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Ethical Considerations of Ovarian and Testicular Tissue Cryopreservation in Pre-Pubertal Children Who Cannot Assent

Katarina Lee

Ethical Considerations of Ovarian and Testicular Tissue Cryopreservation in Pre-Pubertal Children Who Cannot Assent

Katarina Lee†

Introduction

In the last two decades, fertility preservation options have become a part of medical treatment for individuals undergoing gonadotoxic treatments, most typically as a result of oncology therapy.[1] However, the majority of studies and literature surrounding these procedures have focused on adults who have the ability to consent and pubertal children who have the ability to assent. The ethical considerations of experimental pre-pubertal fertility cryopreservation techniques have not been adequately addressed. The purpose of this Article is to argue that while parents and guardians normally have the best interests of their wards in mind when they make medical decisions, pre-pubertal fertility cryopreservation is ethically too problematic to permit parental or guardian consent without the child's assent. There are five parts to this Article: Part I will provide a background of the different fertility cryopreservation techniques available and their success rates; Part II will explain the guidelines governing pediatric experimental research; Part III will discuss informed consent and assent in the pediatric medical context; Part IV will provide the ethical arguments in opposition to pre-pubertal fertility cryopreservation without assent; and Part V will address the counter-arguments permitting pre-pubertal fertility cryopreservation without assent.

I. Current Fertility Preservation Technologies

There are several different fertility preservation techniques for those who are undergoing gonadotoxic treatments, including

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† The author holds a B.A. in Philosophy from the University of Dallas, a M.A. in Bioethics from New York University, and a J.D. with a concentration in Health Law and Bioethics from the University of Minnesota Law School. The author is a Clinical Ethics Fellow at Baylor College of Medicine's Center for Medical Ethics and Health Policy and an Adjunct Professor of Law at South Texas College of Law.

1. Anahad O'Connor, *After Cancer, Fertility Is Often Within Reach*, N.Y. TIMES: WELL (Sept. 23, 2013, 4:03 PM), http://well.blogs.nytimes.com/2013/09/23/after-childhood-cancer-fertility-is-within-reach-for-many/?mcubz=1.

hormonal therapies, gonad shielding during treatments, and creative surgical techniques to prevent damage to the gonads.[2] These treatments are often less invasive than fertility cryopreservation techniques and as a result are less ethically controversial. Additionally, both male and female pubertal patients may cryopreserve their mature gametes. Sperm from male pubertal patients is either retrieved through ejaculation or when "ejaculation is not possible," sperm may be retrieved through "electroejaculation, testicular biopsy, testicular sperm extraction, or epididymal sperm aspiration."[3] Ova from female pubertal patients are retrieved through a process of hormonally stimulating the ovaries to produce ova that are then aspirated from the ovary.[4] Patients may then cryopreserve their gametes independently while others may choose to create embryos with their gametes; afterwards, these embryos are cryopreserved.

Female patients have the additional option of cryopreserving ovarian tissue, a procedure that is currently experimental.[5] Ovarian tissue cryopreservation entails removing either "part of an ovary or a whole ovary."[6] In partial ovarian tissue cryopreservation, the ovarian cortex, or "the ovary's outer layer,"[7] is removed, then sliced into small strips and cryopreserved.[8] Eventually, these slices are thawed and placed back into the woman's body so that she can conceive naturally.[9] The benefit of cryopreserving ovarian tissue is that "[m]ost oocytes are located within the primordial follicles in the ovarian cortex; therefore, obtaining a small volume of cortical tissue potentially enables cryopreservation of large numbers of oocytes."[10]

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2. Stephanie J. Lee et al., *ASCO Recommendation on Fertility Preservation in Cancer Patients: Guidelines Summary*, 2 J. ONCOLOGY PRAC. 143, 143–44 (2006).

3. Am. Soc'y for Reprod. Med., *Fertility Preservation and Reproduction in Patients Facing Gonadotoxic Therapies: A Committee Opinion*, 100 FERTILITY & STERILITY 1224, 1226 (2013).

4. *Tests and Procedures: In Vitro Fertilization (IVF), What You Can Expect*, MAYO CLINIC, http://www.mayoclinic.org/tests-procedures/in-vitro-fertilization/basics/what-you-can-expect/prc-20018905 (last visited Oct. 23, 2017).

5. Am. Soc'y for Reprod. Med., *Ovarian Tissue Cryopreservation: A Committee Opinion*, 101 FERTILITY & STERILITY 1237, 1237 (2014).

6. *Fertility Preservation by Ovarian Tissue Banking (Ovarian Tissue Freezing)*, CTR. FOR HUMAN REPROD., https://www.centerforhumanreprod.com/services/fertility-preservation/ovarian-tissue-freezing/ (last updated Nov. 15, 2014).

7. *Id.*

8. *Female Cancer, Cryopreservation, and Fertility*, AM. SOC'Y FOR REPROD. MED. (2014), http://www.reproductivefacts.org/globalassets/rf/news-and-publications/bookletsfact-sheets/english-fact-sheets-and-info-booklets/female_cancer_cryopreservation_and_fertility_factsheet.pdf.

9. *Id.*

10. Am. Soc'y for Reprod. Med., *supra* note 5.

There have been successful pregnancies that have resulted from the re-transplantation of ovarian tissue,[11] including one recent patient who underwent the procedure prior to puberty.[12] If total ovarian failure is anticipated, an entire ovary may be removed and cryopreserved.[13] Notably, whole ovary cryopreservation is not as medically developed as partial ovarian tissue cryopreservation. There have not been any successful pregnancies resulting from a whole ovary being cryopreserved and then re-transplanted into the female.[14] There has been a successful pregnancy from a whole ovary being donated to another woman[15] and a successful pregnancy in which a whole ovary was removed, tissue was then removed from the ovary, and that tissue was then grafted to the woman's remaining ovary.[16]

The gametes of pre-pubertal patients cannot be retrieved through ejaculation or ova retrieval.[17] As a result, the only means of fertility cryopreservation for female children is ovarian tissue cryopreservation, which is identical to pubertal ovarian tissue cryopreservation.[18] The only option for male children is testicular tissue cryopreservation, as they are unable to produce semen and do not produce mature sperm.[19] Pre-pubertal testicular tissue contains stem cells that have the possibility of becoming mature sperm.[20] The idea is that the testicular tissue is either "reimplanted

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11. Rob Stein, *Freezing Ovaries Before Cancer Treatment May Preserve Fertility*, NPR (Oct. 7, 2015, 2:29 PM), http://www.npr.org/sections/healthshots/2015/10/06/446324220/freezing-ovaries-before-cancer-treatment-may-preserve-fertility (noting that Danish researchers found roughly one-third of participants who underwent the procedure succeeded in having a child).

12. Meera Senthilingam, *Woman Is First to Have Baby with Ovaries Frozen in Childhood*, CNN (Dec. 16, 2016, 3:40 PM), www.cnn.com/2016/12/15/health/first-birth-from-frozen-ovarian-tissue/index.html.

