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FMUP FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

LESBIAN SHARED IVF –THE *ROPA* METHOD

PEDRO MIGUEL BRANDÃO LEITE

TESE DE DOUTORAMENTO APRESENTADA À
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Pedro Miguel Brandão Leite

Supervisor:
José Bellver Pradas | MD, PhD
Faculty of Medicine and Odontology, University of Valencia | Valencia, Spain
IVIRMA Valencia | Valencia, Spain

Co-supervisors:
Ricardo Filipe Sousa Santos | MD, PhD
Faculty of Medicine, University of Porto | Porto, Portugal
Hospital da Senhora da Oliveira | Guimarães, Portugal

Sérgio Reis Soares | MD, PhD
IVIRMA Lisboa | Lisbon, Portugal

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COLLABORATING AUTHORS

José Bellver | MD, PhD
Faculty of Medicine and Odontology, University of Valencia | Valencia, Spain.
IVIRMA Valencia | Valencia, Spain

Ricardo Sousa Santos | MD, PhD
Faculty of Medicine, University of Porto | Porto, Portugal
Hospital da Senhora da Oliveira | Guimarães, Portugal

Sérgio Reis Soares | MD, PhD
IVIRMA Lisboa | Lisbon, Portugal

Anita Ungure | MD
Riga Stradins University | Riga, Latvia

António de Pinho | MD
Faculty of Medicine, University of Porto | Porto, Portugal
Centro Hospital Tâmega e Sousa | Penafiel, Portugal

Bodil Sandvik | NP
IVIRMA Valencia | Valencia, Spain

Brent Monseur | MD, MSc
Stanford University | Stanford, California, United States of America

Fábio Cruz | MD
IVIRMA Valencia | Valencia, Spain

Jakob Doblinger | MD
IVIRMA Valencia | Valencia, Spain

Lavinia Iftene | MD
Clinical Hospital Nicolae Malaxa | Bucharest, Romania

Manuel Gonçalves Henriques | MD
Hospital Prof. Doutor Fernando da Fonseca | Amadora, Portugal

Maria Liz Coelho | MD
Centro Hospital Tâmega e Sousa | Penafiel, Portugal

Nathan Ceschin | MD
Felicittá Fertility Institute | Curitiba, Brazil

Pedro Melo | MD
Oxford University Hospitals | Oxford, United Kingdom

Rafał Zadykowicz | MD
Medical University of Warsaw | Warsaw, Poland

Rebecca Miscioscia | MD
Fertility Center Aarhus | Aarhus, Denmark

Stefania Paolelli | MD, PhD
IVIRMA Valencia | Valencia, Spain

Victor Hugo Gómez | MD, PhD
IVIRMA Valencia | Valencia, Spain

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ABSTRACT

There is a growing number of homosexual women who wish to become mothers, resulting in an increasing demand for assisted reproductive treatments for same-sex couples observed during the last decades. Most female homosexuals report a high wish to be a mother, mostly as part of a couple, mainly through assisted reproduction or step adoption of their partner's child. In general, they report feeling well informed about the assisted reproductive techniques available.

The ROPA (Reception of Oocytes from Partner) method, also known as lesbian shared IVF (*in vitro* fertilization), is an assisted reproduction technique for female couples, in which one of the women provides the oocytes (genetic mother), and the other receives the embryo and gestates (gestational mother). As a double parented method, it is the only way a female couple may biologically share motherhood.

Up to 2022, 35 articles were published on ROPA, 10 of which focused on the motivations for undergoing this treatment, 13 on ethics or legislation, 4 on motherhood, and 8 reporting on clinical outcomes.

As with any medically assisted reproduction technique, ROPA raises several ethical questions regarding patients, future offspring, gametes, and embryos. Furthermore, the fact that it is intended for homosexual women poses its own biological and social issues. Its practice is legal in 13 European countries.

ROPA introduces a new perspective on the biological dimension of motherhood as it distinguishes between the gestational and genetic dimension. The importance of a genetic or gestational relationship with their future child varies greatly between women, although most believe they will have the same connection to their child compared to their partner, regardless of the type of assisted reproductive treatments and the roles they play, both active or passive patients and gestational or genetic mothers. Most female couples have no difficulty choosing a reproductive treatment or role to play, primarily based on factors such as cost, success rates, and the possibility of sharing biological motherhood with ROPA.

Regarding the outcomes of this technique, the rates per embryo transfer of positive pregnancy tests, clinical pregnancies, and miscarriages were found to be between 61% and 63.3%, 54.3% and 57%, and 16.2% and 17.2%, respectively. The live birth rate per transfer was between 44.7% and 46.1%. The live birth rate per ROPA cycle ranged between 48.6% and 79%, and ultimately, 61.6% to 78.3% of couples who

underwent ROPA were able to have at least one live newborn. No significant differences were observed in the outcomes when compared to one-way IVF.

Despite its possible ethical and legal issues, the ROPA method is a desirable alternative for female couples aiming to share biological motherhood. The outcomes of this technique are reassuring and similar to one-way IVF.

RESUMO

Um número cada vez maior de mulheres homossexuais deseja ser mãe, o que se reflete na crescente procura de tratamentos reprodutivos assistidos para casais do mesmo sexo observada durante as últimas décadas. A maioria das mulheres homossexuais refere um elevado desejo de ser mãe principalmente como parte de um casal, através da reprodução assistida ou da adoção de um filho da sua parceira. No geral, consideram-se bem informadas sobre as técnicas de reprodução assistida disponíveis.

O método ROPA (Receção de Ovócitos da Parceira), também conhecido como FIV (fecundação *in vitro*) lésbica partilhada é uma técnica de reprodução assistida para casais femininos, em que uma das mulheres fornece os ovócitos (mãe genética) e a outra recebe o embrião e gesta (mãe gestacional). Como método duplamente parental, é a única forma de um casal de mulheres poder partilhar biologicamente a maternidade.

Até 2022 foram publicados 35 artigos com referência ao método ROPA, 10 sobre as motivações para a escolha deste tratamento, 13 sobre ética ou legislação, 4 sobre maternidade e 8 estudos relatando resultados clínicos.

Tal como qualquer técnica de reprodução medicamente assistida, o método ROPA levanta várias questões éticas relacionadas com as pacientes, futura descendência, gâmetas e embriões. Além disso, o facto de ser dirigida a mulheres homossexuais coloca as suas próprias questões, tanto de natureza biológica como social. A sua prática é legal em 13 países europeus.

O método ROPA introduz uma nova perspetiva sobre a dimensão biológica da maternidade, pois distingue entre as componentes gestacional e genética. A importância dada às relações genética ou gestacional com o seu futuro filho varia muito entre as mulheres, embora a maioria das mulheres acredite que terá a mesma ligação com o seu filho, independentemente do tipo de tratamento de reprodução assistida ou dos papéis que desempenharam, tanto as pacientes ativas ou passivas, como as mães gestacionais ou genéticas. A maioria dos casais femininos não tem dificuldade em escolher um tratamento reprodutivo ou papel a desempenhar, escolha essa baseada essencialmente nos custos, taxas de sucesso e na possibilidade de partilhar a maternidade biológica com o método ROPA.

No que diz respeito aos resultados desta técnica, as taxas por transferência de embrião de teste de gravidez positivo, gestação clínica e aborto espontâneo encontradas

foram de 61% a 63,3%, 54,1% a 57% e 16,1% a 17,2%, respetivamente. A taxa de nascimentos vivos foi de 44,7% a 46,1%. A taxa de recém nascido vivo por ciclo ROPA variou entre 48,6% e 79%. No final, 61,6% a 78,3% dos casais que se submeteram a ROPA obtiveram pelo menos um recém-nascido vivo. Não foram observadas diferenças significativas nos resultados em comparação com a FIV unidirecional.

Apesar das suas possíveis questões éticas e legais, o método ROPA é uma alternativa desejável para casais femininos que pretendam partilhar a maternidade biológica. Os resultados desta técnica são semelhantes aos da FIV unidirecional.

ABBREVIATIONS

AFC: antral follicle count

AMH: antimullerian hormone

ART: assisted reproductive technology

ASEBIR: Spanish Association for the Study of Reproductive Biology

AT: Austria

BE: Belgium

BG: Bulgaria

BMI: body mass index

CH: Switzerland

CI: confidence interval

cm: centimeters

CPR: clinical pregnancy rate

CY: Cyprus

CZ: Czech Republic

DE: Germany

DET: double embryo transfer

DK: Denmark

EE: Estonia

ES: Spain

ESHRE: European Society of Human Reproduction and Embryology

EU: European Union

FI: Finland

FR: France

FSH: follicle stimulating hormone

g: grams

GR: Greece

HR: Croatia

HU: Hungary

ICSI: intracytoplasmic sperm injection

IE: Ireland

ILGA: International Lesbian, Gay, Bisexual, Trans and Intersex Association

IS: Iceland

IT: Italy

IUI: intrauterine insemination

IVF: *in vitro* fertilization

Kg: kilograms

L: liter

LBR: live birth rate

LGBTQIA+: lesbians, gays, bisexuals, transexuals, queers, intersexuals, asexuals and others

LT: Lithuania

LV: Latvia

LX: Luxembourg

m2: square meters

MII: metaphase II

MR: miscarriage rate

MT: Malta

NL: Netherlands

NO: Norway

OR: odds ratio

PCOS: polycystic ovarian syndrome

PGT-a: preimplantation genetic testing for aneuploidy

PL: Poland

pmol: picomole

PN: pronuclei

PT: Portugal

RO: Romania

ROPA: Reception of Oocytes from Partner

SD: standard deviation

SE: Sweden

SK: Slovakia

SL: Slovenia

UK: United Kingdom

vs.: versus

I. INTRODUCTION

STUDY 1
Lesbian shared in vitro fertilization – the ROPA (Reception of Oocytes from Partner) method – a review.
Brandão P, Ceschin N.
Porto Biomedical Journal 2023; 8:e202

Throughout human history, the way in which homosexuality is regarded has varied considerably, ranging from being considered a sin or a crime punishable by the highest penalties to societies where it is well-regarded and generally accepted. Despite the diversity of beliefs and attitudes towards gay individuals, there has been a growing acceptance of homosexuality. In 1973, the first amendment to the Diagnostic and Statistical Manual of Mental Disorders regarding this matter took place, but it was only in 1987 that homosexuality was definitively removed from the list of mental illnesses.[1,2] Since then, many countries have changed their policies concerning same-sex relationships, marriage, adoption, and access to medically assisted reproduction techniques (ART). Consequently, gay civil unions and marriages have been progressively accepted in more countries worldwide, and the possibility of raising a family, including children, is becoming a reality for more and more non-heteronormative families.

In contrast to heterosexual couples, same-sex couples cannot biologically procreate by themselves; therefore, they have to turn to adoption, arranged conception with other people, or ART.[3,4] The inability to conceive naturally can be one of the most challenging aspects for same-sex couples who desire to have children. From a biological perspective, male couples require an oocyte donor and a gestational carrier in order to have a child, whereas a woman or a female couple can conceive as long as they are provided with male gametes – sperm. With the advancements in medically assisted reproduction, there are now a variety of options available, including intrauterine insemination (IUI), *in vitro* fertilization (IVF), and the ROPA method (from Spanish: *Recepción de Ovocitos de Pareja* - Reception of Oocytes from Partner) for female couples and surrogacy for male couples.[5,6] IUI is simpler, cheaper and requires less medication. IVF (including ROPA), however, has higher success rates and allows for the creation of surplus embryos that can be used in future treatments in case of failure or for a second child.[7,8]

The ROPA method is an assisted reproduction technique designed for female couples. In this method, one partner provides the oocytes, also known as the egg provider, donor, genetic mother, or giving partner, while the other partner receives the embryo and gestates, also referred to as the recipient, gestational or gestating mother, or receiving partner.[9] It is also known by several other names, including co-IVF, lesbian shared IVF, intra-partner oocyte donation, lesbian reciprocal IVF, or partner IVF.

ROPA allows couples to share biological motherhood, but it can also be used in cases where one partner has impaired ovarian function or has any condition precluding pregnancy. It is also an option for transgender patients who have undergone gender reassignment after preserving fertility.[10] Additionally, ROPA offers a wide range of possibilities for couples. They can choose to do it unidirectionally, with one partner as the donor and the other as the recipient. Alternatively, they can both play both roles, either at the same time (reciprocal ROPA) or in different cycles (reverse ROPA). If an unsuccessful cycle occurs, couples can choose to invert roles to try to improve the outcomes.[11]

There is a key difference between ROPA and conventional one-way IVF: the embryo will not share any biological links with the gestational carrier. It is similar to IVF treatments with donated oocytes, but it is entirely within a couple and not an external previously screened young and healthy woman.

In the context of assisted reproductive techniques such as IUI or IVF using donated semen, both partners in a female couple may be recognized as legal mothers, but biologically speaking, these methods are generally regarded as single-parent techniques.[5,11,12] In contrast, the ROPA method is considered a double-parent technique, as it allows both partners to actively participate in the conception of their child.[13] While the gestational carrier in this case may not share a genetic link with the child, she will carry and deliver the baby, resulting in a child with two biological mothers. This makes ROPA a particularly attractive option for same-sex couples seeking to share biological motherhood and fully participate in the conception of their child.

