Formative development of a fertility decision aid for transgender adolescents and young adults: a multidisciplinary Delphi consensus study

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Abstract

Purpose No educational and decision support tools exist to aid transgender and non-binary (TNB) adolescents and young adults (AYA) in making decisions about fertility preservation in the context of initiating gender-affirming medical care that can impair fertility. This study identified critical content areas and learning objectives to include in a decision aid about fertility preservation targeted for TNB AYA.

Methods Delphi methodology was leveraged to engage 80 multidisciplinary experts in reproductive medicine and pediatric transgender health care in a two round consensus building procedure. Proposed content areas rated as “probably keep” or “definitely keep” by 75% of experts were retained. Proposed learning objectives reaching 75% agreement on ratings of importance and priority were also identified.

Results The Delphi procedure identified five priority content areas (Basic Reproduction; Gender-Affirming Medical Interventions: Impacts on Fertility; Established Fertility Preservation Options; Benefits and Risks of Established Fertility Preservation Procedures; Alternative Pathways to Parenting) and 25 learning objectives to prioritize in a fertility-related decision aid for TNB AYA.

Conclusion A multidisciplinary panel of experts achieved agreement around content areas and learning objectives to incorporate into a decision aid about fertility preservation for TNB AYA.

Keywords Fertility preservation · Shared decision-making · Gender diversity · Gender-affirming care · Expert consensus

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Introduction

In recent years, fertility and fertility preservation have garnered increasing attention in the context of gender-affirming medical care for transgender and non-binary (TNB) adolescents and young adults (AYA) [1, 2]. Both the World Professional Association for Transgender Health (WPATH) standards of care [3] and the Endocrine Society clinical practice guidelines [4] recommend that health professionals counsel TNB patients on fertility and fertility preservation as part of the informed consent process for gender-affirming hormones. Despite these recommendations, TNB AYA in the USA rarely pursue fertility preservation, with reported rates ranging from 2.7 to 4.7% across three studies [1, 5, 6].

Little is known as to why relatively few TNB AYA pursue fertility preservation, given comparatively higher rates of reported interest in biological parenthood (20 to 36%) in this population [7–9]. One qualitative study identified factors affecting TNB AYA's decisions to pursue fertility preservation, including AYA's desires to parent in the future, their experiences of gender dysphoria and perceptions of how fertility preservation procedures may affect gender dysphoria, family values and expectations of biological parenthood, financial considerations given costs of fertility preservation, and perceived comprehensiveness of fertility counseling by clinical providers [10]. Fertility preservation utilization may be low because TNB AYA are not being adequately counseled on their options. Research demonstrates variable clinician knowledge of fertility treatment options to support gender-affirming care [11]. Clinicians possessing more fertility-related knowledge more frequently discuss fertility preservation options with patients [11]; however, these discussions may be insufficient in meeting patient education and decision-making needs. In the aforementioned study of fertility preservation decision-making in TNB AYA, all AYA reported that their primary medical and/or mental health team discussed fertility [10]. However, while some felt the counseling they received was adequate to make an informed decision about fertility preservation, others felt counseling was incomplete, which hindered their fertility preservation decision-making and satisfaction.

Fertility counseling and patient decision-making is complicated by limited and conflicting research on the effects of gender-affirming hormones on fertility [12]. Some studies show that estrogen leads to histologic changes in the testicles of transgender women [13–15], whereas other studies demonstrate normal spermatogenic activity following estrogen discontinuation [16, 17]. Similarly, some studies document definitive adverse effects of testosterone on ovarian histology among transgender men [18–21], whereas other studies report minimal to no adverse effects [22–24]. Conflicting research evidence of the effects of gender-affirming hormones on fertility contribute to the challenges TNB AYA experience when making an informed choice regarding fertility preservation.

Standardized fertility counseling is needed to support informed decision-making about fertility preservation among TNB AYA [25]. Fertility-related decision aids are useful in supporting fertility preservation decision-making among parents of pediatric patients [26] and adult patients within the oncology context [27, 28]. No decision aids exist to support TNB AYA education and decision-making about fertility preservation. To guide the development of such a decision aid, this study aimed to identify key content domains and critical learning objectives for inclusion. Considering the complexity of fertility-related decision-making and the inconsistencies within the literature on the impact of gender-affirming medical interventions on fertility, we employed a Delphi consensus process to achieve expert agreement on priority content areas and learning objectives for inclusion in a decision aid about fertility for TNB AYA.

Method

The Delphi process reported herein is part of a larger overall study to develop a decision aid about fertility for TNB AYA. Formative work included a needs assessment of TNB AYA and their parents to identify factors affecting fertility decision-making [10] and preferences for timing and delivery of fertility preservation information in this population [29]. The goal of this Delphi process was to ensure that the decision aid about fertility we develop to meet the decision support needs of TNB AYA and their families also meet clinicians' expectations for covering content areas deemed important by the treating clinicians—pediatric transgender health clinicians and reproductive medicine/fertility specialists.

