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Review Article

Ovarian Tissue Cryopreservation / Transplantation for Social Reasons: Between (“Good”) Medicalization and Medical Treatment

Abstract

Background: Ovarian tissue cryopreservation / transplantation (OTC/OTT) has recently been considered as a well-established rather than an experimental method (at least adopting *pragmatic optimism*) and turned into a realistic option for a healthy woman needing to delay her childbearing and defer her menopause. Thus, going beyond “normality” through medicalizing a normal aspect of a woman’s life or addressing a medical problem?

Discussion: Ovarian tissue has a dual nature: it is an organ with a dual function: endocrine and gametogenesis. Premature ovarian failure may be an unhealthy state insofar as health is captured in a holistic way according to Nordenfelt’s or especially Richman’s theory, especially if Elson’s theory of hormonal hierarchy is true. Childbearing age is broadly captured, involving what for the time being is meant as early post-menopausal stage, since human life expectancy has expanded significantly but the childbearing lifespan of a woman has not. On the other hand, it is not clear whether the social environment represents a social determinant of public health or a mere cause of a woman’s ill health at least in so far as autonomy is captured through the relational model of autonomy.

Conclusion: OTC/OTT for a “healthy” woman are carried out in a blurred and clearly shifting gray zone between normality and pathology when performed at a childbearing age, thus fostering an already existing situation. OTT/OTC constitute “good” (ethically acceptable) medicalization which is subtly diversified from medical treatment as being divided from it with a thin blurring borderline, thus being on the cusp of becoming medical treatment based on solid medical reasons.

Abbreviations

OTT: Ovarian Tissue Transplantation; OTC: Ovarian Tissue Cryopreservation; OT: Ovarian Tissue; HRT: Hormone Replacement Treatment.

Background

In spite of the hitherto supported experimental nature of ovarian tissue cryopreservation and transplantation (OTT/OTC) as methods implying unsafety, inefficiency and uncertainty [1-5], most recently they tend to be categorized as well-established [6-7] rather than experimental procedures, although they are invariably optimized [7]. OTT represents a solution for women that suffer premature ovarian menopause (POM) and infertility, especially in the field of oncofertility (preservation of fertility threatened by oncologic diseases or gonadotoxic treatment) [8], thus restoring their “quality

of life”. Moreover, OTC/OTT might be turned into a realistic option (and a viable alternative to social oocyte freezing) for a healthy woman to prolong her childbearing lifespan and defer her menopause [9-10]. The social reasons for opting OTC/OTT methods by women is that in their relatively short reproductive lifespan they may find it difficult to combine starting a family (after having found a suitable partner) with pursuing a career, education and achieving economic stability, especially under the holding social circumstances which are male-centered, if not oppressive (patriarchy). Hence, OTC/OTT can afford a leap towards expanding the woman’s reproductive autonomy which –as is argued below– seems to be threatened with restriction for social/cultural reasons. Reproductive autonomy has an intrinsic value [11] for a woman and should be captured broadly [12], including whether, with whom, how many and when she will have children, ranking her life plan reproductive priorities according to her genuine choice. Recently, women tend to have a positive attitude towards the eventuality to

expand their childbearing age for lifestyle reasons [13]. The risk of premature ovarian failure (for idiopathic or pathologic reasons) and social reasons seem to increasingly skew young women towards resorting to fertility preservation methods [7]. Thus, is it attainable with a method going beyond “normality” (through medicalizing a normal aspect of woman’s life) or addressing a medical problem?

The alternative option of oocyte cryopreservation has also uncertainties (albeit of a different nature); it only serves the purpose of reproduction, and the yield of oocytes per cycle is limited [14].

OT has a dual nature, and consequently a dual ethical consideration. From an ethical (and legal) standpoint it may be considered as being both an organ (having endocrine function) and a gamete (being ovulating tissue) [15]. Is it the donation of a gamete or an organ for transplantation? The answer occupies the intersection of organ transplantation and “assisted reproductive technologies”. What seems more salient is the nature of OTT as gamete donation but it actually depends on an unreliable and absolutely subjective criterion, the woman’s intention [15]. Andersen and Kristensen reasonably state [16] that heterotopic OTT would serve exclusively to postpone menopause (produce hormones) but this is –at least for the time being – an unreliable criterion as transplant’s functionality remains doubtful [10]. Ovarian tissue as having a dual nature is serving both reproduction (reproduction health) and gender identity (sexual health). As I argue below, both of them are highly socially determined. According to the “hormonal hierarchy theory” identified by Elson [17], a woman’s sense of her femininity (experience of herself as woman, gender identity) is proportional to the rate of ovarian tissue existing in her body. Keeping the two ovaries is assumed to be the highest hierarchy. OTC/OTT can be preserving for both a woman’s fertility and her sense of femininity.

OTT may be either homologous (autologous) transplantation (that is currently into place) using the recipient’s her own cryopreserved cortical tissue (the ovarian tissue, the autograft, is inserted back into the donor’s body, either into the anatomic area of ovary (orthotopic) or into a nearby area as abdomen or skin (heterotopic) or heterologous transplantation using fresh tissue donated by the recipient’s monozygotic twin (iso-transplantation, thus without using immunosuppressive agents) or another woman (allo-transplantation, thus using immunosuppressive agents, a very risky method that makes the implementation of allo-transplantation out of place).

Among the advantages of OTC/OTT are the following: A big number of oocytes can be frozen “in one shot” and within a very short timeframe. This is a major advantage in comparison to oocyte or embryo freezing. Besides, OTC/OTT is a considerably important method (perhaps the only viable option) of fertility preservation for prepubertal girls. On the other hand, among the major disadvantages of OTC/OTT methods are the two following: a) post-grafting ischemia (it has already been mostly addressed by development of vascularization stimulating

surgical methods), b) retransferring of cancer cells in the body of the recipient after the autografting (it has been mostly addressed by development of screening of the graft methods).

Structure and Content

As I argue below, the existence of functioning ovarian tissue in female body can promote the total health of a woman, since it has been conceptualized through holistic theories of health. Furthermore, most probably a) The significant expanding of lifespan should be accompanied by an (at least marginal) childbearing lifespan expanding, b) The social and cultural environment in all likelihood restrict the childbearing age woman’s reproductive autonomy (affecting her autonomous volition to remain childless), especially if autonomy is captured through the “relational” model. Regarding an OTC/OTT sought by a childbearing age woman, there is no sharp categorical distinction in terms of having reproductive “vital options” between a clearly selfish childless woman, a proactive woman, a woman being “prevented” by her social/cultural environment in making genuine autonomous reproductive decisions, finding a suitable partner or more widely reaching her reproductive goals, and an oncologic woman being threatened with immediate (iatrogenic or medical) premature menopause. In addition, in light of holistic theories of health, a woman’s health may be considered harmed or threatened by her social and cultural environment. It is rightly stated that there is no categorical distinction between medical and non-medical reasons for resorting (a healthy woman) to fertility preservation methods. OTC/OTT can counterbalance the abovementioned restriction to a woman’s reproductive autonomy by expanding it. c) Modern medicine aims at promoting health and current longevity along with quality of life and anti-ageing. d) The distinction between idiopathic (premature) and menopausal (normal) ovarian failure remains blurred as it varies with regard to each single woman.