A review of the ROPA method was published in 2023, encompassing all relevant articles listed in Pubmed, SCOPUS, and Cochrane Library until November 2022, excluding editorials, letters to the editor, comments, corrigenda, replies, book chapters, and study protocols. The query used for the search was: ropa or "shared motherhood" or "reciprocal ivf" or "reciprocal in vitro fertilization" or ((lesbian or lesbians or gay or lgbt or homosexual or "same sex" or "same-sex") and (ivf or "in vitro fertilization" or

"in vitro fertilization" or "assisted reproduction" or "assisted reproductive"). In total, 1415 articles were retrieved (Pubmed: 558, SCOPUS: 831, Cochrane Library: 26), and after screening, 35 articles were deemed relevant to the review. Among these, 10 addressed preconception issues and motivations for undergoing ROPA treatment, 13 focused on ethical and legal aspects, 4 discussed resulting motherhood, and 8 were quantitative studies evaluating the outcomes of the technique (Figure 1).[14]

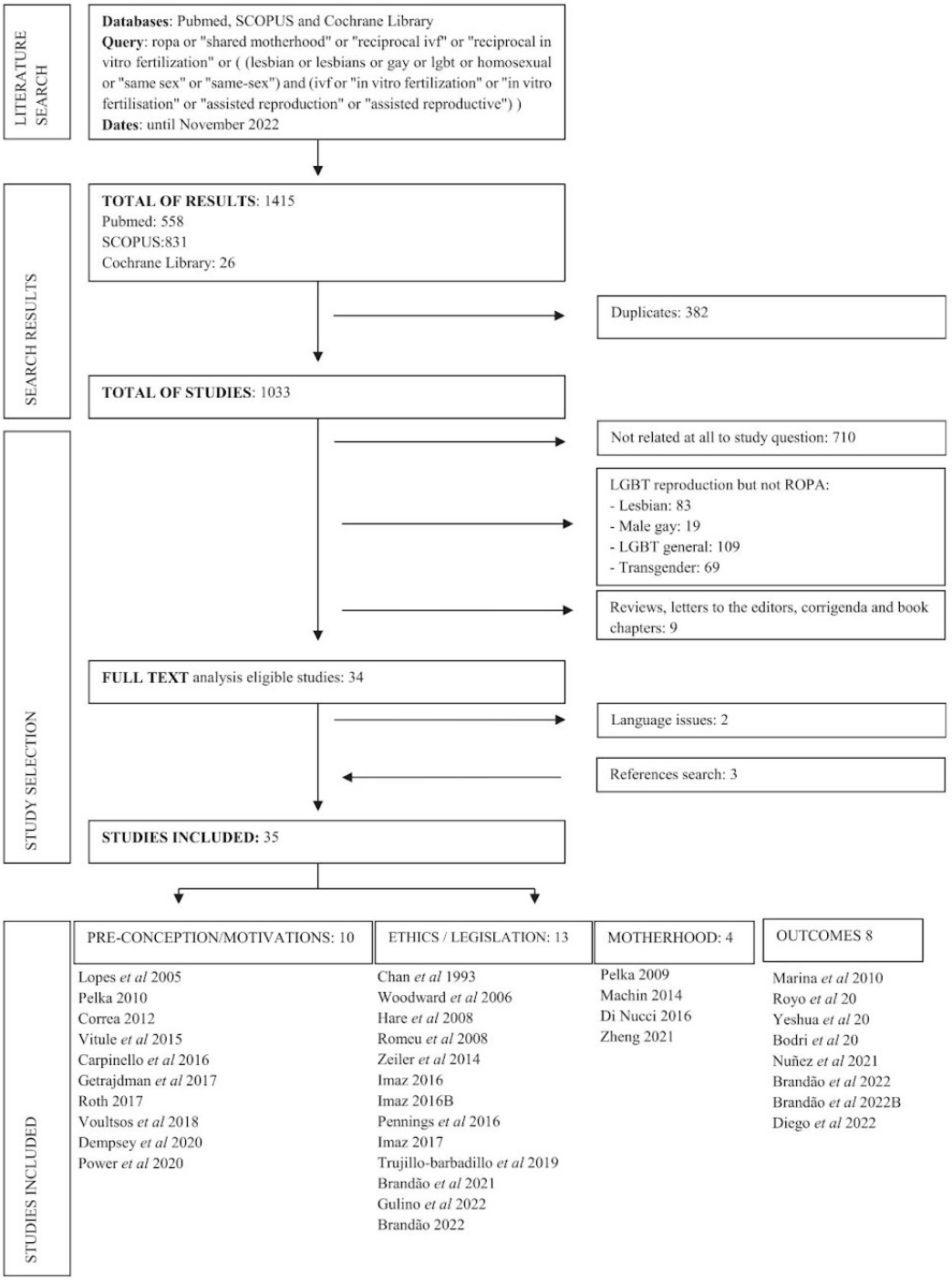


Figure 1: flowchart of the review about the ROPA method – Brandão *et al* 2023.[14]

II. ETHICS

STUDY 2

ROPA – Lesbian shared in vitro fertilization – Ethical aspects.

Brandão P, de Pinho A, Ceschin N, Sousa-Santos R, Reis-Soares S, Bellver J. European Journal of Obstetrics and Gynecology and Reproductive Biology 2022;272:230–233.

The right to procreate is universally accepted as a basic human right.[15]

On the one hand, to accept ROPA treatments is to open one more door to procreation. On the other hand, denying these treatments would create a limitation for female couples at the time of reproduction, particularly couples who, for medical reasons, have no other means of reproduction.[16]

The four bioethical principles defined by Beauchamp and Childress also apply to ART, which include autonomy (individual's, couple's, physician's, and offspring's autonomy), beneficence, non-maleficence (including safety and balancing risks and benefits) and justice or equality.[17] In addition, the respect for everyone's dignity must be met. Furthermore, it must be kept in mind that more than one party is involved in ART, but only one of them, the child, does not have an opinion and is not able to give an informed consent. Thus, protecting the best interest of the child is of paramount importance.[18]

A. Principle of autonomy

To comply with the principle of autonomy, patients must be offered the possibility to choose their treatment. Moreover, ROPA gives patients the opportunity to define which role they intend to play – gestational mother, genetic mother or both.[19]

B. Principle of beneficence

From a demographic perspective, the availability of different methods of assisted reproduction for female couples presupposes an increase in fertility in this population.[20]

The ROPA method allows both mothers to share the child's biological motherhood. Many women opt for a single-parented (biologically speaking) method, since the concept of family does not imply biological ties. Nevertheless, for some patients this may be an explicit dream which cannot be fulfilled in any other way.[21]

Likewise, when both partners express a shared explicit desire for the treatment, it is in the best interest of both parties to undergo the procedure, assuming that they will both benefit from it.

In respect to the offspring, accepting that existing is better than not existing, this method is in their best interest as well.[22]

While there are only few studies on the subject compared to biologically single-parent methods, shared motherhood may reduce the risk of an uneven relationship with children due to the absence of biological motherhood links. However, this is not guaranteed and will depend on the importance attributed to genetics and pregnancy by both mothers and children. Even in cases of reciprocal or reverse ROPA, in which each mother plays both roles (gestational and genetic) simultaneously or at different times, respectively, there is a risk of a distinct bond between the mother and her "gestational" and "genetic children".[23–25]

C. Principle of non-maleficence

The ROPA technique requires the donor mother to undergo ovarian stimulation, imposing a significant physical, psychological, economic, and relational burden, along with the inherent risk of Ovarian Hyperstimulation Syndrome. Similarly, the recipient will conceive with a biologically unrelated embryo, comparable to treatments involving donated oocytes or embryos. Although not yet conclusively established, some studies suggest poorer obstetric outcomes in pregnancies involving donated oocytes or embryos, notably an increased risk of hypertensive disorders, fetal malformations, and low birth weight.[26–28]

These issues are relevant in ROPA treatments, where in most cases, it would be possible to perform insemination with donated sperm—a simpler and less invasive technique with lower risks and associated costs.[21] Some ethical concerns have been raised regarding the submission of biologically fertile women to these treatments.[29] Nevertheless, a parallel can be drawn with heterosexual couples facing an isolated male factor. These couples may require Intracytoplasmic Sperm Injection (ICSI) to achieve pregnancy with their own gametes, but they could also opt for donated sperm and undergo artificial insemination. If the goal is to avoid the drawbacks of a more complex treatment, in both cases, one could forego the genetic link and opt for a mere insemination with donated sperm.[30]

Likewise, it is questionable whether it is ethical to define roles solely based on patients' preferences if the risks would be clearly lower if carried out the other way around. For instance, pregnancy in an older woman poses a greater obstetric risk.[31] On the other hand, ovarian reserve and oocyte quality decrease with age, so if the older woman is providing the oocytes, worse reproductive technique outcomes and higher rates of aneuploidies may be expected.[32]

Regarding offspring, questions have been raised about same-sex couples raising children. Numerous studies have been conducted on this matter, often focusing on adoption or simpler techniques such as insemination. It is important to note that the comparisons are consistently made with children from heterocisnormative families. Consequently, it is always assumed that these families serve as the reference, and their children are seen as the "good example" or the "gold standard".[33]

Regardless, systematic reviews and meta-analyses report similar outcomes regarding behavior, emotional and cognitive functioning, stigmatization, sexual preferences, sexual identity, and quality of life when comparing children raised by straight and gay parents.[24,34]

Interestingly, some studies have reported differences in self-esteem and psychological well-being in favor of children raised by lesbian parents. Based on these findings, one might argue that heterosexual couples should not have access to ART. Certainly, this idea is absurd, but for the same reason, these conclusions must also not be drawn regarding same-sex couples.[23,33,35]

D. Principle of justice

In a society guided by the principles of non-discrimination, access to ART becomes essential for female couples as it represents the sole means to ensure their right to procreation.

The ROPA technique enables both members of a female couple to actively participate in the creation of a new being, establishing both as biological mothers.[22]

This method also allows biological procreation by patients who had undergone a gender change process with cryopreserved oocytes prior to oophorectomy. These patients, now males in a heterosexual relationship, can use their vitrified oocytes for further procreation with their partners.[22]

To date, the ROPA technique is the way female couples become closer to heterosexual couples in what concerns biological connection with their offspring. However, it opens a new opportunity for women only, with no unmatchable alternative for male couples, putting this gender in disadvantage. The male contribution to the procreation consists merely in the supply of the male gamete, while women contribute not only with the female gametes, but also as the gestational carrier. Therefore, and in the light of current knowledge, there is no way both members of a male couple may contribute simultaneously to the generation of a new human being. Moreover, for a male couple to embark on the journey of procreation, they must turn to surrogacy—a process entailing more intricate biological, social, economic, legal, and ethical implications.[6,36]

Another pertinent question is whether it is acceptable to offer a complex assisted reproduction technique in the absence of a medical reason. A parallelism can be established with the use of ART by perimenopausal women. Menopause is a physiological process that marks the end of women's reproductive age. As a physiological process, there is also no medical reason supporting the use of ART in these cases. The same goes for elective fertility preservation for postponing procreation.[30]

In many countries, ART is performed in public facilities, or there is governmental funding for ART in a private setting. Many of these countries offer public funding for ROPA or allow these treatments to be performed in a public setting. Nevertheless, in many cases, public funding applies only to specific situations, usually when patients have no other viable, easier, or cheaper alternatives.[37]

It is questionable whether a biologically single-parented method can be considered an alternative to ROPA. Nevertheless, it is expected that the same criteria applied to other kinds of treatments will also be applied to the ROPA method.[38]

E. Reciprocal or reverse ROPA

In the case of reciprocal ROPA, both patients undergo an ovarian stimulation, oocyte retrieval and the resulting embryos are transferred to the uterus of the partner. This brings to discussion whether it is acceptable to perform two simultaneous treatments in the same couple. Not only must the risks be weighed, but also the fact that more embryos will be generated, thereby assuming a higher risk of having surplus embryos.[25]

Another challenging situation arises when a couple has frozen embryos but decides to undergo a reverse ROPA, meaning they want to redo the treatment by exchanging roles so that both can be genetic and gestational mothers at least once. One may question the acceptability of creating new embryos within the same couple when there are already existing surplus embryos.[39]

F. Disagreement and posthumous

Any IVF technique may end up in the creation of surplus embryos. The disposition of surplus embryos poses important ethical dilemmas.[40–43] Difficult questions may be raised in case of a couple's disagreement in respect to the future of surplus embryos.

Despite all the efforts to define the concept of embryo and its legal framework, no consensus has been reached so far. As such, in certain situations it may be hard to define whose "property" is the embryo.[44]

In general, in countries where gay co-parenting following ART is allowed, before generating embryos patients must sign a contract committing themselves to share motherhood of any resulting beings. If so, it may be assumed that both "own" the embryos. What if there is disagreement in respect to their fate? At this point, only the genetic mother has any biological connection to the embryo, must she have the last word? This is like what happens with a straight couple resorting to donated gametes, only one of them has a biological link with the embryos but both have the same legal rights over them.[25]

Furthermore, pregnancies within female couples may present another significant dilemma. Despite any prior contractual agreements, legal motherhood typically automatically attributes to the woman who gives birth. The other woman may only *de facto* claim the right to shared motherhood in the act of registering the child, immediately after birth. If so, what if the couple disagrees about the fate of pregnancy when the possibility of pregnancy termination is raised? While the best interest of the pregnant patient usually prevails, this raises concerns regarding the autonomy and justice of the other patient – the donor mother finds herself in an unequal position and forfeits the right to decide her own child's future.[25]

Another interesting matter pertains to the use of embryos by one of the patients after a divorce. Generally, when patients opt for medically assisted reproduction as a

couple, they create embryos intended for conjugal use. However, after the dissolution of the union or marriage, one of the members may express a desire to use these embryos individually. While it's true that only one of them may have a biological link with the embryo at this point, both parties typically retain the same legal rights over them.[45]

In contrast to divorce, in post-mortem circumstances, the deceased individual cannot provide consent unless it was duly expressed, written, and legally recognized *in vivo*. However, many countries do not accept this practice due to concerns about creating orphans and the potential for falsifying consent.[44,46] If embryos are considered mutual property while both partners are alive, it may seem intuitive to transfer ownership to the surviving partner in the event of one partner's death. Yet, in case of death of the genetic mother, it seems logical that the widow shall not use the embryos without her consent. If this is true, the same should apply if it is the genetic mother asking for the posthumous use of the embryos, as both patients have the same legal rights over them. If so, this woman has frozen embryos resulting from her own oocytes, but she won't be allowed to use them. Instead, she would need to create new embryos, and the existing ones would be discarded.[25]

G. Is it an oocyte donation?

In procedural terms, ROPA is similar to common oocyte donation, with one partner donating oocytes for the other to become pregnant. If ROPA is to be regarded as an oocyte donation, it raises a legal problem in countries where donation is anonymous, or the choice of gamete donors is not allowed. In such a scenario, a woman with low ovarian reserve or poor oocyte quality could visit a fertility center with a chosen donor, claiming to be a couple seeking ROPA treatment. However, in contrast to traditional gamete donation, both members of the couple would be assumed as mothers, granting legal motherhood rights to the donor. In this hypothetical scenario, the donor would also have to assume maternal rights over the offspring.[25]

As mentioned earlier, certain national laws stipulate automatic recognition of motherhood for the gestational mother, with her partner only able to request shared motherhood recognition after the child's birth. In the same hypothetical scenario, the egg donor, acting as a partner, could potentially refuse to assume motherhood at birth. Consequently, it is common for a contract to be signed at the beginning of a ROPA treatment, ensuring that both women will be recognized as mothers after birth. Fertility

clinics often advise or require couples to legally formalize their relationship, either through a legal union or marriage. This step helps prevent potential fraudulent situations and streamlines the process of acquiring shared motherhood rights postnatally. In extreme cases, formalizing the relationship and having a contract in place can preemptively address issues in the event of a couple's separation or death before or during childbirth.[25]

Likewise, if ROPA is to be regarded as an oocyte donation, the requirements for donor selection would also apply, such as age or the absence of known genetically transmitted diseases. This would limit the access of many women to these treatments, thus calling into question the principle of justice.[47]

Based on the principles of justice and equality, ROPA is a gamete transfer process, similar to any heterosexual couple resorting to ART, wherein sperm is transferred from the male partner to the wife. However, the acronym ROPA is misleading, as it implies that one of the patients donates her oocytes to her partner. In reality, the procedure is performed to create embryos jointly owned by the couple. Therefore, this treatment does not involve the donation of unfertilized oocytes, which would suggest that the recipient patient could use them independently. Additionally, this method may be a way to avoid a third party donation in cases of poor ovarian reserve within a female couple.[47–49]

H. Is it an embryo donation?

The aim of this technique is to create embryos artificially, similar to conventional IVF, which will then be transferred to her partner. If so, ROPA may be regarded as a specific form of embryo donation, as the person becoming pregnant receives a biologically unrelated embryo. This could pose significant legal problems in countries where embryo donation is not permitted.

