Tha Fate of Surplus Embryos

by Fakultas Ilmu Kesehatan

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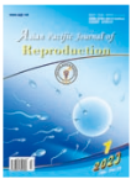

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The fate of surplus embryos in the setting of assisted reproductive technology: A scoping review

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ABSTRACT

Objective: To identify the attitudes of infertile couples toward their surplus frozen embryos.

Methods: This study was according to PRISMA-ScR as the guideline for scoping review. Studies that assessed the attitudes of patients or infertile couples who had surplus embryos were included. We conducted systematic searches in English studies from April 2011-April 2021 using 7 databases: PubMed, Science Direct, EBSCO, Scopus, the Cochrane Library, Sage Journals, and Google Scholar. Data were charted based on author, year of publication, country, purpose, data collection, key findings, and research focus/domain.

Results: A total of 37 research articles were included in the analysis. Their attitudes encompassed: supporting the donation of the surplus embryos for both research and reproductive purposes, continuing to store the frozen embryos, and disposing of the surplus embryos.

Conclusions: Most of the infertile patients support donating their surplus embryos for research and reproductive purposes.

KEYWORDS: Attitude; Decision making; Infertile patients or couples; Male infertility; Female infertility; Surplus embryos; Embryo disposition; Embryo leftover

1. Introduction

Rapid developments in the field of assisted reproductive technology, and a consequent greater success rate in achieving pregnancy at the first cycle of *in vitro* fertilization (IVF) programs, have led to a surplus of embryos. The number of surplus embryos that could be stored is limited by the storage capacity. This limitation certainly affects the number of embryos that could be kept by an infertility clinic that performs assisted reproductive technology procedures. In addition, a woman's ability to conceive embryos and become pregnant was also a limitation.

Surplus embryos are the excess of frozen embryos achieved by a woman after she is successfully treated in the IVF program and she also had the desired number of children as a result of the program. The excess of frozen embryos has been increasing in numbers due to the increasing number of oocytes obtained during ovum pick-up and the increase in the cumulative rate of live births[1]. A previous study found that there were various attitudes towards the excess of frozen embryos, including continuing to or ceasing to store the frozen embryos[1,2]. In the 1990s, patients generally preferred to dispose of the excess embryos, but since the early 2000s, this attitude has been reversed[2]. Another proposed option against the need for further storage by the clinician was a transfer method, which included thawing and transfer of a surplus embryo into the patient's vagina/cervix or the uterus during infertile periods in the patient's menstrual cycle without hormonal therapy[3]. Various factors could influence the attitude of infertile couples who have surplus embryos, including environmental conditions, parental experiences, information obtained, personal value, and psychosocial or demographic factors[4]. In addition, the conceptualization of embryos, trust in medical science, and the lack of acceptable options are also the contributing factors that influence infertile couples' attitudes toward their surplus embryos[5]. However, attitudes will vary among couples. Therefore, this study aimed to analyze the attitude of patients or infertile couples toward excess/surplus embryos.

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2. Materials and methods

2.1. Protocol

This scoping review was conducted based on a framework developed by Joanna Briggs Institute and following the PRISMA-ScR checklist[6]. This scoping review was described to identify the attitude of infertile couples toward their surplus frozen embryo.

2.2. Eligibility criteria

The inclusion criteria in this scoping review were research articles with clinical trial design, library reviews, case studies/series, and other descriptive studies that discussed the choice of patient/infertile partner attitudes towards surplus embryos.

The exclusion criteria in this scoping review were source data in the form of commentaries, such as letters to editors, the manuscript which did not have full text, and the article that was not in English.

2.3. Information source

A three-step search strategy was utilized based on Joanna Briggs Institute's recommendations. A systematic literature search was conducted to identify studies/articles reporting on the attitudes of infertile patients or couples who have surplus embryos. A search was conducted on seven databases including PubMed, ScienceDirect, EBSCO, Scopus, the Cochrane Library, Sage Journals, and Google Scholar from April 2011 to April 2021.