Delphi methodology

The Delphi procedure entailed multiple iterations of surveys completed by a panel of experts to build consensus [30]. This process allows for controlled feedback (i.e., an anonymous summary of results), which permits experts to reconsider their initial judgments, provide new insights, and clarify information from one round to the next [30], and statistical aggregation and analyses of group data that weighs responses of each participant equally [31]. Two rounds were planned so that experts could first review, rate, and suggest changes to an initial list of content areas and learning objectives, and then, in Round 2, rate a revised list of content areas and learning objectives after reviewing the average ratings for each from Round 1.

Development of the Round 1 Delphi survey

We engaged a 5-person multidisciplinary advisory board to generate content areas for inclusion in a decision aid about

fertility targeted for TNB AYA. Advisory board members specialized in the following areas: (1) bioethics, reproductive ethics, and gender theory; (2) pediatric and adolescent gynecology, transgender health; (3) reproductive endocrinology and infertility, transgender health; (4) reproductive endocrinology and infertility; and (5) reproductive biology and infertility. The advisory board identified six content areas for inclusion: Basic Reproduction, Gender-Affirming Medical Interventions: Impacts on Fertility, Established Fertility Preservation Options, Benefits and Risks of Established Fertility Preservation Procedures, Alternative Pathways to Parenting, and Experimental Fertility Preservation Options. The study team then developed learning objectives for each content area, resulting in 25 initial learning objectives.

The Round 1 survey included seven closed-ended questions regarding participant expertise and five closed-ended questions about their training, a list of the six proposed content areas, their 25 associated learning objectives, and 14 statements reflecting what is currently known about how gender-affirming medical treatments affect fertility, established fertility preservation options, and benefits and risks of fertility preservation. Experts rated whether each proposed content area should be included in the decision aid using a 4-point Likert scale: “Definitely Cut”, “Probably Cut”, “Probably Keep” or “Definitely Keep”. Experts rated the importance of each learning objective on a 5-point Likert scale: “Not at all important”, “A little important”, “Somewhat important”, “Very important”, or “Extremely important.” Experts also rated the degree to which they agreed or disagreed with statements reflecting the field’s current understanding of fertility effects of gender-affirming medical treatments and fertility preservation options using a 5-point Likert scale: “Strongly disagree”, “Disagree”, “Not sure”, “Agree”, and “Strongly agree.” A comment field enabled experts to suggest additional content areas, learning objectives, and other key considerations related to how pubertal suppression and gender-affirming hormones affect fertility and the benefits and risks of established fertility preservation options that they believed should be included in the decision aid.

Participants

We used purposive sampling (by discipline and areas of expertise) to recruit a sample of clinicians and/or researchers with expertise in transgender health, reproductive health (i.e., reproductive endocrinology, infertility, obstetrics and gynecology, reproductive biology), or both to participate in the Delphi study. Potential experts were identified through their membership in professional society LGBTQ+ Special Interest Groups (i.e., Pediatric Endocrine Society; American Society of Reproductive Medicine), were listed as primary medical or behavioral health clinicians at gender-affirming pediatric clinics across the USA and Canada [32], or were professional

contacts of the research team known to be providers who are either experts in transgender health or reproductive health. Eligibility criteria included at least 2 years of post-graduate training/experience in either reproductive medicine or pediatric transgender health care. Additional inclusion criteria for individuals with primary expertise in reproductive endocrinology, infertility, obstetrics and gynecology, and reproductive biology included caring for at least two transgender patients clinically within the past year or publishing at least 10 relevant peer-reviewed papers. Additional inclusion criteria for individuals with primary expertise in pediatric transgender health care included caring for more than 50 transgender adolescents and young adults (ages 8–24) or publishing at least one peer-reviewed paper related to fertility or reproductive health in transgender populations.

Data collection procedures

Informed consent was obtained prior to potential experts completing a screening questionnaire to determine eligibility using REDCap, an online research survey application. Experts meeting eligibility criteria were automatically directed to the Round 1 Delphi survey. Frequencies of experts’ inclusion ratings and importance ratings along with qualitative feedback were synthesized by the research team, who removed, added, combined, modified, and revised content areas and learning objectives to create a revised survey for Round 2. Consensus was operationalized a priori as 75% agreement or greater between experts that (1) a content area should “definitely” or “probably” be kept and (2) a learning objective was “very important” or “extremely important.”

The Round 2 survey included five content areas and 49 associated learning objectives for expert ratings and consensus building. Experts were informed that the content areas and learning objectives had been revised based on Round 1 comments, instructed to reconsider their ratings of importance for each learning objective, and rate revised and new learning objectives on importance. In addition, experts were prompted to prioritize two-thirds of the learning objectives within each domain. There were initially 61 learning objectives following revisions and additions from the Round 1 survey; however, 15 learning objectives were collapsed into three overarching learning objectives for priority ratings (e.g., To describe psychosocial implications, including (1) peace of mind/sense of relief that gametes are preserved for future since it is difficult to predict future fertility desires during childhood/adolescence; (2) minimizes potential regret related to infertility; (3) allows for consideration of role/desires of future partners if gametes are preserved; (4) may help one’s family members to be more supportive of medical transition if fertility is preserved). This study was approved by the Ann & Robert H. Lurie Children’s Hospital of Chicago Institutional Review Board.

