risks of PS are increased chances of infertility, impaired sexual function, and more complicated genital surgery. PS, especially early start at Tanner 2, will negatively impact fertility, while fertility preservation options are invasive, expensive, and by no means guarantee success (Stolk et al. 2023; Brik et al. 2019). The Position Paper's extensive reference to these issues with fertility is an appropriate acknowledgement of their seriousness. However, unfortunately, PS is not the reversible intervention that could ease NEK-NCE's worries. Early

[5] At this point, it should be noted that the natural history of GD, even in the classic childhood onset presentation, is largely unknown (Byrne 2024; Abbruzzese, Levine, and Mason 2023). If we would know that after Tanner 2, any present GD is very unlikely to resolve, this would support the use of PS at Tanner 2. Dutch gender clinicians claim such knowledge (Kreukels and Cohen-Kettenis 2011; de Vries and Cohen-Kettenis 2012), mainly based clinical experience and on a qualitative study of so-called persisters (Steensma et al. 2011). However, these were all children who already received a GD diagnosis from the Amsterdam clinic in early childhood, before the age of 12. So, these children knew that if their GD would persist upon entering puberty, at age 12 they could return to the clinic to receive puberty blockers (presented as a fully reversible intervention). Unfortunately, we lack epidemiological studies into the prevalence of GD in the general population. Therefore, we simply do not know what would happen when children with GD were not treated with PS, and hence the risk of overdiagnosis and harmful overtreatment is high.

start of PS is also likely to lead to anorgasmia (Women's Voices [@WomenReadWomen] 2022).[6] And finally, early start of PS, at Tanner stage 2/3, typically results in too little penile tissue to enable standard inversion techniques in genital surgery. To solve this problem, a piece of colon is taken from the person to create an artificial vagina, which is a surgical procedure with more risk (Biggs 2023; Negenborn et al. 2017). In fact, one of the 70 participants of the seminal Dutch PS study (de Vries et al. 2011) later died from complications after her genital surgery (Negenborn et al. 2017).

All this further undermines the framing of PS as a reversible intervention safeguarding an open future, for clearly, these are potential harms that, if materialized, substantially impact the adult life of affected persons. Crucially, these harms are *irreversible*, and hence, these harms constitute another sense in which PS is not reversible at all, in addition to the above explained psychological irreversibility. It might be objected that, lacking good quality scientific evidence on both the harms and benefits of PS, these harmful side effects are 'merely' potential. However the burden of proof to show that puberty blockers are safe and are in fact reversible in the relevant sense, rests with those offering these medical interventions, and on those who propose PS as a solution to the ethical problem of (too) early intervention, i.e., on the NEK-CNE. Add to this that the harms are, as argued above, not merely potential, but all have clear underlying rationales and some empirical evidence in support.

In conclusion, the Position Paper's appeal to PS as a reversible medical intervention that help to solve the dilemma between watchful waiting and early medicalization of GD, and that it keeps the children's future open, is unwarranted. Given that this is the corner stone of the NEK-CNE Position Paper's analysis and argument in support of offering minors with GD PS and CSH, this is a highly significant result.

3 The changed profile of adolescents seeking medical gender treatment

One of the most central issues in the current scholarly and societal debate is the changed patient profile (Aitken et al. 2015; Kaltiala-Heino et al. 2015; 2018; Zucker 2019; De Vries 2020; Littman 2018; Bauer, Lawson, and Metzger 2021; Cass Review 2024; Leonhardt et al. 2024; Ashley 2020). Whereas the Dutch Approach is based on treating roughly equal numbers of relatively psychologically stable natal males and females, presenting with severe GD persisting from early childhood on (de Vries et al. 2011; de Vries and Cohen-Kettenis 2012; Delemarre-van de Waal and Cohen-Kettenis 2006), currently

[6] A recent Dutch article claims that there is no relation to early versus late puberty start of PS when it comes to capacity for orgasm and sexual function more broadly (van der Meulen et al. 2024). However, the sample size was so small, that this conclusion is unwarranted on the basis of the study results.

the predominant patient group consists of natal females, whose gender problems typically emerged after the onset of puberty, and who present with significantly more psychiatric co-morbidity (Arnoldussen, de Rooy, et al. 2022; de Rooy et al. 2024; Kaltiala-Heino et al. 2015; 2018). The changed sex ratio is observed in several Western countries (Aitken et al. 2015).

