

# Factors associated with the donation and non-donation of embryos for research: a systematic review

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**BACKGROUND:** Systematic knowledge on the factors that influence the decisions of IVF users regarding embryo donation for research is a core need for patient-centred policies and ethics in clinical practice. However, no systematic review has been provided on the motivations of patients who must decide embryo disposition. This paper fills this gap, presenting a systematic review of quantitative and qualitative studies, which synthesizes the current body of knowledge on the factors and reasons associated with IVF patients' decisions to donate or not to donate embryos for research.

**METHODS:** A systematic search of studies indexed in PubMed, ISI WoK and PsycINFO, published before November 2013, was conducted. Only empirical, peer-reviewed, full-length, original studies reporting data on factors and reasons associated with the decision concerning donation or non-donation of embryos for research were included. Eligibility and data extraction were performed by two independent researchers and disagreements were resolved by discussion or a third reviewer, if required. The main quantitative findings were extracted and synthesized and qualitative data were assessed by thematic content analysis.

**RESULTS:** A total of 39 studies met the inclusion criteria and were included in the review. More than half of the studies ( $n = 21$ ) used a quantitative methodology, and the remaining were qualitative ( $n = 15$ ) or mixed-methods ( $n = 3$ ) studies. The studies were derived mainly from European countries ( $n = 18$ ) and the USA ( $n = 11$ ). The proportion of IVF users who donated embryos for research varied from 7% in a study in France to 73% in a Swiss study. Those who donate embryos for research reported feelings of reciprocity towards science and medicine, positive views of research and high levels of trust in the medical system. They described their decision as better than the destruction of embryos and as an opportunity to help others or to improve health and IVF treatments. The perception of risks, the lack of information concerning research projects and the medical system and the conceptualization of embryos in terms of personhood were the most relevant motives for not donating embryos for research. Results relating to the influence of sociodemographic characteristics and reproductive and gynaecological history were mostly inconclusive.

**CONCLUSIONS:** Three iterative and dynamic dimensions of the IVF patients' decision to donate or not to donate embryos for research emerged from this review: the hierarquization of the possible options regarding embryo disposition, according to the moral, social and instrumental status attributed to embryos; patients' understanding of expectations and risks of the research on human embryos; and patients' experiences of information exchange and levels of trust in the medical-scientific institutions.

**Key words:** embryo disposition / human embryo research / *in vitro* fertilization / assisted reproductive technologies / systematic review

## Introduction

Research on human embryos, and in particular on embryonic stem cells (hESCs), has engendered promising results and high expectations in society, but also controversial issues in ethics, practices and policies (Vayena et al., 2002; UNESCO, 2008; European Science Foundation, 2013). The development of innovative clinical solutions aiming to improve public and individual health is expected (Lancet, 2013), with eventual impact on the levels of satisfaction and confidence among both caregivers and patients (Genuis, 2008). The value of recent achievements through research on hESCs for neurodegenerative disorders (Marchetto et al., 2010), transplants onto damaged human corneas (Hanson et al., 2013) or organ transplantation (Elliott et al., 2012), is widely recognized. However, differences in national and transnational laws and policies on human embryo research have given rise to reflections concerning the governance of global flows of embryos, scientists and capital (Zaraczny and Caulfield, 2009; Salter and Faulkner, 2011; Salter and Salter, 2012; Nielen et al., 2013). Critical approaches also focus on issues related to the management of institutional and individual responsibilities and the protection of human rights, namely in the following domains: status and protection of human embryos (Mulkay, 1997; Leist et al., 2008; Zaraczny and Caulfield, 2009); lack of public involvement in decision-making regarding funding for hESC research (Árnason et al., 2007) and in regulation of the information conveyed by the media in this process (NHS, 2011; Vicsek, 2011); and dissemination of unrealistic expectations concerning the results of research on human embryos (Burns, 2009).