Therefore, and considering the division of normality from pathology regarding pregnancy at an early post-menopausal stage much more subtle, I attempt to argue that OTC/OTT can interpret as “(good) medicalization” an aspect of human life pending between normality and pathology, at least when performed before the upmost end of childbearing age. Moreover, the acceptance that it is about a “good” medicalization is supported by the fact that OTC/OTT is fostering an already existing situation, extending it for a few more years. OTC/OTT may be regarded as a method being on the cusp of becoming medical treatment based on solid medical reasons.

In this study, OTC and OTT are considered a united entity since (auto-) OTT is performed on the promise of previous OTC. Besides, OTC/OTT has uncertainties (especially long term ones) and ambiguities (e.g. in obtaining a vial pregnancy or an adequate and relatively long-term endocrine function). These are supposed to be overcome in this approach from the viewpoint of *pragmatic optimism*. The hereby attempted ethical approach is rooted in an exhaustive review of the relevant literature. The deep exploration of the meaning of health and autonomy is of a great importance in this paper.

Discussion

Holistic theories of health and well-being

Under the holistic theories of health, especially Nordenfelt's theory [18] or Richman's theory [19] of embedded instrumentalism, premature ovarian failure, having as a consequence infertility and a considerably diminished feeling of femininity (womanhood), may constitute an unhealthy state. Hereby, the term "premature" is captured widely including even the state of ovarian failure at an early post-menopausal stage, for the reasons mentioned below.

Within the viewpoint of the holistic theories of health, healthy is considered the individual who has abilities (and dispositions, as well as the use of them) to reach goals that are vital, ordinary or typical. According to Nordenfelt [18] (mostly representing these holistic theories), healthy is an individual whose abilities (perhaps second-order abilities-capabilities which provide first-order abilities that) allow him, under standard or reasonable circumstances, to reach or strive for his vital goals, which are "necessary and sufficient" [18] to provide minimal happiness or flourishing or a minimally decent life. These goals are argued to be interpreted as the "central human capabilities" identified by Sen [20] and Nussbaum [21] (whose line is followed by Venkatapuram who conceptualized even broader the notion of health making extremely blur the borderline between health and well-being) [22] and based on human liberty and equal dignity. These goals have values in themselves (intrinsic values), whereas in accord to Richman's theory [19] the actual goals of an individual assume variable external values because they are set by himself. Interestingly, it is to be stressed that, as Purdy [11] reliably states, reproductive autonomy has an intrinsic value for women. According to Richman's theory [19] ("embedded instrumentalism") of health (that extends Richman-Budson's theory [23]), healthy is an individual whose abilities as an organism match with the goals as a person. These goals are determined mainly by the individual himself and not by the circumstances as Nordenfelt's theory [18] advocates. The subjective preferences of an individual are objectified by trying to determine his actual goals. For instance, an individual's goals may be having biological offspring; thus, infertility may be assumed to be ill-health [14].

This theory distinguishes between the health of an individual as a biological organism (trying to survive and reproduce) and the health of an individual as a person (moral agent). Like the distinction between death of an individual as an organism and as a person.

In the modern, positive and holistic sense of "health", well-being is of great importance [24]. The modern conception of the "new public health" (meant in a positive-holistic sense) includes "well-being", which is determined by social determinants [25], especially in a society of interdependence [26]. Well-being is usually captured as the positive feeling and evaluation of self-fulfillment according to Haybron's [27] non-essentialist/perfectionist (and thus non Aristotelean) but subject-dependent eudemonistic theory or- as Raibley states

[28] –the realization of personal, 'ownmost', 'wholehearted' values that are central to one's identity and unchangeable through lifespan. Having biological offspring and being in a marriage based on love are most likely such values. Interestingly, one's "general ability" (and therefore health) may be affected (positively or negatively) by her "well-being" and *vice versa*. This is strongly emphasized by the "two-dimensional" theory of health developed by Tengelnd [29]. Moreover, well-being may impose health as long as it is considered an essential component of it [24]. However, health is the minimal capture of well-being [22]. Health is captured by Sen [20] and Nussbaum [21] (in an approach overlapping with that of Nordenfelt [18]) in the broader conception.

Ovarian failure as an unhealthy state

For a woman, having functional ovarian tissue in the body is an issue strongly related to her health, in particular to her reproductive and sexual health. The health of a woman should be considered from a gender perspective. Women's gender identity is an issue of much more importance in comparison to men [17]. Besides, as is argued below, involuntary infertility may have an overwhelmingly negative impact on a woman's health and well-being.

Having offspring and developing healthy and well-functioning relationships based on love (or triggered by it) impose human flourishing / well-being (conceptualized as an entity being wholly separated to health). A woman's reproductive autonomy is central to her well-being [11]. Developing happy relationships is apparently central to the well-being of any human being seeking (as such) to be a member of societal formulations. A robust feeling of femininity probably facilitates it.

In light of the holistic theories of health, suffering from ovarian failure at a childbearing age (and even in early post-menopausal age as hereby is argued) is ill-health state since a woman having the secondary ability to ovulate gains the primary ability (to conceive) to reach (or strive for) the goal of having biological offspring. Besides, her ability to feel adequately woman enables her to reach the goal of forming and developing happy and functional relationships.

The attainment of both of these goals (having biological offspring and forming happy relationships) is beneficial in itself as being of critical importance for enhancing her well-being (since marriage or family are her 'ownmost' values [28]) which, in turn, impacts positively on her general ability (health), and which, in turn, impacts positively on her well-being and *vice versa* (according to the "two-dimensional" theory of health developed by Tengelnd [29]). Especially, if it is about developing countries (such as Pakistan) which are strongly pro-natalist, the stigma of infertility may have a seriously negative impact on the well-being of a woman. It threatens her marriage stability, identity, social position, and ability to adhere to the cultural norms of her social environment [30]. It also threatens her health as she is at risk of domestic abuse and depression (among other things) [30]. Even with regard to western societies, according to what Purdy most reliably

states [11], pronatalism together with other cultural factors, such as sexism and geneticism, may severely constrain (after being internalized) a woman's genuine autonomy. As I argue below, cultural and social environmental factors probably have in any case a restrictive impact on a woman's reproductive autonomy, thus putting her at health risk and thus rendering her a vulnerable person, whether infertility is considered a socially determined disease or not, especially in light of holistic theories of health.