A clear concern in the literature and societies is whether this new patient group may include adolescents who identify as transgender on the basis of interpreting their pre-existing challenges through the lens of gender (Bechard et al. 2017; Bradley 2022; Cass Review 2024). Obviously, if this would be the case, medical treatment seems unlikely to benefit them especially in the long term, while careful explorative psychotherapy and psychosocial interventions may help reduce these adolescents' psychological distress and improve their global functioning. Several authors argue for such non-medical approaches as the first intervention, and a number of case reports in the literature indicate that this indeed does happen and hence is a real possibility (Churcher Clarke and Spiliadis 2019; Spiliadis 2019; Lemma 2018; D'Angelo 2023; D'Angelo et al. 2021).

Notably, the Position Paper completely side-steps these issues.[7] Its section "2.2.1 Psychological, systemic, and psychotherapeutic support", mainly discusses psychotherapeutic approaches as an aid for trans persons in dealing with discrimination and exclusion, and as a support when commencing on a medical treatment pathway. There is no recognition of the changed patient profile, nor its implications for the evidence base (which is already weak for the original Dutch patient cohort (Abbruzzese, Levine, and Mason 2023)), nor for the question as to what should be the best first line interventions. From a medical ethical and legal point of view, invasive medical treatment can only be justified if less invasive psychotherapeutic approaches to help resolve the distress in adolescents with GD have been tried and failed. Contrary to claims made in the literature (Ashley 2022), such therapy can certainly be ethical and should not be equated to conversion therapy (D'Angelo 2023; Spiliadis 2019; Sinai and Sim 2024).

4 The Position Paper's discussion of the medical information and risks

At several places, especially in chapter 2, the Position Paper's presentation and discussion of the relevant medical information and risks of PS, CSHs, and surgery is incomplete, insufficiently balanced, or even incorrect. I will briefly discuss the most salient problems.

[7] This omission is also visible in the recommendations under section 4.3

Starting PS at Tanner stage 2 is not best practice

The claim that current best practice is to start PB "at the earliest from Tanner 2 if indicated" (p10) is unfounded. The fact that this is recommend by the Standard of Care 8 from the World Professional Association for Transgender Health (Coleman et al. 2022) is not a good foundation, as this is a problematic guideline (Block 2024; Cass Review 2024). The Position Paper does not acknowledge the fact that the recently changed Swedish guideline requires Tanner 3 before adolescents can be eligible for PS.[8] Notably, together with the Finnish guidelines, these were the only guidelines qualified as 'evidence-based' by the Cass review (Cass Review 2024; Taylor, Hall, et al. 2024).

It should be noted that the age of onset of puberty has consistently dropped over the last decennia, and Tanner 2 happens currently around age 10-11 for girls and age 11 for boys (Brix et al. 2019). And as noted by prominent Dutch gender clinician Annelou De Vries, "A child who starts puberty blockers at the age of nine, will be taking these for a long period. We have to question if that is perhaps too long" (in: A. Bakker 2021, 163–64).

There are no reassuring findings regarding the impact of puberty blockers on brain development

Under "Risks and side-effects", the framing of the influence of PB on brain and cognitive development as something that "cannot be ruled out" is too weak in the light of the total evidence. The signals of possible negative impact all come from studies that do not provide strong evidence, but together they can be regarded as concerning, and urgently warranting further study (Baxendale 2024; Chen et al. 2020; Biggs 2023). The appeal to a Dutch study on the association of pre-treatment IQ and post-treatment educational achievement to suggest that there may be no problems is unfounded, since it has too severe methodological limitations to draw any reassuring conclusion, as anyone reading the study itself (Arnoldussen, Hooijman, et al. 2022), or reading the systematic review by (Baxendale 2024) will discover.[9] Similarly, the Position Paper's brief discussion of another Dutch study