Embryo donors have no legal obligation or the possibility to claim offspring paternity, there is a complete transfer of embryo “property”. Embryos resulting from ROPA are generated within a couple - there is no transfer of “embryo’s property”, they belong to the couple since their creation and both participants show their intention to assume motherhood since the beginning of the process.[50]

In some countries, embryo donation is only possible if embryos are left over from another reproduction treatment. In this case, ROPA treatments would have to be

initiated as conventional IVF cycles, which would later be changed to ROPA once the embryos were created.[48]

I. Is it surrogacy?

From a purely biological standpoint, ROPA can be considered a form of gestational surrogacy, as one mother becomes pregnant with an unrelated embryo. However, ROPA treatments are conducted within a couple, and the pregnant woman does not relinquish her maternity rights. The pre-treatment contract signature and legal formalization of relationships help prevent fraudulent cases where women in need of surrogacy falsely present themselves as female couples in regions where these treatments are not allowed.[36,51,52]

J. Treatment denial

May doctors or healthcare providers refuse to carry out this type of treatment? In a free society, any person has the right to refuse to perform any act if it goes against their principles, whether for cultural, religious, or reasons of any other nature. Based on this, any physician must have the right to refuse to perform or assist in a ROPA treatment. However, if a healthcare professional consents to and conducts treatments with donated gametes or embryos but refuses to perform a ROPA treatment, they would be engaging in an act of discrimination based on sexual orientation. This is because all of these treatments are technically and biologically similar; only the sexual orientation of the patients differs.[53]

III. EUROPEAN LEGAL BACKGROUND

STUDY 3
European policies on same-sex relationships, adoption and assisted reproduction.
Brandão P.
International Journal of Reproduction, Contraception, Obstetrics and Gynecology
2022;11:2306.

Neither the formalization of relationships, nor procreation or adoption by same-sex couples are consensual between and within different countries, cultures, and societies. In addition, ART poses several ethical issues of its own. These are some of the reasons countries take so long to adopt more liberal policies concerning the matter.[54,55]

In most countries, assisted reproduction was first legalized for heterosexual couples. However, more and more nations have gradually extended the availability of ART to single people and same-sex couples.[50]

When same-sex couples become parents, either through adoption or assisted reproduction techniques, the child's registration does not adhere to the traditional heterocisnormative family structure, which includes a mother and father. For a female couple to undergo ART, the country must not only accept the registration of two mothers but also acknowledge the absence of a father.

Rainbow Europe's annual benchmarking tool identified Malta and Belgium as the leading nations in 2021 regarding LGBTQIA+ family policies and rights in European countries, followed by Sweden, Portugal, Spain, Denmark, the United Kingdom, and the Netherlands (Figure 2).[56]

RANKING (FAMILY)	COUNTRY	ILGA SCORE 2021 (FAMILY)	ILGA SCORE 2021 (GLOBAL)
1	MALTA	100	94
1	BELGIUM	100	74
2	SWEDEN	93	65
3	PORTUGAL	90	68
3	SPAIN	90	65
3	DENMARK	90	64
3	UK	90	64
3	NETHERLANDS	90	61
4	LUXEMBOURG	83	72
4	FINLAND	83	65
4	ICELAND	83	54
5	NORWAY	78	64
5	AUSTRIA	78	50
6	IRELAND	76	53
7	FRANCE	57	57
7	GERMANY	57	52
8	SLOVENIA	43	42
9	ESTONIA	40	38
10	SWITZERLAND	33	38
11	GREECE	31	47
11	CYPRUS	31	31
12	CROATIA	28	46
12	HUNGARY	28	31
13	ITALY	15	22
14	CZECH REPUBLIC	14	26
15	BULGARIA	13	20
15	LATVIA	13	17
16	SLOVAKIA	0	30
16	LITHUANIA	0	23
16	POLAND	0	13
16	ROMANIA	0	19

Figure 2: Ranking of European countries based on Rainbow Europe (ILGA Europe) score 2021 concerning family aspects (untied by global score). From 1 to 16 and from green to purple, ranked from best to worst.[57]

In 2021, a review was conducted to assess national policies regarding gay relationships and families.[57] This review encompassed all European Union (EU) member states, as well as Iceland, Norway, Switzerland and the United Kingdom, covering a total of 31 nations: Austria (AT), Belgium (BE), Bulgaria (BG), Croatia (HR), Cyprus (CY), Czech Republic (CZ), Denmark (DK), Estonia (EE), Finland (FI), France (FR), Germany (DE), Greece (GR); Hungary (HU), Iceland (IS), Ireland (IE), Italy (IT), Latvia (LV), Lithuania (LT), Luxembourg (LX), Malta (MT), Netherlands (NL), Norway (NO), Poland (PL), Portugal (PT), Romania (RO), Slovakia (SK), Slovenia (SL), Spain (ES), Sweden (SE), Switzerland (CH) and the United Kingdom (UK).

The first step of the review involved an online search for national legislation.If the national language was not comprehended and an English version was unavailable, assistance was sought from native or proficient speakers. In situations where the official legislation was unavailable, the websites of ILGA Europe and ESHRE were

consulted.[56,58] The retrieved information was subsequently confirmed by reaching out to official entities: an official national LGBTQIA+ association for relationships, marriage, and adoption, and a representative of the national society of reproductive medicine for issues relating to assisted reproduction. In cases where complete information was not obtained through the previous steps, at least two national experts on the matter were consulted, and data was considered only if there was a consensus.

All countries included recognized homosexual activity. The first countries to officially recognize homosexual activity were France, Belgium, and Luxembourg during the 18th century, followed by Italy and the Netherlands in the 19th century. All remaining countries legalized homosexual activity during the 20th century.[55] The most recent country to officially allow homosexual activity was Romania in 1996.[59]

The definition of civil union or recognized partnership varied widely across countries. Additionally, the rights granted to same-sex partnerships also differed from country to country.[60] As a general rule, in countries where same-sex partnerships were allowed, their rights were usually the same or similar to those of heterosexual couples.[61,62] Out of the 31 countries included in this study, 10 recognized civil unions or registered partnerships, while 16 allowed same-sex marriage. Only 5 countries did not officially recognize any kind of gay partnership - Bulgaria, Lithuania, Poland, Romania, and Slovakia (Figure 3).[63,64] Some nations have explicitly rejected gay marriage after referendums or parliament decisions, such as Hungary in 2012, Croatia in 2013, and Slovakia in 2014. Meanwhile, the Czech Republic and Switzerland have passed new laws allowing gay marriage, which are yet to come into effect.[65–67]

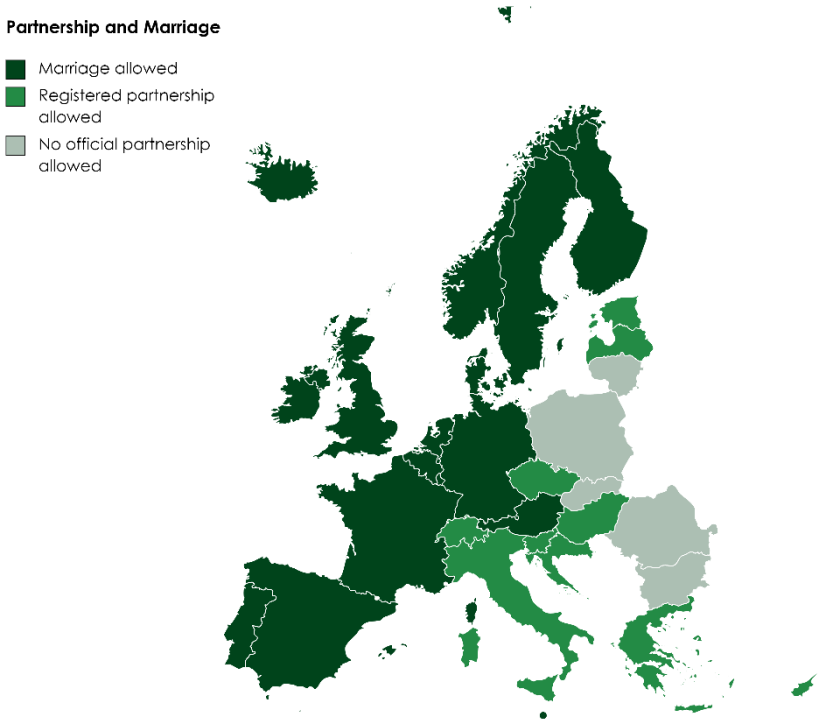


Figure 3: European map according to national policies on the official recognition of same-sex partnership and marriage and/or single female rights on 2021.[57]

Adoption was possible in all European countries.[68] Nevertheless, some countries only authorized the adoption of a child by married couples (only heterosexual or also gay couples, depending on the country), while others also accepted adoption by single people. As expected, the 5 countries where no gay partnerships were recognized, the co-adoption by gay couples was not allowed as well (BG, LT, PL, RO, SK). Additionally, 5 other countries did not allow adoption by gay couples as well (CY, CZ, GR, HU, IT). In the remaining countries where gay partnerships, but not marriages, were recognized (HR, EE, LV, SK, CH), gay couples were allowed to adopt a partner's child (second child adoption) but not engage in joint adoption (adoption of a child without any previous legal paternal connection to either member of the couple).[18] Interestingly, all and only the 16 countries where gay marriage was recognized also allow the joint adoption of a child by gay couples (AT, BE, DK, FI, FR, DE, IS, IE, LX, MT, NL, NO, PT, ES, SE, UK) (Figure 4).[69] Some of these countries recognized gay marriage and adoption at the same time, since national laws of child adoption refer to "married couples", implicitly granting the same rights of adoption to same-sex couples.

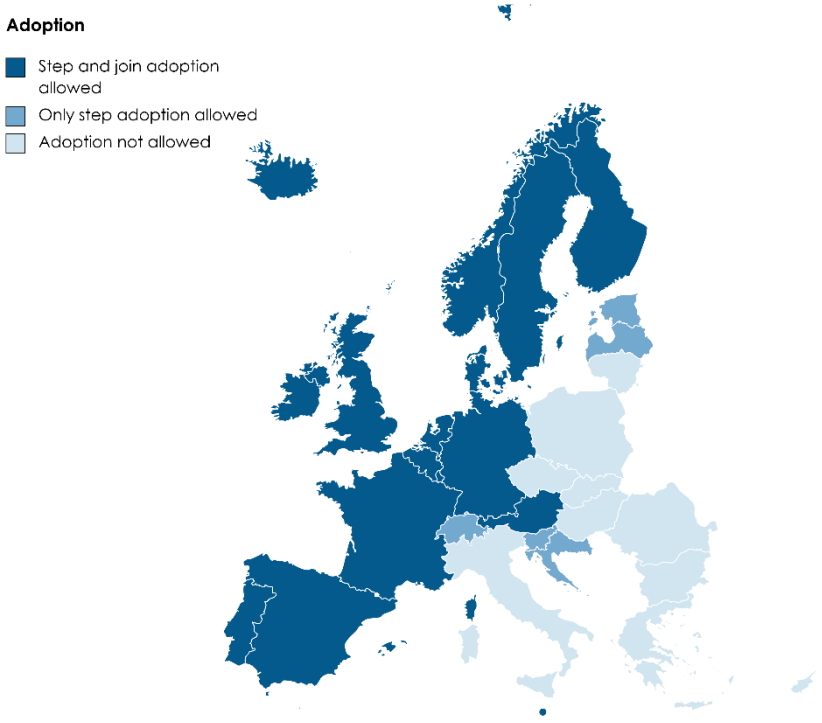


Figure 4: European map according to national policies on child adoption by same-sex couples (second child adoption: adoption of partner's child; joint adoption: simultaneous adoption in 2021.[57]

The world's cultural diversity has led to a wide variety of national laws related to both homosexuality and ART. Consequently, the ability of gay individuals to exercise their procreative rights often depends on their place of origin or current residence. Many countries have progressive laws regarding same-sex relationships and families but lack specific legislation regarding gay individuals' access to ART. However, some of these countries permit single people to undergo ART, resulting in many cases in the same regulations applying to same-sex couples automatically.[70]

The regulations governing the access to IUI and IVF in Europe were the same for single women and female couples.[71] Romania did not have specific legislation for assisted reproduction.[50] Seven countries only offered ART to heterosexual couples (CZ, IT, LT, PL, SK, SL, CH). In seven other nations, single women were allowed to undergo ART, but female couples were not, thereby preventing homosexual women from legally or biologically sharing motherhood (BG, HR, CY, EE, GR, HU, LV).[72,73] The remaining 15 countries allowed both single women and female couples to access fertility treatments (AT, BE, DK, FI, FR, DE, IS, IE, MT, NL, NO, PT, ES, SE, UK).[74] Notably, Austria permitted female couples to receive ART, but only as a couple, single women were ineligible for treatment (Figure 5).[75] France was the most recent country to approve ART for single women and female couples in June 2021.[76]

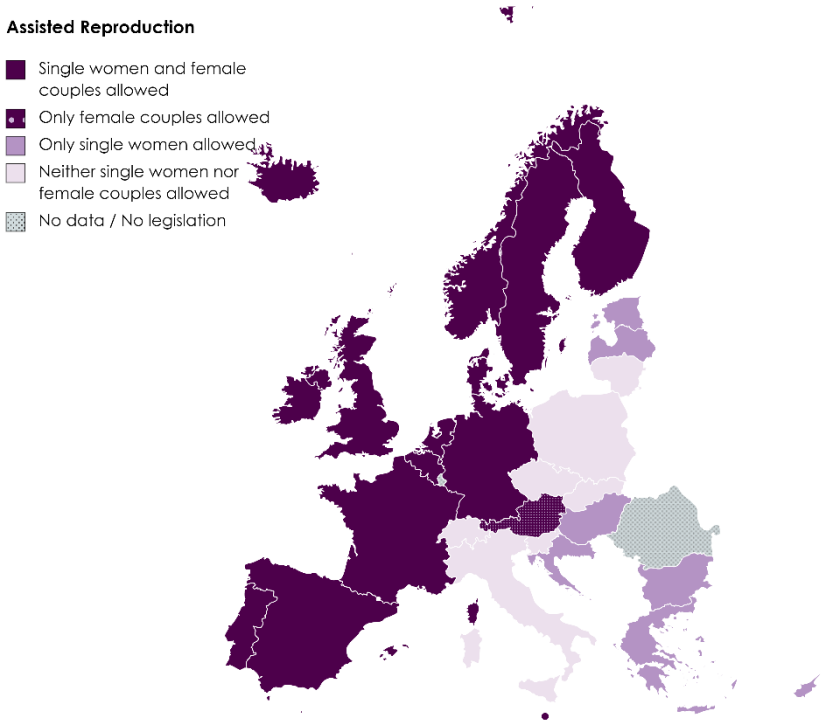


Figure 5: European map according to national policies on the access of female couples and/or single women to assisted reproduction in 2021.[57]

Gamete donation policies exhibited notable variations among countries. In all jurisdictions providing ART to single women, the usage of donated sperm was permitted. Likewise, in the 15 countries offering ART to female couples, the use of donated sperm was also allowed.[77] The same regulations applied to oocyte donation, except in Germany, where this type of treatment was universally prohibited.[71]

Embryo donation is more intricate than gamete donation, primarily due to ethical concerns associated with the existence of an embryo. The process involves the use of embryos with a genetic background entirely unrelated to the receiving patient or couple, akin to a double gamete donation. Consequently, in some countries, embryo donation is not permitted.[78] Furthermore, in addition to the seven countries that only permitted heterosexual couples to receive fertility treatments, six other countries prohibited single women and female couples from using donated embryos. (AT, BG, DK, DE, IS, NO) (Figure 6).[79]

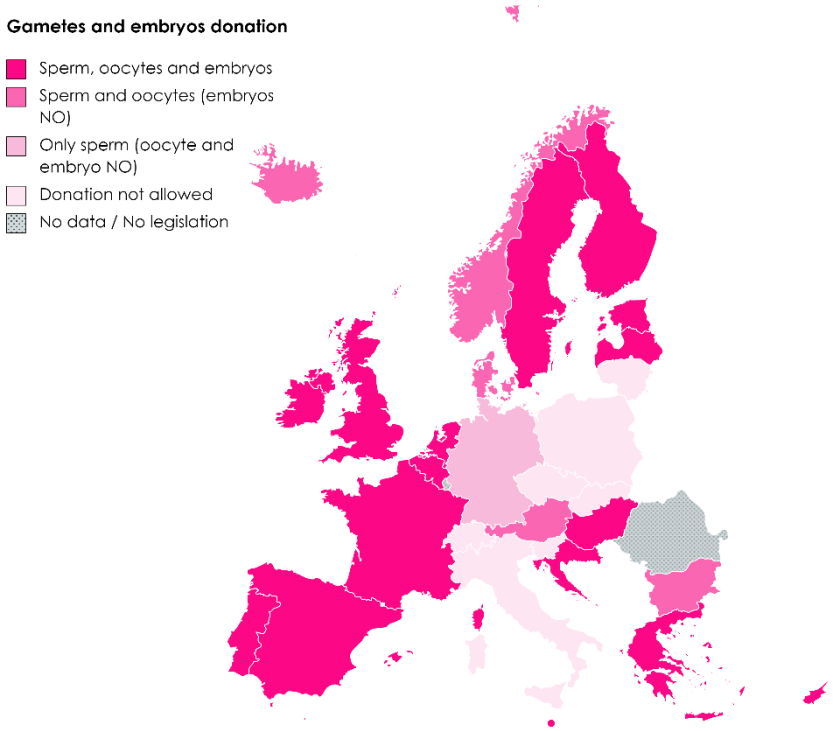


Figure 6: European map according to national policies on gametes and embryos donations to female couples or single women. in 2021.[57]

Most European countries currently lack specific legislation addressing the ROPA method. Some countries categorize ROPA as a form of oocyte donation, while others consider it an embryo donation. This variability makes it challenging to determine the feasibility of this technique in countries with diverse policies regarding different types of donations.