In case that Nordenfelt's theory of health [18] is adopted, the chance of having biological offspring and forming happy and functioning mating or marriage, thus developing a family, may be categorized as typical vital goals, thus "central human capability", necessary to provide "minimal happiness". Therefore, by depriving a woman of her own ability to produce her own oocytes, the sense of her femininity is respectively reproductively and sexually unhealthy, especially if Elson's theory of "hormonal hierarchy" [17] is true. This can also be assumed within the viewpoint of Richman's theory of health [19]. A woman being in "premature" ovarian failure, should be interpreted as being in an unhealthy state, since: a) She is unhealthy *qua organism* as she is prevented from reproducing and even from surviving (as ovarian hormones prevent physical disease either directly or indirectly insofar as the establishment of happy relationships positively affects physical and mental health). b) She is an unhealthy *qua person* as she is prevented from reaching or striving for her goals, thus having biological offspring and developing happy and functional relationships based on love.

The consideration of a woman's health, especially in light of feminist scholarship, is inevitably environment-sensitive [31]. Besides, most probably the social/cultural environment prevents a childbearing age woman from using her abilities to reach or strive for sustainable reproductive goals. Moreover, most probably the impact of social/cultural environment results in a woman being prevented from making autonomous reproductive decisions, thus setting goals. Certain intersecting components of social environment (usually criteria or activities) most probably play the role of "health determinants of public health" since they can put the woman at high risk of undesired childlessness (unhealthy state as is herein advocated), and thus of vulnerability, apart from her inherent biologic vulnerability regarding reproduction (that is limited childbearing lifespan). This gives rise to a moral obligation for beneficence based on solidarity (especially within a communitarian standpoint) [32], in terms of considering OTC/OTT as preventive medicine aiming to address a public health issue as is the undesired childlessness rooted in a social environment.

Ovarian endocrine function as a health-related issue

According to the "hormonal hierarchy theory" [17], the ovarian tissue that exists in the female body is of great symbolic and essential importance regarding her sense of her own femininity. This is the case even if it is about a little piece of ovarian tissue, while two ovaries represent the highest hierarchy. It is argued that this results from socially and culturally constructed understanding (which highlights the

social constructive theories for gender identity) that interact with bodily biology (which highlights the essentialist theories for gender identity) [17]. As Elson states [17], in his relevant study, it highlights "the degree to which cultural discourse regarding biological determinism influences subjective bodily experience and how this, in turn, becomes social fact". Furthermore, the woman's sense of her femininity may affect her behavior which, in turn, under the theory of gender performativity creates her gender identity which is an ever continuing process [33].

It is reported that, while the conventional "hormone replacement treatment" (HRT) has more advantages, women usually prefer to maintain their hormone-producing ability by resorting to OTT, not only because the "hormonal hierarchy theory" is now in force, but also because they are afraid of the side effects of HRT, although OTT has more disadvantages [15]. This is probably the case because, intuitively, they experience the production of hormones as their own production. OT is the primary source of ovarian hormones.

Ovarian hormones have an overwhelmingly positive impact on all the components of health and well-being as being key determinant factors of secondary sex characteristics. Therefore, ovarian hormones may enhance the pair bond-related well-being of a woman. There are also other human hormones that may play a role in this prospective. It is argued that oxytocin and vasopressin (both produced in hypothalamus and secreted by posterior pituitary) are considered "pro-social" hormones as they promote pair binding behaviors [34]. Moreover, it is argued that marriage and happy pair-bond love relationships promote well-being (happiness, feeling of social safety, life satisfaction) [34,35]. As Nyholm remarks [36], Sen [37] and Nussbaum [38] consider "the capacity to experience positive and satisfying emotions (hedonic well-being)" as essential to human well-being. According to Seligman's [39] approach, in the context of "positive psychology", love is not simply a means to health and well-being but a "key element of human flourishing", as Nyholm notes [36]. In addition, marriage and happy love relationships decrease stress, depression, blood pressure, mortality and increase the immune status of the organism [34]. In addition, the deficiency of ovarian hormones threatens cardiovascular health and bone density [34]. However, it is worth noting that recent publications [9] hold ambiguities whether OT auto-transplant: a) can establish long-term (>5 years), beneficial and sufficient endocrine ovarian function, and b) does not put at risk the woman's other health (e.g. her uterus or mammary gland).

A woman having functional OT in her body is a condition promoting her sexual (apart from reproductive) health, insofar as the enhancement of sexual satisfaction, comfort and self-confidence is based on the feeling of existing womanhood (insofar as the theory of hormonal hierarchy is true). This is coupled with the fact that ovarian endocrine function, as being "pro-social", promotes physical health, either directly (by decreasing osteoporosis, atherosclerosis etc) or indirectly by promoting both social support through maintaining relationships, marriages, love-based mating etc (which, as

exhibited previously, have positive effects on health and well-being) and well-being with positive repercussions to health, according to Tengland's two-dimensional theory of health [29].

It is not to be overlooked that the theory of hormonal hierarchy may lead to a perceptual bio-reductionism of a woman's feeling of her womanhood. Furthermore, it has to be stressed that such a bio-reductionism fosters the medicalization (that is e.g. OTC/OTT): it takes the responsibility from the social context and shifts it onto the individual's biologic functions, thus widening the medical paternalism.

The attachment to biological motherhood

OTT provides the opportunity to experience biological (genetic in the case of autologous transplantation or non-genetic in the case of heterologous (allo)transplantation which however is not at all currently into practice) motherhood, something common and typical of the (childbearing age) female group of our society, which – in my opinion – constitutes a “vital goal” for the purposes of Nordenfelt's theory [18] of health as necessary to provide minimal flourishing or happiness in our social circumstances. Despite the theoretical equation of biological and socio-emotional kinship, in some laws, including Greek law, at a psychological level (intuitively?), biological motherhood is preferred in our individual-centered society, where genetic determinism is still present [15]. This is “biological egocentrism” [40], which is probably associated with an intuitive attachment to “naturalness”. Therefore, “sharing motherhood” between female partners in lesbian couples is desirable. OTC/OTT, even if it is only a marginally established method, is probably preferable to alternative options, which are much more established. The costly intracytoplasmic sperm injection is preferable to insemination from a donor [14]. Certainly, biological motherhood also constitutes an “essential function” (according to article 37 of the Italian Constitution) of a woman, since only fecundation (not procreation) can occur without a mother's body. A mother's body is the only mode of reproduction of society and of human species [41]. According to a study [42] relied on interviews, masculine lesbians, while they regard pregnancy as socially constructed, highlight the essentialist concept of pregnancy as being strictly associated with femininity.

Attachment to biological motherhood is argued to “have deep roots, both culturally and biologically” [14]. The desire for biological motherhood and gender identity is socially determined to a considerable extent.