2.4. Searching evidence

The search string used was as follow: Medical Subject Heading (MeSH) namely (((((((((("Attitude"[Mesh]) OR "Attitude to Health"[Mesh]) OR "Decision Making"[Mesh]) OR "Decision Making, Shared"[Mesh]) OR "Decision Theory"[Mesh]) OR "Reproductive Behavior"[Mesh]) OR "Directive Counselling"[Mesh]) OR "Patient Self-Determination Act"[Mesh]) OR "Patient Participation"[Mesh]) OR "Involuntary Fertility Control"[Mesh] AND ((("Infertility"[Mesh]) OR "Infertility, Male"[Mesh]) OR "Infertility, Female"[Mesh]) OR "Fertility Clinics"[Mesh] AND (((((“Surplus Embryo”[Mesh]) OR "Research Embryo Creation"[Mesh]) OR "Embryo Research"[Mesh]) OR "Embryo Disposition"[Mesh]) OR "Cryopreservation"[Mesh]) OR "Fertilization *in Vitro*"[Mesh]) OR “Embryo Leftover”[Mesh]).

2.5. Selection of source of evidence

By working independently and avoiding duplication, two authors (IG and SA) decided upon which titles and abstracts to include. Duplication was avoided by using the software Mendeley Desktop version 1.19.8. Abstracts that had the potential to meet the criteria but with a lack of information were further studied using the full document if they did not meet the criteria were excluded.

2.6. Data charting process

All data from articles included in the scoping review were extracted. Extracted data included author, year of publication, country, purpose, data collection, key findings, and research focus/domain.

2.7. Data item

These extracted data were listed in the table by using Microsoft Excel 2010 and were classified based on author, year of publication, country, purpose, data collection, key findings, and research focus/domain.

2.8. Summarizing evidence

The extracted data were summarized and classified based on the country of origin of the articles, study design of articles, methods to conduct the articles, and options against the storage of surplus embryos.

3. Results

3.1. Selection of source and characteristic of evidence

From the seven database sources, 4 196 studies were obtained, and after the separation of duplication, it was reduced to 2 729 research articles. From this, 246 papers met the eligibility criteria, and 37 papers met the inclusion criteria. Figure 1 shows the results of this systematic search process. Characteristics of studies that meet inclusion criteria are available in Table 1. The countries of origin, the study design and the methods of the included studies are mentioned in Table 2.

3.2. Attitudes options toward surplus embryos

Several options can be extracted from the studies regarding the attitudes toward the surplus embryos, which are described in Table 3.

3.2.1. Embryo donation

There were 31 studies discussing donation options from surplus frozen embryos. These studies came from Canada, the United States of America (the USA), Mexico, Italy, Israel, Portugal, France, Sweden, Belgium, China, Japan, India, Iran, and Australia. The donation option was divided into two types that are: donations for the reproductive purposes of other infertile couples and donations for research purposes. Based on the continent of origin of the studies, most of the subjects who chose to donate surplus embryos were from Europe followed by Asia, America, and Australia. Countries from Latin America such as Brazil, Venezuela, Colombia, Peru, Bolivia, Uruguay, and Ecuador also tended to donate surplus embryos for research purposes[7]. Study showed that in Italy (n=832) donation

