

Altruistic Donation of Surplus Embryos to Known and Unknown Recipients, The Dutch Approach

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Abstract

Background: Previous studies have shown that embryo donation can be a successful treatment for infertile couples, however the willingness of Dutch couples to donate or accept embryos was unknown. The aim of this article is to describe the protocol and results for altruistic embryo donation of the only embryo bank in the Netherlands.

Materials and Methods: This is a descriptive study. Since 2011, donated cryo-embryos from couples that have undergone *in vitro*-fertilization/intracytoplasmic sperm injection (IVF/ICSI) treatments, are being stored in our embryo bank. The majority of the donated embryos were frozen on day 3 or 4 by slow freezing techniques. We perform a thorough medical and psychological screening of donor couples and recipients, according to the protocol drawn up in close collaboration with the Dutch Ministry of Health.

Results: Up to June 2021, 54 women have received embryos from our embryo bank, all single embryo transfers. While the clinical pregnancy rate in ‘unknown’ embryo donations was relatively high (25.3%), the live birth rate shows limited success (12.6%), partly due to high pregnancy loss through miscarriage. In known donation procedures, the recipients tend to undergo more procedures, depending on the number of donated cryo-embryos. Twenty-eight women received embryos from known donors, with a clinical pregnancy rate per embryo transfer of 24%, and live birth rate of 14%. In total, 82 recipients were granted donated cryo-embryos, twenty had an ongoing pregnancy (24.4%), nineteen of whom have given birth to a healthy child (23%).

Conclusion: Altruistic embryo donation of embryos appears to be satisfying for the donors, as they are not obliged to destroy their embryos, but instead help others build a family. Although success rates are still limited, partly due to the relatively high miscarriage rates and inferior freezing techniques, to this date nineteen out of 82 recipients have given birth to a healthy child.

Keywords: Altruism, Embryo Donation, Protocol, Screening

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Introduction

Many women and couples have to face the fate of unsuccessful infertility treatments and childlessness. They are left with the option of remaining without a child or decide to build a family through adoption. Embryo donation may create an ultimate possibility to have a child, in women who have no more options for treatment. Hundreds of thousands, perhaps millions of surplus embryos are stored at fertility laboratories all over the world. They may be forgotten after successful treatments, or parents are not able to decide what to do with them after their family is complete. The feeling of preciousness of these embryos could make the option to destroy very difficult (1). Couples may have endured a long road of multiple fertility treatments, before becoming parents themselves. Donating their surplus cryo-embryos provides a possibility of life for these embryos and therewith a feeling of satisfaction in the people who have decided that their family is complete (2, 3). While many countries have implemented embryo donation as a standard care for

infertile couples, embryo donation was not an option in the Netherlands until 2011 when we set up the first embryo bank in our country. This innovation of care for the Dutch health system now enables embryo donation procedures for childless couples, and as yet we remain the only Dutch fertility center facilitating embryo donation (2).

The option to receive a donated surplus embryo provides a unique possibility of parenthood in patients that have no more possibilities and remain childless or perhaps decide to adopt. Accepting a donated embryo is not comparable to adoption. By Dutch law, the woman who is pregnant and gives birth to the child, is biologically and juridically the mother of this child, hence there is no need to adopt. Nor does her partner (when wedded or legally bound) need to adopt the child, but this may be different in other countries. The description “embryo-adoption” has been widely used and can be found in literature, but as such is not a correct term. The child will indeed not be genetically one’s own, but will be “biologically, juridically and psychologically

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one's own" from the very beginning of the pregnancy and has no juridical relation to the donating couple.

Many articles have been written on the procedures of embryo donation and the medical pregnancy risks for mother and child (4-7), on the possible psychological and social risks for donors and recipients (8, 9) and on the psychological development of the children and their bonding mechanism (10, 11). Different countries have different points of view on disclosure or non-disclosure, matching or not matching, and commercializing or non-commercializing (12-15).

In the Netherlands, gamete donation is only possible in a non-commercial and disclosed way (ie non-anonymous and registered). Dutch law was changed in 2004 in order to prevent anonymity, now stating that all donors must be registered and agree to share person identifying details. Thus, children of 16 years of age and older may request identifying information about their donor. In numerous countries gamete donation is commercial and anonymous. Even within Europe, there is a big difference in laws and insight on this matter between the different countries. Recently, the Council of Europe has stated that anonymous donation should not be permitted as non-anonymous donation is in the best interest of the child. The aim of this article is to describe the protocol and results for altruistic embryo donation of the only embryo bank in the Netherlands.