Results

Of 176 potential experts, we were unable to locate contact information for 17 individuals, and 9 individuals' email addresses were invalid. Thus, 150 potential experts received the email invitation to participate in the Delphi study. Four declined participation; 46 did not respond. Of the 100 potential experts completing the screening questionnaire, 80 met eligibility criteria. Seventy-eight of 130 potential experts participated in the Round 1 survey (60% response rate). All 80 eligible experts were invited to complete the Round 2 survey. Fifty-nine experts participated in the Round 2 survey (45% response rate). Table 1 presents expert panel demographic characteristics.

Round 1 survey

Five of the six content areas met consensus to retain for the decision aid: 95% of experts endorsed retaining the Basic Reproduction content area, 100% endorsed retaining the Gender-Affirming Medical Interventions: Impacts on Fertility and Established Fertility Preservation content areas, and 99% endorsed retaining the Benefits and Risks of Established Fertility Preservation Procedures and Alternative Pathways to Parenting content areas. Only 73% of experts endorsed keeping the Experimental Fertility Preservation Options content area; thus, this content area was cut. In total, 13 out of 25 initial learning objectives met the 75% agreement threshold for being “very important” or “extremely important” (Table 2). None of the five learning objectives in the Experimental Fertility Preservation Options met 75% agreement for importance.

Experts were asked to suggest additional learning objectives they felt should be included in the decision aid. Twenty-five experts provided learning objective recommendations to include within the Basic Reproduction content area (e.g., anatomy of the human reproductive system; role of puberty on gamete production). Twenty-one experts suggested learning objectives within the Gender-Affirming Medical Interventions: Impact on Fertility content area (e.g., address the unknown long-term impacts of these interventions on fertility). Thirteen experts suggested learning objectives within the Benefits and Risks of Established Fertility Preservation Procedures content area (e.g., potential risk of future regret if patients decide not to pursue fertility preservation). Twenty-two experts suggested additional learning objectives within the Established Fertility Preservation Options content area (e.g., possible stress reduction and peace of mind resulting from preserving fertility which will allow for future parenting decisions). Twenty-seven experts suggested learning objectives for the Alternative Pathways to Parenting content area (e.g., unique

Table 1 Expert panel demographics (*N* = 80)

	<i>n</i> (%)
Highest degree earned	
MD/DO	69 (86)
PhD	9 (11)
MD and PhD	1 (1)
MA	1 (1)
Primary role	
Clinician	52 (65)
Clinician-researcher	26 (33)
Researcher	2 (3)
Area(s) of expertise	
Transgender health	34 (43)
Reproductive health	41 (51)
Both transgender health and reproductive health	5 (6)
Primary discipline/area of practice	
Reproductive endocrinology	35 (44)
Pediatric endocrinology	20 (25)
Adolescent medicine	9 (11)
Clinical child/pediatric psychology	5 (6)
Obstetrics and gynecology	3 (4)
Reproductive biology	2 (3)
Urology	2 (3)
Other (footnote)	4 (5)
Race	
White	55 (69)
Asian	12 (15)
Black or African American	4 (5)
More than one race	1 (1)
No response	8 (10)
Ethnicity	
Not Hispanic/Latinx	66 (83)
Hispanic/Latinx	6 (8)
No response	8 (10)
Gender	
Cisgender woman	52 (65)
Cisgender man	21 (26)
Genderqueer/nonbinary	1 (1)
No response	6 (8)

Note. “Other” primary discipline/area of practice is comprised of experts in child/adolescent psychiatry, family practice/family medicine, and pediatric gynecology

parenting experiences among gender diverse individual; surrogacy as an additional option).

Experts were also asked to consider whether any additional content areas should be included and, if so, identify relevant learning objectives within their proposed content area(s). Twenty-four experts proposed content areas for inclusion in the decision aid, and 15 experts included learning objectives