As of 2021, ROPA could be performed with no restrictions in 13 of the 15 European countries that offered ART to female couples (AT, BE, FI, FR, IS, IE, MT, NL, NO, PT, ES, SE, UK). The remaining two countries had limitations due to their restrictions on oocyte and/or embryo donations (DK, DE). However, in Denmark, ROPA could still be performed if there was a medical reason justifying the treatment (Figure 7).[57]

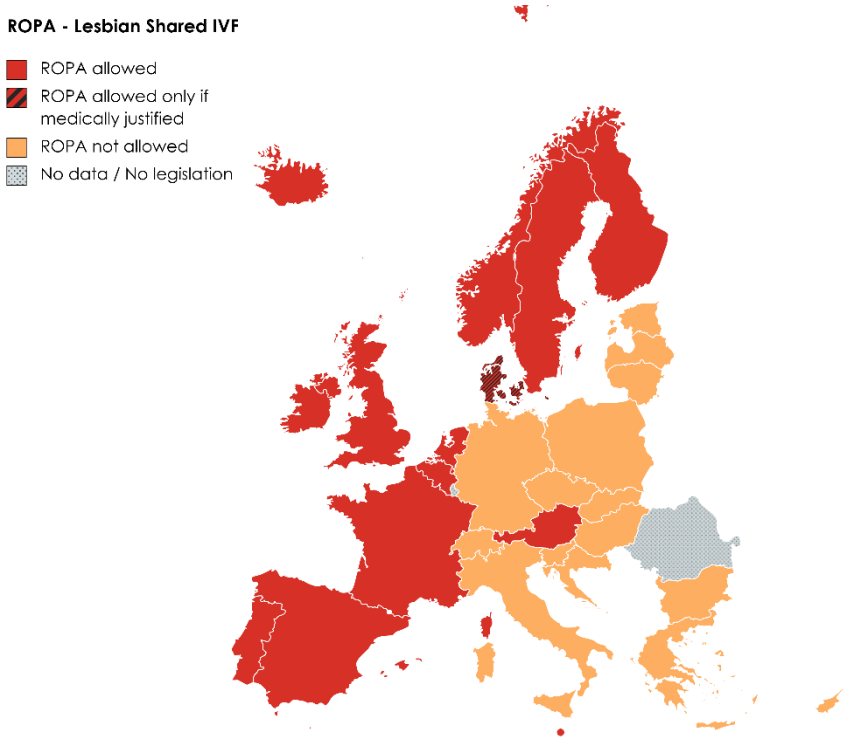


Figure 7: European map according to national policies on Lesbian Shared IVF – the ROPA method in 2021.[57]

IV. LESBIAN PROCREATION AND THE ROLE OF GENETICS AND PREGNANCY

STUDY 4
Reproductive plans and knowledge of assisted reproductive techniques among lesbian women: an international survey study.
Brandão P, Zadykowicz R, Miscioscia R, de Pinho A, Liz-Coelho M, Iftene L, Ungure A, Ceschin N.
JBRA Assisted Reproduction 2023; 27:602-609.
Poster presented at the 10th IVIRMA Congress 2023.

STUDY 5
Female couples undergoing assisted reproduction - choices and the importance of pregnancy and genetics.
Brandão P, Ceschin N, Sandvik B, Paolelli S, Doblinger J, Reis-Soares S, Sousa-Santos R, Bellver J.
JBRA Assisted Reproduction 2023; 27:442-452.

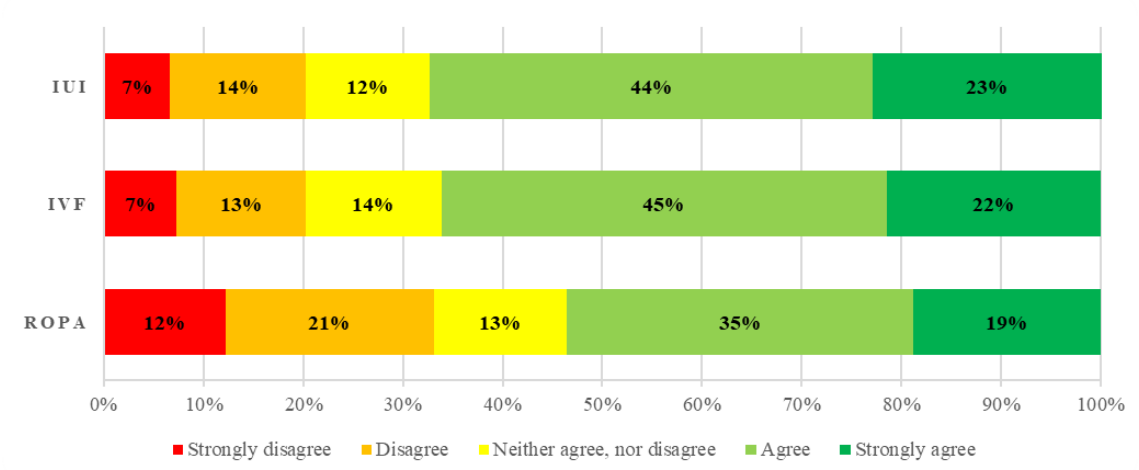
A. Knowledge on assisted reproductive techniques

In the past, homosexual women were only mothers in conjunction by step adopting the partner's child. This is the same as saying that in most cases, the maternity project was not a common project, often resulting from prior heterosexual relationships or as single women.[80] Homosexual women would often engage in intravaginal inseminations using sperm from a friend or a stranger. However, this method is not exempt from the risk of sexually transmitted diseases, and the man involved in the process will possess the same parental rights and obligations toward the child.[81] Nowadays, female couples may easily procreate through IUI, IVF or ROPA with donated sperm.

A cross-sectional international study was conducted to gather insights from individuals who identify as homosexual females. This observational study was based on an anonymous survey distributed through social networks, primarily via LGBTQIA+ associations across the globe, and was conducted between May and November 2021. The survey was originally composed in English and was later translated into French, German, Italian, Latvian, Polish, Portuguese, Romanian, and Spanish by proficient or native speakers. A second proficient speaker reviewed each translation to ensure its accuracy. The survey was distributed using Google Forms® and comprised five sections: personal information, prior knowledge of assisted reproductive techniques, current family status, the significance of genetics and pregnancy, and future

reproductive plans. A total of 549 responses were collected from individuals across 49 countries on all continents.[82]

The majority of women (67%) agreed or strongly agreed that they felt well-informed about IUI and IVF. However, this percentage was slightly lower (54%) for the ROPA method (Graph 1). These findings suggest that, in general, homosexual women feel informed about the available methods to achieve biological motherhood.[82]



Graph 1: Level of knowledge about assisted reproduction techniques - Answers to the question "To what extent do you agree with the following statements? I feel informed about …" on a survey on 549 homosexual women[82]

B. Choice of treatment and roles

Traditionally, assisted reproduction units were primarily designed and set up to treat heterosexual couples. Some of these units have been attempting to adjust their operations to cater to other types of patients, such as single patients and homosexual couples. Previous research has shown that same-sex couples often experience a sense of neglect regarding their unique circumstances, including marketing strategies targeted at heterosexual couples, decorations that emphasize heteronormative families, paperwork that refers to "husband and wife," clinics specializing in fertility disorders, etc.[83–87]

Unlike heterosexual couples, female same-sex couples do not typically visit assisted reproduction units due to infertility.[88] Therefore, they are not expected to have any conditions impairing fertility. However, like the general population, there remains a possibility of underlying fertility issues. Some couples arrive at the clinic with well-defined plans for procreation, while others seek information on available treatments and their suitability.[89–91]

According to current evidence, sexual orientation does not seem to have an impact on the outcomes of fertility treatments.[92–95] Nevertheless, it is important to note

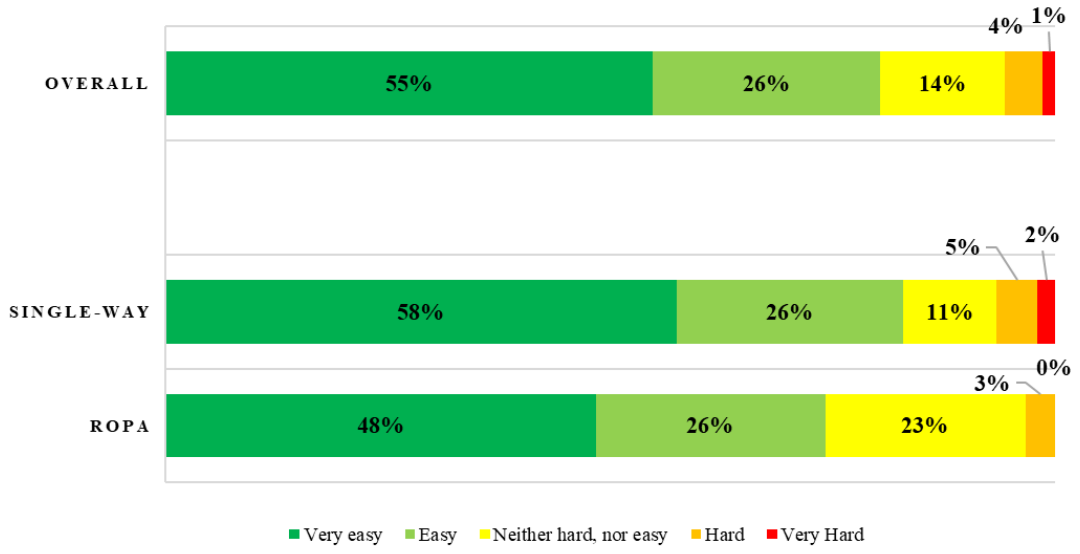
that most female couples have never attempted natural conception, so their fertility potential is unknown. These couples may also experience fertility issues or have underlying conditions affecting their ability to conceive. In fact, it is not uncommon for fertility workups or unsuccessful fertility treatments to reveal infertility factors in patients. Therefore, it is crucial for same-sex couples to undergo thorough fertility evaluations and assessments to determine the most appropriate and effective course of action.[96,97]

This can be particularly challenging for same-sex couples with well-defined plans for family building. Unlike heterosexual couples, altering the treatment approach for same-sex couples may also entail redefining roles. In the case of ROPA, couples must determine who will serve as the gestational or genetic mother. This decision can be intricate, necessitating thoughtful consideration and effective communication between partners and their physician.[98,99]

There are many reasons driving female couples to choose a reproductive treatment, including personal preferences, cost, simplicity of the process, availability of treatments, and medical reasons, such as poor oocyte quality, low ovarian reserve, a genetic disease of the gestational mother or a medical contraindication for pregnancy.[100–102] In the case of ROPA, couples may choose the role they are playing, avoiding those they do not want.[19,49] For instance, a woman may have a strong desire to have genetic related children but may not want to be pregnant.[103,104]

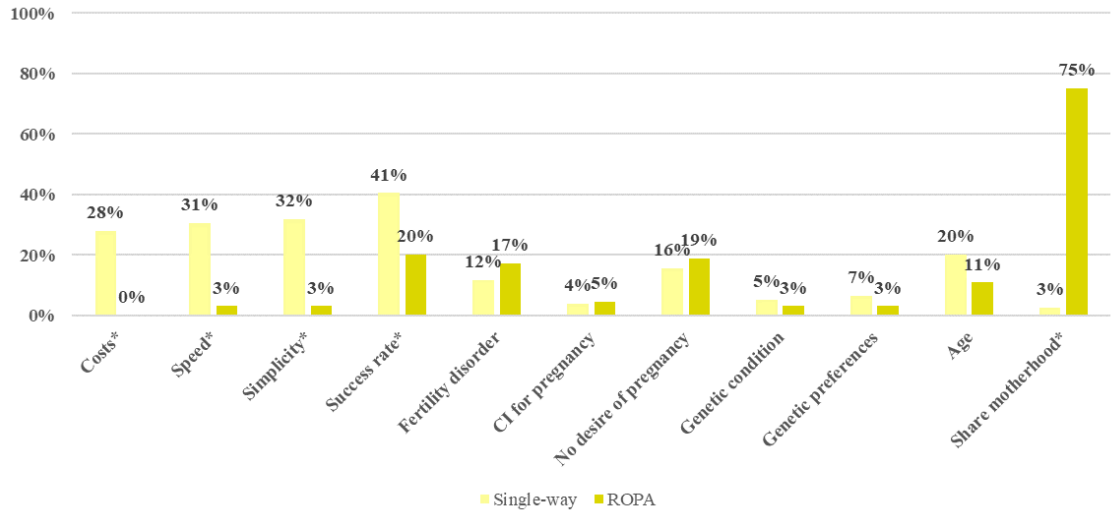
In 2021, a qualitative study was conducted using an anonymous survey to collect insights from female couples undergoing assisted reproductive treatments, such as IUI, IVF, or ROPA. The survey was originally crafted in English and distributed as a paper-based questionnaire comprising two pages with five sections: personal information, prior motherhood experience, current treatment, the significance of pregnancy and genetics, and future reproductive plans. Subsequently, the survey was translated into French, Italian, Portuguese, and Spanish by proficient or native speakers. Each translation was reviewed by a second proficient speaker to ensure accuracy. The study included a total of 217 patients from 117 female couples.[105]

More than three quarters of the patients found it easy or very easy to choose treatment and roles to play, with no differences between single-way and ROPA patients (Graph 2).[105]