[8] https://segm.org/Swedish-2022-trans-guidelines-youth-experimental

[9] Baxendale (p9): "Arnoldussen et al.52 reported the results of an assessment of IQ, before the commencement of GnRH analogue treatment in 72 children and examined the relationship between this measure and a highly simplified, dichotomised index of educational progress/ achievement ('vocational educated' vs. 'higher vocational educated/ academic educated'). Prior to treatment, the mean and standard deviation of the IQ score in the group was comparable to the general population (mean = 100, standard deviation = 15). Forty per cent of the eligible subjects declined to participate in the follow-up. No conclusions can be drawn from this study with respect to the impact of puberty suppression on the development of cognitive function."

Adding to Baxendale's analysis, here is one reason for why the 40% non-participants may have included a relatively higher number of 'vocational educated' adolescents. The study states that "some agreed to participate but did not fill out the questionnaires despite repetitive reminders". One strong predictor for educational achievement is good 'executive functioning', and failing to follow up on repetitive reminders can

(Staphorsius et al. 2015) incorrectly claims that in this study "no significant differences in [cognitive] performance … were found" (p12).[10] It is notable that instead of referring to this systematic review by Baxendale, the Position Paper chooses to provide a brief and selective narrative discussion of the literature. Also absent is a refence to the consensus statement on the cognitive effects of PBs as an urgent research topic (Chen et al. 2020).

Incomplete and unbalanced discussion of regret and regret rates

Here is the core of the Position Paper's discussion of the prevalence of regret:

"Only a few people regret the procedure. According to a meta-analysis, in which data on the satisfaction of around 8,000 people after various gender reassignment surgeries was evaluated, 77 people regretted the surgery (approx. 1%) (Bustos et al.2022)."

There two major problems with this statement. First, the meta-analysis by (Bustos et al. 2021) has serious flaws (Expósito-Campos and D'Angelo 2021).[11] And not mentioned by the Position Paper is the

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plausibly be taken as an indicator of less developed executive functioning. And there are several more sources of bias in this study.

Another instance of a problematic reference to the Arnoldussen paper, with omittance of reference to all studies with concerning results, was in a Dutch article by a number of prominent Dutch gender clinicians (Claahsen - van der Grinten et al. 2023), as discussed in (Smids and Vankrunkelsven 2023).

[10] The Position Paper: "No significant differences in performance (time, error rate) were found between the two groups of gender dysphoric children with and without pubertal blockade."

The abstract of the study: "We found no significant effect ofGnRHa on ToL performance scores (reaction times and accuracy) when comparing GnRHa treated. male-to-females (suppressed MFs, *n* = 8) with untreated MFs (*n* = 10) or when comparing GnRHa treated female-to-males (suppressed FMs, *n* = 12) with untreated FMs (*n* = 10). *However, the suppressed MFs had significantly lower accuracy scores than the control groups and the untreatedFMs*. (emphasis added (Staphorsius et al. 2015))"

And Baxendale on this study (p8): "While the groups did not differ with respect to reaction time on the Tower of London Test, suppressed male to females had significantly lower accuracy scores compared to the control groups. This pattern remained significant after controlling for IQ. Despite this, the reaction time finding has been subsequently been reported as evidence for no detrimental effects on performance in citations in the subsequent literature44 and in policy documents". The NEK-NCE Position Paper is a case in point.

[11] From (Expósito-Campos and D'Angelo 2021) : "In this letter, we argue that the conclusions of their systematic review and meta-analysis are questionable due to limitations in their methods and shortcomings of the studies selected. Starting with methods, the authors overlooked numerous relevant studies, including one of the best-known,2 raising
questions about the adequacy of their search strategy. One study3 was inappropriately included as it only investigated regret regarding choice of surgical procedure, not of surgery itself. In addition, there are significant data extraction errors, leading to erroneous conclusions. For instance, the sample for surgical regret in their largest included study4 was inflated from 2627 to 4863, likely due to a miscalculation from a table reporting the treatment patterns of that paper's total study population."

fact that many of the selected studies have substantial loss to follow-up. For example, the largest paper contributing about half of the participants, reports a loss to follow-up of 36% (Wiepjes et al. 2018). This means that the finding of the very low regret rate in this study is of questionable validity (Cf. Dettori 2011).