13. Am. Soc'y for Reprod. Med., *supra* note 5, at 1238.

14. *Freezing and Storing Eggs*, HUMAN FERTILISATION & EMBRYOLOGY AUTH., http://hfeaarchive.uksouth.cloudapp.azure.com/www.hfea.gov.uk/46.html (last accessed Oct. 23, 2017).

15. James Randerson, *Woman to Give Birth After First Ovary Transplant Pregnancy*, THE GUARDIAN (Nov. 9, 2008, 7:52 AM), http://www.theguardian.com/science/2008/nov/09/health; Sherman J. Silber, Gedis Grudzinskas & Roger G. Gosden, *Successful Pregnancy After Microsurgical Transplantation of an Intact Ovary*, 359 NEW ENG. J. MED. 2617, 2617 (2008).

16. *Baby Born from Ovary Frozen in Mother's Childhood*, BBC NEWS, (June 10, 2015), http://www.bbc.com/news/health-33063838.

17. Christine Wyns et al., *Options for Fertility Preservation in Prepubertal Boys*, 16 HUMAN REPROD. UPDATE 312, 315 (2010).

18. Am. Soc'y for Reprod. Med., *supra* note 5.

19. Wyns, *supra* note 17, at 312–315.

20. *Fertility Preservation Program*, CHILDREN'S HOSP. OF PHILA., http://www.chop.edu/services/fertility-preservation-program#.VkYOb4RDm51 (last visited Nov. 21, 2017).

as is or matured" prior to transplantation back into the grown and healthy child.[21] There has not been any proven success in humans, but animal studies have shown that testicular tissue can feasibly be removed and cryopreserved.[22] The Fertility Preservation Program at The Children's Hospital of Philadelphia (CHOP) is one of the most advanced and widely publicized centers in the United States providing these experimental treatments.[23]

II. Experimental Treatment in Pediatrics

These fertility cryopreservation techniques are experimental, meaning that children undergoing them should be protected by standard human research protocols for pediatrics. As a result, clinicians have developed protocols in order to comply with ethical standards in pediatric clinical trials.[24] In 2010, CHOP published its protocol for testicular tissue cryopreservation.[25] Similarly, in 2012, the University of Pennsylvania, in conjunction with CHOP, the Oncofertility Consortium, and the National Physicians Cooperative, published a protocol for pre-pubertal ovarian tissue cryopreservation.[26] Institutional Review Board (IRB) approval for pre-pubertal ovarian tissue cryopreservation was originally granted in April 2007 at the Hospital of the University of Pennsylvania (HUP) and in May 2009 at CHOP.[27]

Generally, research that is either funded by federal dollars or performed by certain government agencies or individuals is subject

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21. *Id.*

22. *Id.*; Honor Whiteman, *Deep-Freezing Testicular Tissue Produces Healthy Baby Mice*, MED. NEWS TODAY (July 2, 2014, 8:00 AM), http://www.medicalnewstoday.com/articles/279093.php.

23. *Fertility Preservation Program*, *supra* note 20. Note that many premier hospitals have begun offering fertility preservation programs in recent years.

24. Jordan Reese, *Penn Researchers Find Reproductive Germ Cells Survive and Thrive in Transplants, Even Among Species*, U. PENN NEWS (Dec. 14, 2009), http://www.upenn.edu/pennnews/news/penn-researchers-find-reproductive-germ-cells-survive-and-thrive-transplants-even-among-species.

25. J.P. Ginsberg et al., *An Experimental Protocol for Fertility Preservation in Prepubertal Boys Recently Diagnosed with Cancer: A Report of Acceptability and Safety*, 25 HUMAN REPROD. 37, 38 (2010). *See* PENN CTR. FOR BIOETHICS, THE PENN CENTER GUIDE IN BIOETHICS 335–36 (Vardit Ravitsky, Autumn Fiester & Arthur L. Caplan eds., 2009) ("If children cannot ejaculate or are too young, then testicular biopsy for sperm extraction or biopsy to use as germ cell repository can be done under IRB experimental conditions.").

26. Clarisa R. Gracia et al., *Ovarian Tissue Cryopreservation for Fertility Preservation in Cancer Patients: Successful Establishment and Feasibility of a Multidisciplinary Collaboration*, 29 J. ASSISTED REPROD. & GENETICS 495, 495 (2012).

27. *Id.* at 496.

to the *Common Rule*.[28] The *Common Rule*, codified in the Code of Federal Regulations, requires human subjects research, including research conducted on children, to abide by specific guidelines and ethical standards. Non-governmental institutions "that engage in human subject research that is conducted or supported by any U.S. federal department or agency that has adopted the Common Rule are required to"[29] adopt the Federalwide Assurance (FWA). This means, "an institution commits to HHS [Health and Human Services] that it will comply with the requirements in the HHS Protection of Human Subjects regulations at 45 CFR part 46 [The Common Rule]."[30] A pre-requisite of receiving FWA designation is that the institution is required to designate an IRB to perform "ethical review of proposed research."[31] The University of Pennsylvania[32] and CHOP[33] have adopted the FWA; as a result, research conducted at these institutions is required to follow the federal guidelines.

Using these federal guidelines, IRBs are to analyze pediatric experimental procedures under the following four categories: (1) "[r]esearch not involving greater than minimal risk,"[34] (2) "[r]esearch involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects,"[35] (3) "[r]esearch involving greater than minimal risk and no prospect of direct benefit to the individual subjects, but likely to yield generalizable

28. 45 C.F.R. § 46.101 (2016); *Federal Policy for the Protection of Human Subjects ('Common Rule')*, U.S. DEP'T. OF HEALTH & HUMAN SERVS.: OFFICE OF HUMAN RESEARCH PROTECTIONS, http://www.hhs.gov/ohrp/humansubjects/commonrule/index.html (last visited Nov. 8, 2017); Stanley G. Korenman, TEACHING THE RESPONSIBLE CONDUCT OF RESEARCH IN HUMANS (RCRH) ch. 3 (2006), https://ori.hhs.gov/education/products/ucla/chapter2/page04b.htm (last accessed Nov. 8, 2017).

29. Jennifer S. Geetter & James W. Kim, *OHRP Revises Federalwide Assurance*, NAT'L L. REV. (July 14, 2011), http://www.natlawreview.com/article/ohrp-revises-federalwide-assurance.

30. *Federalwide Assurances (FWAs)*, U.S. DEP'T OF HEALTH & HUMAN SERVS., http://www.hhs.gov/ohrp/assurances/assurances/index.html (last visited Sept. 23, 2017) (alteration in original).

31. OFFICE FOR HUMAN RESEARCH PROTS., U.S. DEP'T OF HEALTH & HUMAN SERVS., IRBS AND ASSURANCES, https://www.hhs.gov/ohrp/irbs-and-assurances.html (last visited Oct. 8, 2017).