Non-commercial, non-anonymous embryo donation, a prospective and ongoing study

Fertility Clinic TFP Medisch Centrum Kinderwens in Leiderdorp, is the first and only government approved embryo bank in the Netherlands. We opened for procedures of embryo donation in 2011, to meet repeated requests from parents who had completed their family after IVF procedure and were facing a decision on their stored cryo-embryos. Some of these parents decided they want to give these surplus cryo-embryos "a chance at life" and help others build a family. We set-up a protocol for embryo donation procedures, in close collaboration with and monitored by the Dutch Ministry of Health. We followed the existing guidelines by ESHRE (16) and ASRM (17-20). We established a protocol that has been thoroughly checked and finally approved by the Dutch Ministry of Health in 2011.

In this article, we describe our embryo donation procedures, from counseling and screening in donation to accepting surplus cryo-embryos through our embryo bank, and share the results of these procedures.

Materials and Methods

Information brochures

Brochures for potential donors and acceptors can be found on our website: <https://tfp-fertility.com/en-nl/tfp-mc-kinderwens-leiderdorp>.

The Dutch approach

Since 2011, we have performed embryo donation

procedures in a standardized protocolled manner, approved by the Medical Ethical Committee of TFP Medisch Centrum Kinderwens.

Intake of donating couples

Embryo donors are heterosexual couples, who have completed family building and wish to donate their surplus cryo-embryos to unknown or known others. We do not accept surplus cryo-embryos that were established using donor gametes, for two important reasons: i. future difficulties in explaining its genetic origin to the child and just as importantly: ii. So as not to surpass the limit of the number of offspring of a donor (in the Netherlands, a maximum of 25 children per donor is decreed in the appropriate guidelines, recently we have set the limit to a maximum of 12 families per donor). Cryo-embryos will only be accepted for donation in the embryo bank after the youngest child has reached the age of one year, this is to ensure that parents have enough time to rethink their donation and are completely sure of not wanting another child (21).

During the first consultation with the gynaecologist (J.P.), medical files are reviewed, and a medical and genetic anamnesis is performed to acquire information for possible genetic or health risks for the future child. In the majority of donating couples no clear cause of infertility was found, hence the cause was documented as idiopathic (Fig.S1, See Supplementary Online Information at www.ijfs.ir). Other couples were subjected to *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI) due to reduced sperm quality or tubal pathology (Figs.S1, S2, See Supplementary Online Information at www.ijfs.ir). Donated embryos were frozen years ago, when slow freezing of embryos on day 3 or 4 was the standard in most Dutch laboratories (Fig.S3, See Supplementary Online Information at www.ijfs.ir). We assess donors' health, medication, smoking habits and the health of their children, as well as the possible medical problems of their own parents and brothers and sisters (genetic family tree). If a serious physical and/or psychological disorder is present in the donors -or their family, we cannot accept the embryos for our bank (Supplementary 1, See Supplementary Online Information at www.ijfs.ir). Next, the couple has a consultation with a social worker who discusses all consequences of embryo donation, checking for risks of not being able to let go. Relevant articles of Dutch law are discussed and explained, which entails that a child will have the right to know his or her genetic parents and may even try to get in touch with them and their children, who are 100% genetic siblings to these children. After the consultation with a social worker, the couple is screened for infectious diseases as has been done at the time of their IVF-treatment. This is stated by European law on donation of cells and tissues (12, 22): HBV, HBC, HIV and lues. This screening accounts for unknown as well as for known donating procedures.

Donating couples complete our anamnestic file by signing a contract to "give up their ownership" of their surplus

embryos (Supplementary 2, See Supplementary Online Information at www.ijfs.ir). Donating couples are informed that they will not receive any identifying information on a child that may be born as a result of their donation. If they like, they may write a letter to the future child, explaining their donation and express their best wishes for the child. These letters are evaluated to assure that the content will never negatively affect the child. We only accept surplus cryo-embryos for donation, if we find no risk for medical or genetic diseases and we ask the donating couples to keep us informed of any medical problems that may occur in the future. Of course, in fully disclosed donating procedures, donors and recipients will be able to meet with each other from time to time. We inform them on the importance of contractual agreements and we counsel on the change in mutual relationship.