The legal and regulatory landscape on human embryo research was recently analysed by the European Science Foundation (2013), the European Society of Human Reproduction and Embryology (ESHRE, 2013) and the International Federation of Fertility Societies (International Federation of Fertility Societies (IFFS), 2013). Considering the 58 countries with coherent data on national policies or guidelines regarding research on human embryos in these three sources of information, more than one-third ( $n = 22$ ) bans such research, and 19 countries permit research only on surplus IVF embryos, prohibiting the creation of embryos solely for research purposes. Six countries allow the creation of human embryos for research purposes, while four permit research only on imported embryos. The remaining seven countries have no legislation on human embryo research.

Responsible governance of hESC research needs to find a balance between expectations and controversies, empirically grounded on the assessment of the moral and ethical spectrum involving both scientists and stakeholders (European Science Foundation, 2013) and the public (Etchegary et al., 2013), in particular those people who must make embryo disposition decisions. Listening to the patients' voice is a core need for patient-centred policies on hESC research, as they are key actors in this research practice (WHO, 2007; Dancet et al., 2010; European Commission, 2012).

Existing literature reviews on the factors that influence the decisions of couples to donate embryos, both for research and to other couples, are not systematic reviews. The review authored by de Lacey (2013) mainly focuses on the perception of the embryo status and its implications for counselling, while Hug (2008) only provides information about studies published between 2002 and 2007, with a more specific focus on prospective donors and their motivation to donate or not to donate cryopreserved embryos for medical research. Additionally, these reviews did not identify essential dimensions involved in the decision-making process concerning embryo donation for research. This could serve as a relevant tool for future research and policy on hESCs, allowing the comparison of real-world decisions among different cultural, economic and political contexts.

We aimed to synthesize the current body of knowledge about the motivations of IVF patients to donate or not to donate embryos for research, by providing a systematic review on the factors and reasons associated with such a decision.

## Methods

We followed the PRISMA principles and our reporting complies with this approach (Moher et al., 2009). Qualitative data analysis followed the main guidance for qualitative research and Cochrane reviews, by the Cochrane Qualitative Research Methods Group (Noyes et al., 2008), and a protocol for content analysis (Stemler, 2001) and for thematic analysis (Mays et al., 2005). A review protocol was developed in advance.

## Search strategy

A search of the publications on three electronic databases (PubMed, ISI WoK and PsycINFO) was undertaken in November 2013, with no restriction set for language or time of publication, using the MeSH term 'embryo

disposition', which was adapted according to the requirements of each database (e.g. PubMed syntax: (embryo disposition[mh] OR 'embryo disposition') NOT (Animals[mh] NOT Humans[mh])). Embryo disposition was introduced as a MeSH term in 1999, defined as the 'utilization or disposal of an embryo that is fertilized but not immediately transplanted and resulting course of action'. The search was followed by reference tracking, examining the references of the selected publications based on full-text assessment.

## Study selection

The inclusion criteria allowed only empirical, peer-reviewed, original full-length studies that: (i) reported the proportion of IVF patients (couples or individuals) who agreed to donate embryos for research; or (ii) assessed factors associated with the decision concerning donation of embryos for research; or (iii) explored the reasons reported by IVF patients to justify their decision regarding the donation or non-donation of embryos for research.

The exclusion criteria disallowed: studies focusing on donation to other couples, studies of the ethical or legal issues surrounding embryo donation to research or medical procedures, as well as studies about the decision to continue/discontinue storage. Non-original full-length studies (reviews, meta-analyses, comments, editorials, notes, newspapers articles, conference proceedings, reports and guidelines) were also excluded.

## Screening and quality assessment

The first two authors (C.S. and M.P.) independently screened all the papers retrieved initially, based on the title and abstract, and afterward, based on the full-text; this was crosschecked in both phases. The study selection was guided by the research question, inclusion/exclusion criteria and consensus by both authors. Agreement was reached > 92% of the time. Disagreement was solved by joint discussion until consensus could be reached or, when consensus was not achieved, by the assessment of a third author (S.S.), based on the implementation of the same inclusion and exclusion criteria defined for study selection.