32. *Assurances*, U PENN THE INSTITUTIONAL REVIEW BD., http://www.upenn.edu/IRB/mission-institutional-review-board-irb/assurances (last visited Nov. 22, 2017) (hereinafter IRB GUIDEBOOK).

33. *Federalwide Assurance (FWA): Compliance with Federal Regulatory Requirements and Guidelines*, CHILDREN'S HOSP. OF PHILA. RESEARCH INST., https://irb.research.chop.edu/federalwide-assurance-fwa# (last visited Nov. 22, 2017).

34. 45 C.F.R. § 46.404 (2016).

35. § 46.405.

knowledge about the subject's disorder or condition,"[36] and (4) "[r]esearch [that is] not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children."[37] *Minimal risk* "means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests."[38] The Institute of Medicine (IOM) has defined *greater than minimal risk* to be "a slight increase in the potential for harms or discomfort beyond minimal risk."[39] Additionally, IOM has defined *direct benefit* as "a tangible positive outcome," for example, "cure of disease, relief of pain, and increased mobility."[40]

In all four categories, IRBs are required to make sure "[a]dequate provisions are made for soliciting the assent of the children and permission of their parents or guardians."[41] Additionally, for research in Category 2, the following two requirements are needed: "(a) [t]he risk is justified by the anticipated benefit to the subjects; [and] (b) [t]he relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches."[42] For research in Category 3, the following are required:

> (a) [t]he risk represents a minor increase over minimal risk;
> (b) [t]he intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical . . . situations; [and]
> (c) [t]he intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or

36. § 46.406.

37. § 46.407; ROBIN LEVIN PENSLAR, PROTECTING HUMAN RESEARCH SUBJECTS: INSTITUTIONAL REVIEW BOARD GUIDEBOOK ch. 6, 19–21 (2nd ed. 1993); Michelle Roth-Cline et al., *Ethical Considerations in Conducting Pediatric Research*, *in* PEDIATRIC CLINICAL PHARMACOLOGY (Hannsjörg W. Seberth, Anders Rane & Matthias Schwab eds. 2011) 219, 225–30.

38. § 46.102(i).

39. Paul Litton, *Non-Beneficial Pediatric Research and the Best Interests Standard: A Legal and Ethical Reconciliation*, 8 YALE HEALTH POL'Y ETHICS 359, 377 (2008) (quoting COMM. ON CLINICAL RESEARCH INVOLVING CHILDREN, INST. OF MED., THE ETHICAL CONDUCT OF CLINICAL RESEARCH INVOLVING CHILDREN 17 (Marilyn J. Field & Richard E. Berman eds., 2004)).

40. COMM. ON CLINICAL RESEARCH INVOLVING CHILDREN, INST. OF MED., THE ETHICAL CONDUCT OF CLINICAL RESEARCH INVOLVING CHILDREN 132 (Marilyn J. Field & Richard E. Berman eds., 2004) [hereinafter CLINICAL RESEARCH INVOLVING CHILDREN].

41. § 46.404–07.

42. § 46.405 (alteration in original).

> condition which is of vital importance . . . [to] ameliorat[ing] [the] . . . disorder.[43]

Lastly, for research in Category 4, the IRB must "find[] that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children" and the Secretary, after significant review, finds the research permissible.[44]

III. Informed Consent and Assent in Pediatric Patients

Informed consent in pediatric patients can create significant legal and ethical concerns. Parents and guardians are legally able to consent and make decisions for their wards provided these medical decisions are in the best interests of the child.[45] Under the legal doctrine of *parens patriae*, the state has the authority to take action to protect children if a parent or guardian "demonstrably act[s] contrary to [the best] interests of the child."[46] As Professor Anne Tamar-Mattis states:

> The basis for parental control over the medical decisions for treatment of children is two-fold. It arises out of both the concept of a constitutional right to family privacy and the legal presumption that parents are best situated to make good decisions because "natural bonds of affection lead parents to act in the best interests of their children."[47]

Parents have been given significant deference to make medical decisions for their children as a result of the legal and social upholding of autonomous parenting.[48] However, disagreements do

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43. § 46.406.

44. § 46.407.

45. Jennifer L. Rosato, *Using Bioethics Discourse to Determine When Parents Should Make Health Care Decisions for Their Children: Is Deference Justified?*, 73 TEMP. L. REV. 1, 7–8 (2000); Mary Koll, *Growth, Interrupted: Nontherapeutic Growth Attenuation, Parental Medical Decision Making, and the Profoundly Developmentally Disabled Child's Right to Bodily Integrity*, 2010 U. ILL. L. REV. 225, 243 (2010).

46. J. Steven Svoboda, Robert S. Van Howe & James G. Dwyer, *Informed Consent for Neonatal Circumcision: An Ethical and Legal Conundrum*, 17 J. CONTEMP. HEALTH L. & POL'Y 61, 84 (2000).

47. Anne Tamar-Mattis, *Exceptions to the Rule: Curing the Law's Failure to Protect Intersex Infants*, 21 BERKELEY J. GENDER L. & JUST. 59, 79 (2006) (quoting Parham v. J. R., 442 U.S. 584, 602 (1979)). Opinions differ regarding the use of the best interests standard in pediatric experimental research. *See* Doriane Lambelet Coleman, *The Legal Ethics of Pediatric Research*, 57 DUKE L. J. 517, 609–10 (2007) (explaining how a balance between child protection and parents' consent is the right approach); Seema Shah, *Does Research with Children Violate the Best Interests Standard? An Empirical and Conceptual Analysis*, 8 NW. J. L. & SOC. POL'Y 121, 165–66 (2013) (arguing that a child's interest should not be absolute, but rather that the value of research and the public good should also matter).

48. Lee Black, *Limiting Parents' Rights in Medical Decision Making*, 8 AMA J.

arise in the medical treatment of children. There have been several legal actions where the religious beliefs of a parent have come into conflict with medical decision making of a child.[49] Generally, medical practitioners are obligated to provide treatment to pediatric patients if the treatment would reverse a life-threatening condition regardless of parental or guardian disagreement.[50] This long-standing concept is derived from the Supreme Court decision in *Prince v. Massachusetts*, when the Court concluded, "[p]arents may be free to become martyrs themselves. But it does not follow they are free, in identical circumstances, to make martyrs of their children before they have reached the age of full and legal discretion when they can make that choice for themselves."[51] Considering this legal framework, the American Academy of Pediatrics (AAP) has created guidelines that assist in obtaining informed consent from parents as well as assent from children; the AAP states: (1) "[p]ractitioners should seek the informed permission of parents before medical interventions (except in emergencies when parents cannot be contacted)" and (2) "[d]ecision-making involving the health care of older children and adolescents should include, to the greatest extent feasible, the assent of the patient as well as the participation of the parents and the physician."[52] As was noted in the federal guidelines, child assent should be solicited, but is not always legally required; as a result, it is usually left to IRB or ethics committee discretion.[53] Assent is defined as "a child's affirmative agreement to participate in research."[54] Notably, there is no specific age at which a child can assent; however, in practice, assent is sought from children above the age of six or seven.[55] Instead, determining the capacity to assent is analyzed by a variety of

OF ETHICS 676, 676 (2006); Koll, *supra* note 45, at 245–246 (discussing child organ donation and sterilization).