Medical files of the donating couples and embryos are given a unique code to ensure the privacy of the donating couple. If the embryos are stored at a different clinic, we will assist to transport the embryos to our embryo-bank (Fig.1).

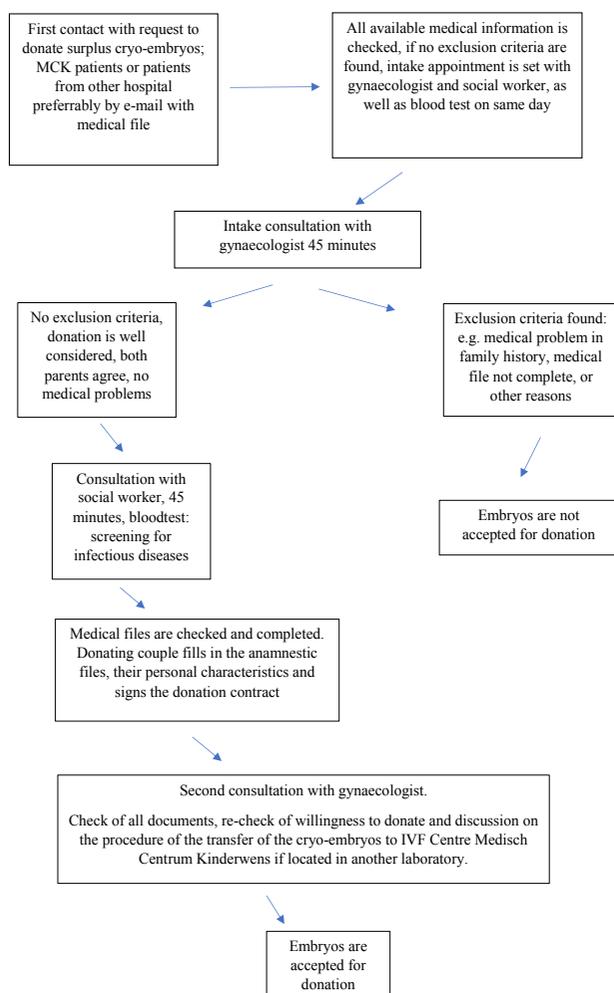


Fig.1: Donating couples.

Intake of recipient(s)

The accepting party, being heterosexual, lesbian or single, is counseled in a similar manner to donating couples: two or more consultations with the gynaecologist (J.P.), as well

as at least one consultation with our social worker. During these consultations, an assessment is made to ensure that no other option for parenthood is left, which is one of the strict indications for an embryo donation procedure. We perform a medical and psychological screening and assemble all information on former treatments in the recipients' medical file. This screening accounts for unknown as well as for known donating procedures. Most recipients were diagnosed with idiopathic or male subfertility (Fig.S1, See Supplementary Online Information at www.ijfs.ir). All recipients were selected to have a healthy BMI, they had no concurrent diseases, they did not smoke and were advised to take folic acid on a daily basis (since 2018 daily vitamin D is also advised).

In these women, special attention is focused on their past fertility treatment and their ability to accept their infertility. At the moment of discussing the option of embryo donation, they have reached the point where they will remain childless or choose to adopt. Medical, social and psychological status is evaluated, as well as their willingness to be open to the child on disclosure of its genetic background (23, 24).

Pregnancy as a result of embryo donation has specific medical risks, comparable to egg donation pregnancies, such as miscarriage, bleeding, placental problems, hypertensive disorders, intra-uterine growth retardation and premature birth (4, 6, 7). These higher risks for complications in pregnancy urge us to evaluate the physical condition of the recipient and counsel her on these specific risks (Fig.2).