Quality assessment on the included articles was based upon the protocol recommended by the Cochrane Database of Systematic Review. It was grounded on the following criteria, according with the characteristics and objectives of this review: (i) Database: studies should be peer-reviewed and be available in an electronic database; (ii) Selection of participants: study participants should be clearly defined as couples or individuals who have been involved in an IVF treatment and have effectively or hypothetically decided about embryo donation or non-donation for research; (iii) Outcome measurements: they should include values of statistical significance in quantitative studies, and research questions in qualitative studies; and (iv) Study methodology: the methods should be clearly described in sufficient detail, including the recruitment of participants, method, time of assessment and outcome measures.

## Data abstraction

A standardized data extraction sheet was developed and completed by two independent researchers (C.S. and M.P.), including both quantitative and qualitative data. Descriptive data for the characterization of studies included: information about the authors and publication year; type of methodology (quantitative, qualitative and mixed-methods); period of data collection, country and setting where the study was developed; sample size; and time of assessment (categorized as 'pre-decision' and 'post-decision', the latter being when patients had already formalized their decision on embryo disposition, or both pre- and post-decisions).

Data concerning the proportion of patients who agreed to donate embryos for research (in percentage) were gathered only from quantitative studies. Specific choices were made: (i) in longitudinal studies, where data from the last evaluation were extracted; and (ii) when the response

options included mutually exclusive categories, where all the proportions were retrieved and added up.

Quantitative data on variables whose association with embryo donation for research was statistically tested were retrieved and the directions of the associations were registered. Whenever adjusted Odds Ratios (ORadj) were provided, these were extracted.

Based on the protocol for content analysis developed by [Stemler \(2001\)](#), the first two authors analysed, independently, all the studies presenting data about the reasons to donate or not to donate embryos for research, aiming to identify, quotation by quotation, all the reasons reported by IVF patients to justify their decision. These quotations were synthesized into categories, defined as 'a group of words with similar meaning and connotations', by the first and the last authors (C.S. and S.S.), and the number of papers where each category emerged was recorded. Such categories were then grouped into three main themes by C.S. and S.S., according to the protocol for thematic analysis developed by [Mays et al. \(2005\)](#): 'sociotechnical context', which included the IVF patients' understanding of science, technology and medicine, and the leading values in the doctor-patient relationship; 'societal benefits', when quotations pointed out the advantages of research on human embryos for the society, for IVF patients, and for individuals; and the 'views about embryos' where the reasons included references to their moral status and quality, as well as to the hierarchization of the fates of embryos. Disagreements in abstractions were discussed and resolved by consensus. An almost perfect strength of agreement between reviewers was achieved (>0.80) ([Stemler, 2001](#)).