Infertility: harmful to health and well-being

It is disputed whether infertility (absence of conception after one year of unprotected intercourse) [43] is a disease. Both WHO and gynecologists consider infertility an illness (whenever there is a desire for a child) [44]. It is greatly relevant that, as Purdy notes, “medical environment” considers pregnancy as a “medical condition” [11]. Israeli National Bioethics Council (INBC) 2011 qualifies the egg freezing for social reasons, aiming to address future age-related infertility (which is interpreted

as disease), as “preventive medicine”, thus regarding infertility as a public-health issue [45]. Along the same lines is a relevant Israeli Minister of Health directive of 2011 [45]. For example, “undesirable childlessness” because of a missing partner, (or diminishing reproductive autonomy or impeding ability to reach reproductive goals) constitutes a (*latu sensu*) medical reason, since it renders “childlessness” not exclusive “by choice”. The distinction between such “childlessness” and clearly “undesirable childlessness” for clearly lifestyle reasons is both subtle and blurred (e.g., a carrier may put obstacles in partner finding) [12].

Infertility is a socially determined “illness”, but it is not the only one. The distinction between good and ill health is based not only on medical facts, but also on social conventions, especially when the concept of “health” is meant in a wide, holistic and positive way. Infertility is not a threat to human life and it does not cause any physical suffering; however, it causes some mental and social distress [46], which is not at all negligible, and it may be assumed to be a disease. As Greil et al. observe, scholars stress that “the experience of infertility is shaped by social context” [47].

It is rightly argued that the early loss of fertility seriously harms the quality of life [48]. This entails considerable vulnerability for the patient, both psychologically and socially, in the strict sense of the word, since she is at a significant risk of harming her mental health [49,50]. The inability to achieve biological motherhood has negative effects on the woman's psychology (e.g., anxiety, distress, depression) [51], social role, gender identity, and well-being [51, 52]. Childlessness constitutes a “major” [53] life stressor, a life crisis [54]. Childlessness is associated with serious negative psychological effects [54, 55] similar to those caused by long-term diseases [56].

Childlessness is associated with serious negative psychological effects: serious anxiety, stress [55], feelings of grief, mourning [57], experience loss, low self-esteem, social isolation, relationship problems and sexual dysfunction [58].

The ability to achieve biological motherhood is a critical part of a woman's life [59]. Infertile and childless women are stigmatized and underrated [60-62]. Social stigmatization, as is argued below, may strongly negatively affect a woman's reproductive autonomy which is central to her well-being, which in turn may affect her total health, at least according to the two-dimensional theory of health developed by Tengland [29]. It is worth noting that as Campo-Engelstein states [15], fertility is “intrinsically intertwined” with a woman's identity. Identity is –as is stated below– central to a woman's reproductive autonomy which, in turn, is considered to be central to women's well-being [11].

Is biological motherhood attainable even through (iso-) allotransplantation of ovarian tissue?

In OTT, with the use of an allo-/isograft, in my opinion, the OT may be perceived by the recipient as if it were her own tissue, which is a part of her selfhood. According to phenomenologists,

the identity process starts from the preconscious level of self-awareness (embodied selfhood), followed by the process of the mind (self-reflection) and the social-cultural process (social-narrative identity) [63]. These are three layers linked with an interactive relationship. The higher the ability to feel the new organ, i.e., the more functional and symbolic its meaning, and the higher the “visibility” of the organ (by means of inner perception) in the internal realms of the body, the more it refers to “another person” and the more the recipient of the organ has the experience of intrusion to herself (her body), i.e., the experience of intimate alienation. In the case of OTT, the graft is not functionally perceivable, it does not have any direct symbolic meaning (as, for example, the heart or the hand), but it only has an indirect symbolic meaning, through the determination of female gender markers, including the formation of the body, pregnancy, or motherhood, and it is not visible as an internal organ. It lacks a clear shape or its own vascularization, and it is an indefinite functional unit of tissue. Thus, the recipient probably experience the ovarian graft as her own. This remains to be proved by further research. And the function (ovulation, hormone production) of this graft is “her” function. Apart from any social influence, in the framework of the deeply intimate experiential relationship of a human being with his/her body [41], the sensation of an OT recipient that this is her “own” OT is enhanced by the holistic view about the human body in the context of the Mediterranean bioethics (contrary to the view of dualism, which distinguishes between brain and body with spare organs [64], a distinction that becomes vague again as science develops, since the distinction between the “parts of ourselves” and the “tool-like parts of the world” also becomes vague [65].

In my view, even in the case of iso- or allo- ovarian transplantation, the recipient’s own ovulation represents an interim type of biological motherhood (between the genetic and gestational one), thus promoting her reproductive health. In addition, if Elson’s theory of “hormonal hierarchy” is true, the existing OT in a woman’s body determines her own “womanhood” as it is perceived to be her own tissue.

Is fertility preservation for healthy women preventive medicine?

A premenopausal woman, similarly to a cancer patient, has no “viable option” for preventing infertility problems (to meet a suitable partner is beyond her control [12, 14]; it is absolutely certain that she will lose her fertility within the next years), there is no categorical denying her the opportunity on the basis of a sharp distinction between medical and non-medical reasons [14]. Reversely, even a cancer patient may face infertility problems because she has chosen late childbearing [66]. Nowadays, age-related infertility is considered a medical problem to be prevented [44, 67]. In addition, since health is conceptualized according to Richman’s or Venkatapuram’s theory of health, the already blurred demarcating line between medical and non-medical (social) indications [12-14], [68, 69] becomes much more blurred. These theories make the distinction between health and well-being much more unclear. Besides, age-related infertility is now considered a medical problem

to be prevented [44, 67]. Incidentally, some interventions are characterized as “medical”, whereas their scope is non-medical (sterilization, abortion) or non-pathologic (e.g. facing idiopathy) [12]. Moreover, a woman threatened by age-related loss of fertility should be considered as a vulnerable person, in the over-inclusive sense of the term ‘vulnerability’, related to our common humanity [32]. As phenomenologists argue, we share the same “being-in-the-world” with other people as “embodied persons” [65]. Reproduction creates “embodied persons” and relations between them [14]. In a wide approach, ovarian ageing is a public health-related issue [12] because of women’s vulnerability related to their gender inequity in reproduction due to biological (natural) inequity [70-72]. Besides, as exhibited above, infertility is assumed to be socially determined ill-health.

Most importantly, I consider OTC/OTT for healthy women as preventive medicine because of the restriction of a woman’s reproductive autonomy due to social/cultural environmental influences resulting either in diminishing her health or in threatening it (insofar as undesirable childlessness is meant to be ill-health).