49. Black, *supra* note 48, at 676–677; Svoboda, *supra* note 46, at 84–88.

50. Danielle Chaet, *The AMA* Code of Medical Ethics' *Opinions Relevant to Patient- and Family-Centered Care*, 18 AMA J. OF ETHICS 45, 45–46 (2016).

51. 321 U.S. 158, 170 (1944).

52. Comm. on Bioethics, Am. Acad. of Pediatrics, *Informed Consent, Parental Permission, and Assent in Pediatric Practice*, 95 PEDIATRICS 314, 315 (1995) (emphasis omitted) [hereinafter Am. Acad. of Pediatrics].

53. CLINICAL RESEARCH INVOLVING CHILDREN, *supra* note 40, at 194–195 (providing examples of how IRB has practiced discretion); NAT'L INST. OF HEALTH, NAT'L CANCER INST., CHILDREN'S ASSENT (June 22, 2016), https://www.cancer.gov/about-cancer/treatment/clinical-trials/patient-safety/childrens-assent.

54. CLINICAL RESEARCH INVOLVING CHILDREN, *supra* note 40, at 157–158.

55. *Id.* at 156.

factors such as: psychological capacity, emancipation status, and whether the child is a "mature minor."[56]

The AAP requires that medical practitioners receive assent from capable pediatric patients by: (1) helping the pediatric patients understand their condition, (2) explaining the tests and treatments they will undergo, (3) making an assessment of how much the pediatric patient is understanding, and (4) "[s]oliciting an expression of the patient's willingness to accept the proposed care."[57] Furthermore, in regard to the expression of assent, the medical practitioner is required to weigh the child's assent "seriously," when considering appropriate medical care.[58] In human subjects research there is disagreement as to whether child assent is always required.[59] Notably, Ravitsky et al., argue the following in regard to assent in ovarian and testicular tissue cryopreservation,

> Child assent and parental consent should always be sought. If the child is too young to give assent, no procedure involving more than minimal risk and not for their proven benefit should be permitted. The consent should cover the possible use of the reproductive tissue, the duration of storage, and the disposal of the tissues in event of mental incapacitation or death.[60]

Given the federal and medical framework within which IRBs are to analyze the ethical permissibility of experimental fertility cryopreservation techniques, one can begin discussing the ethical arguments in favor of and opposed to testicular and ovarian tissue cryopreservation in pre-pubertal children who cannot assent.[61]

IV. Arguments in Opposition to Pre-Pubertal Ovarian and Testicular Tissue Cryopreservation Without Assent

This section of the Article will address the four main arguments in opposition to pre-pubertal ovarian and testicular tissue cryopreservation with children who cannot assent: (a) that these procedures are too medically risky, (b) that there is an impermissible conflict of interest in allowing parents and guardians

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56. *Id.* at 324–25 (explaining that the mature minor rule means a child is "sufficiently mature to make (certain) health care decisions"); 45 C.F.R. § 46.408(a) (2016); IRB GUIDEBOOK, *supra* note 32, at 6–22.

57. Am. Acad. of Pediatrics, *supra* note 51, at 315.

58. *Id.* at 315–16.

59. D.S. Wendler, *Assent in Paediatric Research: Theoretical and Practical Considerations*, 32 J. MED. ETHICS 229, 230 (2006).

60. PENN CTR. FOR BIOETHICS, *supra* note 24, at 336.

61. Note, for the few children who will reach puberty prior to the age of assent, parents and guardians should also be prohibited from cryopreserving their gametic material, as most of the arguments in this Article remain persuasive.

to consent, (c) that these procedures create secondary ethical problems through issues of control over gametic material, and (c) that given the federal guidelines and the lack of proven success, it is questionable whether this research should be conducted altogether on children.

a. Medical Risks

One of the major ethical concerns with childhood ovarian and testicular tissue cryopreservation is the issue of subjecting individuals who cannot assent or consent to non-medically necessary procedures. As will be discussed later, it is foreseeable that individuals will differ on determining the medical riskiness of ovarian and testicular tissue cryopreservation. However, any additional medical procedure has potential medical consequences,[62] and each additional procedure performed on a child will increase their medical risks.[63] There are several different types of medical risk associated with this form of fertility preservation: (i) procedural risk, (ii) reproductive organ and gametic risk, (iii) re-transplantation risk, and (iv) psychological risk.

i. Procedural Risk

Ovarian tissue is procured through laparoscopy surgery,[64] while testicular tissue is procured through removal of a testicle[65] or through a biopsy.[66] Testicular and ovarian tissue can either be procured simultaneously as the child is undergoing an unrelated medical procedure or the procedure can occur independently.[67] Children are required to undergo general anesthesia in order that the surgery can be performed to remove the tissue.[68] The argument

62. Heidi Stevens, *What Does the Future Hold for Kids with Cancer?*, STAR TRIB. (June 7, 2012, 8:10 AM), http://www.startribune.com/what-does-the-future-hold-for-kids-with-cancer/157559905/ (discussing fertility preservation for young children diagnosed with cancer).

63. *Id.*

64. Marie-Madeleine Dolmans et al., *A Review of 15 Years of Ovarian Tissue Bank Activities*, 30 J. ASSISTED REPROD. & GENETICS 305, 312 (2013).

65. U. PITTSBURGH, MANUAL OF OPERATIONS: TESTICULAR TISSUE CRYOPRESERVATION 5 (Sept. 2014), http://oncofertility.northwestern.edu/sites/oncofertility/files/TTC_Manual_of_Operations.pdf.

66. CHILDREN'S HOSP. OF PHILA., *supra* note 20.

67. Lindsey Tanner, *Kids with Cancer Get Futuristic Fertility Chance; Experimental Tissue-Freezing Even for Babies*, U.S NEWS & WORLD REP. (Sep. 28, 2017, 9:28 AM), http://health.usnews.com/health-news/news/articles/2015/08/11/kids-with-cancer-get-futuristic-chance-at-saving-fertility.