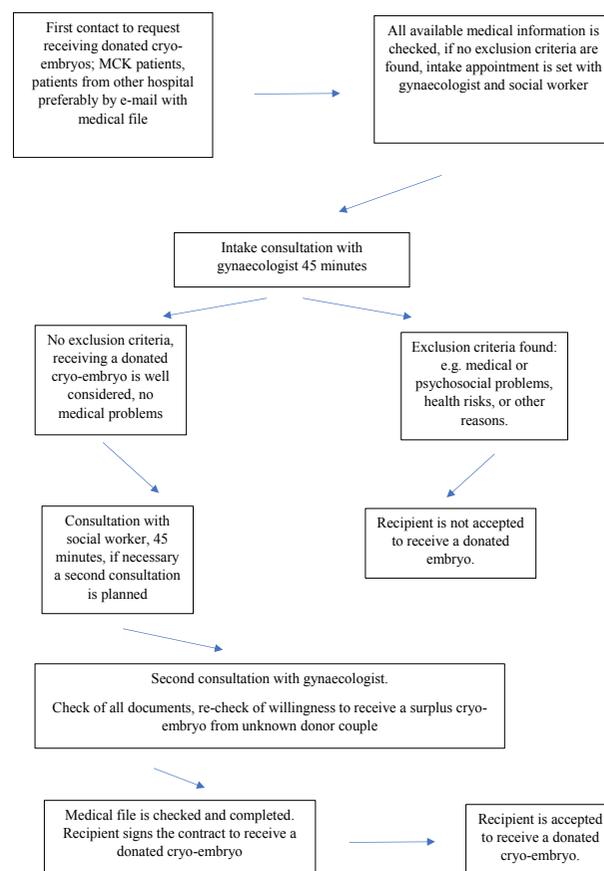


Fig.2: Recipients.

Embryobanking for donation of surplus cryo-embryos to an unknown other or to a relative or friend

In performing procedures of embryo donation in our fertility clinic, we thoroughly check and re-check the donor's motivations for donating their surplus cryo-embryo(s) to unknown recipients in multiple counseling sessions with a gynecologist (J.P.) and our social worker. We discuss the screening protocol of the (known or unknown) recipients and the in- and exclusion criteria (MCK brochures in English, Supplementary 3, See Supplementary Online Information at www.ijfs.ir). After having completed the counseling procedure of the donors and finishing all the paperwork, an extra telephone appointment with the donors is planned, in order to tell them the negative result of their infection screening tests and moreover, to check again their wish to donate. If there are no missing data, all questions have been answered and all test results have checked to be good, they are asked to complete and sign the donation contract and, if applicable, the cryo-embryos are transported to our laboratory (supervisor M.v.M.). Most donated embryos were frozen on day 3 and 4 using a slow freeze protocol (Fig.S3, See Supplementary Online Information at www.ijfs.ir), their morphological grades ranging from 6-cell embryos to the morula stage. Only a small proportion of embryo donation transfers were blastocyst transfers (Fig.S3, See Supplementary Online Information at www.ijfs.ir), with morphological grades ranging from early blastocysts to hatching blastocysts. Morphological classification of embryos/blastocysts was performed using the scoring method described in the Istanbul consensus on embryo assessment (25). Donated embryos are stored in our embryo bank with a personal, anonymous code that is linked to their medical file.

Follow-up research among donors and recipients

We inform all donating couples that we would like to re-contact with them in a few years to assess how they feel at that moment in time about having donated their cryo-embryo(s). Also, we ask them to keep us informed on any changes in medical or psychiatric circumstances. This accounts for themselves as well as their currently healthy and well-developing children.

We will re-connect with the recipients who had a successful embryo donation and will try to contact them yearly in order to follow up with the parents and children. We intend to publish the results of our follow-up research in the coming years.

Results

Procedures and results

Since our start in 2011, 54 unknown and 28 known recipients have received embryos from our embryo bank, all single embryo transfers. We describe the diagnoses and fertility treatments of donors and recipients in Figure S1 (See Supplementary Online Information at www.ijfs.ir).

Considering that some of the donated embryos were frozen over a decade ago, it is evident that the quality of embryos donated was variable. Freezing methods at that time were inferior to current freezing methods such as vitrification. Therefore, on average, more than one embryo was thawed in order to transfer one qualitatively good embryo (Tables 1, 2). Given the limited availability of embryos in our bank, women were granted a maximum of two embryo transfers. In donating procedures with a known recipient, all donated surplus cryo-embryos were specifically linked to the file, giving these recipients sometimes more than two options for pregnancy.

We performed 95 embryo transfers resulting in 24 clinical pregnancies (25%) and 12 live-births (12.6%) in donating procedures with an unknown recipient. The average age of embryo acceptors was 39 years, the average age of the donating women was 34.9 years.

We performed 50 donating procedures with a known recipient, resulting in 12 clinical pregnancies (24%) and 7 live births (14%). In known donation procedures, the average age of the acceptor was 37.8 years and the average age of the donating women was 33.9 years.