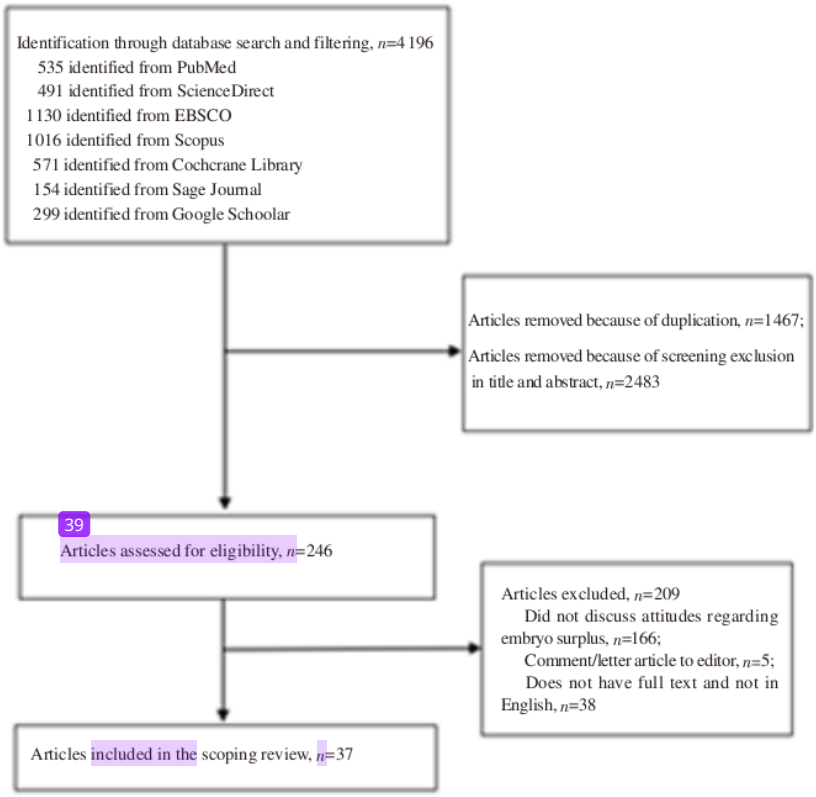

Figure 1. PRISMA-ScR flowchart in article and result search.

options for research were also very high which was approximately 84% of the surplus of aneuploidy embryos[11]. The Zoroastrians in Iran (*n*=143) also donated surplus embryos for reproduction purposes (71.3%)[24].

In Portugal (*n*=221), 87.3% of the subject under the age of 36 chose to donate embryos[22]. Studies showed that in the USA (*n*=224), the percentage going to the two choices of donations, in general had not reached 50%, whereas in 2019 research showed the choice of donations for research was only 29% and donations for reproduction by 13%[10]. Even a subsequent study in 2020 showed that the choice of donation for research only reached 45.4%[2]. The results of the study in Belgium (*n*=326) showed that the percentage of donation options for research purposes was 50.8% and the percentage of donations for reproduction was 16.1% from the group of 61.3% of couples who did not continue to store the surplus embryos[33]. Donation for research in Belgium (*n*=2 334) has been increasing year by year compared to donations for reproduction[32]. Overall, the percentage of subjects who donated surplus embryos in Japan (*n*=2605) was 36.2% while in China (*n*=718) and Canada (*n*=498), embryo donation options for research were 16.4% and 56.0%[15,16,25]. When viewed by gender, infertile in Japan (*n*=2 605) tended to donate embryos[15]. In China (*n*=718), women over the age of 30 preferred to donate their embryos. Donation options for research and reproduction in India were 11.5% and 46.0% respectively (*n*=87) with the percentages of male and female patients choosing embryo donation being 23.7% and 15.7%, respectively (*n*=594)[12,13]. The donation option for research in Israel (*n*=674) was only 7%[8]. Research in Sweden (*n*=471) showed that the percentages for the two embryo donation options were 73%, with 55% for research and 45% for reproduction[29,30].

3.2.2. Continuing to keep frozen embryos

There were eleven studies discussing the continuation of surplus embryo storage. These studies came from Canada, the USA, Israel, Belgium, China, and Japan. The option to continue the storage of surplus embryos had increased in Israel (*n*=674)[8]. Research in the United States (*n*=1053) also showed the option to continue the storage of frozen embryos was 79%[10], meanwhile, in China (*n*=769) it was 64.3%[16]. Qualitative research in Canada (*n*=45) showed that the option to continue the storage of frozen surplus embryos was 50% of the sample group[19]. Between 30% and 50% of the patients who participated in the study in Belgium (*n*=231) and the Netherlands (*n*=95) expressed a desire to keep keeping frozen embryos[34,36].

Table 1 Data extraction from individual studies.