68. Mark F. H. Brougham & W. Hamish B. Wallace, *Male Infertility Following Childhood Cancer: Special Considerations for Fertility Preservation in Children*, *in* FERTILITY PRESERVATION IN MALE CANCER PATIENTS 164 (John P. Mulhall et al.

in favor of a simultaneous procedure is that the child does not need to undergo an additional anesthesia. This is especially important in young children, as there is significant concern about the effects of anesthesia on their brains.[69] Studies have shown "an association between learning problems and multiple exposures to anesthesia early in life—though not single exposures."[70] However, there are also concerns about keeping a child anesthetized for a lengthier period of time to complete the additional procedure, as there is some evidence that suggests spending more time under anesthesia can negatively impact recovery.[71] Usually, the risk of lengthier anesthesia is less than multiple anesthesias.[72] Notably, there has been at least one death reported due to an anesthesia complication during ovarian tissue cryopreservation.[73] In addition to anesthetic concerns, ovarian tissue retrieval can cause "discomfort, pain, bleeding from cicatrices,"[74] and urinary tract infection.[75] Another medical concern is whether ovarian or testicular tissue cryopreservation may compromise medically necessary care for the child, for example, if the child were to contract an infection and then not be eligible to undergo their medically necessary oncology treatments because of a weakened immune system.

ii. Reproductive Organ and Gametic Tissue Risk

There is both a risk to the tissue that is cryopreserved and a risk of damaging reproductive organs or material that are not surgically removed. There is a concern that testicular tissue

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eds., 2013).

69. Denise Grady, *Researchers Warn on Anesthesia, Unsure of Risk to Children*, N. Y. TIMES (Feb. 25, 2015), http://www.nytimes.com/2015/02/26/health/researchers-call-for-more-study-of-anesthesia-risks-to-young-children.html; Tara Haelle, *More Evidence That General Anesthesia May Affect Young Brains*, HEALTHDAY NEWS, https://consumer.healthday.com/cognitive-health-information-26/brain-health-news-80/more-evidence-that-general-anesthesia-may-affect-young-brains-700124.html (last updated June 8, 2015).

70. Grady, *supra* note 68.

71. Catherine Sharoky, *Time Spent Under Anesthesia Could Up Risk*, MED. ONLINE (July 20, 2005), http://www.medicineonline.com/news/12/1129/Time-spent-under-anesthesia-could-up-risk.html; Robert A. Yoho, Deborah A. O'Neil & Jeremy J. Romaine, *Duration of General Anesthesia and Surgical Outcome*, http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.501.7332&rep=rep1&type=pdf (last accessed Oct. 23, 2017).

72. Sharoky, *supra* note 71.

73. R. Imbert et al., *Safety and Usefulness of Cryopreservation of Ovarian Tissue to Preserve Fertility: A 12-Year Retrospective Analysis*, 29 HUM. REPROD. 1931, 1938 (2014).

74. *Id.*

75. Dolmans, *supra* note 64, at 310.

retrieval may cause trauma to the testicle.[76] Similarly, it is foreseeable that there could be trauma to the ovary (a concern with ova retrieval).[77] In one study reporting on whole ovary removal, twenty-seven percent of individuals reported complications due to the procedure, including the need to have "additional surgeries for cutaneous infections or bladder lesions."[78] Furthermore, cryopreservation can damage gametes through the process of being cryopreserved and then thawed.[79] Additionally, cryopreserving a full ovary can "fracture . . . the ovarian pedicle, preventing successful vascular transplantation; fracture of the surface of the ovary as a whole, which then provides an interface for ice crystal formation; inconsistent permeation of the cryoprotectant; and potential for ice crystal formation in the ovarian pedicle or ovary during warming."[80]

iii. Re-transplantation Risk

Another major concern about the reimplantation of cryopreserved gametic tissue is the potentiality of reintroducing cancerous cells into the patient.[81] This is a concern for both testicular[82] and ovarian[83] tissue cryopreservation. Typically, testicular and ovarian tissue cryopreservation is sought prior to gonadotoxic treatments to prevent damage to the tissue, but as a result, there may be cancerous tissue removed simultaneously with the gametic tissue.[84] The type of cancer that the patient suffers from may impact whether there is the possibility of re-transplanting cancerous cells from their gametic tissue.[85] Tissue taken from individuals who suffer from blood-borne cancers, such

76. G. Bahadur, R. Chatterjee & D. Ralph, *Testicular Tissue Cryopreservation in Boys. Ethical and Legal Issues*, 15 HUM. REPROD. 1416, 1419 (2000).

77. COMM. ON ASSESSING MED. RISK, ASSESSING THE MEDICAL RISKS OF HUMAN OOCYTE DONATION FOR STEM CELL RESEARCH: WORKSHOP REPORT 32 (Linda Giudice, Eileen Santa & Robert Pool eds., 2007), http://www.nap.edu/download.php?record_id=11832# (describing the connection between the surgical process and potential complications).

78. Imbert, *supra* note 73, at 1938.

79. Batuhan Özmen & Safaa Al-Hassani, *Techniques for Ovarian Tissue, Whole Ovary, Oocyte and Embryo Cryopreservation*, 11 J. REPROD. & INFERTILITY 3, 4–6 (2010); Dolmans, *supra* note 64, at 311; Jason Pacchiarotti et al., *Developing a Clinical-Grade Cryopreservation Protocol for Human Testicular Tissue and Cells*, 2014 BIOMED RESEARCH INT'L 1, 4 (2013).

80. Am. Soc'y for Reprod. Med., *supra* note 5, at 1238.

81. *Id.*

82. Pacchiarotti, *supra* note 79, at 9.

83. BBC NEWS, *supra* note 16.

84. Bahadur, *supra* note 76, at 1418; Dolmans, *supra* note 64, at 312.

85. Bahadur, *supra* note 76, at 1418; Dolmans, *supra* note 64, at 312.

as leukemia, have tested positive for cancerous cells.[86] In one study, tissue taken from breast cancer patients did not indicate cancerous cells, but the researchers cautioned that more screening was necessary.[87] Another study concluded that the possibility of reintroducing cancer was high in leukemia patients, moderate for gastrointestinal cancer patients, and low for Hodgkin's and Non-Hodgkin's Lymphoma, breast cancer, gynecological cancers, and sarcomas of the bone and connective tissue.[88]

iv. Psychological Risk

In addition to the physiological risks discussed above, it is worth noting the potential psychological impact ovarian and testicular tissue cryopreservation may have. This is a risk that can affect the child, the parents, and guardians who consent to the procedure.[89] There are three main concerns: (1) individuals will experience great emotional loss if the procedures do not work; (2) individuals may build up unrealistic faith and reliance upon the idea of using this gametic material in the future; and (3) if there are complications, the negative emotional impact this may have on the parents or guardians who consented to the procedure. Parents and guardians as well as the child are at risk for experiencing loss if these procedures are unsuccessful—the loss of potential genetically-related children and grandchildren. Furthermore, reliance upon frozen gametic tissue may impact choices and decisions cancer survivors make in their future, such as delaying procreation. Lastly, if there are negative complications, or if these procedures impact a child's medically-necessary treatment, it is foreseeable that parents and guardians may experience guilt or remorse.