The contradictory influence of environment on a woman’s reproductive autonomy

We live in a “pro-reproductive” [73] society which encourages the ‘healthy’ woman to undergo fertility preservation methods [45,74], such as OTC, although, as is rightly argued, social constraint seems not to be straightforwardly related to an eventual woman’s choice for OTC/OTT. For Harwood [74], inadequate information “in a commercial exploitative context” threatens a woman’s autonomy, intensively encouraging her to undergo such methods. OTC may protect a woman from getting involved in an unhappy marriage [71] for reasons of parenting “in time”. It is demonstrated [13] that healthy young women have a positive attitude towards the eventual use of fertility preservation methods (for social reasons) in the future (although inadequately informed about these methods [75]). Nevertheless, in our “pro-reproductive” society, for a young healthy woman the state of being “proactive” [76] should be interpreted as reasonable (or wise). For some women, the fear of idiopathic premature ovarian failure at a pre-menopausal age is probably a reason for social freezing of oocytes. Besides, in case that a woman resorts to OTC/OTT, the freezing of the ovarian issue should take place up to the age of 30 in order to be safer and more efficient [77]. This intensifies the pressure that is exerted on a woman reflecting on the option to undergo OTC/OTT.

At the same time, reportedly, there is an increasing trend for women toward postponing their first pregnancy [71]. The impact of our societal/cultural environment most probably results in a young (fertile) woman being prevented from reaching the reproductive goals she set or making autonomous decisions concerning her reproduction. It is argued that we live in a male-oriented society that makes it difficult for the woman to combine career/education pursuing with child rearing. From a mere feminist viewpoint, this combination is extremely difficult since our society is a “patriarchal” society that

victimizes the childbearing aged woman [78]. As Petropanagos argues, pro-natalism and biologism (as exhibited above regarding infertility) are two different social ideologies that can affect oppressively the woman's reproductive autonomy blurring the distinction between an oncologic and a healthy woman seeking fertility preservation [78]. Even if our society is not "patriarchal", it is true that we live in a mildly male-oriented society. In any case, as Lockwood rightly states [77], if the environment does not prevent a woman from having children, it encourages her to postpone it. It is also true that the social and cultural environment most probably have a negative impact on the autonomous decision-making of the woman (her reproductive choices), affecting her autonomous decision-making process both positively (as "pro-reproductive" society) and negatively (encouraging career pursuing). The social environment may exert significant coercion on the woman's reproductive autonomy by preventing her from reproductive decision-making as it sends her contradictory messages: pro-reproductive and pro-career are probably equally prevailing expectations to which a woman at an early reproductive age has to attempt to conform to. Therefore, it is extremely difficult to draw a sharp demarcation line between "desirable/voluntary" and "undesirable/involuntary" childlessness. Such a blurred distinction may be due either to the complexity of the reasons or to the complexity of the impact of the circumstances on a woman. Furthermore, women's perception with regard to circumstances and choices seems to be blurry. As Kelly states [79], in a study they reported themselves as "transitional," "postponers," "ambivalent," or "passive decision makers". A woman may as well be heavily skewed towards the pro-reproductive or the alternative direction. It has been demonstrated that women underestimate the speedy age-related decline of their fertility [80], while the number of voluntary childless women has been increasing [81].

Besides, the modern age of over-specialization, while being "pro-reproductive", is time-consuming and highly demanding to a young woman that pursues a socially recognized professional position and economic stability. Moreover, for a demanding career pursuing woman it is probably difficult to spend time seeking a long-term stable relationship with a partner.

The contradictory influence of the social/cultural environment on women of childbearing age may diminish their capacity for critical reasoning and thus for autonomous decision. Therefore, in my opinion, the social and cultural environment include intersecting "social health determinants" [32] that are able to render a woman a vulnerable person as they put her at high risk of undesirable childlessness, which is a disease, as is argued here. Therefore, OTC/OTT for a "healthy" fertile woman can qualify as "preventive medical treatment" [45], insofar as it may address her vulnerability [32]. It is about a public health issue, regardless of interpreting "infertility" itself as a disease or not.

Do childbearing age women have restricted reproductive autonomy?

Reproductive autonomy has an intrinsic (not instrumental) value and as such it should be approached philosophically, not

legally (minimally). Reproductive autonomy, for the purposes of the present study is conceptualized as relational (feminist) autonomy, not as individual (based on Kantian tradition). Reproduction is a strongly relational issue. We are embedded in a relational social net characterized by interdependence and care. Being a parent means developing relationships of care and interdependence. Besides, reproductive autonomy is in the present study captured in its so-called "programmatically" conception as regards the major life plan issue of setting priority between a career and being a mother. According to Meyers, who makes such a distinction (graduation of relational autonomy), programmatic autonomy is much more likely to be restricted than the local one [82]. Regarding the issue under discussion here, restriction of programmatic autonomy leads to restriction of local autonomy.

When the conception of autonomy is conceptualized as individual autonomy, it is captured through the 'in-control agent' [83,84] model, the model of autonomy that highlights the individual, a woman is considered self-sufficient, capable of making sovereign decisions regardless of any influence of her environment. She is considered capable of self-reliance and rationality to the point of being resistant to societal emotional pressures [83,85]. According to this model of autonomy, a childbearing age woman has the authenticity to be herself. She is capable of interpreting the facts (this is the cognitive information provided to her) and having critical self-reflection to which her actions are subjected. Or -from another standpoint- she develops a "real" identity with which her actions accord. She is able to conflict with the input of the others, manipulate the situation and overcome it.

As long as the "content-neutral" ("procedural" or "hierarchical", not substantive) account is adopted for autonomy [82, 86-88] with her "autonomy competency", a reproductive decision of a childbearing age woman may be autonomous even if it is socially constructed, since her first-order desires are in congruence with her second-order volitions and thus she "wholeheartedly" [86] identifies with them, with her "true self" [87], as having "autonomy competency" [82]. One is considered autonomous by making their own decisions authorized by a certain and appropriate (evaluative) procedure. According to the "split-level self" approach developed by Frankfurt [86], the lower-order desires should be in congruence with the higher-order desires. However, there is a lot of skepticism about the authenticity of second-order volitions (this is considered as *ab initio* dilemma). A solution based on the "need for self-worth as the appropriate mental state" is invoked [89].

Under other theories, in order for the agent to be autonomous it is sufficient to be committed normatively to certain values. These substantive accounts of autonomy are based on the agent's capability of developing normative commitments to certain values that are strictly linked to autonomy or "normative competence" [90,91] evaluative of social norms or values that affect a woman's decision-making process. In these views, a woman may be autonomous in spite of the oppressive environmental norms. Under other self-regarding accounts of

autonomy, an agent, in order to be autonomous, should develop a robust conception of self, self-worth, self-respect and self-trust to secure the authenticity of her decision and her capability of proper evaluation and reflection. For McLeod, self-trust is an “attitude of optimism about our own competence and moral integrity” [92]. However, the development of such capability is doubtful under circumstances of strong, profound and complex environmental impact on a woman, especially when it is about a weak-willed woman. The self-regarding accounts of autonomy may be either “substantive” or “content-neutral” [93] like the dialogical accounts arguing for “interrelation between self-interpretation and interpretation of the self by others” [93]. Within this account, Westlund states that an agent “holds herself answerable, for her action-guiding commitments, to external critical perspectives” [94].