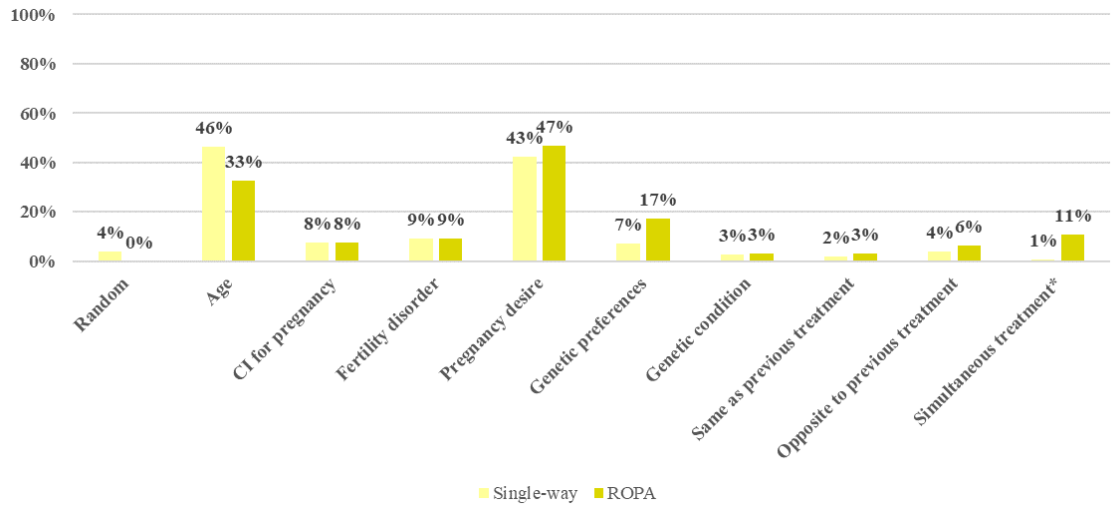


Graph 2 – Answers to the question - "How difficult was it to decide who is going to get the treatment or what roles you are going to play?" on a survey on 217 patients from 117 female couples under ART - The overall results and the comparison between single-way and ROPA patients (p=0.151).[105]

The primary reasons for choosing single-way treatments were success rates, simplicity, speed, and cost (Graph 3). As for the reasons for selecting roles (active/passive if single-way, pregnant/genetic/both if ROPA), the main reasons were the preference of one partner for being pregnant and age (Graph 4). In the case of ROPA, 75% of the patients reported the possibility of sharing biological motherhood as the reason for undergoing this treatment (Graph 3). The preference for one's genetics and the ability to simultaneously perform both roles were also important considerations when choosing roles (Graph 4).[105]



Graph 3 – Reasons for choosing a single-way or a ROPA treatment, based on a survey on 217 patients from 117 female couples under ART. CI: contraindication, *: p<0.05.[105]



Graph 4 – Reasons for choosing roles – active/passive role for single-way treatments, gestational/genetic mother for ROPA treatment. CI: contraindication, *: $p<0.05$.[105]

Some couples may have a clear idea about which ART they want to undergo or which role they want to play, while others may come to the fertility clinic with no prior conceptions.[106] There are reports of a practice called "mixing of eggs," which involves randomly combining the eggs of both women so that no one knows whose fertilized eggs they are.[106]

A study conducted on a sample of 242 female couples undergoing ART found that only a small percentage (11.8%) of couples had the intention of undergoing double parented treatment, and interestingly, all these couples intended to do the treatment in a single direction, i.e., no couple had the initial intention of doing a reciprocal or reverse ROPA. In the end, only 4.1% of the couples underwent a ROPA treatment, but in 40% of these couples, both partners became pregnant, either by reciprocal, reverse ROPA, or using the embryos of one of them to get both pregnant.[98]

Another study that included all 129 couples treated in a fertility clinic in Spain in a 2-year period found that only one third had no condition potentially affecting fertility, including advanced age. Initially, most couples intended to undergo IUI or IVF, and the majority adhered to their plans. In contrast, 38% of couples initially considering the ROPA method changed their plans. Ultimately, 11% of couples opted for ROPA.[21]

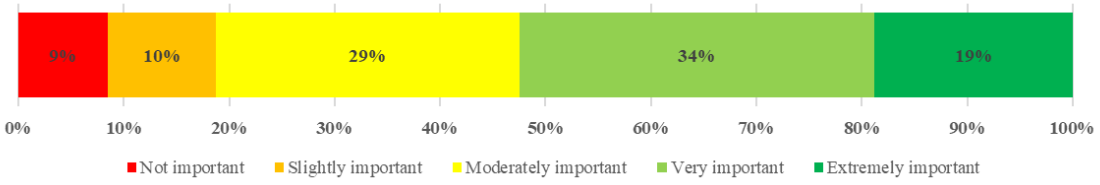
Studies report that the main reasons for female couples to quit treatments or not to pursue ART are the costs and the lack of insurance coverage.[98]

C. Importance of motherhood

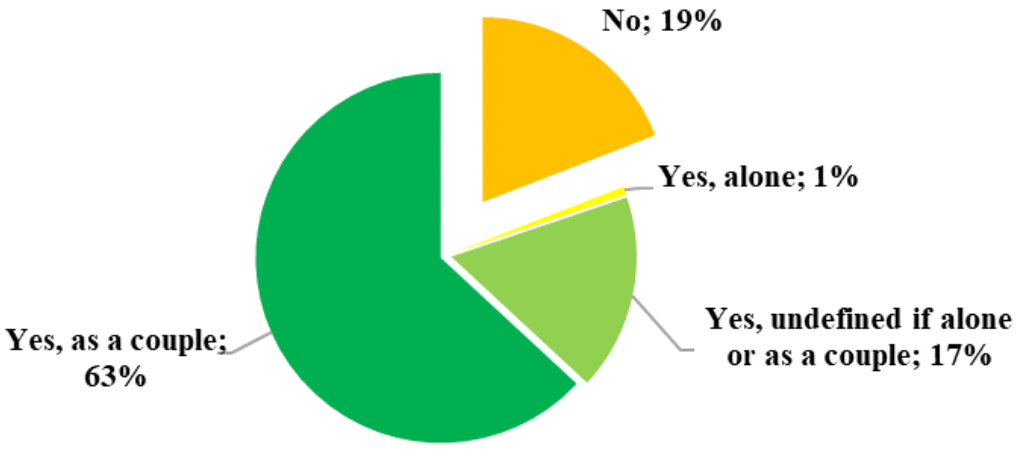
The right to conceive is generally accepted as a fundamental principle in most societies worldwide, if not all. However, the circumstances under which procreation can occur through means other than natural conception are not consistently defined, resulting in varying policies among countries.[57] The right to procreate may be considered both a positive and negative right. This means that states are responsible not only for providing individuals with the means to procreate, but also neither to impose compulsory sterilization nor to deny fertility treatments.[15,107]

The number of homosexual women who desire to become mothers has been rapidly increasing, as evidenced by the growing demand for reproductive treatments among same-sex couples in recent decades.[108–110] This trend has led to the coining of the term "homobaby-boom," which was first used in 2008 to describe this phenomenon.[111]

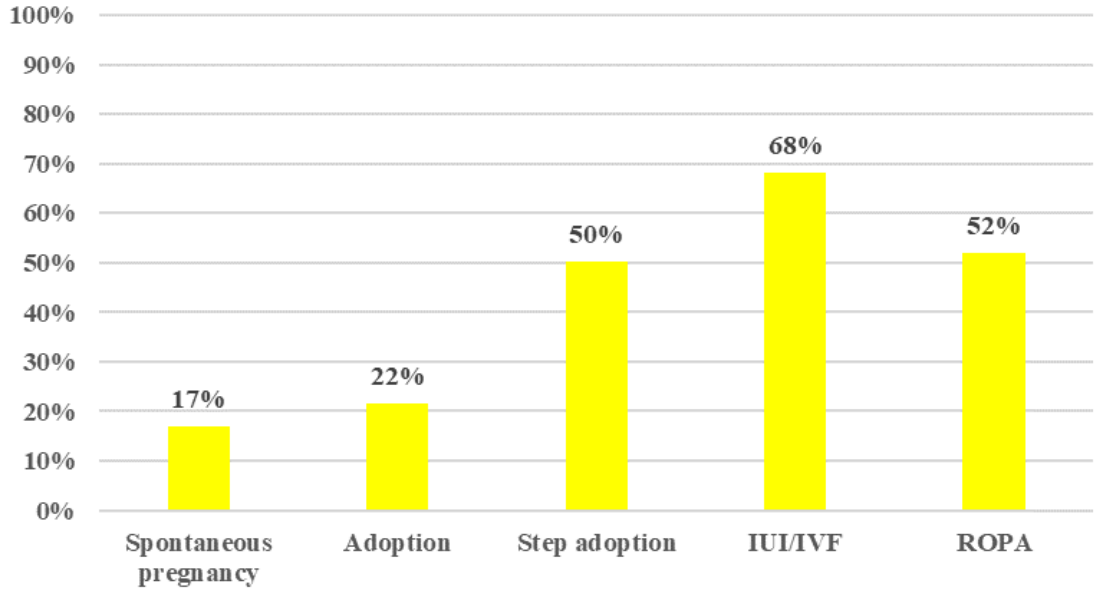
According to the international survey on female homosexuals, only 19% of the 549 women reported that motherhood was of little or no importance to them (Graph 5). Likewise, only 19% of the respondents stated that they did not intend to have children in the future, with the majority (63%) planning to do so as a couple (Graph 6). Among those who planned to have children, 68% intended to use IUI or IVF, and 52% planned to use the ROPA method. In addition, 50% of respondents indicated they would consider adopting the child of their partner, while 22% planned to pursue joint adoption of a new child. Interestingly, 17% of respondents reported that they would attempt spontaneous pregnancy with a friend or acquaintance (Graph 7).[82]



Graph 5: Importance of becoming a mother - Answers to the question “How important is it to you to be a mother?” on a survey on 549 homosexual women.[82]

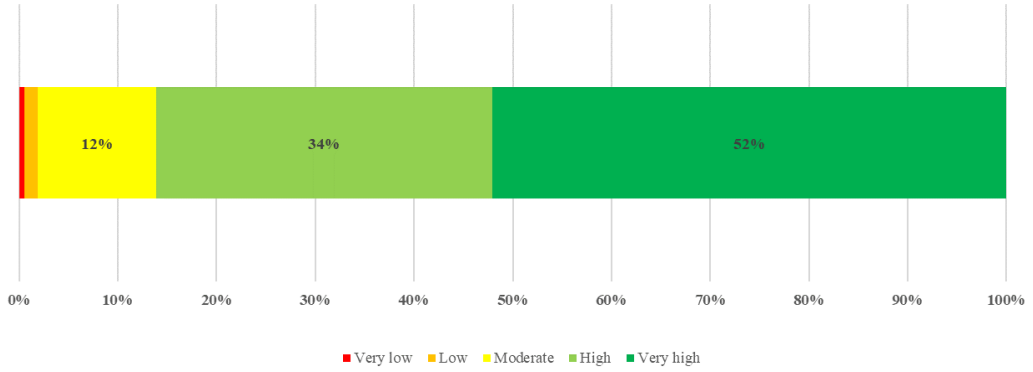


Graph 6: Intention to have children. Answer to the question "do you intend to have (more) children?" on a survey on 549 homosexual women[82]



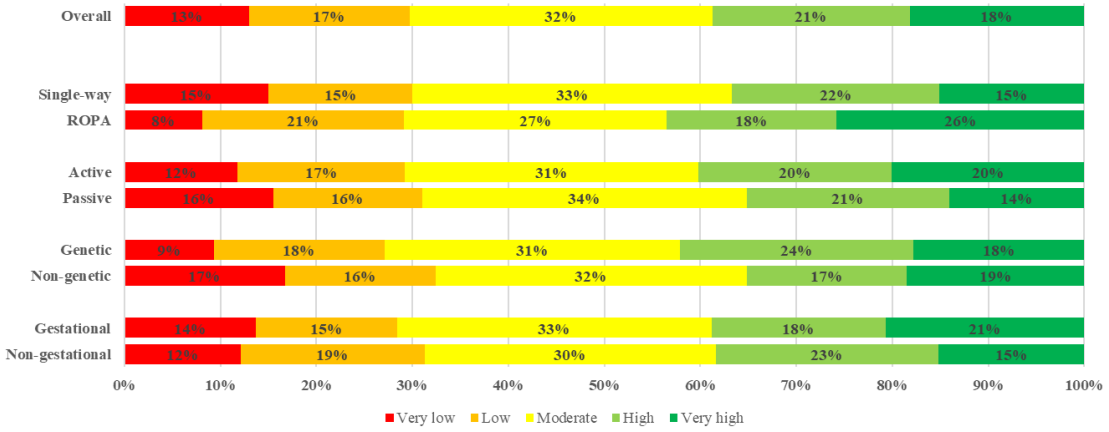
Graph 7: Plans for future procreation based on a survey on 549 homosexual women.[82]

According to the study on female couples under reproductive treatment, a significant majority of the patients expressed a strong or very strong desire to become a mother (Graph 8).[105]



Graph 8: Answers to the question - "How would you rate your wish to be a mother?" on a survey on 217 patients from 117 female couples under ART.[105]

When patients were asked about their desire to have more children in the future after finishing their current treatments, opinions diverged. Almost half of the patients expressed their willingness to undergo another treatment playing the same roles, while 36.6% indicated a preference to invert roles. Notably, there were no differences in the desire to have more children based on the type of treatment or the role they were playing (Graph 9).[105]



Graph 9 – Answers to the question - "How would you rate your wish to have more children after this treatment?" - on a survey on 217 patients from 117 female couples under ART – the overall results and the comparison between single-way and ROPA patients (p=0.19), active and passive patients (p=0.78), genetic and non-genetic mothers (p=0.42), and gestational and non-gestational mothers (p=0.66).[105]

D. Importance of genetics and pregnancy

There has been ongoing debate and controversy surrounding parenting by same-sex couples. However, the majority of research conducted to date suggests that these concerns are unfounded. Several studies have examined the well-being of children raised by same-sex parents, and have found no significant differences in the

psychological or social development of these children compared to those raised by heterosexual parents. When compared to heteronormative families, children raised by two mothers exhibit equal levels of self-esteem, academic performance, social interaction, behavioral, psychological, and cognitive development, mental health, sexual orientation, gender identification, and the quality of parent-child relationships.[34,112–114] Some authors report children of same-sex couples fare just as well as the children of opposite-sex couples across a wide range of well-being measures and note that there is no evidence to suggest that lesbian mothers or gay fathers are unfit to be parents or that psychosocial development among children of same-sex parents is compromised relative to that among offspring of heterosexual parents.[115–117]

In fact, the criteria for adoption are often stricter than those for assisted reproduction, so one may assume that couples who are able to adopt must also be able to have a child through ART.[4,118,119]

In most countries, motherhood is automatically attributed to the woman who gives birth.[36,120] However, ROPA introduces a new perspective on the biological dimension of motherhood as it distinguishes between the gestational and genetic dimension.[121–123] This presents a challenge when defining legal motherhood, as the birth mother is neither the genetic mother nor a mother resulting from a third-party donation process.[124] This can escalate into an even greater issue if the couple is not married, in the case of divorce, and the issue of child custody arises.[125,126] Furthermore, seeking reproductive treatments abroad may also pose difficulties when trying to register the child in the patient's home country.[36,127]

The impact of biological ties on mother-child bonding is not yet well understood.[128] Children naturally form bonds with various caregivers, but the type of connection they develop with their mother, father, or other caregivers can vary considerably. Some previous studies have reported that some individuals experience feelings of fear or concern about being neglected by a non-biological child.[129] Moreover, some authors argue that children often develop a primary attachment to one caregiver.[130]