The second major problem is that this meta-review includes several studies reporting on less recent patient cohorts, who transitioned in another time and do not include the new cohorts of natal female adolescents discussed in the previous section. In these more recently transitioned patients, the regret rate is unknown, even though there are clear signals that their regret may come sooner after transition and that regret rates may be higher (Cohn 2023; Jorgensen 2023; Hall, Mitchell, and Sachdeva 2021; Expósito-Campos and D'Angelo 2021).[12]

Unfounded reference to "acute suicidal tendencies" when arguing against watchful waiting

On page 20, the Position Paper states that:

> However, this [i.e.taking a watchful waiting approach instead of halting puberty and potentially causing harmful side-effects] ignores the fact that medical intervention that is too late can also cause great harm, for example because it can make extensive surgical interventions necessary during a later medical transition that could otherwise have been avoided or because the symptoms of gender dysphoria worsen as puberty progresses, which can greatly increase the suffering of those affected, *even to the point of acute suicidal tendencies* (see Bauer et al. 2015). (emphasis added).

The reference to suicidal tendencies to support the argument that a wait and see approach could be harmful, is very problematic. As acknowledged by a WPATH commissioned systematic review, there is no proof that medical treatment reduces actual suicide (Baker et al. 2021). This finding is confirmed by a Finnish study that also shows that the actual number of suicide thankfully is low (Ruuska et al. 2024). Of course, suicidal tendencies are a serious matter as well, however, they are very common in people with mental health problems and may be due to present psychiatric comorbidity as much as to suffering from GD. It belongs to the profession of mental healthcare to deal adequately with suicidality, and should not be taken as justification for medically transitioning vulnerable adolescents.

The discussion of harms and side-effects is incomplete

[12] See also (Boyd, Hackett, and Bewley 2022, 12): *"Thus, the detransition rate found in this population is novel and questions may be raised about the phenomenon of overdiagnosis, overtreatment, or iatrogenic harm as found in other medical fields."*

Several serious side effect are lacking in the Position Paper's discussion. For example, not mentioned are pelvic floor problems (such as pelvic pain, which may lead trans men to opt for otherwise unwanted hysterectomy), vaginal atrophy, and sexual dysfunction (da Silva et al. 2024; Tordoff et al., n.d.; Zwickl et al. 2023; Dominoni et al. 2025).

In relation to the risks of cross-sex hormones, the Position Paper states that: "In addition to the aforementioned effects of hormone therapy on fertility, the main side effects are bone health and the risk of thrombosis and cancer. The available scientific evidence suggests that hormone therapy does not have any serious health disadvantages in healthy people (Hembree et al. 2009)". This is peculiar, since (Hembree et al. 2009) is the previous and not the current guideline (Hembree et al. 2017) of the Endocrine Society. Absence of evidence for serious health disadvantages is of course no evidence of absence of these harmful side effects. It should be noted that since 2009 and especially the last five years, the amount of medical literature on gender medicine has increased exponentially.

A large Dutch retrospective cohort study into health outcomes for transgender adults shows various elevated health risks and elevated mortality risks, notwithstanding that causality may be difficult to distribute between the effects of CSHs, life-style factors, minority stress, and still other factors (Blok et al. 2021). Some preliminary research suggests altered cardiometabolic changes in transgender youth (Nokoff et al. 2020). While there are clear signals of health risks and harmful side-effect, the main message of the recent reviews performed in service of the Cass review is high quality studies that could provide reliable information on medical harms are lacking (Taylor, Mitchell, Hall, Langton, et al. 2024; Taylor, Mitchell, Hall, Heathcote, et al. 2024).

Summarizing, the Swiss discussion should be informed by a much more complete, balanced, and accurate discussion of the medical harms and risks than is currently provided in the Position Paper.