Table 2 Initial learning objectives generated by the study team

Learning objective	Importance rating: <i>n</i> experts who rated item as “very important” or “extremely important”/ <i>n</i> experts who responded to the item (%)
Content Area 1: Basic Reproduction	
1. To identify the kinds of gametes your body can produce for reproduction	62/76 (82)
2. To explain the role of puberty in facilitating reproduction	56/76 (74)
3. To describe how a baby is conceived	52/75 (69)
Content Area 2: Gender-Affirming Medical Interventions: Impacts on Fertility	
4. To explain how gender-affirming hormone treatment impacts fertility	75/77 (97)
5. To describe what pubertal suppression treatment is	72/77 (94)
6. To explain how pubertal suppression treatment impacts fertility	71/76 (93)
7. To describe what gender-affirming hormone treatment (testosterone/estrogen) is	69/76 (91)
8. To identify how gender-affirming “bottom” surgery impacts fertility	68/77 (88)
9. To describe how gender-affirming hormone treatment (testosterone/estrogen) works	60/76 (79)
10. To identify types of gender-affirming “bottom” surgery	57/77 (74)
11. To describe how pubertal suppression works	54/76 (71)
Content Area 3: Established Fertility Preservation Options	
12. To identify established fertility preservation options in the United States	74/77 (96)
13. To summarize the process for obtaining mature gametes for cryopreservation and timeline to complete gamete cryopreservation	68/77 (88)
14. To identify costs associated with gamete harvesting, long-term storage, and future gamete use	68/77 (88)
15. To describe the process for using cryopreserved gametes in the future	62/76 (82)
Content Area 4: Benefits and Risks of Established Fertility Preservation Procedures	
16. To summarize the benefits and risks of established fertility preservation	75/76 (99)
Content Area 5: Alternate Pathways to Parenting	
17. To identify two alternative pathways to parenting aside from being a biological parent (including choosing not to parent)	62/75 (83)
18. To describe unique considerations pursuing adoption or fostering as a transgender or gender-expansive individual	47/75 (63)
19. To summarize the process for adoption	46/75 (61)
20. To describe costs associated with adoption	39/75 (52)
Content Area 6: Experimental Fertility Preservation Options	
21. To define what it means for a procedure to be considered “experimental”	51/75 (68)
22. To identify costs associated with gonadal tissue harvesting, long-term storage, and future use	48/74 (65)
23. To identify experimental fertility preservation options (ovarian and testicular tissue cryopreservation)	42/76 (55)
24. To describe the process for obtaining gonadal tissue for cryopreservation (including need for IRB-approved protocol)	39/75 (52)
25. To describe the necessary scientific advancements needed to use cryopreserved testicular/ovarian tissue	33/75 (44)

Note. Learning objectives that met 75% agreement for importance are listed in bold

for their proposed content areas. We reviewed each proposed content area and determined that some were less relevant to our aims (i.e., “adolescent decision-making” and “contraception/menstrual suppression”) or addressed medical interventions (i.e., gender-affirming surgery) outside the intended scope of the decision aid. Thus, these additional content areas and learning objectives were not incorporated into the Round 2 survey. Some suggestions overlapped with existing content areas and learning objectives (i.e., “timelines and possible

options for fertility preservation after initiation of hormone therapy”) or recommended expanding on existing learning objectives (i.e., “It may be helpful to be more specific about gender dysphoria symptoms that may occur as a result of preservation”). These suggestions were incorporated into the revised learning objectives for the Round 2 survey.

Experts also rated their level of agreement with 14 statements about the effects of gender-affirming medical interventions on fertility, established fertility preservation options, and

benefits and risks for fertility preservation procedures (Table 3). These statements reflect the study team's synthesis of the existing literature. Given that research is limited and existing findings are mixed, expert ratings were used to ensure broad agreement with interpretation of current research findings. Only 3 of 14 statements reflecting the current understanding of how gender-affirming medical treatments affect fertility potential failed to meet the 75% agreement threshold.

Thirty experts also responded to an open-ended question requesting additional key considerations on the impact of pubertal suppression treatment on fertility. Their responses reflected the potential reversibility of this treatment's impact on fertility. Thirty-one experts provided additional considerations on the impact of gender-affirming hormones on fertility which pertained to unknown long-term impact and cost.

Round 2 survey

Of the 49 revised learning objectives, 40 reached the 75% agreement threshold for importance (Table 4). Experts prioritized 25 learning objectives. See Table 5 for the list of learning objectives that met consensus for prioritization.

We conducted post hoc analyses on items that did not meet consensus to explore whether 75% agreement was reached when considering different subgroups of experts (i.e., experts in transgender health, experts in reproductive health, and experts in both transgender health and reproductive health). Some items reached 75% agreement on ratings of importance within subgroups of experts. Specifically, 79% of transgender health experts (22/28) and 80% of experts in both transgender health and reproductive health (4/5) endorsed the learning objective "To describe how pubertal suppression works" as "very important" or "extremely important." Similarly, 76% of transgender health experts (19/25) endorsed the learning objectives "To describe psychosocial implications of pursuing fertility preservation, including: allows for consideration of roles and desires of future partners if gametes are preserved" and "To describe the lived experience of transgender and gender expansive individuals who have chosen to pursue adoption or other family building options" as "very important" or "extremely important". In addition, six items that did not reach the 75% agreement threshold for the entire sample reached consensus on ratings of importance among experts in both transgender health and reproductive health, including "To describe potential barriers to adoption or fostering as a

Table 3 Expert agreement ratings for statements reflecting effects of gender-affirming medical treatments, established fertility preservation options, and benefits and risks of fertility preservation