Relational autonomy highlights not the individual but the social environment and perceives the individual as interdependent with and embedded in the complicated net of social and cultural relationships [83,85]. As Baier states, in a world of interdependence the way to self-realization passes through the relations with others [95]. A profound impact of social/cultural environment on a woman may probably result in her being hindered from obtaining genuine autonomous decisions. The relational autonomy model focuses on social inter-subjective relationships and intersecting and complex environmental determinants that interact (subtly but significantly) with the individual’s ends, beliefs, goals, interests etc, thus forming the social dimensions of selfhood, selfhood and self-understanding and what is meant as self-directed, especially when the constitutively relational autonomy is adopted, a strongly substantive account of autonomy developed by Oshana through her “social-relational” approach, a non-psychological, content-neutral account [96]. It is argued that one’s autonomy may be restricted by only the narrow range of real options in her society without being affected by her psychology necessarily [96,97]. Strong substantive (constitutively relational) accounts are defined as self-rule considering an agent autonomous if she decides morally correctly or according to her objective interests [93]. Emotion is getting involved in procedures of reasoning and decision-making. However, it is rightly stated that relational autonomy facilitates decision-making process.

A social and cultural environment may lead to “uncritical acceptance” of social norms related to “stigmatization” existing in a society at large (as is childlessness or professional instability), especially if persons of a woman’s close relationships adopt the same norms [98]. Uncritical acceptance of social norms may lead to what Meyers (who is skeptical about authenticity in autonomy) calls “warped desires” [82]. Meyers rightly states that “not all desires should be afforded equal credence or weight” [82]. The internalization of norms and values of an oppressive social environment may adopt “what is meant to be” her “self-directed” [96], that is, her own genuine preferences and choices, may result in a woman’s “adaptive or deformed” desires or preferences (that however certain theorists [94] consider autonomous). The internalization of fears of stigmatization (ostracism) is

probably dependent on the degree of stigmatization (especially adopted by persons close to the woman). Autonomous decision may be prevented by the social context of a woman as it may affect the development of capacities that are essential to autonomy, such as self-direction, self-reflection and self-discovery/knowledge/mastering (as Mackenzie and Stoljar argue) [99]. The woman’s so-called “normative competence”, that is, the capability of identifying the right and wrong [100], thus the capability of detecting, evaluating and responding to the external norms (or values or roles), is necessarily acquired by making autonomous reproductive decisions. Such capability should not be taken for granted when the social environment is oppressive or social norms are strong. Nevertheless, when social norms are weak a woman may be able to make genuine autonomous decisions [98].

The impact of social/cultural environment on a fertile woman is an extremely sensitive and complex issue. The factors that determine it are overlapping. Indicative is the fact that the portrayals of OTC/OTT seeking healthy women (selfish / career pursuing, proactive, victim) are considered overlapping [76]. Selfish career-pursuing women are not a category sharply distinct from those not yet having found a suitable partner for social reasons. In addition, the European Society of Human Reproduction and Embryology [12] argues for a possible blurred distinction between an oncologic childbearing age woman and a not having yet found a suitable partner healthy one regarding their reproductive prospective. Indeed, they have similarly no “vial options” [101] to reproduce. Besides, as mentioned above, women’s perception with regard to circumstances and their reproductive choices seems to be blurry [79]. Importantly, the indication that social/cultural environment most probably sends a woman oppressive or at least contradictory demands, in my opinion, is of crucial importance either for forming clear and robust psychological capacities or for forming clear perceptions by a woman regarding the values and norms of her social environment. Most of the accounts of autonomy developed above focus on the woman’s psychology, some of them on the social environment and some others on the interaction-interrelation between individual and social environment. There is not a consensus between them, despite the fact that most are overlapping. Whatever account of autonomy is adopted, a robust psychology and perception of the clear values and norms of the social environment are necessary for making a genuine autonomous reproductive decision. Most probably, the social environment plays a restrictive role (as having oppressive or contradictory influence) with regard to women’s reproductive autonomy. Our social environment *most probably* sends contradictory or prohibitive messages (*most probably* strong messages) to a childbearing age woman with regard to her reproductive life plan (decision-making process or reaching her goals), and these messages *most probably* restrict her genuine autonomy. In the light of the relational account of autonomy, such contextual influence may reduce the woman’s capability of consciousness, critical reasoning, self-esteem and self-trust. The authenticity of a woman’s desires regarding her reproduction is not straightforward. The reproductive decisions of a woman are most probably beyond her control. As is rightly stated, not having a child may be “beyond the

woman's direct control" [102]. It may be the result of "an 'accidental' combination of circumstances" [103]. As Smajdor rightly states, a woman is likely to remain childless without it being "necessarily attributable to any conscious decision" [103]. However, studies argue for an increasing rate of women with desirable childlessness, whereas that rate remains low [81].

As the social environment impedes the childbearing aged "healthy" woman from having offspring, it puts her at a situation similar to that of an oncologic woman of the same age whose fertility is threatened by the gonadotoxic treatment which she has to undergo. A woman's reproductive autonomy is in "all likelihood restricted". The ability of each single woman to act autonomously, thus to make a decision or reach a goal that she set regarding her reproduction or strive for it (e.g. by searching for a suitable partner) without being coerced by her social context remains ambiguous and probably does not exist, as is the case with oncologic women (since there are equally not "vial options") [101]. Hence, the existence of "medical reasons" for a healthy woman to undergo OTC/OTT cannot be ruled out, since there is no categorical distinction between medical and non-medical reasons [14]. The restriction of the woman's autonomy either harms or threatens her health, since an intrinsic and not instrumental value is attributed to her reproductive autonomy. Notwithstanding this, the intrinsic value of reproductive autonomy remains to be proved with plausible arguments [104]. The threatening of a woman's reproductive autonomy with restriction may be counterbalanced through OTC/OTT that leads to its expansion. Or at least, OTC/OTT, in our common perception, may be assumed to be an abnormal situation addressing method.

A woman should by no means be blamed for being exclusively responsible for her (potential) childlessness, thus viewing the society as blameless by considering OTC/OTT for the 'healthy' woman as a "medicalization" of a clearly normal aspect of human life. Such a "medicalization" would bear a negative meaning and be categorized as "bad" medicalization (over-medicalization) [105].