The literature on the importance of gestational or genetic mother-child bonds is conflicting. Some studies suggesting that children may have different connections with their mothers depending on their biological ties, while others suggest a fairly balanced family situation.[128,129,131,132]

Regarding the impact on the couple, some authors argue that the intrinsic value of biological ties between parents and children is negligible, asserting that the

distribution of roles within a parental project should be independent of biological considerations.[121]

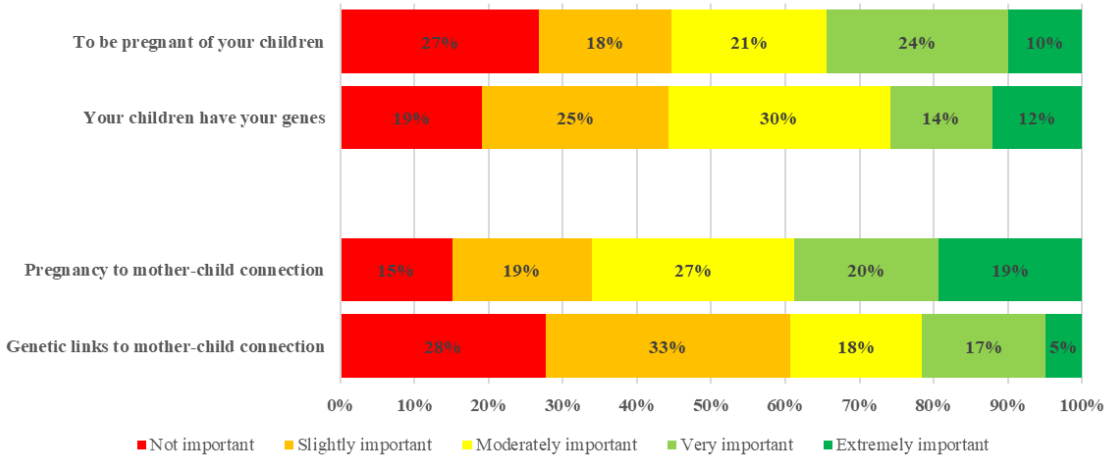
On the other hand, some studies show that the absence of biological connection does not go unnoticed by these couples, the unequal power dynamics derived from a genetic or gestational relationship may lead to inter partner jealousy.[129,132,133] Although female couples show more equity in childcare than heterosexual couples, birth mothers have a more marked role than their partners. Research suggests that children born after single-parented methods seek the biological mother when they are hungry and the other mother when they want to play.[129] Nevertheless, other studies have shown that female couples are capable of reconciling the various parenting roles and establishing a balanced relationship with their children.[113,134,135]

In general, women prefer to have an active and equal role in procreation and not be mere spectators. For some, it is a way to immortalize the union of two people.[106] Another interesting fact mentioned by some women is that if one partner has a fertility problem and does not participate in the process, she may experience mourning for her own fertility. Additionally, non-biological mothers may experience feelings of exclusion and jealousy.[129] ROPA allows both partners to share the challenges of reproductive treatments at physical, mental, and emotional levels, ensuring that neither is relegated to a passive role, promoting a more equitable distribution of the treatment's burdens (one of them will have to undergo ovarian stimulation and oocyte retrieval, while her partner will carry out pregnancy).[49,136] Some patients suggest that involving both partners in the treatment may alleviate the reliance on donor sperm contribution and lessen the dependence on IVF procedures and clinicians.[103] Nevertheless, some women believe this method may paradoxically be a setback in the process of accepting non-biological motherhood, particularly within the LGBTQIA+ community. This could ultimately have discriminatory consequences both for couples who have opted for single parented methods or adoption, as well as for male or trans couples, in which shared motherhood may not be possible.[49]

Some authors argue that the insistence on active and biological participation from both women in the procreation process may stem from an attempt to adhere to heteronormative ideals, thereby reinforcing subordinate parenting roles for women. Additionally, donor mothers frequently report experiencing a sense of assuming a “father” role.[80]

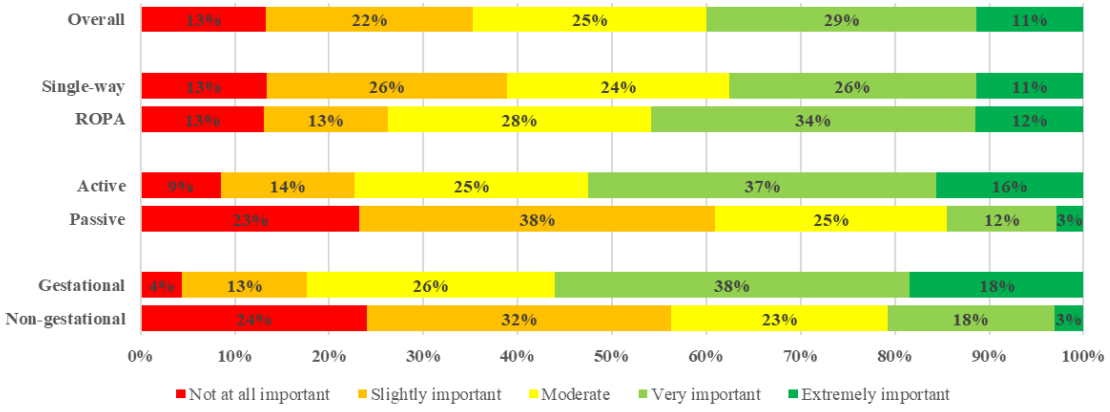
In theory, the possibility of sharing biological motherhood with ROPA could improve the mother-child bond, although studies on this subject are quite contradictory. Some women believe the biological links affirm the social bond and the "role of mother" – it is not a “child of mine”, a “child of her”, it is a “child of hers” and may facilitate the answer to the question "who is the mother?" – it will always be "both”.[49,110] Some studies indicate that ROPA may strengthen the relationship between partners, and some patients acknowledge choosing this treatment to fulfill their partners’ desire to experience “true shared motherhood”. [104] Additionally, from a societal standpoint, accepting a non-biological child may be more challenging due to its complexity and and somehow unnatural process.[80,137]

According to the international survey on 549 homosexual women, when assessing the importance of genetics and pregnancy to the participants themselves, 27% and 18%, respectively, indicated that pregnancy was either not important or only slightly important. In contrast, 24% and 10% considered it very or extremely important. Similarly, for genetics, 19% and 25% expressed that it was not or slightly important, while 14% and 12% deemed it very or extremely important, respectively. Therefore, no significant differences were observed in the importance assigned to pregnancy and genetics. On the other hand, when considering the expected impact of pregnancy and genetics on the future mother-child connection, there was a tendency to assign more importance to pregnancy, although this difference was small: 15% and 19% reported that pregnancy was not or slightly important, while 20% and 19% considered it very or extremely important, respectively. As for genetics, 28% to 33% assigned little or no importance, while only 17% and 5% considered it very or extremely important, respectively (Graph 10).[82]



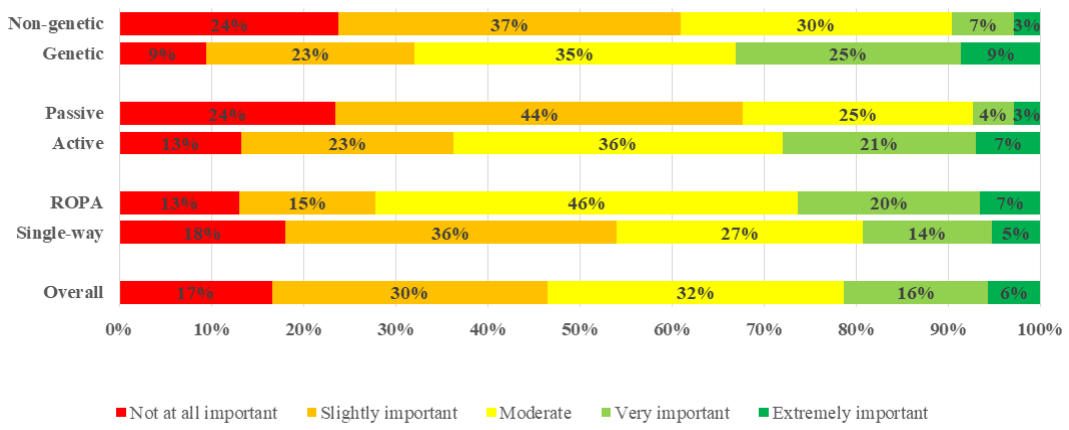
Graph 10: Importance of pregnancy, and genetics - Answers to the question "How important is it to you…?" on a survey on 549 homosexual women.[82]

Moreover, the study on the 217 patients under reproductive treatments evaluated differences on the importance given to pregnancy and genetics between patients doing ROPA or single-way reproductive treatments and patients with an active or passive role. Of the participants, 40% reported that pregnancy was very or extremely important, while 35% stated that it was only slightly important or not important at all. Mothers with an active role, especially gestational mothers, tend to ascribe more importance to pregnancy. However, no differences were observed between ROPA and non-ROPA patients (Graph 11).[105]



Graph 11: Answers to the question - "How important is it to you to be pregnant of your children?" on a survey on 217 patients from 117 female couples under ART – the overall results and the comparison between single-way and ROPA patients ($p=0.35$), active and passive patients ($p<0.01$) and gestational and non-gestational mothers ($p<0.01$).[105]

In contrast, fewer women considered genetics to be very or extremely important, with more reporting little or no importance, compared to pregnancy. Once again, women with an active role, in particular the genetic mothers, tended to attribute more importance to genetic links than patients with no active role (Graph 12).[105]



Graph 12: Answers to the question - "How important is it to you that your children have your genes?" on a survey on 217 patients from 117 female couples under ART – the overall results and the comparison between single-way and ROPA patients (p=0.1), active and passive patients (p<0.01), and genetic and non-genetic mothers (p<0.01) .[105]

Interestingly, despite these facts, most patients were confident that their offspring will have a similar bond with themselves and their partner, regardless of the role they played in the conception process. No differences were observed at this level between ROPA and non-ROPA patients, as well as patients with or without any active role (Graph 13).[105]

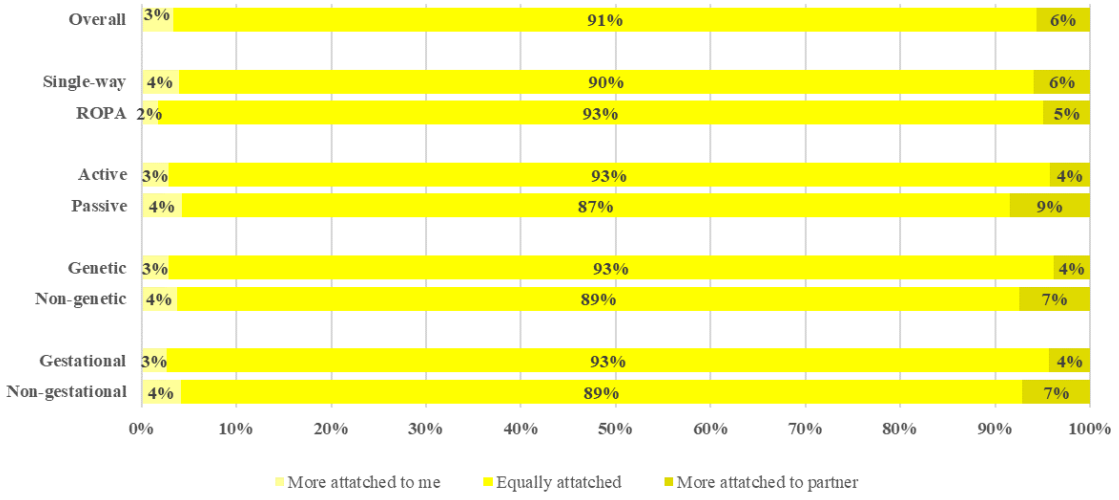


Figure 13: Answers to the question - "How attached do you think your child will likely be to you and your partner?" - on a survey on 217 patients from 117 female couples under ART – the overall results and the comparison between single-way and ROPA patients (p=0.67), active and passive patients (p=0.37), genetic and non-genetic mothers (p=0.47), and gestational and non-gestational mothers (p=0.54).[105]

V. OUTCOMES

As of November 2022, eight studies were published describing the outcomes of the ROPA method, including six case series and two cohort studies (Figure 1). An additional cohort and a case series were published in 2023. Tables 1 and 2 summarize the primary outcomes of each study.

	Positive pregnancy test rate	Clinical pregnancy rate	Miscarriage rate	Live birth rate
Marina *et al*[8]	-	46.0%	15.0%	30.8%
Bodri *et al*[9]	60.0%	52.0%	-	41.9%
Nuñez *et al*[138]	70.0% (IVF: 47.5%; p=0.004)	60.0% (IVF: 40.0%; p=0.011)	-	57.1% (IVF: 29.8%; p=0.001)
Brandão *et al*[139]	63.3% (IVF: 58.3% ; p=0.27)	57.0% (IVF: 50.2%; p=0.15)	17.2% (IVF: 16.9%; p>0.99)	46.1% (IVF: 40.9% ; p=0.14)
Matorras *et al*[28]	45.3%	-	13.4%	29.2%
Brandão *et al*[140]	61.0%	54.3%	16.2%	44.7%

Table 1: Rates per embryo transfer after the ROPA method according to the different studies.

	Positive pregnancy test rate	Clinical pregnancy rate	Miscarriage rate	Live birth rate
Royo *et al*[141]	58.0%	42.0%	15.0%	-
Yeshua *et al*[142]	69.4%	-	-	25.0%
Bodri *et al*[9]	-	-	-	60.0%
Nuñez *et al*[138]	81.7% (IVF: 64.2%; p=0.016)	71.7% (IVF: 55.8%; p=0.04)	-	66.1% (IVF: 43.4%: p=0.005)
Brandão *et al*[21]	-	-	-	79.0%
Brandão *et al*[139]	-	-	-	73.7%
Diego *et al*[143]	-	77% (IVF: 50%)	7% (IVF: 6%)	61% (IVF:42%)
Brandão *et al*[140]	-			48.6%

Table 2: Rates per ROPA cycle according to the different studies.

A. Case Series – Marina *et al* – 2010 (Spain)

The first case series, published in 2010, covered 14 cycles involving 14 couples. Donor patients had an average age of 35.1 years, while recipients averaged 34.6 years. Per cycle, an average of 9.4 mature oocytes (MII) and 5 embryos were obtained. Approximately 35% of couples had surplus embryos, with one couple having no viable embryos. Notably, the authors exclusively reported outcomes related to fresh embryo transfers.

The clinical pregnancy rate (CPR) was reported at 46%. The study documented one live newborn and three ongoing pregnancies during the study period, revealing a miscarriage rate (MR) of 15% and a potential live birth rate (LBR) of 30.8% (Table 1). Most cases involved a double embryo transfer (DET), resulting in one twin pregnancy (7.7%).[8]

B. Case series – Baviera-Royo *et al* – 2014 (Spain)

In 2014, another Spanish research group published a case series of female couples undergoing ART. The study included 8 cycles of ROPA, which resulted in a positive pregnancy test rate of 58%, a CPR of 42%, and a MR of 15% per cycle, which they considered similar to those of conventional IVF (Table 2).[141]

C. Case series – Yeshua *et al* – 2015 (USA)

In 2015, a study was published describing a series of 20 couples and 36 ROPA cycles. The mean age of the donor patients was 35.7 years, and the mean age of the recipients was 38.1 years. The study reported a positive pregnancy test rate of 69.4% per cycle and 66.7% per couple (including all cycles). Ultimately, the LBR was 25% per cycle and 42.9% per couple (Table 2).[142]

D. Case series – Bodri *et al* – 2018 (UK)

In 2018, another case series was published including 141 ROPA cycles performed by 121 couples. The study found statistically significant differences between donors and recipients regarding their basal characteristics. Specifically, recipients had a higher number of previous births and previous ART treatments, while donors had better ovarian reserve. However, no differences were found between the groups regarding age or BMI. Additionally, 40% of the cycles were performed for medical reasons such as failed previous inseminations, advanced maternal age, or low ovarian reserve.