	Agreement rating: <i>n</i> experts rating "agree" or "strongly agree"/ <i>n</i> experts who responded to the item (%)
1. Sperm cryopreservation is considered an established method of fertility preservation.	76/77 (99)
2. Oocyte preservation is considered an established method of fertility preservation.	73/77 (95)
3. Specific benefits of fertility preservation procedures are unique to the individual, depending on an individual's desires to have genetically-related children.	72/76 (95)
4. Embryo cryopreservation is considered an established method of fertility preservation.	71/77 (92)
5. Testosterone and estrogen are not effective forms of contraception.	68/76 (89)
6. Worsening gender dysphoria due to delaying GAH initiation is a risk of fertility preservation procedures.	64/75 (85)
7. Ovarian hyperstimulation is a physical/medical risk of fertility preservation procedures.	62/74 (84)
8. Worsening gender dysphoria due to invasiveness of obtaining eggs or sperm is a risk of fertility preservation procedures.	63/76 (83)
9. Cryopreserving gametes may result in "false hope" or the belief that completing fertility preservation procedures guarantees that someone will be able to have genetically-related children in the future.	59/76 (78)
10. There are financial risks to cryopreservation gametes because it is possible that someone can discontinue hormonal treatment and conceive naturally.	58/75 (77)
11. Hemorrhage or injury during follicular aspiration are physical/medical risks of fertility preservation procedures.	57/75 (76)
12. Pubertal suppression using GnRHa prevents the maturation of germ cells when used in early puberty, thus reducing fertility preservation options.	51/77 (66)
13. Estrogen may damage testicular tissue and prevent sperm production.	48/76 (63)
14. Testosterone may damage ovarian tissue and negatively affect oocyte quality.	40/76 (53)

Note. GnRHa = gonadotropin releasing hormone agonist (i.e., pubertal suppression treatment). GAH = gender-affirming hormones (i.e., testosterone/estrogen). Statements that met 75% agreement are listed in bold

Table 4 Revised learning objectives based on Round 1 expert feedback

Learning objective	Importance rating: <i>n</i> experts who rated item as “very important” or “extremely important”/ <i>n</i> experts who responded to the item (%)
Content Area 1: Basic Reproduction	
1. To describe the effect on the body of testosterone and estrogen in people with testicles and ovaries	55/59 (93)
2. To identify the type of gametes one’s body can make for reproduction	53/59 (90)
3. To describe the body parts needed to make a baby (egg, sperm, uterus)	52/59 (88)
4. To explain the role of puberty in reproduction (i.e., gamete production)	47/59 (80)
5. To describe basic anatomy of the human reproductive systems	47/59 (80)
6. To introduce the idea that no one knows their future fertility potential, cisgender or transgender	46/59 (78)
7. To identify the stage of puberty when mature gametes are typically made	40/59 (68)
8. To compare conceiving a baby to carrying a pregnancy	40/59 (68)
9. To explain that oral and anal sex do not result in pregnancy	29/59 (49)
Content Area 2: Gender-Affirming Medical Interventions: Impacts on Fertility	
10. To describe what pubertal suppression treatment is	58/58 (100)
11. To describe what gender-affirming hormone treatment is (e.g., testosterone/estrogen)	56/58 (97)
12. To describe what is known/unknown about reversibility of negative effects on fertility if gender-affirming hormones are stopped	56/58 (97)
13. To describe what is known/unknown about how pubertal suppression treatment impacts fertility. This includes: discussing the timing of treatment initiation, used alone or concurrent with gender-affirming hormones	54/57 (95)
14. To describe the potential to reverse the effects of pubertal suppression treatment on fertility. For example, the time one would need to be “off” blockers in order to become fertile again.	54/57 (95)
15. To describe what is known/unknown about how gender-affirming hormone treatment impacts fertility. This includes: the timing of starting treatment and previous treatment with puberty blockers	53/57 (93)
16. To describe irreversibility of gender-affirming genital surgeries that negatively affect fertility (e.g., orchiectomy; hysterectomy; oophorectomy)	52/57 (91)
17. To identify which gender-affirming genital surgeries negatively affect fertility	52/58 (90)
18. To describe how gender-affirming hormone treatment works	50/57 (88)
19. To explain that gender-affirming hormones will not allow an individual to make gametes from reproductive organs they do not have	51/58 (88)
20. To describe the availability of other gender-affirming medical treatments that have differential effects on fertility (e.g., menstrual suppression using oral contraceptives, spironolactone)	51/58 (88)
21. To explain that the effects of testosterone/estrogen treatment on future children is unknown	49/58 (85)
22. To describe how pubertal suppression works	41/57 (72)
23. To identify types of gender-affirming genital surgery	39/58 (67)
Content Area 3: Established Fertility Preservation Options	
24. To identify established fertility preservation options in the United States (oocyte, sperm, and embryo cryopreservation)	56/56 (100)
25. To identify financial costs associated with gamete harvesting, long-term storage, and future gamete use	54/56 (96)
26. To explain that fertility preservation is possible even after being on testosterone/estrogen for several years	53/56 (95)
27. To describe when in puberty eggs/sperm can be obtained/frozen using non-experimental methods (e.g., after menses in someone assigned female at birth; after testes are about 12–15 ml in someone assigned male at birth)	51/56 (91)
28. To identify which financial costs may or may not be covered by insurance	51/56 (91)
29. To summarize the process for obtaining mature gametes for cryopreservation	49/56 (88)
30. To summarize the timeline to complete gamete cryopreservation as it relates to initiation of gender-affirming medical interventions	47/56 (84)
31. To describe success rates of current cryopreservation options	44/55 (80)
32. To recognize the possibility of multiple cycles of oocyte harvesting/sperm banking to have a reasonable chance of success with future use	44/56 (79)
33. To describe the process for using cryopreserved gametes in the future	44/56 (79)
34. To recognize the possibility of using sperm or egg donation from a relative (e.g., sibling)	43/56 (77)
35. To describe the lived experience of transgender individuals who have chosen to seek fertility preservation	41/55 (75)