However, clinical psychologist Dan Shapiro of the Humanities Department at Pennsylvania State University, College of Medicine, disagrees with many of these psychological concerns. Shapiro argues that "[g]iven what we know about the psychological challenges of infertility, which is enormously stressful—about as stressful as having a chronic pain condition—and the exciting promise of ovarian cryopreservation techniques, I think parents of

86. *See* Dolmans, *supra* note 64, at 312; *see also* Bahadur, *supra* note 76, at 1418 (discussing the risk of such transmission and trial evidence from mice).

87. Dolmans, *supra* note 64, at 312.

88. Mikkel Rosendahl, Tine Greve & Claus Yding Andersen, *The Safety of Transplanting Cryopreserved Ovarian Tissue in Cancer Patients: A Review of the Literature*, 30 J. ASSISTED REPROD. & GENETICS 11, 11 (2013).

89. Stevens, *supra* note 62.

children facing cancer treatments would be mistaken not to try this."[90]

From a utilitarian ethical analysis, conducting these procedures in pre-pubertal children who cannot assent to these risks is ethically impermissible. Parents and guardians should not risk the life and health of their children for the mere possibility that their children may be able to use this tissue in the future. Moreover, as was mentioned earlier in this Article, gonadotoxic treatments do not necessitate infertility. The most significant counter-argument to the medical-risk concern is that researchers and medical practitioners could mitigate some of the risk by following a criterion to determine which patients are the best candidates for tissue cryopreservation.[91] While selection criteria will limit who these procedures will be offered to, it does not address the fact that parents and guardians should not be risking the health and life of their children for a medically unnecessary procedure. If a child can and is willing to assent to this procedure, then medical practitioners should engage in a conversation about the risks and potential outcomes, but parents and guardians should not be permitted to subject their already-compromised child to additional medical risk, even at the risk of infertility. Potential procreative capability does not outweigh the health and life of the child.

b. Conflict of Interest

One of the major ethical concerns about cryopreservation is whether parents and guardians who consent to their pre-pubertal children undergoing these procedures have a conflict of interest. The conflict argument stems from the concern that parents, by cryopreserving their children's ovarian or testicular tissue, are either (1) acting in their self-interest in that they want genetically-related grandchildren, or (2) that they are imposing their preference of procreation on their children. Regarding the first concern, the

90. *Id.*

91. *See* W. Hamish B. Wallace et al., *Fertility Preservation for Girls and Young Women with Cancer: Population-Based Validation of Criteria for Ovarian Tissue Cryopreservation,* 15 LANCET ONCOLOGY 1129, 1130 (2014). In 2014, the University of Edinburgh set forth a criterion called the "Edinburgh Selection Criteria" to determine which female patients should be eligible for ovarian tissue cryopreservation. The following were used as selection criteria: (1) the patient was younger than 35 years; (2) had not received chemotherapy or radiotherapy if aged 15 or older, but mild, non-gonadotoxic chemotherapy was acceptable in female patients under 15; (3) a likely chance of living for five years; (4) a greater than 50% risk of developing premature ovarian insufficiency; (5) informed consent and assent (if possible); (6) negative HIV, syphilis, and hepatitis B tests; and (7) the patient was not pregnant and had no existing children. *Id.*

parent or guardian may have a great desire to have grandchildren and therefore may be cryopreserving their child's ovarian or testicular tissue so that they will be able to fulfill that desire to become a grandparent. The second concern is that parents or guardians will impose a sense of duty and pressure upon their child to eventually procreate in the future if they cryopreserve their ovarian or testicular tissue.

There are no persuasive counter-arguments to the concern that parents or guardians may be acting in their own self-interest, as it is nearly impossible to determine whether the parent or guardian simply wants to provide an option for future fertility for their child or if they are acting based upon their desire to become a grandparent. It is arguable that parents and guardians may not even realize that they are acting in their own self-interest, as they are too emotionally invested in their child's fertility. Notably, in the testimonies of parents who are a part of the experimental work being done at the University of Pennsylvania, many of the parents reiterated that they wanted to be grandparents.[92] Moreover, medical staff state that it is part of their job to "let [patients] know why [ovarian and testicular tissue cryopreservation] is important, and to . . . set the scene," even when the children stated that they did not know if they wanted to have kids.[93]

Furthermore, allowing parents and guardians to consent without a child's assent imposes certain values about procreation on children, when many individuals do not wish to procreate or may have different values regarding how they wish to build their families. Quinn et al., argued that these concerns are not justified because a child's values are already impacted by their upbringing, including the decision to have children, and that a child may feel pressure regardless of the situation to abide by their parent's wishes.[94] However, these counterarguments are unconvincing, as these children will eventually have to make decisions whether to implant, destroy, or donate their cryopreserved ovarian or testicular tissue, a situation they may not have desired to be in. Moreover, they may feel even more compelled to procreate because of the burden their families underwent to cryopreserve their

92. *See Fertility Options for Young Female Cancer Patients*, CHILDREN'S HOSP. OF PHILA. (Oct. 7, 2014), http://www.chop.edu/video/fertility-options-young-female-cancer-patients#.VkoyooRDm50; *see also Fertility Preservation for Boys Treated for Cancer*, CHILDREN'S HOSP. OF PHILA. (July 14, 2014), http://www.chop.edu/video/fertility-preservation-boys-treated-cancer#.VkoyJIRDm50.

93. *Fertility Preservation for Boys Treated for Cancer*, *supra* note 92.

94. Gwendolyn P. Quinn et al., *Preserving the Right to Future Children: An Ethical Case Analysis*, 12 AM. J. BIOETHICS 38, 39 (2012).

ovarian or testicular tissue. I do not intend to argue that procuring a child's assent will alleviate all of these conflicting concerns, as parents or guardians may still pressure their children to assent, but arguably, based upon the AAP's ethical guidelines stated earlier in this Article, assent will provide a better opportunity that a child's wishes will be abided by.

c. Decision-Making Concerns Regarding Cryopreserved Ovarian and Testicular Tissue

Another ethical concern is the issue of "control" of the ovarian or testicular tissue. The control issue has several components: (1) control over the tissue while the child is minor, (2) disposition of tissue, (3) claims to the tissue, and (4) addressing conflict. In regard to the first concern, if a child has the ability to assent, they would have the ability to partake in the decision-making process regarding their gametic tissue. However, if the child cannot assent, who should have the ability to make decisions over the gametic material? Will the material be cryopreserved until the child can assent? Additionally, it is unclear if the tissue would be re-transplanted when the child is healthy, when they can assent, or when they have reached majority. Regarding the second concern, as was mentioned above, Ravitsky et al. argue that the tissue needs to be destroyed if the child dies *or* is incapacitated.[95] Not only is permitting a parent or guardian to consent to destroying another independent individual's gametic material ethically problematic, it is foreseeable that a child may want their tissue donated and not destroyed.