5 The Position Paper's discussion of the ethics of medical treatment of gender dysphoria

In itself, it is helpful to provide an ethical analysis of medical treatment of adolescent GD based on the four principles of beneficence, non-maleficence, respect for autonomy and justice (Beauchamp and Childress 2019; Varkey 2021), as the Position Paper undertakes. However, the discussion lacks balance, both when it comes to space devoted to each of them separately, and the weight given to each of them in the final weighing of the pros and cons of medical treatment.

The basic medical ethical consideration is that to offer medical treatment, it should have a positive balance of benefit over harm, as these are established by scientific evidence of sufficient quality (cf. 3.2.1, p 19). As will be argued below, however, the Position Paper's discussion of beneficence (3.3) does not identify clear and scientifically established benefits that could justify the serious harms and risks. Somewhat surprisingly, (3.3) provides a lengthy discussion of the role of family and social context in the wellbeing of adolescents with GD, but no discussion of the potential benefits of medically treating them with PS, CSHs, and surgery. One would have expected a brief discussion of the conclusions of the various systematic reviews, which all conclude that there is only low or very quality evidence for psychological benefits of PS and CSHs. (NICE 2020; Ludvigsson et al. 2023; Zepf et al. 2024; Taylor, Mitchell, Hall, Langton, et al. 2024; Taylor, Mitchell, Hall, Heathcote, et al. 2024).

Regarding the ethical principle of non-maleficence, the discussion of this principle (3.2) naturally suffers from the Position Paper's incomplete and at times imbalanced, or even inaccurate, presentation and discussion of the various risks and harms of PS and CSHs in earlier sections (in its chapter 2). The bulk of the discussion in (3.2) is on the gaps in scientific evidence, and how to deal with these gaps in the medical decision-making with minors regarding medical treatment. The Position Paper refers to research results on PS for the indication *pubertas praecox*: "these results cannot be directly transferred to the treatment of minors with gender dysphoria, but they nevertheless provide valuable information on possible risks and side effects." While these results are indeed not without value, there are several disanalogies that render the comparison of only limited value. Most notably, PS for *pubertas praecox* is given to reduce sex hormones to age and developmentally appropriate levels and it is stopped at the time when normal pubertal development should occur; thus, it does not give rise to worries about a lock-in effect, and does not put children on a pathway to further medicalization. Furthermore, the condition that is being treated--*pubertas praecox*--has observable, biologically measurable symptoms (i.e. signs of puberty before a certain age) and a clear natural course (i.e., premature sexual maturation, fusing of growth plates leading to short adult stature); in contrast, there is no biological marker for GD and the natural history is unknown. Third, there have been trials for the use of blockers in precocious puberty, they are approved in the EU by the EMA and in the US by the FDA, unlike use for GD.

The Position Paper clearly recognizes the limitations of the evidence, but still argues that medical treatment can be justified:

> In the absence of effective treatment alternatives and in view of promising treatment results with regard to the mental health and quality of life of those affected (cf. Nobili et al. 2018) and the presence of sometimes enormous suffering, the threshold for ethically justifying a general decision not to treat is particularly high (cf. de Lara et al. 2020).

This reasoning does not hold. Implicit in this quote, and rightly so, the Position Paper recognizes the need for benefit to justify medical treatment. However, the reference to (Nobili, Glazebrook, and Arcelus 2018) is to a study with adults and not with minors who are treated with PS and CSHs. It is evidently problematic to appeal to a systematic review of treatments provided to adults to justify treatment of minors, especially when systematic reviews of studies of treatments for minors consistently report only low or very low quality evidence of benefit (see the reviews cited in the discussion above on (3.3). No matter how severe the suffering from GD, given the substantial harms and risks of PS and CSHs, there must be sufficient evidence of benefit to outweigh these harms. For, evidence of suffering, even strong evidence of suffering, is completely independent of clinical evidence for the relief of suffering.

It is therefore highly significant that, among others, Sweden has done that weighing of risks and benefits and comes to a different conclusion:

> At group level (i.e. for the group of adolescents with gender dysphoria, as a whole), the National Board of Health and Welfare currently assesses that the risks of puberty blockers and gender-affirming treatment are likely to outweigh the expected benefits of these treatments.[13]

Unlike the Position Paper's weighing, that of Sweden is based on a proper systematic review of studies about adolescents.