Table 4 (continued)

Learning objective	Importance rating: <i>n</i> experts who rated item as “very important” or “extremely important”/ <i>n</i> experts who responded to the item (%)
36. To describe potential barriers in using cryopreserved gametes including ability to use gestational carrier (varies by U.S. state)	35/56 (63)
37. To describe the limited research on viability of using gametes that have been frozen for 10+ years	33/55 (60)
38. To describe what happens to frozen gametes that are not used	20/56 (36)
Content Area 4: Benefits and Risks of Established Fertility Preservation Procedures	
39. To identify the over-arching risks/side effects of established fertility preservation techniques, including: Possibility of permanent physical changes should one opt to stop pubertal suppression or gender-affirming hormone treatment for a period of time to complete fertility preservation	52/55 (95)
40. To explain that fertility preservation is an individual decision with varying benefits dependent on how much one values fertility	49/54 (91)
41. To identify the over-arching risks/side effects of established fertility preservation techniques, including: Possibility that multiple rounds of gamete retrieval may be needed	45/54 (83)
42. To identify the over-arching risks/side effects of established fertility preservation techniques, including: Potential failure of saved gametes to result in a live birth in the future	45/55 (82)
43. To identify the over-arching risks/side effects of established fertility preservation techniques, including: Inability to produce sperm or retrieve oocytes	44/55 (80)
44. To identify risks/side effects of oocyte cryopreservation including: Side effects of hormonal stimulation like breast tenderness and menses can worsen gender dysphoria	43/55 (78)
45. To identify the over-arching risks/side effects of established fertility preservation techniques, including: No long-term information on effects of gender-affirming hormone on future offspring if using gametes obtained after taking gender affirming hormones	41/55 (75)
46. To identify risks/side effects of sperm cryopreservation, including masturbation or ejaculation can worsen gender dysphoria	41/55 (75)
47. To describe psychological implications of pursuing fertility preservation, including: Allows for consideration of role/desires of future partners if gametes are preserved	39/54 (72)
48. To identify the over-arching risks/side effects of established fertility preservation techniques, including: Anesthesia for oocyte retrieval surgery or surgical testicular sperm extraction	39/55 (71)
49. To describe psychological implications of pursuing fertility preservation, including: Minimizes potential regret related to infertility	39/55 (71)
50. To describe psychological implications of pursuing fertility preservation, including: Peace of mind/sense of relief that gametes are preserved for future use since it is difficult to predict future fertility desires during childhood/adolescence	38/55 (69)
51. To identify risks/side effects of oocyte cryopreservation including: Ovarian hyper-stimulation syndrome	31/55 (56)
52. To identify the over-arching risks/side effects of established fertility preservation techniques, including: Loss of cryopreserved gametes due to technical issues	28/55 (51)
53. To describe psychological implications of pursuing fertility preservation, including: May help one’s family members to be more supportive of medical transition if fertility is preserved	23/54 (43)
54. To identify risks/side effects of oocyte cryopreservation including: Infection	23/55 (42)
55. To identify risks/side effects of oocyte cryopreservation including: Injury to bowel or bladder	22/55 (40)
Content Area 5: Alternate Pathways to Parenting	
56. To identify other parenting options, including choosing not to parent, adoption, fostering, donor gametes, surrogacy	52/55 (95)
57. To recognize that desires for genetically-related children may change over time, in either direction	48/55 (87)
58. To describe the lived experience of transgender and gender-expansive individuals who have chosen to pursue adoption or other family building options	38/53 (72)
59. To describe potential barriers to adoption or fostering as a transgender or gender-expansive individual depending on location/agency	35/54 (65)
60. To describe financial costs associated with adoption and variable nature of financial costs based on location/agency	34/55 (62)
61. To describe the process for adoption, including challenging parts of the process	32/55 (58)