There is also a potential concern that a parent or guardian may have a claim to the gametic material if the child dies. There are already controversies that occur when parents of deceased children stake a claim to the gametic material of their children.[96] Lastly, if the child cannot assent, it is unclear how conflict will be dealt with. The Office of the Human Research Protection Program states that when there is a conflict, a child should not be part of a study until the conflict is resolved.[97] But what happens if parents

95. PENN. CTR. FOR BIOETHICS, *supra* note 25, at 336.

96. *See* Hall v. Fertility Inst. of New Orleans, 94-1135 (La. Ct. App. 1994) 647 So. 2d 1348; *see also* Jessica Elgot, *Mother Loses Bid to Use Dead Daughter's Frozen Eggs to Give Birth to Grandchild*, THE GUARDIAN (June 15, 2015, 11:59 AM), http://www.theguardian.com/society/2015/jun/15/mother-loses-bid-to-use-dead-daughters-frozen-eggs-to-give-birth-to-grandchild; Yoram Yarkoni, *Fallen Soldier's Sperm at Center of Battle*, YNET (March 25, 2015, 10:54 PM), http://www.ynetnews.com/articles/0,7340,L-4640932,00.html.

97. *See* U.C.L.A.: OFFICE OF HUM. RESEARCH PROT. PROGRAM, *Guidance and*

and guardians do not agree after the tissue is cryopreserved? The current solution for conflict surrounding gametic material has been litigation. A simpler solution would be to conduct these experimental procedures only on children who can assent.

d. Should We Be Doing This Research?

Fundamentally, underlying all of the opposition arguments to pre-pubertal ovarian and testicular tissue cryopreservation without a child's assent is the question of whether this type of experimental research is permissible at this time. Determining whether pre-pubertal ovarian and testicular tissue cryopreservation should be conducted requires an analysis of the four federal guidelines discussed in Part II of this Article. Based upon potential medical risks stated in Part IV, Section a of this Article, it is arguable that ovarian and testicular tissue cryopreservation does not fit in the category of research that is of *minimal risk*, as subjecting a child to these risks seems greater than the risks a child would encounter in daily life or during routine medical tests.[98]

If one considers these fertility preservation procedures as research that involves *greater than minimal risk*, then the next question is whether fertility preservation provides a *direct benefit* to the child. According to the IOM, *direct benefit* means that there is a "tangible positive outcome"; a likely conclusion from the discussion in Part IV of this Article is that there is no "tangible positive outcome," there is only a mere *possibility* of a positive outcome. As a result, ovarian and testicular tissue cryopreservation would be subject to the additional requirements of Category 3 research. It is unclear whether pre-pubertal ovarian and testicular tissue cryopreservation could withstand the Category 3 requirement; "[t]he intervention or procedures present experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical . . . situations."[99] Arguably, the cryopreservation procedure is not something a child experiences with their expected oncology care. Moreover, if one considers these fertility preservation techniques to be outside the scope of Categories 1, 2, and 3 of the federal regulations, then pre-pubertal

Procedures: Child Assent and Permission by Parents of Guardians, http://ora.research.ucla.edu/OHRPP/Documents/Policy/9/ChildAssent_ParentPerm.pdf (last updated June 9, 2016).

98. 45 C.F.R. § 46.102(i) (2016) (defining "[m]inimal risk"). Note, interpreting the definition of minimal risk is controversial. D. B. Resnik, *Eliminating the Daily Life Risks Standard from the Definition of Minimal Risk*, 31 J. MED. ETHICS 35, 35 (2005).

99. § 46.406(b).

fertility cryopreservation is subject to significantly higher standards. The research would have to alleviate "a serious problem affecting the health or welfare of children" and the Secretary would have to review the research.[100] It is extremely unlikely that pre-pubertal fertility cryopreservation would meet this standard.

Determining whether these procedures follow appropriate federal guidelines and determining what category, if any, they are governed by greatly impacts whether these procedures should be ongoing. As mentioned earlier, Ravitsky et al. state that experimental procedures that are *greater than minimal risk* and that have no proven benefit should not be conducted without a child's assent.[101] Conceivably, the IRBs at the University of Pennsylvania and CHOP have concluded that ovarian and testicular tissue cryopreservation is of *minimal risk*, or of *greater than minimal risk* with a direct benefit to the child. However, considering the lack of successful data and the minimal animal trials, especially in the situation of testicular tissue removal,[102] it is imperative to question whether pre-pubertal ovarian and testicular tissue cryopreservation should be conducted at this time, regardless of assent.

V. Counter-Arguments in Favor of Pre-Pubertal Ovarian and Testicular Tissue Cryopreservation Without Assent

This section of the Article will address the three most compelling arguments in favor of pre-pubertal ovarian and testicular tissue cryopreservation without assent: (a) these procedures will potentially preserve a child's fertility; (b) parents and guardians have a moral responsibility to safeguard an "open future" for their children; and (c) these experimental procedures should be conducted for the advancement of science.

a. Potentially Preserving Future Fertility

The most persuasive argument in favor of cryopreservation of pre-pubertal ovarian or testicular tissue is that these procedures may potentially preserve fertility for children who may become infertile due to gonadotoxic treatment. Studies have shown that individuals who have been treated for childhood cancers have an increased risk of infertility.[103] Male survivors rank testicular

100. § 46.407.
101. PENN. CTR. FOR BIOETHICS, *supra* note 25, at 336.
102. Whiteman, *supra* note 22.
103. Denise Grady, *Childhood Cancer Survivors Face Increased Risks Later*, N.Y.

dysfunction as one of the major side effects of oncology treatments, while female survivors have experienced damage to their ovarian tissue and uterine function.[104] Determining the certainty of infertility in these situations is unpredictable and difficult, as infertility symptoms usually manifest much later in an individual's life. As a result, determining whether infertility is a direct result of gonadotoxic treatments or other secondary factors such as age is onerous and sometimes inconclusive.[105] Moreover, oncology treatments themselves vary and as a result will have different gonadotoxic severities.[106] Nonetheless, proponents of these procedures argue that the increased risk of infertility is sufficient reason to undertake these preventative measures. Additionally, there have been successful pregnancies after re-transplantation of ovarian tissue into women who have had their tissue cryopreserved, and animal trials have shown success with re-transplantation of testicular tissue.[107]

However, even though there is the potentiality of preserving fertility by cryopreserving ovarian or testicular tissue, there are two significant problems with this argument. First, there is no guarantee that re-transplantation of ovarian or testicular tissue later in life will result in fertility, as there are risks associated with removal, cryopreservation, and re-transplantation. Initially, ovarian tissue cryopreservation had a low success rate because the cryopreserving process damaged the tissue.[108] Eventually a new type of "freezing" called vitrification was developed in order to prevent damaging crystallization.[109] While vitrification proved more successful, the exact number of how many women have been re-implanted with their ovarian tissue remains unknown.[110] Therefore, the success rate may actually be inconsequential

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TIMES (Oct. 12, 2006), http://www.nytimes.com/2006/10/12/health/12chemo.html ?_r=0.