The LBR per transfer was 41.9% per transfer and 60% per cycle (Tables 1 and 2). The prematurity rate was 17.7%, which was mainly attributed to multiple pregnancies (14%), and the cesarean section rate was 47.2%. Most of the cycles (88%) involved a synchronous fresh embryo transfer. No significant differences were found in outcomes between this group and the freeze-all group.[9]

E. Cohort – Núñez *et al* – 2021 (Spain)

The first comparative study was a retrospective cohort comparing 60 ROPA cycles with 120 cycles of IVF. While no significant differences were found in the age of ROPA donors, recipients, and women undergoing single parented IVF (around 34 years old), the partners of the latter group were significantly older, with a mean age of 36.5 years (p=0.001). ROPA donors had a significantly higher antral follicle count (AFC) than IVF patients (17.4 vs. 14.6, p=0.045), and a significantly higher number of mature oocytes were retrieved in ROPA cycles compared to IVF cycles (9.4 vs. 7.8, p=0.019). There were no significant differences in the fertilization rate or the mean number of embryos obtained. The majority of embryo transfers in both groups were DET (81.7%) and in cleavage stage (87.2%). All clinical outcome rates analyzed, including positive pregnancy test, CPR, and LBR, were significantly better in the ROPA group (Table 1). The LBR per ROPA cycle was 66%, compared to 43.4% for IVF (p=0.005) (Table 2). These differences remained significant after multivariate analysis considering age, BMI, and number of MII.[138]

F. Case series – Brandão *et al* – 2022 (Spain)

STUDY 6
The Pathway of Female Couples in a Fertility Clinic.
Brandão P, Ceschin N, Gómez VH.
Revista Brasileira de Ginecologia e Obstetrícia 2022;44:660–666.

A retrospective study was conducted to describe the journey of all female couples having their first appointment at an IVF clinic in Spain over a two-year period. The patients' mean age at the start of the first treatment was 36.6 years, with a body mass index (BMI) of 23.7, an anti-Mullerian hormone (AMH) value of 19.1 pmol/L, and an AFC of 13.4. Active patients (in the case of single-parented methods) and recipient patients (in the case of ROPA) tended to be younger and had a higher ovarian reserve. Most patients (92%) had no previous children (Table 3).[21]

	Total	Single-parented methods (n= 107 couples)			Double-parented method (ROPA) (n=22 couples)		
		Patient	Partner	p	Recipient	Donor	p
Mean age (years)	36.6	35.1	36.4	**0.03**	34.6	32.2	0.15
Women with advanced age (percentage)	25%	18.5%	37.1%	**0.003**	19%	0%	**0.04**
Women without previous children (Percentage)	91.9%	92.5%	95.2%	0.54	96%	96%	>0.99
BMI	23.7	23.3	23.3	0.9	23.4	23.1	0.79
AFC	13.4	12.9	11.8	0.7	9.9	19.7	**0.03**
AMH (pmol/L)	19.1	23.4	13.4	**0.02**	17.7	23.2	0.59

Table 3: Baseline features according to type of first reproductive treatment performed in a study including all female couples in a fertility clinic in a two-year period.[21]

Upon completing the medical workup, it was revealed that 46.1% of the couples had at least one member affected by one or more fertility impairing conditions. When considering advanced age (defined as 40 years or older), this figure increased to 68% of patients. Among these individuals, 28.9% received at least one diagnosis during the medical workup by the fertility specialist. In the end, only 32% of all couples had no known conditions potentially affecting fertility or advanced age. Notably, endometriosis was the predominant condition among previously known diagnoses (found in 5% of patients). Conversely, low ovarian reserve (5.5% of patients) and uterine disorders (4.7% of patients) were the most frequent *de novo* diagnoses discovered during the medical workup. These findings are intriguing. Although female couples are typically regarded as fertile, just under one-third of the couples were found to have no conditions impairing fertility or advanced age, and almost half of the couples had at least one member affected by an organic fertility disorder.[21]

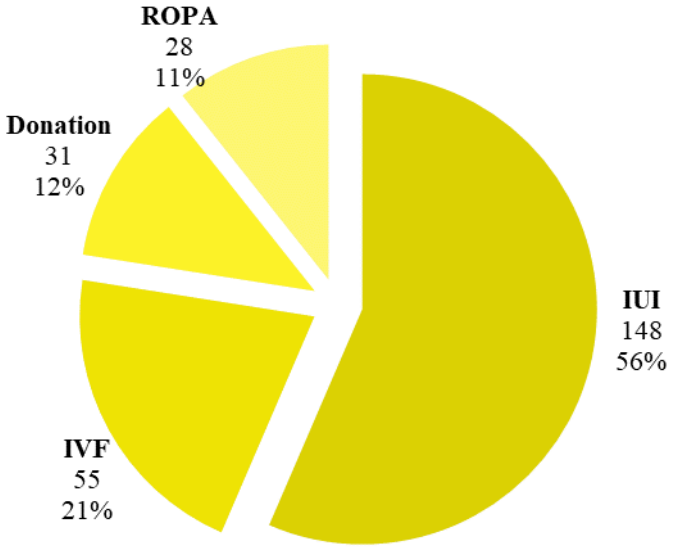
Before receiving medical counseling, a notable proportion of couples expressed their intentions regarding fertility treatments, with 41% considering IUI, 26.4% opting for ROPA, 17% leaning towards IVF with their own oocytes, and 9.4% considering donated oocytes/embryos. Intriguingly, 6.2% of patients had no predefined treatment

preference. Following the medical workup and counseling, a majority of couples intending to undergo IUI or IVF ultimately received their initially desired treatment (only 11.3% and 9%, respectively, ended up with an alternative treatment as their first choice). Conversely, a significantly higher percentage of couples (38.2%, p=0.005) who initially planned on ROPA as their primary treatment ended up pursuing a single-parent method, with 20.6% opting for IVF and 17.6% choosing IUI (Table 4). Interestingly, the percentage of couples changing their treatment preferences was similar between groups that did and did not receive a *de novo* diagnosis of a fertility issue during the medical workup (27% and 23%, respectively, p=0.39).[21]

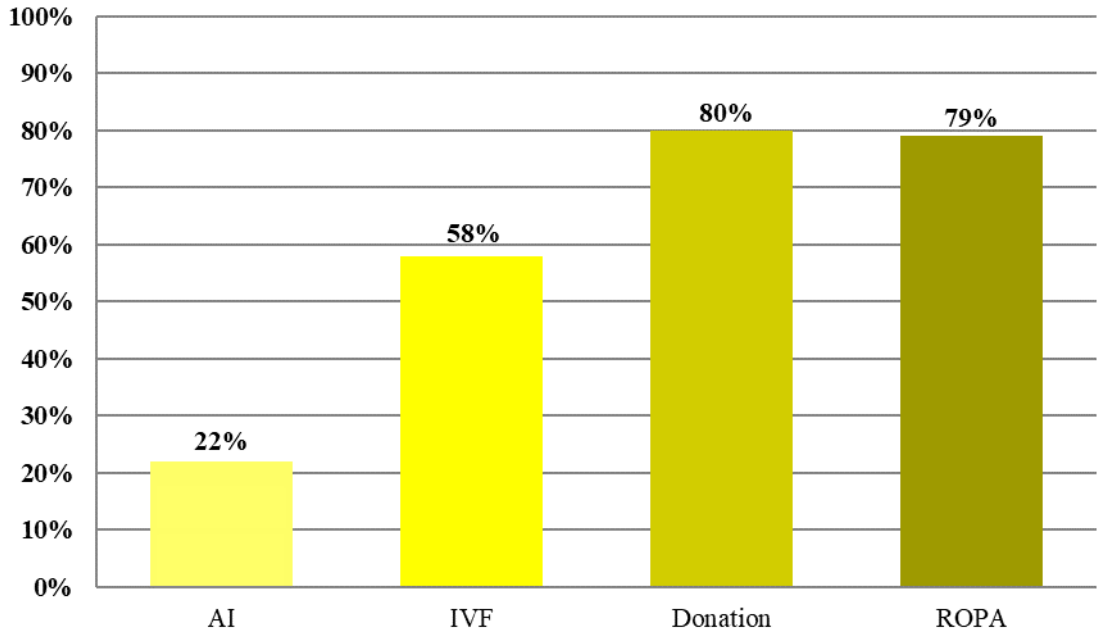
		FIRST TREATMENT PERFORMED			
		IUI (59)	**IVF (36)**	**Donation (12)**	**ROPA (22)**
PRETENDED TREATMENT BEFORE MEDICAL WORKUP	**Unknown (8)**	4 (50%)	4 (50%)	-	-
	IUI (47)	41(88,7%)	6 (11,3%)	-	-
	IVF (22)	1 (4,5%)	20 (91%)	-	1 (4,5%)
	Donation (12)	-	-	12 (100%)	-
	ROPA (34)	7 (20,6%)	6 (17,6)	-	21 (61,8%)

Table 4: First reproductive treatments performed according to patients' previous intentions before medical workup in a study including all female couples in a fertility clinic in a two-year period.[21]
(n and percentage within pretended treatment group) (Grey: went on with the pretended treatment)

Considering all the 262 treatments carried out during the study period, 56% were IUI, 21% were IVF, 12% were oocyte donation, and 11% were ROPA. The LBR per treatment (including frozen embryo transfers) was 80% for treatments with donated oocytes/embryos, 79% for ROPA, 58% for IVF with their own oocytes, and 22% for IUI (Graphs 14 and 15). However, it's crucial to acknowledge the limitations of this study, including its small sample size, retrospective and descriptive nature, and reliance on data from a single private clinic.[21]



Graph 14 – Total number of ART performed, in a study including all female couples in a fertility clinic in a two-year period.[21]



Graph 15 – Live birth rate per treatment, in a study including all female couples in a fertility clinic in a two-year period.[21]

The LBR per ROPA cycle (including frozen embryo transfers) was 79%, with one successful twin gestation. The majority of couples (86.4%) achieved a live birth after one or two embryo transfers, with only a small minority requiring three (4.5%) or four (9.1%) transfers. In half of the cycles, patients had surplus frozen embryos, with a mean of 2.8 surplus embryos per cycle (Table 5). The LBR per treatment was higher

compared to single-way IVF (79% versus 58%), and almost the same as oocyte donation (79% versus 80%) (Graph 10). The authors hypothesize this could be explained by the fact that ROPA offers the possibility of choosing the best of each side. However, it is important to note that the study was based on only 25 ROPA cycles.[21]

Number of couples		25
Number of cycles		28 (22 as first reproductive treatment, 3 following other type of ART, 3 as second ROPA in same couple)
Outcomes		
	Number of live newborns	23
	Live births (rate per cycle)	22 (79%)
	Twin pregnancies	1 (4.5%)
Number of embryo transfers needed to achieve a LB		
	1	10 (45.5%)
	2	9 (40.9%)
	3	1 (4.5%)
	4	2 (9.1)
Surplus embryos		
	Number of couples with surplus embryos (percentage)	12 (48%)
	Number of surplus embryos per couple (mean)	2.8
Couples who repeated ROPA		3
	Case 1	Same-way ROPA for a second child (successful)
	Case 2	Same-way ROPA after an unsuccessful first cycle, last embryo transferred to the donor mother (single parented) due to recurrent implantation failure (successful)
	Case 3	Reverse ROPA for a second child (successful)

Table 5: Main outcomes of the ROPA method in a study including all female couples in a fertility clinic in a two-year period.[21]

G. Case series – Diego *et al* – 2022 (USA)

Another study from 2022 reported on 31 cycles of ROPA, with a CPR per cycle of 77%, a live birth rate LBR of 61%, and a MR of 7% (Table 2). All these rates were higher compared to one-way IVF, but the authors did not conduct a statistical comparison.[143]

H. Cohort – Brandão *et al* – 2022 (Spain)

STUDY 7

Similar reproductive outcomes between lesbian-shared IVF (ROPA) and IVF with autologous oocytes.

Brandão P, Ceschin N, Cruz F, Sousa-Santos R, Reis-Soares S, Bellver J.
Journal of Assisted Reproduction and Genetics 2022;39:2061–2067.

Lesbian Shared IVF (ROPA) and IVF with donated semen – changing the recipient has no impact on reproductive outcomes

Brandão P, Ceschin N, Cruz F, Sousa-Santos R, Reis-Soares S, Bellver J.
Poster presented at the 38th Congress of the European Society of Reproductive Medicine 2022.

A cohort study compared young patients without fertility disorders undergoing single-way IVF and ROPA. It included 99 ROPA cycles (73 couples) and 2929 IVF cycles with autologous oocytes (2334 patients). Only patients aged 37 or younger and without any known infertility factors were included. There were no significant differences in age, BMI, or AFC between the ROPA donors and recipients. However, when comparing the ROPA and non-ROPA groups, the mean age of the patients in the non-ROPA group was 2.5 years higher (Tables 6 and 7).[139]

	ROPA recipient mean (SD)	ROPA donor mean (SD)	p
Age	32.6 (3.4)	32.7 (3.1)	>0.99
Body mass index	24.0 (3.9)	24.4 (5.5)	0.72
Antral follicle count	13.7 (7)	15.5 (12.2)	0.67

Table 6: Comparison of patients' main basal features within the ROPA group (recipients versus donor) in retrospective cohort study including 99 ROPA cycles (73 couples) and 2929 IVF cycles with autologous oocytes (2334 patients).[139]

	ROPA	Non-ROPA	p
Age (recipient)	32.6 (3.4)	35.14 (2.8)	**<0.01**
Age (donor)	32.7 (3.1)		**<0.01**
BMI (recipient)	24.0 (3.9)	23.8 (4.2)	0.22
BMI (donor)	24.4 (5.5)		0.47
Stimulation and PGT-a			
FSH total dosage	1675 (778)	1709 (677)	0.74
Estradiol levels on day of triggering	2177 (1760)	1750 (1375)	0.11
PGT-a	6.4%	6.9%	>0.99

Table 7: Comparison of patients' basal characteristics and cycle details between the ROPA and the non-ROPA groups in retrospective cohort study including 99 ROPA cycles (73 couples) and 2929 IVF cycles with autologous oocytes (2334 patients).[139]

The ROPA group obtained more mature oocytes (10.1 vs. 7.7; $p < 0.01$) and good quality embryos, according to the Spanish ASEBIR classification [144–146] (embryos grade A: 0.59 vs. 0.44; $p = 0.03$; embryos grade B: 1.47 vs. 0.81; $p < 0.01$) (Table 8).[139]