Note. Learning objectives that met 75% consensus are listed in bold

Table 5 Final learning objectives

	<i>Priority rating: n experts who rated “yes, prioritize”/n experts who responded to the item (%)</i>
Content Area 1: Basic Reproduction	
1. To describe the body parts needed to make a baby (egg, sperm, uterus)	52/57 (91)
2. To describe the effect on the body of testosterone and estrogen in people with testicles and ovaries	49/57 (86)
3. To identify the type of gametes one’s body can make for reproduction	46/57 (81)
4. To describe basic anatomy of the human reproductive systems	45/57 (79)
5. To explain the role of puberty in reproduction (i.e., gamete production)	45/57 (79)
Content Area 2: Gender-Affirming Medical Interventions: Impacts on Fertility	
6. To describe what is known or unknown about how pubertal suppression treatment impacts fertility. This includes: discussing the timing of treatment initiation, used alone or concurrent with gender-affirming hormones.	48/50 (96)
7. To describe what is known or unknown about how gender-affirming hormone treatment impacts fertility. This includes: the timing of starting treatment and previous treatment with puberty blockers.	46/50 (92)
8. To describe what is known or unknown about the reversibility of negative effects on fertility if gender-affirming hormones are stopped	46/50 (92)
9. To describe what is known or unknown about how pubertal suppression treatment impacts fertility. This includes: the time one would need to be “off” blockers in order to become fertile again.	43/50 (86)
10. To describe irreversibility of gender-affirming genital surgeries that negatively affect fertility (e.g., orchidectomy, hysterectomy, oophorectomy)	42/50 (84)
11. To describe what gender-affirming hormone treatment is (e.g., testosterone, estrogen)	41/50 (82)
12. To describe what pubertal suppression treatment is	40/50 (80)
Content Area 3: Established Fertility Preservation Options	
13. To identify established fertility preservation options in the United States (oocyte, sperm, and embryo cryopreservation)	49/49 (100)
14. To explain that fertility preservation is possible even after being on testosterone or estrogen for several years	46/49 (94)
15. To summarize the process for obtaining mature gametes for cryopreservation	44/49 (90)
16. To describe when in puberty eggs or sperm can be obtained or frozen using non-experimental methods (e.g., after menses in someone assigned female at birth; after testes are about 12–15 ml in someone assigned male at birth)	44/49 (90)
17. To identify financial costs associated with gamete harvesting, long-term storage, and future gamete use	44/49 (90)
18. To summarize the timeline to complete gamete cryopreservation as it relates to initiation of gender-affirming medical interventions	43/49 (88)
19. To describe success rates of current cryopreservation options	41/49 (84)
20. To describe the process for using cryopreserved gametes in the future	40/49 (82)
Content Area 4: Benefits and Risks of Established Fertility Preservation Procedures	
21. To identify the over-arching risks and side effects of established FP techniques, including: (1) anesthesia for oocyte retrieval surgery or surgical testicular sperm extraction; (2) inability to produce sperm or retrieve oocytes; (3) loss of cryopreserved gametes due to technical issues; (4) possibility that multiple rounds of gamete retrieval may be needed; (5) possibility of permanent physical changes should one opt to stop pubertal suppression or gender-affirming hormone treatment for a period of time to complete fertility preservation; (6) potential failure of saved gametes to result in a live birth in the future; (7) no long-term information on effects of gender affirming hormone on future offspring if using gametes obtained after taking gender-affirming hormones	45/53 (85)
22. To explain that fertility preservation is an individual decision with varying benefits dependent on how much one values fertility	42/53 (79)
23. To describe psychosocial implications of pursuing FP, including: (1) peace of mind and sense of relief that gametes are preserved for future use since it is difficult to predict future fertility desires during childhood/adolescence; (2) minimizes potential regret related to infertility; (3) allows for consideration of role/desires of future partners if gametes are preserved; (4) may help one’s family members to be more supportive of medical transition if fertility is preserved	41/53 (77)
Content Area 5: Alternate Pathways to Parenting	
24. To identify other parenting options, including choosing not to parent, adoption, fostering, donor gametes, surrogacy	51/54 (94)
25. To recognize that desires for genetically-related children may change over time, in either direction	48/54 (89)

transgender or gender-expansive individual depending on location or agency.”

For priority ratings, post hoc analyses showed fewer instances of 75% agreement within subgroups of experts. However, experts in both transgender health and reproductive health met 100% agreement (5/5) on prioritizing “To explain that gender-affirming hormones will not allow an individual to make gametes from reproductive organs they do not have.”

Discussion

This study leveraged Delphi methodology to engage multidisciplinary experts in pediatric transgender health care and reproductive medicine in a consensus building process to identify critical content areas and learning objectives to incorporate into a fertility-related decision aid for TNB AYA. Despite growing recognition that fertility matters are important to discuss and consider in the context of gender-affirming medical care, medical and mental health providers caring for this population identify significant barriers to counseling [25]. One possible point of intervention is to develop standardized patient education and decision support tools [10].