As a further problem, this section (3.2) repeats the problematic reference to supposedly low regret rates discussed in section 4 above.

Finally, the Position Paper rightly states that treatment decisions should be made on an individual basis. The suggestion seems to be that a careful individualized assessment of risks and benefits may

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[13] https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/kunskapsstod/2023-1-8330.pdf The above quote continues as follows: "The National Board of Health and Welfare therefore gives the following weak, negative recommendations as guidance to the healthcare system:
• Treatment with GnRH analogues, gender-affirming hormones, and mastectomy can be administered in exceptional cases.
Care must be provided on the basis of scientific evidence and proven experience and according to the principle of doing good and not harm. In revising its recommendations, the National Board of Health and Welfare has taken account of the fact that the efficacy and safety, benefits and risks of treatments are not proven [2] and that three factors have shifted the balance between benefit and risk in a negative direction:
• The uncertainty resulting from the lack of clarity about the causes, that the number of people diagnosed with gender dysphoria has continued to rise since the publication of the guidelines in 2015, particularly in the 13 to 17 age group and especially among people whose registered sex at birth is female. 4
• The documented prevalence among young adults of medical detransition, which is the process by which a person discontinues gender-affirming medical treatment for any reason or seeks to reverse the medical effects of completed gender-affirming treatment [3, 4]. According to the SBU, it is not possible to assess how common it is for young people to later change their perception of their gender identity or to discontinue a gender-affirming treatment [2].
• The experience-based knowledge of participating experts is less uniform than it was in 2015."

lead to the conclusion that 'in this individual case', there is a positive balance of benefit over harm. However, it should be noted that the lack of scientific evidence on known and unknow risks and on potential benefits is so weak that even individualized assessments are too fraught with uncertainty to confidently reach such judgments even for individual adolescents. The Position Paper therefore rightly notes (p22) that informed consent procedures should involve comprehensive disclosure and discussions of risks and harms, if, of course, the treatments were medically indicated and could be offered on the basis of a favorable risk-benefit profile.

Regarding the principle of justice, the Position Paper gives a rather extensive discussion of the importance of equal access to medically necessary care (Cf. Daniels 2008). However, European healthcare systems generally do not grant a right to medical care that is insufficiently evidence-based. For, such treatments do not qualify as medically necessary: there can only be medical need for treatment that indeed is effective in curing a condition, relieving suffering, etc. Hence, to emphasize just access to medical gender treatment presupposes effectiveness of these treatments, which as we have seen, is questionable.

This leads, finally, to the Position Paper's discussion of the principle of respect for autonomy. Here the discussion can be rather brief, because much has been said already above in connection to PS and the right to an open future. A strong point of the analysis is the emphasis on the weight of the decision of a minor to start a medical treatment pathway. Similarly, it is accurately noted that minors have the right to participate in shared decision-making. And indeed, expert clinicians should try their best to support minors in that process of shared decision-making, and therefore build a trusting relationship.

Yet, despite all these valuable observations, as discussed extensively above in section (2), the idea that PS is a reversable medical intervention that enables the minor to mature until decisional capacity is evidently present, is unfounded. This means that starting PS is not consistent with the Position Paper's strong statement that only minors themselves should give informed consent to starting a medical treatment pathway, and not their parents or other proxies. Summarizing, the Position Paper's strong commitment to true informed consent by the minor seems directly incompatible with PS, especially when starting PS at Tanner stage 2.

Finally, the Position Paper's extensive discussion of autonomy and self-determination, taking clearly more pages than the other medical-ethical principles, could invite the misunderstanding that this is the most important principle. While it should be stressed that this is not the approach defended by the Position Paper, sometimes respect for autonomy is taken to justify initiating a treatment, or to entail a right to one's preferred treatment (Cf. Goodman and Houk 2022). This is a mistake, as respect for autonomy first and foremost entails the right to be adequately informed about risks and benefits,

and to consent to or to refuse a treatment that has prior medical indication (i.e., has a scientifically established favorable risk-benefit profile (Cf. Gorin 2024)). Patient autonomy just does not guarantee a patient's right to medical interventions that do more harm than good.