	ROPA	Non-ROPA	p
Oocytes and Embryos - mean (SD)			
Number of oocytes retrieved	12.4 (7.9)	10.3 (7.0)	**<0.01**
Number of mature oocytes obtained	10.1 (6.4)	7.7 (5.6)	**<0.01**
Number of embryos classified as A	0.59 (1.2)	0.44 (1.1)	**0.03**
Number of embryos classified as B	1.47 (2.3)	0.81 (1.5)	**<0.01**
Number of viable embryos	2.84 (3.8)	1.76 (2.6)	**0.02**

Table 8: Comparison of features related to oocytes and embryos between the ROPA and the non-ROPA groups in retrospective cohort study including 99 ROPA cycles (73 couples) and 2929 IVF cycles with autologous oocytes (2334 patients).[139]

There was no significant difference in positive pregnancy test rates (63.3% vs. 58.3%; $p = 0.27$), clinical pregnancy rates (57% vs. 50.2%; $p = 0.15$), miscarriage rates (17.2% vs. 16.9%; $p > 0.99$), ectopic pregnancy rates (0% vs. 0.5%; $p > 0.99$), and live birth rates (46.1% vs. 40.9%; $p = 0.14$). Additionally, there were no significant differences in gestational age at delivery (39.1 weeks vs. 38.7 weeks; $p = 0.17$), preterm birth rates (7.9% vs. 12.1%; $p = 0.61$), and newborn weight (2809g vs. 3072g; $p = 0.17$) between the two groups (Table 9).[139]

	ROPA	Non-ROPA	p
Positive pregnancy test rate	63.3%	58.3%	0.27
Clinical pregnancy rate	57.0%	50.2%	0.15
Miscarriage rate	17.2%	16.9%	>0.99
Ectopic pregnancy rate	0%	0.5%	>0.99
Live birth rate	46.1%	40.9%	0.14
Gestational age at delivery	39.1 weeks	38.7 weeks	0.26
Preterm birth rate	7.9%	12.1%	0.61
Weight of the newborn	2809g	3072g	0.17

Table 9: Comparison of the main reproductive outcomes between ROPA and non-ROPA (rates are per transfer). in retrospective cohort study including 99 ROPA cycles (73 couples) and 2929 IVF cycles with autologous oocytes (2334 patients).[139]

Whether the analysis was conducted by considering only frozen embryo transfers, first embryo transfers, or all embryo transfers, no significant differences were observed (Table 10). [139]

	ROPA	Non-ROPA	p
Fresh embryo transfer			
Positive pregnancy test rate	56.9%	58.8%	0.80
Clinical pregnancy rate	47.7%	50.2%	0.71
Miscarriage rate	16.9%	16.9%	>0.99
Ectopic pregnancy rate	0%	0.6%	>0.99
Live birth rate	40.0%	41.3%	0.47
Gestational age at delivery	38.1 weeks	38.9 weeks	0.56
Preterm birth rate	17.6%	11.4%	0.44
Weight of the newborn	2568g	2980g	0.10
Frozen embryo transfer			
Positive pregnancy test rate	69.8%	59.5%	0.12
Clinical pregnancy rate	66.7%	51.4%	**0.02**
Miscarriage rate	17.4%	18.3%	>0.99
Ectopic pregnancy rate	0%	0.3%	>0.99
Live birth rate	52.4%	41.3%	0.05
Gestational age at delivery	39.2 weeks	39.1 weeks	0.39
Preterm birth rate	0%	12.3%	0.15
Weight of the newborn	3098g	3169g	0.81

Table 10: Comparison of the main reproductive outcomes between ROPA and non-ROPA IVF in fresh and frozen embryo transfers (rates are per transfer) in retrospective cohort study including 99 ROPA cycles (73 couples) and 2929 IVF cycles with autologous oocytes (2334 patients).[139]

In the end, the cumulative live birth rate per cycle was 73.7% and 78.3% of couples achieved at least one live birth across all their ROPA cycles (Table 11). The odds ratio for a live birth between ROPA and non-ROPA IVF was 1.19, but this was not statistically significant (p = 0.55) (Table 12).

The study revealed that there was no impact on live birth rates when there was no genetic link between the embryo and the recipient. This was shown by comparing ROPA to single-way IVF with autologous oocytes and donated sperm in patients with good prognosis. Therefore, the study not only demonstrated similar live birth rates between ROPA and single-way IVF, but also showed that the absence of genetic ties has no impact on reproductive outcomes.

	Live Birth Rate
Per embryo transfer	46.1 %
Per ROPA cycle (including all transfers)	73.7%
Per couple (including all ROPA cycles)	78.3%

Table 11: Live birth rate of ROPA per embryo transfer, per cycle and per couple in retrospective cohort study including 99 ROPA cycles (73 couples) and 2929 IVF cycles with autologous oocytes (2334 patients).[139]

	Odds Ratio (ROPA vs. IVF with autologous oocytes)	p
Positive pregnancy test rate	1.24	0.47
Clinical pregnancy rate	1.18	0.55
Miscarriage rate	1.78	0.46
Live birth rate	1.19	0.55

Table 12: Odds ratio of main clinical outcomes between ROPA and IVF with autologous oocytes (after multivariate analysis excluding age and BMI of both donors and recipients) in retrospective cohort study including 99 ROPA cycles (73 couples) and 2929 IVF cycles with autologous oocytes (2334 patients).[139]

I. Cohort – Matorras *et al* – 2023 (Spain)

In 2023, a retrospective cohort study was published comparing the perinatal outcomes of 660 ROPA cycles to 4349 IUI in female couples.[28]

As expected, they found higher positive pregnancy test rates in the ROPA group compared to IUI (artificial insemination with donor sperm), 45.3% versus 21.8%, respectively ($p<0.001$).[28]

This was the first study to primarily focus on the obstetric and perinatal outcomes of the technique. As previously mentioned, it is well-established that pregnancies resulting from oocyte donation are linked with a higher incidence of obstetric complications, including preeclampsia, low birth weight, preterm birth, and cesarean section.[147–149] Some hypothesize that these complications are likely caused by inadequate immunological recognition resulting from the use of a genetically unrelated embryo, which can lead to deficient placentation.[150–152] Whether pregnancies resulting from donated semen are similarly associated with an increased risk of preeclampsia remains uncertain, given the absence of prior maternal exposure and recognition.[153,154] Moreover, carrying a genetically unrelated embryo can result in immunological maladaptation, which can adversely affect reproductive outcomes such as lower pregnancy rates and a higher risk of miscarriage.

In this study, no significant differences were found between ROPA and IUI in terms of gestational age (278 days (268-285) versus 279 (272-284), $p=0.24$), preterm rates (8.3% versus 7.3%, $p=0.80$), preterm births occurring before 28 weeks (0.6% versus 0.4%, $p>0.99$), newborn weight (3195 g (2915-3620) versus 3270 g (2980-3600), $p=0.296$), low birth weight rates (6.4% versus 6.4%, $p>0.99$) or extremely low birth weight rates (0.6% versus 0.5%, $p>0.99$). Rates of cesarean section, newborn malformations, and perinatal mortality were also similar between ROPA and IUI. However, there was a non-significant trend in hypertensive disorders towards an

increase in pre-eclampsia/hypertension among ROPA patients (recipient's age-adjusted Odds ratio (OR) =1.9, 95% CI=0.7-5.2). Overall, the authors acknowledge perinatal data as consistent with what is reported in the general population. In twin pregnancies, the perinatal parameters showed no significant differences between ROPA and IUI, except for a higher incidence of hypertensive disorders in the ROPA group. (recipient's age-adjusted OR = 21.7, 95% CI = 2.8-289.4, p=0.01).[28]

J. Case series – Brandão *et al* – 2023 (Spain)

STUDY 8

Shared in vitro fertilization among female couples: clinical outcomes of the Reception of Oocytes from the Partner (ROPA) method.

Brandão P, Monseur B, Melo P, Ceschin N, Cruz F, Sousa-Santos R, Reis-Soares S, Bellver J.

Reproductive Biomedicine Online; *in press.*

Another case series on ROPA included all cases of this treatment in a group of clinics in Spain over a 10-year period, involving 356 ROPA cycles (281 couples) and 580 embryo transfers..[132] Of these couples, 232 (82.5%) underwent only one ROPA cycle, while 36 (6.2%) had 2 cycles, 8 (2.8%) had 3 cycles, 4 (1.4%) had 4 cycles, and 1 (0.4%) underwent 7 cycles. Among the couples having 2 cycles, 5 (13.9%) had a reverse ROPA (opposite roles between cycles). The mean age of the patients was 34.8 years (+/- 4.6), with a BMI of 24.2 kg/m2 (+/- 4.6) and AMH of 2.5 ng/mL (+/- 1.9). Donors were 2.5 years younger than recipients (33.5 vs. 36.0 years old), but no differences were found regarding BMI or AMH (Table 13).[140]

	Overall	Recipient	Donor	p
Age (years, mean and SD)	34.8 (+/- 4.6)	36.0 (+/- 4.9)	33.5 (+/- 4.4)	<0.01
Advanced age (defined as ≥ 38 years old)	30.0%	41.4%	18.7%	<0.01
BMI (Kg/m2, mean and SD)	24.2 (+/-4.6)	24.1 (+/-4.4)	24.2 (+/-4.7)	0.8
Anti-müllerian hormone (ng/mL, mean and SD)	2.5 (+/-1.9)	2.4 (+/- 2.2)	2.7 (+/- 1.6)	0.5
Previous IUI	9.1%	15.3%	2.9%	0.3
Previous IVF	40.1%	60.7%	19.5%	<0.01
Previous pregnancy	3.8%	5.0%	2.5%	0.7

Table 13: description of baseline patients' characteristics and comparison between donors and recipients in a case series including 356 ROPA cycles.[140]

The study found that poor ovarian reserve was the leading fertility disorder, with 6.8% of the couples diagnosed with this condition. Endometriosis was the second most common disorder at 2.9%, followed by polycystic ovary syndrome (PCOS) at 2.2%, genetic alterations at 1.1%, and tubal dysfunction at 0.7%. Almost half of the couples (48.6%) had at least one partner who was 38 years or older. Overall, 53.6% of the couples had a known condition that could potentially affect their fertility.[140]

The study also found that the mean number of oocytes obtained per cycle was 12.0, with a mean maturity rate of 83.3%, resulting in a mean of 10.0 mature oocytes. The average number of zygotes (2 *pronuclei* - PN) was 7.9, which represents a mean fecundation rate of 74.5%. The mean number of embryos obtained per cycle was 3.2 (+/-1.5), with the majority of the embryos being blastocysts (97.2%). According to the ASEBIR classification, 15.6% of the embryos were graded as A, 43.8% as B, 25% as C, and 21.9% as D (Table 14).[140]

	Mean	SD
Oocytes (total)	12.0	6.6
Mature oocytes	10.0	5.7
Zygotes (2 PN)	7.9	4.9
Fecundation rate	74.5%	18.8
Embryos grade		
A	0.5	1.1
B	1.3	2.0
C	0.8	1.3
D	0.7	1.6

Table 14: description of the laboratory outcomes in a case series including 356 ROPA cycles.[140]

In 50.4% of cycles, surplus embryos were present, with a mean of 4.3 (+/-1.8) embryos cryopreserved per cycle. Of the embryo transfers, 61% resulted in a positive pregnancy test, with a clinical pregnancy rate of 54.3%. The miscarriage rate was 16.2%, with one ectopic pregnancy (0.2%) and two fetal demises (0.5%). The twin pregnancy rate was 5.4%, while the live birth rate per embryo transfer was 44.7%. The mean gestational age at delivery was 38 weeks and 6 days, with 11.6% of preterm deliveries. Vaginal deliveries accounted for 66.4% of deliveries, while the cesarean section rate was 33.6%. The newborns had a mean weight of 2925g (+/- 612.8), mean length of 49.8 (+/- 2.5) cm, and mean head diameter of 34.5 cm (+/- 1.4). Five percent of newborns had an APGAR score of 8 at 1 minute after birth, while the remaining newborns had a score of 9 or 10 at 1, 5, and 10 minutes after birth (Table 15).[140]

	Number	Rate (per embryo transfer)
Positive pregnancy test	354	61.0%
Clinical pregnancy	315	54.3%
Miscarriage	57	16.2%
Ectopic pregnancy	1	0.2%
Fetal dismiss	2	0.5%
Multiple pregnancy	19	5.4%
Live birth	259	44.7%
Preterm delivery	30	11.6%
Vaginal delivery	173	66.3%
Cesarean section	88	33.7%
	Mean	SD
Gestational age at delivery	38 weeks and 6 days	-
Newborn’s weight	2925.0g	612.8
Newborn’s length	49.8 cm	2.5
Newborn’s cephalic diameter	34.5 cm	1.4

Table 15: description of the clinical outcomes of ROPA in a case series including 356 cycles.[140]

The LBR per ROPA cycle was 48.6%, with 4.2% of cycles resulting in the birth of 2 singletons. Overall, 61.6% of the couples achieved at least one live birth, and 6.2% of couples had 2 singletons as a result of their ROPA treatments (Table 16).[140]

	Live Birth Rate
Per embryo transfer	44.7 %
Per ROPA cycle (including all transfers)	48.6%
Per couple (including all ROPA cycles)	61.6%

Table 16: Live birth rate of ROPA per embryo transfer, per cycle and per couple in a case series including 356 cycles.[140]

VI. CONCLUSION

In recent years, there has been an increase in the number of female couples who wish to procreate. This trend is reflected in the growing number of ART available for same-sex couples.

Homosexual women generally seem to be well-informed about assisted reproductive technology treatments. Most homosexual women consider it important to become a mother and plan to do so as a couple, mainly through assisted reproduction or step adoption of their partner's child. While a large proportion of couples may present a fertility disorder and may want or need to change their plans after medical counseling, female couples are considered to have good reproductive prognosis.

Female couples tend to report little difficulty in choosing their reproductive treatment or determining roles to play. Most couples end up opting for a single-parented method, despite the growing availability of the ROPA method. This choice is driven mainly by factors such as speed, success rate, simplicity, and cost of the treatment. In contrast, most couples opting for ROPA do so to share biological motherhood.

The importance given to gestation or genetic mother-child relationships varies greatly between women, with gestation being slightly more important. The importance attributed to pregnancy and genetics is higher in patients with an active role, particularly for gestational and genetic mothers, respectively. Nevertheless, most mothers believe that the bond with their children will be similar for both.

The ROPA method is an alternative to conventional ART for female couples in which one partner provides the oocytes (genetic mother) and the other receives the embryos and eventually gestates (gestational mother). This method allows women to share biological motherhood. However, like any ART, the ROPA method brings important ethical issues that are far from being universally accepted. This treatment is legal in 13 European countries.

Regarding the outcomes of this technique, the rates per embryo transfer of positive pregnancy tests, clinical pregnancies, and miscarriages were found to be between 61% and 63.3%, 54.3% and 57%, and 16.2% and 17.2%, respectively. The live birth rate per transfer was between 44.7% and 46.1%. The live birth rate per ROPA cycle varied between 48.6% and 79%. Moreover, 61.6% to 78.3% of couples who underwent ROPA were able to have at least one live newborn. Notably, no significant differences in outcomes were observed when compared to single-way IVF.

In conclusion, the ROPA method provides a viable alternative for female couples willing to share biological motherhood, with outcomes that are reassuring and comparable to single-way IVF.

VII. REFERENCES

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This thesis represents the outcome of years of study and immersion in a field that awakened an enormous passion within me. Throughout this journey, I delved into complex and current issues, seeking to deeply understand the theoretical and practical foundations of this topic.

I believe this thesis reinforces messages with significant social consequences and can help our society progress towards a better world.

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