The Delphi panel determined the following content areas should be included in a decision aid: Basic Reproduction, Gender-affirming Medical Interventions: Impacts on Fertility, Established Fertility Preservation Options, Benefit and Risks of Established Fertility Preservation Options, and Alternative Pathways to Parenting. Experts agreed that foundational knowledge of the anatomy of the human reproductive system, identifying what is needed to make a baby (i.e., egg, sperm, uterus), understanding the role of puberty in reproduction, and recognizing the types of gametes one can contribute for reproduction are necessary to highlight in a fertility decision aid for TNB AYA. There was agreement that a fertility decision aid targeted for TNB AYA must include information about what is known and unknown about how pubertal suppression and gender-affirming hormones can affect fertility—both while an individual is actively receiving treatment, and when treatment is discontinued. Furthermore, experts identified the need for TNB AYA to know what established fertility preservation interventions are available (i.e., oocyte, sperm, and embryo cryopreservation) and understand the process of gamete retrieval and costs of procedures. There was also agreement that TNB AYA must understand the risks and side effects of fertility preservation interventions to make an informed decision. Specifically, experts emphasized the need for AYA to understand that multiple rounds of gamete retrieval may be needed and that the process for gamete retrieval may exacerbate gender dysphoria [2, 33]. Further, experts emphasized that AYA must understand that completing fertility preservation does not guarantee a genetically-related child. Experts also agreed that TNB AYA should be aware of other

parenting choices, including adoption, fostering, using donor gametes, and surrogacy, as well as the financial implications of each of these parenting options. There was also agreement about the importance of explicitly highlighting the choice not to parent as a valid decision.

There were some learning objectives that approached but did not meet our consensus threshold on ratings of importance and/or priority but were deemed by our research team as important to consider retaining for a decision aid based on our clinical experience. Specifically, within the domain of Basic Reproduction, we plan to retain “to identify the stage of puberty when mature gametes are typically made” (met 53% agreement for prioritization) and “to compare conceiving a baby to carrying a pregnancy” (met 54% agreement for prioritization) even though only 68% of experts considered them very important/extremely important. A question commonly posed by TNB AYA and parents of younger TNB youth is when in development fertility preservation may be attempted and how much pubertal progression is associated with that stage of pubertal progression. In addition, a recent study found TNB AYA struggled to separate their understanding of genetic parenthood with carrying a pregnancy [34], emphasizing the need to distinguish these concepts.

Within the Established Fertility Preservation Options content area, the learning objective “to recognize the possibility of multiple cycles of oocyte harvesting or sperm banking to have a reasonable chance of success with future use” met consensus for importance, but only 69% of experts endorsed prioritization. Similarly, within the Benefits and Risks of Fertility Preservation content area, the learning objective “to identify the risks and side effects of sperm cryopreservation, including masturbation or ejaculation can worsen gender dysphoria” met consensus for importance, but only 28% of experts endorsed prioritization. Considering the gamete retrieval process may worsen gender dysphoria [2], and multiple rounds of retrieval may be necessary, we believe these are important considerations for TNB AYA making decisions about fertility preservation.

Experimental Fertility Preservation Options was the only content area that did not meet expert consensus to be retained within the decision aid, and none of the learning objectives within this content area met consensus on ratings of importance. Several experts did not think this should be included due to the limited research available about these options. Multiple experts indicated that all TNB AYA and their families should receive an overview of experimental options available, though some experts indicated that more in-depth details should be offered only if TNB AYA or their parents express interest.

Our study has limitations. We are potentially missing some expert perspectives: 76 potential experts either were unable to be reached or did not complete the screening questionnaire. We were unable to determine differences in characteristics

among experts who did not complete the screening questionnaire; thus, we were unable to determine potential participation bias. Of the 50 potential experts who received the survey link but did not respond or declined to participate, 46% ($n = 23$) were identified from the American Society of Reproductive Medicine LGBTQ+ Special Interest Group, 30% ($n = 15$) were identified from the Pediatric Endocrine Society Transgender Health Special Interest Group, 14% ($n = 7$) were professional contacts of our research team known to be experts in transgender health or reproductive health, and 10% ($n = 5$) were listed as healthcare providers in gender-affirming clinics [32]. Of the 100 experts who completed the screening questionnaire, 29% ($n = 29$) were identified from the American Society of Reproductive Medicine LGBTQ+ Special Interest Group, 29% ($n = 29$) were identified from the Pediatric Endocrine Society Transgender Health Special Interest Group, 27% ($n = 27$) were professional contacts, and 15% ($n = 15$) were listed as health care providers in gender-affirming clinics [32]. Thus, a larger percentage of the 50 non-responders were identified through the American Society of Reproductive Medicine and a smaller percentage of non-responders were professional contacts of the research team. Of the 21 eligible experts who were invited but did not participate in the Round 2 survey, 6 were experts in transgender health and 15 were experts in reproductive health.

This study identified five priority content areas and 25 learning objectives from a multidisciplinary panel of experts to inform the development of a fertility-related decision support tool for TNB AYA. Future research should engage end users—TNB AYA and their parents—to ensure that these content areas and learning objectives are sufficient to meet their fertility decision-making needs.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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