Collectively, 82 recipients (both known and unknown donations) were granted donated cryo-embryos, with an average of 1.76 embryo transfers per recipient. Of these embryo transfers, twenty had an ongoing pregnancy (24.4%), nineteen of them have given birth to a healthy child (23%).

While donation of gametes, such as oocytes, may often be linked to undesired side-effects such as hypertension, intra-uterine growth retardation and premature birth (5, 6, 26); we observed an expected percentage of medical problems in our embryo donation procedures (Table 3). In addition, all children were healthy at delivery and showed normal growth during follow-up.

Table 1: Characteristics of embryo donation procedures with unknown recipients

Variables	n or n (%)
Recipients	54
Embryos thawed	187
Number of embryos thawed per transfer	2.0
Number of embryo transfers	95
Number of embryo transfers per recipient	1.8
Cancelled embryo transfers	0 (0)
Clinical pregnancy per transfer	24 (25.3)
Ongoing pregnancy per transfer	13 (13.7)*
Live births per transfer	12 (12.6)
Average age of embryo donor	34.9 (27-41)
Average age embryo acceptor	39 (29-45)

All transfers were single embryo transfers. *: One pregnancy was terminated, because of multiple malformations.

Table 2: Characteristics of embryo donation procedures with known recipients

Variables	n or n (%)
Recipients	28
Embryos thawed	85
Number of embryos thawed per transfer	1.7
Number of embryo transfers	50
Number of embryo transfers per recipient	1.8
Cancelled embryo transfers	2 (3.8)
Clinical pregnancy per transfer	12 (24)
Ongoing pregnancy per transfer	7 (14)
Live births per transfer	7 (14)
Average age of embryo donor	33.9 (25-41)
Average age of embryo acceptor	37.8 (29-47)

All transfers were single embryo transfers.

Table 3: Follow up: pregnancy, delivery, and complications

Unknown donation	n	Known donation	n
Live birth	12	Live birth	7
Hypertension, pre-eclampsia	3	Hypertension, pre-eclampsia	None
Placental problems, bleeding	None	Placental problems, bleeding	1
Premature birth (<36 weeks), induction	None	Premature birth (<36 wk), induction	1
Premature birth (<36 weeks), caesarian	1	Premature birth (<36 wk), caesarian	None
Fetal distress, vacuum/forceps delivery	None	Fetal distress, vacuum/forceps delivery	None
Fetal distress, caesarian	None	Fetal distress, caesarian	None
Small for gestational age	None	Small for gestational age	None
Healthy child	12	Healthy child	7

Discussion

Embryo donation may create the ultimate possibility to have a child in women who have no more options for treatment. Donating surplus cryo-embryos provides a feeling of satisfaction in the people who have decided that their family is complete (27, 28).

Intensive screening procedures for donating couples as well as the recipients are important, in order to assess all possible medical, social or psychological problems for the future child, its parents and for the donating couples as well. We counsel complete and early openness to the child, as the child will be able to potentially meet its genetic parents and siblings at the age of 16. Dutch law ensures that all children conceived of donor gamete conception, will be able to find and ultimately meet with their donors. The important difference with other children that grow up as a single child, is that the children born through embryo donation procedures have full genetic siblings and may get in contact with their siblings later in life.

The results of embryo donation procedures from 2011 until today from the first government approved embryo

bank of the Netherlands, show that the procedures have a limited success percentage (ongoing pregnancy) per embryo transfer to an unknown recipient of 13.7%. When observing the procedures for known recipients, we find a comparable success percentage of 14%. In most of these donations, the cryopreservation procedures as well as the thawing procedures were done in our own laboratory. It is generally known that blastocyst transfers demonstrate a higher live birth rate (29). As we have performed mostly day 3 embryo-transfers in the beginning years of our embryo bank procedures, this may explain our low ongoing pregnancy rate. Given the recent shift towards donation of day 5 blastocyst vitrified embryos, we anticipate higher pregnancy outcomes in the foreseeable future. Also, the advanced age of the receiving and the donating woman, is an important factor, as is known in oocyte procedures (30, 31). The advanced average age of the recipients in our program with unknown embryo donation may explain the high pregnancy loss through miscarriage (32, 33).