OTC/OTT: carried out in a gray zone between natural and unnatural, normality and pathology

Ovarian failure (that induce infertility, reduced endocrine function resulting in low bone density, increasing risk of cardiovascular diseases, cognitive impairment or dementia and sense of diminished femininity [106]) is in itself ill-health, when it is premature. Under the holistic theories of health, this unhealthy state extends over the post-menopausal ages (at least the early stage).

According to Broer et al., young women with very low level of anti-mullerian hormone may have menopause two years earlier than the average age of 51 [106]. Already, the idiopathic ovarian failure at these ages is considered a medical reason for IVF [12]. Consequently, the pre-menopausal phase might be considered a marginally gray zone between necessitating and not necessitating medical treatment.

Besides, nowadays, human life expectancy is remarkably expanding and this indication is taken seriously into account by current bioethical literature, regarding either fertility [10] or endocrine ovarian function lifespan [107] prolongation. Reportedly, women in about 20 years from now will live, on average, 90 years [10]. In Denmark, reportedly 50% of the existing female population is expected to reach 100 years of life [108]. As a consequence, the woman's life plan and lifestyle may reasonably change. The reproductive lifespan (and the lifespan in which the woman feels having full womanhood) does not follow the lifespan expansion. Therefore and for reasons of consistency, the prolonging of a woman's childbearing age should not be considered an absolutely unnatural procedure.

The focus of modern medicine, especially after the invasion of techno-sciences, is clearly shifting towards the promotion of human flourishing and quality of life, however, along with the pursuit of longevity. Some forms of medicalization enhance the human flourishing/well-being (even if not the health). They allow women to promote their own flourishing/well-being by gaining control over their lives through gaining control over their bodies [105,109]. The ageing/natural death is radically shifting to qualify as a "curable disease", a "technical phenomenon" [110] to be eradicated by offering immortality to human beings. The dying process has already been medicalized as having passed from family environment to healthcare settings. Ageing cellular mechanisms are to be addressed through modern methods as nanotechnology (e.g. nanorobotics) [110]. In the notion "ageing", reproductive ageing is encompassed. Menopause may be viewed as reproductive death. As Parens notes [105], chronic pain due to normal ageing is given the name Complex Regional Pain Syndrome and is on the cusp of being brought within the purview of medicine.

Furthermore, in the purview of medicine, practices such as "labia plasty" have marginally been brought, which are considered to be addressing emotional problems related to labia anatomy [105], birth control [105] as being preventive of poverty and distress, even medicalization of love as long as it fosters a pre-existing situation [105]. Especially when "health" and "well-being" are in a wider way conceptualized. In this context, OTC/OTT may be construed as promoting women's own flourishing/well-being by gaining control over their lives while fostering a pre-existing situation (ovarian function). The "medicalization" OTC/OTT is hence perceived as rather "good" medicalization. This is supported by the argumentation that follows.

Social environment *in all likelihood* diminishes (insofar as restricted reproductive autonomy may be considered unhealthy) or at least threatens (insofar as involuntary childlessness or infertility is considered unhealthy) the woman's reproductive and sexual health and well-being. Furthermore, in light of holistic theories of health, the ability of a woman to reach her vital reproductive and relational goals *may* be prevented by environmental influences. This may be characterized either as unhealthy state (under holistic theories of health as those of Nordenfelt [18] or Richman [19] outlined above) or as a threat to the health (putting it at high risk of future involuntary

childlessness, an unhealthy state from a standpoint outlined above). The social environment *probably* includes “health determinants” that threaten a woman’s reproductive health. The goals of medicine should be a conception inclusive of addressing such threats or aiming at treating problems rooted in the relationship between the individual and the environment. If the goals of medicine would be considered in a narrow conception, as not being inclusive of addressing the social roots of disease, then the next step is the risk of getting even narrower, focusing only on bodily disorders and excluding the mental ones, thus leading to accepting the so-called “mental-body dualism” [105] that is an unacceptable assumption in the context of modern bioethics, though ‘most adults remain “essentialistic mind-body dualists” at heart’ as Forstmann and Burgmer argue in their study [111].

For these reasons, coupled with both the existing possibility of performing OTC/OTT, a not particularly costly method, menopausal ovarian failure may be gradually interpreted (perhaps intuitively) as pathologic, or at least as occupying a blurred gray zone between normality and pathology. In our common perception, OTC/OTT aiming to make ovarian function lasting for a few more years beyond the age considered as menopausal (reportedly up to 10 years the ovarian transplant can last) [112], may qualify as either preventive (insofar as undesirable childlessness is unhealthy state) or mere medical treatment since it counterbalances the environment-rooted restriction of reproductive autonomy, that is, ill-health state or threat to health.

The borderline is shifting toward normality broadening what is meant as pathological

In modern bioethics, the borderline between normality and pathology (health and disease) is vague and volatile, either because of technological development (e.g., genetic enhancement, neurosciences), or because of a redefinition of the concept of “health”, especially when the disease is socially determined. Interestingly, in light of the increasing scientific progress, the “classic” not valued-laden distinction between “species-typical” and “species-atypical” functions, abilities, traits and behaviors tends to lose ground whereas the “individual-differences” model regarding the differentiation between normality and pathology gains ground [105]. When adopting the “individual-differences” model regarding the distinction between normality and pathology the borderline between naturalness and unnaturalness gets blurred.

In the field of reproduction, some practices occupy a gray zone between naturalness and unnaturalness. Moreover, there is a blurred distinction between biological / social and genetic / gestational motherhood. There are “minimal” forms of biological motherhood, either genetic (as in mitochondrial donation/replacement where the genetic-biological “motherhood” is minimal), or non-genetic (e.g., gestational surrogacy). In addition, under the (still experimental) prospect of “in vitro generated gametes” (IVG) [113], biologic motherhood may quantitatively be varying with regard to each single case. Such gametes may enhance the reproductive ability of same-sex couples or post-menopausal women [113], two categories

for which being a parent is considered unnatural. Besides, in case of oocytes shared donation between the partners of a lesbian couple (“shared biologic motherhood”) [114] there is a combination of biologic and gestational motherhood [115]. Non-genetic biological motherhood may also be “minimal”, since the surrogate uterus (potentially for the time being) can be a transplant in the body of the pregnant woman who therefore does not experience any pain or uterus contractions [116].

In addition, it is to be taken into account that natural reproduction may be risky. The advanced father age is said to be positively correlated with offspring’s neuropsychiatric disorders (e.g. schizophrenia) due to damaged DNA in advanced father gametes (low quality gametes) [113].

The abovementioned borderlines seem to be shifting toward normality (naturalness), making “pathology” to gain ground, especially provided that what is qualified as “normal” is based on the statistical average. Aspects of human life that are hitherto assumed to be “normal” (in which the medical intervention is considered as “medicalization”) may gradually transform into pathologic in our common perception, probably based on intuition. What for the time being is characterized as “human” may shift towards “post-human” after having passed through an interim stage of “trans-human” [117].