No.	Author & year of publication	City/Country	Purpose	Data collection	Key findings	Research focus/Domain
1	Álvarez-díaz, 2021[7]	Mexico	To find out of Latin Americans who have undergone assisted reproductive techniques will donate embryos	Multinational analytics descriptive research	Results showed that embryo donation for research purposes was the most frequently chosen option.	Attitudes of Latin Americans undergoing IVF toward embryo donation
2	Raz *et al*, 2021[8]	Israel	To explore misconceptions and miscommunication underlying IVF users' decisions towards surplus Frozen Embryos owned	Semi-structured interviews.	Payments for continuing storage and embryo disposal are the two most frequent options (13%, *n*=89 and 89) followed by donations for research and frozen embryo transfer (7%, *n*=47 and 45).	The perspective of patients undergoing IVF in disposition decision in Israel
3	Hertz, 2021[9]	Wellesley (USA)	To find out how mothers manage their excess stored frozen embryos	Qualitative and descriptive-analytical study	Forty-three percent had given it to other families, another 43% were still deciding whether they will have a second child or find candidate parents, and only 14% used it for scientific research donations.	Management of excess embryos in single mothers in the United States
4	Alexander *et al*, 2020[2]	Washington (USA)	To assess the longitudinal trends of stored frozen embryos disposal	A retrospective cohort study	point six percent. Chose to dispose of embryos, 45.4% donated for research, and 4.1% chose to donate for reproductive purposes.	Embryo disposition options in Washington
5	Zimon *et al*, 2019[10]	Massachusetts (USA)	To assess a patient's knowledge, willingness, and factors related to their willingness to donate.	A two-page anonymous survey	Saving for subsequent reproduction efforts (82%), continued saving (79%), donations for research (29%), discarding (14%), and donations to form a family (13%).	Effect of counseling sessions on participation rates to discuss embryo disposition options in Massachusetts
6	Faustini *et al*, 2019[11]	Rome (Italy)	To assess the patient's attitude toward the fate of the surplus embryos	An observational cohort	Eighty four per cent (*n*=126) choose to donate to research, 9% (*n*=13) disposed of embryos and 7% (*n*=10) kept frozen.	Patient attitudes to surplus aneuploid embryos in Italy
7	Roudsari *et al*, 2019[41]	Iran	To determine the relationship between the sociocultural beliefs and infertile couples' attitude toward reproductive donation	Descriptive observational study	There was a direct correlation between sociocultural beliefs and attitude toward reproductive donation in infertile women ($P<0.001$) and men ($P<0.001$), that is, women and men with a higher score of sociocultural beliefs had a higher score of attitude as well.	Socio-cultural beliefs could influence infertile couple's attitude toward embryo donation
8	Chandy *et al*, 2019[12]	Vellore (India)	To evaluate the knowledge and attitude of infertile couples regarding their surplus frozen embryos	A descriptive-analytical study and two-stage structured interviews	Thirty-three (37.9%) were unaware of the disposition of surplus embryos, 40 (46%) couples preferred donating embryos to other sub-fertile couples, 10 (11.5%) couples preferred donating to research, 24 (27.6%) couples donating to other couples and research, and 3 (3.4%) indicated to stop saving.	Indian sub-fertile patient's attitude to embryo surplus
9	Banerjee & Singla, 2018[13]	New Delhi (India)	To assess the attitudes toward egg, sperm, and embryo donation	Descriptive analytical research	One hundred and eighteen women agreed to donor the eggs (19.9%), 116 women agreed to donor the sperm (19.5%), and 93 women agreed to donor their embryos (15.7%).	Indian infertile patient's preference for egg, sperm, or embryo donation
10	Rosemann & Luo, 2018[14]	China	To find out the point of view of embryo donors for stem cell research	In-depth interviews and a quantitative survey	Perception and cultural specificities concerning human tissue play a crucial role in embryo donation for research or reproductive purposes.	Attitudes, perceptions, and experiences of IVF among patients and students in China regarding embryo donation for stem cell research
11	Yamamoto *et al*, 2018[15]	Tokyo (Japan)	To gauge the public's attitude toward third-party reproduction	Web-based survey	36.2% approved, and 26.6% disapproved of gamete or embryo donation.	Third-party reproductive attitudes in Japan
12	Chun-lin *et al*, 2017[16]	Guangzhou (China)	To investigate infertile patients' attitudes towards frozen embryos and the factors that influence decisions.	A quantitative observational study	Of 718 couples (93.4%) who completed the questionnaire, 462 couples (64.3%) chose to continue storing their embryos, 214 couples (29.8%) chose to dispose of embryos, and 42 couples (5.8%) agreed to donate embryos for research.	Factors associated with attitudes toward the disposition of surplus embryos in infertile couples in China
13	de Lacey, 2016[17]	Australia	To find out how to make decisions to dispose of embryos	Analyzed interview	Women experience emotional distress similar to losing an early pregnancy and experience attachment and sadness.	Perceptions and experiences of IVF patients disposing of surplus embryos in Australia
14	Deniz *et al*, 2016[18]	Ontario (Canada)	To find out the effectiveness of education in preparing decisions on the disposition of surplus embryos.	Descriptive analytical study	Education for couples in preparing surplus embryo disposition decisions before starting IVF treatment met the needs of the majority of participants for making disposition decisions (n = 86 from n=131).	The effect of education on infertile couples' embryo disposition decisions in Canada

Table 1. Data extraction from individual studies (continued).