## Results

### Search strategy and study selection

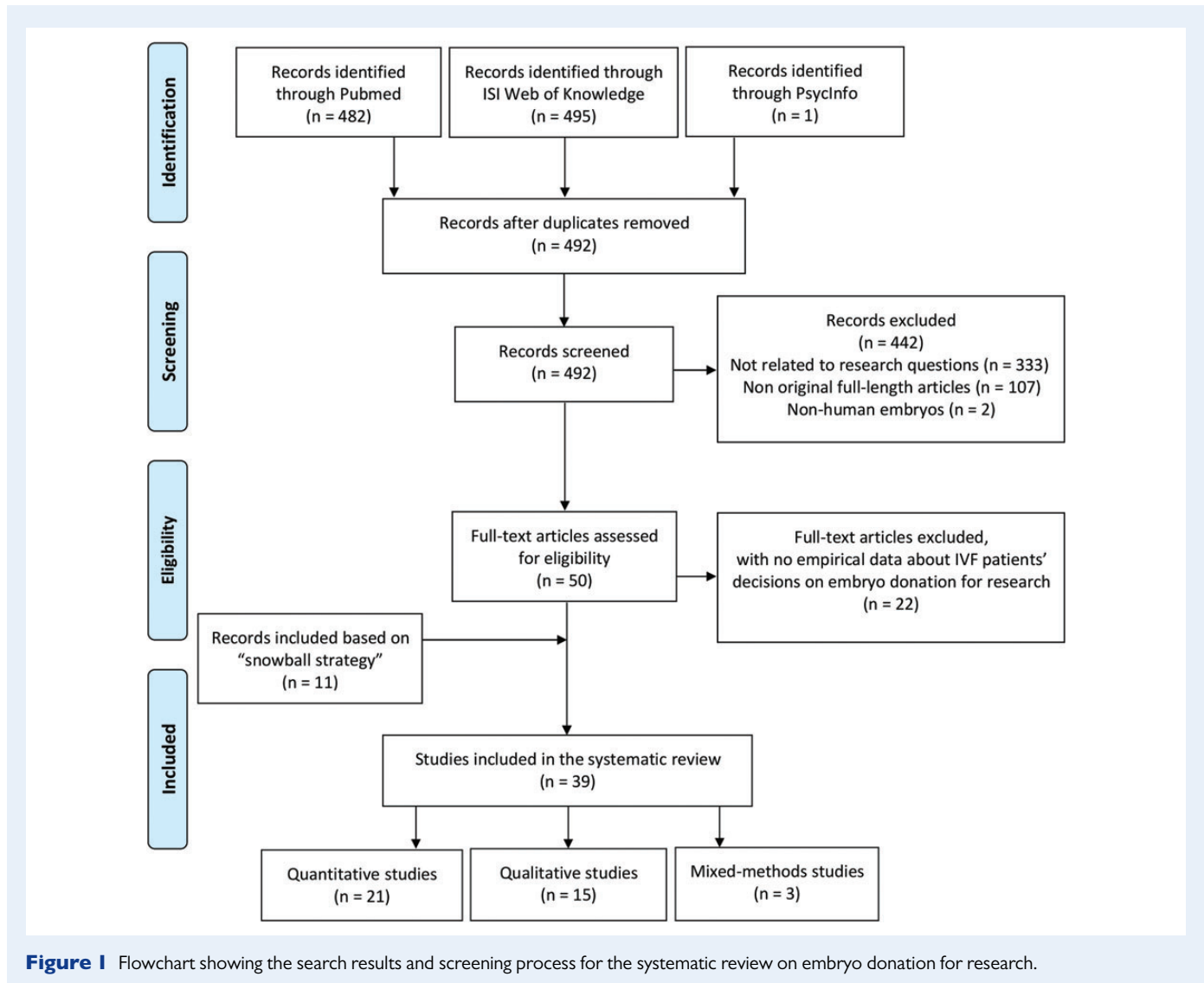
The titles of 978 records were initially screened. The search included publications dating from 1985 until November 2013. After the removal of the duplicates ( $n = 486$ ), 492 records were examined. This led to the exclusion of 442 records based on title and abstract assessment, mainly because they were neither related to the research questions nor original full-length studies. Of the 50 fully read papers, 28 met the inclusion criteria. After the reference tracking, 11 papers were included and the final systematic review was composed of 39 papers, published between 1995 and 2012. The screening process is summarized in the study flowchart (Fig. 1).

### Study characteristics

The main characteristics of the 39 studies included can be found in Table 1. Studies were grouped by type of methodology and ordered by the year of publication.

#### Research design

More than half of the studies ( $n = 21$ ) used a quantitative methodology, 15 used a qualitative approach and 3 used mixed-methods. In quantitative studies, 13 used questionnaires to collect data ([Lornage et al., 1995](#); [Asensio et al., 2001](#); [McMahon et al., 2003](#); [Bangsboll et al., 2004](#); [Burton and Sanders, 2004](#); [Hammarberg and Tinney, 2006](#); [Karpel et al., 2007](#); [Mohler-Kuo et al., 2009](#); [Lyerly et al., 2010, 2011](#); [Provoost et al., 2011, 2012a, b](#)), and 8 used medical records, including consent forms ([Choudhary et al., 2004](#); [Newton et al., 2007](#); [Luna et al., 2009](#); [Van Voorhis et al., 2009](#); [Lanzendorf et al., 2010](#); [Hill and Freeman, 2011](#); [Sharma et al., 2011](#); [Provoost et al., 2012c](#)). All the qualitative studies relied on semi-structured and in-depth interviews ([Lyerly et al., 2004, 2006](#); [Parry, 2006](#); [Fuscaldo and Gillam, 2007](#); [Haimes and Taylor,](#)



**Figure 1** Flowchart showing the search results and screening process for the systematic review on embryo donation for research.