104. Sara E. Barton et al., *Infertility, Infertility Treatment, and Achievement of Pregnancy in Female Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study Cohort*, 14 LANCET ONCOLOGY 873, 873 (2013) (stating that female cancer survivors "are less likely to become pregnant than . . . their siblings"); Jill P. Ginsberg, *New Advances in Fertility Preservation for Pediatric Cancer Patients*, 23 CURRENT OP. IN PEDIATRICS 9, 11–12 (2011); Louise E. Bath et al., *Late Effects of the Treatment of Childhood Cancer on the Female Reproductive System and the Potential for Fertility Preservation*, 109 BRITISH J. OF OBSTETRICS & GYNAECOLOGY 107, 109 (2002).

105. Bath, *supra* note 104, at 107–108.

106. *Id*.

107. Wyns, *supra* note 17, at 316.

108. Quinn, *supra* note 94, at 2.

109. Wallace, *supra* note 91.

110. *Id.*

compared to risking gonad and gametic tissue damage. Second, refraining from cryopreserving ovarian or testicular tissue of children undergoing gonadotoxic treatments does not necessitate that these children will be infertile, as there are childhood cancer survivors who become pregnant.[111] In fact, some studies suggest that while female cancer survivors may take longer to get pregnant than sisters who have not had cancer, two-thirds of female cancer survivors initially deemed infertile eventually became pregnant, becoming so just took longer than their siblings.[112] Furthermore, "fertility cannot be assessed before puberty"; therefore, the effects of oncology treatments are unclear.[113] Lastly, this argument does not take into account the potential of less invasive fertility advancements that may be available in the future, nor does it account for other options in creating a family, such as adoption or the use of donor gametes.

b. Moral Responsibility to Give Children All Options

Parents and guardians have a moral and legal duty to act in the best interest of their child. Defining what is considered to be in the best interest of a child is extremely difficult, especially in the area of medical decision-making. As a result, it is arguable that parents and guardians of children experiencing gonadotoxic treatments should, or are required to, cryopreserve their children's ovarian or testicular tissue as part of their duty as parents and guardians. The argument in "bioethical literature [is coined] as a 'right in trust,' to be safeguarded until the child reaches adulthood."[114] The argument originally stems from the bioethical and philosophical concept of an "open future."[115] An "open future," originally posited by the academic Joel Feinberg, means that there are a "set of moral rights children possess that are derived from the autonomy rights of adults."[116] As a result, children have the right to future fertility because as an adult they would have the capacity to make the autonomous decision whether to procreate. Arguably,

111. Andrew Seaman, *Pregnancy Possible for Many After Childhood Cancer*, REUTERS, July 15, 2013, http://www.reuters.com/article/us-pregnancy-possible-idUSBRE96E0Q120130715.

112. *Id*.

113. Wyns, *supra* note 17, at 313.

114. Pascale Jadoul, Marie-Madeleine Dolmans & Jacques Donnez, *Fertility Preservation in Girls During Childhood: Is It Feasible, Efficient and Safe and to Whom Should It Be Proposed?*, 16 HUM. REPROD. UPDATE 617, 621 (2010).

115. Joseph Millum, *The Foundation of the Child's Right to an Open Future*, 45 J. SOC. PHIL. 522, 522 (2014).

116. *Id.*

fertility is a component of normal human functioning, and as Professor Norman Daniels would argue, "protecting normal functioning contributes to protecting opportunity."[117] Thus, proponents argue that even if a child cannot assent to the procedure, it is the obligation of the parent or guardian to consent. Furthermore, the extension of this argument is that parents could be deemed irresponsible or neglectful if they do not provide this option for children, because of the burden of potential infertility.[118]

While parents and guardians should provide opportunities that are beneficial to their children, it is unconvincing to suggest that they would be morally required to provide an experimental medical treatment to their children. Additionally, if one follows this argument in its entirety, why would ovarian and testicular tissue cryopreservation be only limited to individuals who are experiencing gonadotoxic treatment? There is an argument to be made that if parents have an obligation to create and maintain an "open future" for their children, they should provide fertility preservation mechanisms at an early age because (1) there are many causes of infertility that a child may face in their future, and (2) if ovarian and testicular tissue cryopreservation happen while the child is young, they will have no recollection of the procedures. Most would agree that subjecting an otherwise healthy child to an unnecessary medical procedure is ethically problematic. Realistically, practical financial considerations or religious or philosophical beliefs will prevent parents from permitting ovarian and testicular tissue cryopreservation for their children who are experiencing gonadotoxic treatments; therefore, the moral responsibility argument is unconvincing.

c. Advancement of Science as a Societal Imperative

As was mentioned earlier in this Article, the federal guidelines may permit otherwise not-approvable human subject research using children if it "presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children."[119] There is an argument that even if cryopreservation of a specific child's gametic tissue were unsuccessful in being re-

117. Norman Daniels, *Justice, Health, and Health Care*, 1 AM. J. OF BIOETHICS 2, 3 (2001).

118. *See Global Prevalence of Infertility, Infecundity and Childlessness*, WHO, http://www.who.int/reproductivehealth/topics/infertility/burden/en/ (last visited Oct. 8, 2017) (providing access to sources which outline the prevalence and impacts of infertility).

119. 45 C.F.R. § 46.407 (2016); IRB GUIDEBOOK, *supra* note 31.

transplanted, developing these fertility preservation techniques assists in the advancement of science. Moreover, improving the quality of life of cancer survivors is a beneficial social good. Unlike adult-onset cancer, pediatric patients have approximately an eighty percent long-term survivorship rate, which plausibly warrants development of medical care for their future.[120]

However, as I argued before, it is unlikely that pre-pubertal ovarian and testicular tissue cryopreservation will meet the requirements for research in Category 4. A part of the requirement for Category 4 research is that the IRB must "find[] that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children."[121] It is unlikely to do so, because while infertility is a serious medical concern, potential infertility would not meet this threshold in consideration of the potential medical risks children would undergo during this research. Developing fertility preservation techniques for children who experience gonadotoxic treatments is an ethically worthwhile venture. However, under a utilitarian ethical framework, subjecting children, especially children who cannot assent, to medically risky research that may not directly benefit them, simply for the potential of preserving another child's fertility, is ethically impermissible.

Conclusion

While the intention of ovarian and testicular tissue cryopreservation in pre-pubertal children is to benefit children undergoing gonadotoxic treatments, it is ethically too problematic to be permissible. The potential benefit of preserving fertility does not outweigh the potential medical consequences and the conflicts of interest, nor does it address potential future conflicts that will result due to the cryopreserved material. Assent, while not alleviating all concerns, will mitigate many of them. Moreover, the federal guidelines and the AAP both highly encourage seeking assent when conducting medical and experimental research on children. Finally, the counter-arguments are unconvincing given the potential risks to which children are exposed. As a result, ovarian and testicular tissue cryopreservation in pre-pubertal children without assent should not continue at this time.

120. Quinn, *supra* note 94, at 38.
121. § 46.407.