No.	Author & year of publication	City/Country	Purpose	Data collection	Key findings	Research focus/Domain
15	Cattapan & Doyle, 2016[19]	Halifax, Montreal, and Ottawa (Canada)	To identify factors that contribute to decision-making for the disposition of surplus embryos.	Interviews	Most patients (21 patients, representing 16 households) renewed embryo storage agreements. 6 patients (representing 5 households) used all their embryos, 2 patients (representing one household) decided to keep them in storage, 3 patients (representing 3 households) disposed of their embryos, and 13 patients (representing 9 households) donated their embryos for clinical research or training.	Decision-making of embryonic disposition among infertile couples in Canada
16	Raz *et al*, 2016[20]	Israel	To understand the attitudes, values, and perceptio	In-depth interviews	IVF patients who donated surplus pre-embryo frozen embryos for research view frozen embryos as a valuable resource that does not yet have a human identity.	The moral reasons behind the decision to donate surplus embryos to infertile couples in Israel
17	Samorinha *et al*, 2016[21]	Porto (Portugal)	To analyze the willingness of couples undergoing IVF to donate their frozen embryos for research.	Longitudinal prospective	A significant decrease in the willingness of patients to donate embryos for research over time was observed [86.5% to 73.6%; relative risk (*RR*)=0.85; 95% *CI* 0.76–0.95].	Infertile couple's willingness to donate embryos in Portugal
18	Bruno *et al*, 2016[4]	France	To analyze the factors that influence decisions on embryo disposition	Prospective studies	The option to 'stop frozen storage' and decided to donate or dispose embryo was more often if the embryo is represented as a child [odds ratio (*OR*) adjusted=3.29, 95% confidence interval (*CI*)=1.62–6.66], *P*=0.000 9. The option to choose 'embryo donation' if they represented the embryo as a potential person [*OR* adjusted = 3.77, 95% *CI*=1.45–9.80], *P*= 0.0064.	Factors influencing decision-making for surplus frozen embryos in infertile couples in France
19	Samorinha *et al*, 2015[22]	Porto (Portugal)	To assess the factors related to willingness to donate embryos for research	Questionnaires	Willingness to donate was more often in women younger than 36 years (adjusted *OR* 3.06; 95% *CI* 1.23 to 7.61) and who considered it was important to do research on embryos (adjusted *OR*: 6.32; 95% *CI* 1.85 to 21.64)	Factors that influenced willingness to donate embryos among infertile couples in Portugal
20	Jonlin, 2015[23]	Seattle, Washington (USA)	To study the motivations to donate embryos for research	In-depth interview	Did not want to waste their embryos and often expressed a keen interest in stem cell research	Concerns and questions arising from surplus embryo donors
21	Halvaei *et al*, 2014[24]	Iran	To evaluate the attitude and knowledge toward embryo donation (ED)	Descriptive analytical studies	The majority of participants supported embryo donation for reproductive purposes (71.3%) to infertile patients.	Attitudes and knowledge of infertile couples towards embryo donation in Iran
22	Cote *et al*, 2014[25]	Montreal (Canada)	To report an analysis of users' choice in using surplus embryos	Consent forms	Approximately 68% of individuals approved the use of surplus embryos for embryologist training and the improvement of assisted reproductive techniques.	The willingness of infertile couples toward surplus embryos in Canada
23	Kato, 2014[26]	Japan	To understand the process by which Japan women's efforts are neglected in embryo donation	Narrative analysis	The concept of embryo disposition changed across the process of IVF treatment, as the women's perceptions of gift transactions, led them to decide to donate embryos.	Japanese Infertile couples experience embryo donation
24	Jin *et al*, 2013[27]	China	To find out the attitudes toward surplus embryos and donations for medical research	Study with narrative interviews.	Family size was the main reason for not continuing embryo storage. The cost of storage is an important factor for those who chose embryo disposal.	Attitudes towards surplus embryos frozen in China
25	Millbank *et al*, 2013[28]	Australia	To explore the barriers to embryo donation	Interviewed study	There were several external barriers including inadequate information and support for those who wish to donate embryos to others for reproductive use, ethical-based restrictions, and current practices on donations.	Infertile couples experience embryo donation in Australia
26	Wanggren, Prag, *et al*, 2013[29]	Uppsala (Sweden)	To investigate public opinion on embryo donation.	Questionnaires	The majority of respondents (73%) gave a positive response to embryo donation. Seventy-five percent agreed that it should be possible to donate embryos to infertile couples.	Attitudes toward embryo donation in Sweden.
27	Wanggren, Alden, *et al*, 2013[30]	Sweden	To investigate the attitudes toward the donation of frozen embryos	Analytical descriptive study through questionnaires	Seventy-six percent supported donating surplus embryos to other infertile couples.	Infertile couple's attitudes towards embryo surplus donation in Sweden