In conclusion, the Position Paper's medical ethical analysis raises various valid and important points. Nevertheless, its most central thesis, that currently a sufficient ethical justification can be given for PS, CSHs for minors with GD is unfounded. Especially the principles of beneficence and non-maleficence entail the requirement that PS and CSHs have positive risk-benefit profile, for which there is no sufficient quality evidence.

6 Concluding discussion

In conclusion, the NEK-CEN Position Paper's central argument has been found wanting: puberty suppression (PS) has not been shown to be a psychologically reversible intervention, and on the contrary, there is alarming evidence of the lock-in effect; hence, PS cannot safeguard a minor's right to an open future. That is, PS cannot halt pubertal development and at the same time enable children's further maturation to a point where they have acquired capacity and still possess a meaningful choice to either stop the medical treatment pathway, or to continue with cross-sex hormones. Therefore, even though the Position Paper stresses autonomy and self-determination regarding the decision to medically transition, the NEK-CEN in fact defends a practice in which 10-11 year old children, without any meaningful capacity to give informed consent, start with puberty blockers and subsequently have a near 100 % likelihood that they will enter adulthood as lifelong patients, with a real possibility of infertility, sexual dysfunction, decreased bone health, impeded cognition, and still other health issues. And all this without credible evidence of psychological and psychosocial benefits that could outweigh these risks and harms.

A second and concerning major finding of this commentary is that the Position Paper's presentation and discussion of the various risks and harmful side-effects of puberty suppression and CSHs throughout its analysis is often incomplete, insufficiently balanced, and sometimes even incorrect.

Third, the medical-ethical analysis suffers from a lack of real engagement with, and ethical evaluation of, the total risks and harms in proportion to the potential benefits. Consequently, the Position Paper's recommendation to offer such treatments, even if on an individualized basis, appears unfounded.

These observed shortcomings are unfortunate, for treatment of GD, be it medical or non-medical, is fraught with ethical questions and dilemmas. It is therefore to be recommended that the ethical

discussion among Swiss professionals and society at large should be enriched by the broader ethical reflection available in the literature.[14] In this respect, given that both sides of the debate have felt the need to engage with the very extensive and thorough Cass review (Cheung et al. 2024), it is remarkable that any reference to this landmark review is absent from the Position Paper. Given the impact of the Cass review, it is highly recommended to involve it in the Swiss reflections and discussions as well. Similar considerations apply to the recent plea for caution by the European Society for Child- and Adolescent Psychiatry (ESCAP) (Drobnič Radobuljac et al. 2024).

A final remark concerns the need for more and better research. Throughout its analysis, the Position Paper frankly acknowledges the weakness of the scientific evidence. This is fully appropriate. The use of puberty blockers is "off-label" which ought to be governed by the key requirement that there must be reasonable expectation of benefit (Smeehuijzen and Smids 2024). While in the 2006, the Dutch clinicians noted positive results and used them to promote this "off-label" practice, we now have over 30 years of data that has been subjected to nearly a dozen of systematic reviews that noted that the observation of benefits are not trustworthy due to limited study designs (Abbruzzese, Levine, and Mason 2023).[15] Therefore, the Position Paper's, recommendation 2a states that "Existing research gaps should be identified and closed" (p28) is clearly to be welcomed.

[14] There are several ethics papers on both sides of the debate that seem not yet considered in the Position Paper (Lemma and Savulescu 2021; Gorin 2024; Wenner and George, n.d.; Jorgensen, Athéa, and Masson 2024; Baron and Dierckxsens 2022b; Ashley 2021; Baron and Dierckxsens 2022a; Lieke Josephina Jeanne Johanna Vrouenraets et al. 2015; D'Angelo 2023; Gorin, Smids, and Lantos 2025; Giordano and Holm 2020; Ashley 2023)

[15] If those interested in the debate, but who are not yet very familiar would read one paper, this should be that paper. It convincingly argues that the two Dutch studies (de Vries et al. 2011; 2014) that are the cornerstone of the evidence for pediatric gender medicine, are deeply flawed.

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