In earlier reports on embryo donation, a success percentage of Live Birth Rate was given as 14-40% (34, 35); most publications on embryo donation do not provide any success percentages but focus on ethical, social and moral issues. ASRM Ethics Committee published a statement in which it is clarified that scientific research indicates that even in natural conception, an estimated of 70% of all human embryos fail to result in live birth (36, 37). The Committee states that if the donated embryos are provided by people with impaired fertility, the percentage that will result to live birth may be lower than in natural conceiving population where no need for fertility treatment exists (18).

Dutch guidelines are very strict on medical intervention and fertility treatments, IVF/ICSI is only permitted if there is a clear medical indication. Our limited success percentage of LBR after embryo donation may partly be explained by the fact that the population reaching the stage of IVF/ICSI has a worse prognosis than in countries where these fertility treatments are offered with less restrictions and at a younger age.

In this report of our embryo donation pregnancies, we have observed a high pregnancy loss due to miscarriage; overall, the total pregnancy rate per embryo transfer was 25.5%. We presume that allograft immune reaction might be present in embryo donation, comparable to pregnancies in oocyte donation procedures, which may lead to miscarriage (38, 39).

We registered all pregnancy follow ups and found an expected percentage of pregnancy complications (33% in unknown embryo donation pregnancies and 28.5% in known procedures). The recipients' advanced age may have contributed to the proportion of pregnancy complications. All children that were born, were in good health and they have continued to develop well until now. One pregnancy had to be terminated because of severe fetal malformations.

We accept surplus cryo-embryos in our embryo

bank, in order to donate them to recipients that are unknown to the donors- but well-known to us after the screening consultations. This creates a situation of great responsibility, towards the donors as well as towards the recipients. When donors and recipient are well-known to each other, the existing relationships may change considerably, with the birth of a child but also when the embryo donation procedure is not successful. We feel responsible towards the donor couples, who handed over to us their cryo-embryos in full confidence that we will perform an adequate screening of the (known or unknown) recipients. The donors ask us to take good care of the embryos, they trust us to screen the recipient for her medical, social and psychological health and hope for the future child to have a happy life and a good future. The screening procedure of the unknown recipients is of course a snapshot of the current situation. This point is elaborately discussed with the donor couples, but we always keep the donors' concern in mind.

Our responsibility to the recipients lies in the thorough screening of all medical files of the donors, the search for possible genetic, medical, psychological or other risk for their future child after a successful donation procedure. Also here, we counsel the recipients that we can only screen the situation as is at the moment of screening, but that we ask donors to contact us if any medical or other problems may become clear in later years.

Thus, our embryo bank functions as a mediator, as we are the only professionals that get to know and counsel the donor couples as well as the recipients. The significant responsibility for the happiness of donors, recipients and the future children is always our priority.

Only in many years from now, will we know if the children originating from an embryo donation procedure of our embryo bank to an unknown recipient, will try to get in contact with their genetic family. Only then we can find out how the child, the biological mother and the donor couples have experienced the donation procedure. As has been stated in earlier reports, more data on these topics are warranted (40).

Conclusion

Donating one's surplus cryo-embryo to an unknown recipient shows to be an act of ultimate altruism for all donor couples we have seen in our clinic. In their own words: "we are happy to help someone else with our embryo to give them a chance for creating a family and raising their own child". The donation of these surplus embryos is not considered as giving away children, but the donated embryos are indicated as "a chance at happiness". Donating surplus cryo-embryos to known recipients may have an impact on existing relationships and thorough counseling and screening for medical or psychological risks is mandatory.

The recipients understandably are very happy to have been given this ultimate possibility of having a "child of their own". If the procedure is successful, they may

experience pregnancy and childbirth. Even if the embryo donation procedure is unsuccessful, they are thankful to the donors to have offered them this last opportunity to possibly fulfill their wish for a child.

As a result of donating embryos from our embryo bank, until today 82 women have been offered an additional opportunity for motherhood. Nineteen of these recipients have given birth to a healthy child. We are confident that embryo donation procedures provide a safe addition to our pallet of treatment options when dealing with unsuccessful fertility treatments.

We will certainly aim at collecting data in the coming years, in order to learn more about these precious and vulnerable procedures.

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Authors' Contributions

J.P.; Designed the initial protocol in 2011 for the first and only embryo bank in the Netherlands. Since then, she screens personally all donors and recipients in close collaboration with the medical social workers of the clinic. M.v.M.; Shares responsibility for the embryo bank and provided the data and data analysis for this manuscript. J.P., M.v.M.; Wrote and edited the manuscript. All authors read and approved the final manuscript.

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