Table 1. Data extraction from individual studies (continued).

No.	Author & year of publication	City/Country	Purpose	Data collection	Key findings	Research focus/Domain
28	Veerle Provoost *et al*, 2012b [31]	Belgium	To illustrate the concept of frozen stored embryos identified as symbols of one's relationship (SOR)	Analytical observational study through questionnaires	Sixty-six point eight percent (n=213) agreed with the statement of frozen stored embryos as a symbol of one's relationship (SOR), while 12.2% (n=39) disagreed. Of the patients who viewed their embryos as SOR, only 22.5% were willing to consider donating to others for reproduction, compared to 53% of women without such views (P<0.001). Regarding donations to science, significantly more patients without SOR views (87.2%) were willing to consider donations compared to (65.1%) of patients with SOR display (P=0.018).	Infertile couples' attitudes toward frozen stored embryos identified as a symbol of one's relationship (SOR) to embryo donation in Belgium
29	V Provoost *et al*, 2012[32]	Belgium	To find out how patients respond to up embryo disposal decisions (EDDs)	A retrospective analysis	The increasing trend in decisions to discard became a negative trend with the introduction of donations to research (1997). Since then donations to research have become the most popular choice and its popularity has increased over time	Trends in infertile couples on embryo disposal decisions (EDD) in Belgium
30	Takahashi *et al*, 2012[5]	Tokyo (Japan)	To find out how patients make decisions about their frozen stored embryos	In-depth interview	A model of the patient's decision-making process consists of five steps: 1) a moratorium on embryo transfer is maintained, 2) "Mottainai"-embryos (as having another child by embryo transfer in the future) and having other children considered; 3) cost was taken into account; 4) before a final decision was made, the partner's opinion on continued storage is confirmed 5): the effect of donation.	Decision-making process on surplus frozen storage embryos in infertile couples in Japan.
31	Veerle Provoost *et al*, 2012a [33]	Belgium	To find out how patients decide embryo disposition decisions	Descriptive, analytical study with an anonymous questionnaire	The majority of patients who do not want to continue storing their embryos (87.9%) reported that sufficient information was provided to make a decision. Of the patients who did not want to continue storage, 50.8% decided to donate embryos to science, 27.1% decided to dispose of them, and 16.1% wanted to donate for reproduction.	Information obtained and related to embryo disposition decision (EDD) in infertile couples in Belgium
32	V Provoost, Pennings, De Sutter, Gerris, *et al*, 2011[34]	Belgium	To find out the patient's decision on frozen stored embryos	A descriptive-analytical study through questionnaires	After a period of embryo storage of at least 2 years, 40% of couples wanted to continue storing their embryos. For those who decided to stop storage (60%), the main reason was they already had the desired number of children.	Infertile couple's attitude to surplus stored frozen embryos in Belgium
33	Hill & Freeman, 2011[35]	Tennessee (USA)	To compare embryonic disposition decisions in autologous and donor-recipient oocyte patients.	A retrospective study	Attitudes of infertile patients with autologous oocytes and oocyte donor recipients to surplus embryos in the United States	Attitudes of infertile patients with autologous oocytes and oocyte donor recipients to surplus embryos in the United States
34	V Provoost, Pennings, De Sutter, & Dhont, 2011[36]	Belgium	To compare the perception of accepted services and decisions on embryonic disposition.	Descriptive analytical study with questionnaires	Half of the Dutch patients want to continue storing their embryos compared to a third of Belgian patients.	Differences in the attitudes among couples from Belgium and couples from the Netherlands who were infertile to the decision of embryo disposition.
35	Lyerly *et al*, 2011[37]	USA	To identify predictor factors and correlation of decision conflict in embryonic disposition decisions	Descriptive analytical study	High decisional conflict associated with thinking about future childcare [adjusted odds ratio (aOR)=3.93, P<0.001 and aOR =1.69, P=0.04, respectively], thawed embryos and discarded embryos (aOR=2.08, P<0.0 donations for research (aOR= 1.66, P=0.01) or frozen hold 'forever' (aOR=1.90, P=0.01).	Conflicting decisions and disposition of embryos in infertile couples in the United States
36	Frith *et al*, 2011[38]	USA	To describe the experience of couples who choose to release bryos through the embryo adoption program.	A qualitative explorative study	The factors that contributed to the embryo 'adoption' progr were how the embryo was perceived; dislike of the alternative disposition options available; concepts of parental responsibility and the desire to 'openly' share information between the patient and the embryo recipient's partner.	The views of couples who chose to relinquish their embryos conditionally through an embryo 'adoption' program in the United States
37	Sharma *et al*, 2011[39]	San Francisco, California (USA)	To find out ethnic differences donating embryos for research.	A retrospective study	Asians were more likely than Caucasians to dispose of embryos and less likely to donate to another partner (P=0.02) or research (P< 0005).	Infertil uples' attitudes towards embryo donation in the United States