Such shifting may probably be noticed in our common perception with regard to the age of a woman in which getting pregnant and keeping the sense of her full femininity are not assumed to be “unnatural” states. In light of the holistic conception of health, the increasing progress of science, the increasing life-expectancy, the ongoing further acceptance of practices being characterized as “medicalization”, the increasing pressure exerted on women from their social/cultural environment that increasingly “demands” the building up of a career, are making our common perception to clearly be shifting towards considering OTC/OTT as “technical and artificial” method which, however, works harmoniously with what is meant to be “inherently and intrinsically” natural [73]. Besides, as Smajdor states [118], our career-demanding society should compromise with the consideration that becoming a parent at a marginally advanced age is the price of career pursuing. Therefore, in my view, it might be considered as not (absolutely) unnatural. Our common perception probably might be influenced in this direction by the fact that the uterine functionality does not decline over the years as is the case with ovaries and the advent of the forthcoming “in-vitro generation of gametes” [113] through dedifferentiation and reprogramming of somatic cells that is expected to secure women’s ability to “produce” gametes for life.

The shifting of the borderline should not violate the core of naturalness

The metaphysical concept of “naturalness” is vague, volatile and non-uniformly defined. Naturalness expresses biologic essentialism and usually causes moral prejudices. However, despite the anti-naturalness trends in bioethics, several authors observe that a sharp distinction between

“naturalness” and “artificiality” [119,120] is, nevertheless, rightly accepted by some authors and that an intuitively intrinsic value is also attributed empirically to “naturalness” [121] rendering it preferable to “artificiality”. There is an inviolable core of the “naturalness”. What is given as natural is preferable to what is produced [121-123]. The “artificial intervention in the natural constitution of the human being” – as Birnbacher [124] states – is problematic, “if it pursues purposes which are non-health-related”. Therefore, in my opinion, the expansion of the reproductive lifespan for the time being should not be greater than a certain period of time in order not to be considered as violating the core of the volatile notion “naturalness”. This period may be determined by the actual life expectancy. Currently, this time-frame is, in my view, roughly corresponding to the time-frame which the ovarian transplant is expected to last (up to 10 years) [112].

The OTC/OTT being performed on “healthy” woman and aiming to expand the lifespan of ovarian function beyond the foreseen “natural” limits (and for only a few years) should be considered as carried out in a “gray zone” between normality and pathology (shifting towards the former), and therefore between being categorized as medicalization or medical treatment. Therefore, the heightening of the upper limits of childbearing age for a few more years through OTC/OTT can be categorized as a “good medicalization” when carried out under “ethical responsibility” [105]. It is to be emphasized that “good” medicalization means not over-medicalization, and this is acknowledged by bioethical literature either explicitly or tacitly [105]. In addition, following the line of Savulescu and Sandberg reasoning [34], I am inclined towards the acceptance that OTC/OTT can be perceived as “good medicalization” because OTC/OTT does not “create” as a causal reason “a new situation” (the ovarian function) but fosters an “already existing and established situation” (ovarian function and its consequences). OTC/OTT might also be perceived as “good medicalization” for the additional reason that it promotes the woman’s flourishing through gaining control over her live and body [105,109].

In any case, the social/cultural environment of women should not be viewed as blameless by the acceptance of OTC/OTT as “good medicalization”, thus intensifying the medical paternalism and further restricting women’s autonomy.

Conclusion

Ending up, in light of the arguments I have presented above and on the condition that the repeatedly mentioned *most probably* is true, I have come to conclusions, as follows:

- 1) When “health” is captured within the viewpoint of the holistic theories of health, premature ovarian failure constitutes an unhealthy state as followed by ill reproductive and sexual health of the woman. Involuntary infertility and noticeably diminished femininity are ill-health in themselves negatively affecting the well-being of a woman. The term “premature” should be captured broadly, including women’s ages that statistically are considered as early

post-menopausal. The health of a woman should be considered from a gender perspective.

- 2) Reproductive autonomy has an intrinsic value for a woman and should be captured broadly, including whether, with whom, how many and when she will have children, ranking her life plan reproductive priorities according to her genuine choice. Women’s reproductive autonomy may in all likelihood be restricted by social and cultural environmental factors either by preventing her from pursuing her reproductive goals or by sending to her contradictory messages regarding reproduction and thus encroaching on her decision-making procedure, especially, when either the constitutionally relational or the dialogical count of autonomy is adopted. Therefore, and reproductive autonomy being considered as having an intrinsic and not an instrumental value, the women’s health (especially the reproductive and sexual one, in light of holistic theories of health) and well-being may be considered either as being diminished or as being at high risk of ill-health (future involuntary infertility), and thus rendering her a vulnerable person. OTC/OTT may be considered as medical treatment (insofar as it counterbalances the restriction of autonomy) or as preventive medicine (preventive of future involuntary infertility insofar as it is considered a public health issue).
- 3) The distinction between idiopathic (premature) and menopausal (normal) ovarian failure remains blurred as varying with regard to each single woman.
- 4) Lifespan has significantly expanded. However, it is not accompanied with childbearing lifespan expansion.
- 5) The goals of modern medicine are getting wider, thus bringing in the purview of the institution of medicine practices which are considered “medicalizations”.
- 6) Therefore, OTC/OTT when performed at a childbearing age (even in its terminal stage) should be considered as having been carried out within the gray zone between normality (for non-medical reasons) and pathology (for medical reasons). OTC/OTT constitutes medicalization.
- 7) OTC/OTT can be perceived as “good medicalization” because:
 - a. The previously mentioned gray zone between normality and pathology is clearly shifting towards the latter.
 - b. OTC/OTT allows women to promote their own flourishing/well-being by gaining control over their lives through gaining control over their bodies OTC/OTT.
 - c. In addition, it fosters an already existing and well established healthy-under the holistic conception of health- situation (that is ovarian functioning). OTC/OTT is a technical intervention into human

naturalness that, nevertheless, can marginally work harmoniously with it. It constitutes a “good medicalization” on the cusp of becoming medical treatment.

- 8) OTC/OTT is considered as “good medicalization” on the condition that OTC/OTT can postpone menopause for only a few years. Otherwise, the core of the volatile concept of naturalness would unacceptably be violated.

Authors' contributions

PV (Polychronis Voultzos) is the sole author of the manuscript. The author is solely responsible for all aspects of conception and design, and solely drafted, wrote, approves, submitted and takes responsibility for the manuscript.

Authors' information

I (PV, the author) am assistant professor of bioethics in Aristotle University of Thessaloniki (School of Medicine), Greece. I am a doctor (pulmonologist), graduated also from School of Law and School of Drama. I am also graduated with a master degree in criminal law and hold a doctorate in medical criminal law. I am especially interested in reproductive ethics.

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