Table 2. Country of origin, study design and methods of the included studies.

Country of origin	*n*	Study design	*n*	Methods	*n*
United States of America	8	Cross-sectional	16	Questionnaire	21
Belgium	5	Qualitative-descriptive	7	Interview	8
Portugal	2	Retrospective	5	In-depth semistructured interview	7
Iran	2				
Canada	3	Qualitative	5	Medical record	4
Japan	3	Cohort	3		
China	3	Randomized trial	1		
Others	11				

Table 3. Option, reason, factor, and barrier that influence decision/attitude.

Option, reason, factor, and barrier
Option and reason that influence decision/attitude
1. Embryo donation for reproductive purposes Did not want the embryos to be discarded; Did not want the embryos to be discarded and felt that donating to other couples was better than research/manipulation of an embryo; Wanted to help other infertile couples achieve parenthood[2,4,19,20,22,24,26,28–30,33,35,7,37,38,8–10,12,15,16,18].
2. Embryo donation for research purposes Did not want the embryos to be discarded; Did not want the embryos to be discarded and felt that the research option was better than donating to other couples; Wanted to help other patients with diseases for which cure can be found through stem cell technology[4,8,22–25,28,33,35,37,38,11,12,14–16,18–20].
3. Continuing to keep the frozen embryo The conceptualization of embryos as "children", a "baby" or a "living being"; The need to transfer the cryopreserved embryos; Still deciding if they would have second children with these embryos; To find intending parents for them[8,15,16,19,27,34–38].
4. Embryo disposition Do not want more siblings created after donating to other couples; Do not want manipulations of embryos; The child from donated embryos would trace back genetic parents creating legal/social issues in future; Religious or cultural reasons; Satisfaction with family size; Financial constraints limiting future embryo transfer[4,8,33–35,37,38,12,15,16,18,19,27,28,30].
Factors that influence decision/attitude
1. Reproductive and gynecological history
2. Sociodemographic and age characteristics
3. Storage length
4. Embryo status
5. Helping others than wasting embryos
6. Research interest
7. Family planning
8. Cost
9. Partner opinion
The barrier that influences decision/attitude
1. Unmet information related to donation or disposition
2. Unmet communication need at the level of clinician or fertility clinic provider
3. Unmet wish to donate concerning prohibited by-laws

3.2.3. Embryo disposition

There were ten studies discussing embryo disposition. These studies come from Canada, the USA, Belgium, China, Japan, and Australia. In a study conducted in the United States (n=615), the choice to dispose of the embryos was 50.5%, which was higher in female patients who are less than 30 years old[2]. Meanwhile, in Canada (n=131), the study showed that the percentage of the population that would dispose of surplus embryos was 37%[18]. In Belgium (n=200), 87.9% opted not to continue surplus embryo storage with 27.1% deciding to dispose of the embryos. Other studies in the United States (n=400) showed that embryos obtained from egg donors compared to autologous eggs tended to be discarded (38%). The option to discard embryos was preferred by Asians living in the United States[35,39]. In China (n=363), the study showed that 58.8% of couples chose to dispose of surplus embryos[27].

4. Discussion

These studies determine the attitude of patients or infertile couples toward excess/surplus embryos. The focus of this study is the choice made for embryo disposition that is, to store, donate or discard embryos. There was also another choice mentioned in the paper which is to re-insert the embryo into the uterus, however, it did not become a focus area in this scoping review. Studies from different countries show that most infertile couples choose to donate their surplus embryos. Some of the factors that influence this decision include a belief that it will assist in the development of science: a positive view of research, a great sense of trust in the health system, and a desire to help other infertile couples[23,40]. Further analysis shows the donation of surplus embryos for research was generally made if the couple viewed the embryo as a research sample. However, if the couples viewed the embryo as a potential human being, then it became a factor in choosing to donate for reproduction[4]. One study indicates the attitudes of those who donate embryos for reproduction can be characterized as being pragmatic and optimistic with a greater consciousness of the importance of social bonds[28]. Another study identifies the factors influencing an embryo donation program for reproduction as follows: the perception of the embryo, unwillingness to dispose of embryos or commit to its storage; a sense of responsibility as a parent for the embryos; and the

desire to engage with embryo recipients[38].

Couples who chose to continue with the storage of surplus embryos felt a sense of morality towards the embryos and the desire to save them for subsequent reproductive efforts[10,16,27]. Meanwhile, couples who wanted to dispose of embryos felt that there was: a lack of information/explanation received; a negative perception toward research; high cost of storage, and; now having the desired number of children[22,27]. One study indicates a five-stage decision-making model for frozen embryos comprising 1) a moratorium on transfer; 2) the storage embryo and having additional children are considered; 3) the cost of storage is considered; 4) the partner's opinion is confirmed on continued storage, and; 5) the effect of donation[5]. Differences in the attitudes to choices by infertile couples from each country are likely influenced by local cultural factors, applicable rules, ethical views, and information received. In China, embryo donation is preferred most likely due to sociocultural public perceptions[14]. In Australia, the regulations and practices regarding embryo donation are still lacking[28]. Whereas, in Belgium, there is a perception that embryos are a symbol of a relationship with a partner, which causes difficulties in making choices to dispose of surplus embryos with consequent guilty feelings and regrets[31]. Emotional conflicts in the decision-making for surplus embryos occur in 39% of couples in the USA[37]. There were nine studies that had participation rates below than 90%[11,18,29-31,33,34,36,37] and most of them used descriptive-analytical study method[18,29-31,33,34,36,37]. The results of this review can provide case studies, knowledge, and consideration for fertility experts on establishing a policy toward surplus embryos in their clinical setting.

There were limitations and weaknesses in most of the reviewed studies, such as the participation rate of the sample was still very low and had not reached greater than >90% of the total samples. This certainly affected the aggregate picture of these study results because not all subjects provided information regarding attitudes to choices for surplus embryos disposition. Most studies with descriptive-analytical methods also might influence the analysis of the result, because decisions and attitudes were longitudinal and might change over time during the storage of the embryos.

In conclusion, most infertile couples chose to donate surplus embryos for research and reproduction. In the future, more multinational cohort research with a subject participation rate above >90% is needed to be able to better understand the aggregated picture of couples' attitudes toward surplus embryos.

Conflict of interest statement

The authors declare there is no conflict of interest.

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Authors' contributions

Agung Dewanto provided the definition, concept, and design of intellectual material. Investigation, literature search, and data analysis were all done by I Gusti Agung Ngurah Agung Sentosa and Sarrah Ayuandari. I Gusti Agung Ngurah Agung Sentosa, Sarrah Ayuandari, Rafhani Rosyidah, and Agung Dewanto wrote, edited, and reviewed the paper.

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