2009; Kufner et al., 2009; Melamed et al., 2009; Peddie et al., 2009; Provoost et al., 2009, 2010; Mitzkat et al., 2010; Nachtigall et al., 2010; Frith et al., 2011; Kato and Sleebloom-Faulkn, 2011; Takahashi et al., 2012). Focus groups were also used in two cases (Parry, 2006; Fuscaldo and Gillam, 2007). Mixed-methods studies used a questionnaire, an informed consent document and a psychological interview (Laruelle and Englert, 1995); in-depth interviews in a narrative style, followed by statistical analysis (Jin et al., 2013); and qualitative and quantitative interviews (Zweifel et al., 2007). Regarding the outcomes under analysis in this review, 23 papers had reliable information on the proportion of IVF patients who agreed to donate embryos for research; 18 provided quantitative information on the factors associated with such a decision; and 22 provided information about the reasons underlying the decision to donate and not to donate embryos for that purpose (Supplementary data, Table SI).

#### Country of study origin

Empirical studies about the proportion of embryo donation for research or its associated factors, or reported reasons underlying IVF patients' decision derived from 13 countries: USA ( $n = 11$ ), Belgium ( $n = 7$ ), Australia ( $n = 4$ ), UK ( $n = 4$ ), China ( $n = 2$ ), France ( $n = 2$ ), Japan ( $n = 2$ ),

Spain ( $n = 2$ ), Brazil ( $n = 1$ ), Canada ( $n = 1$ ), Denmark ( $n = 1$ ), Germany ( $n = 1$ ) and Switzerland ( $n = 1$ ).

#### Setting

Most of the 39 studies were performed in University Hospitals ( $n = 22$ ). Ten studies were performed in private clinics, 1 in a public centre, 1 in a fertility clinic, 2 in mixed centres (private and public), and 3 did not mention the setting. Two studies gathered data from various centres: Mohler-Kuo et al. (2009) presented data from 11 of the 19 Swiss IVF centres in existence in 2004 and Lyerly et al. (2010) reported data from 9 fertility clinics operating in the USA between June 2006 and July 2007.

#### Sample size

In quantitative studies sample sizes varied from 149 individual patients (Lanzendorf et al., 2010) to 2334 couples (Provoost et al., 2012c). In qualitative studies, the samples varied from 5 women (Mitzkat et al., 2010) to 184 participants (110 women and 74 men) (Nachtigall et al., 2010); and in mixed-methods studies, there were from 45 couples (Zweifel et al., 2007) to 363 couples (Jin et al., 2013). In the total of

**Table 1** Main characteristics of the included studies in the systematic review on embryo donation for research: period of data collection, country, setting, sample size and time of assessment (*n* = 39).

Authors, year of publication	Period of data collection	Country	Setting	Sample size	Time of assessment (pre/post decision)
Quantitative studies					
Lornage <i>et al.</i> (1995)	1987–1992	France	Public centre	145 couples	Pre
Van Voorhis <i>et al.</i> (1999)	NR	USA	University hospital	365 patients	Post
Asensio <i>et al.</i> (2001)	2000	Spain	University hospital	89 couples	Pre
McMahon <i>et al.</i> (2003)	NR	Australia	Private clinic	152 women; 123 men	Pre
Bangsboll <i>et al.</i> (2004)	NR	Denmark	University hospital	207 couples	Pre
Burton and Sanders (2004)	May 03	Australia	Private clinic	235 couples	Pre
Choudhary <i>et al.</i> (2004)	Jan-Feb 02; Mar-Dec 03	UK	Mixed	300 couples	Post
Hammarberg and Tinney (2006)	Jan 02–Jun 03	Australia	Private clinic	88 women; 35 couples	Post
Karpel <i>et al.</i> (2007)	Oct 04	France	University hospital	84 couples	Pre/post
Newton <i>et al.</i> (2007)	2002–2005	Canada	University hospital	88 couples	Post
Luna <i>et al.</i> (2009)	NR	Spain	University hospital	236 couples	Post
Mohler-Kuo <i>et al.</i> (2009)	Mar and Dec 04	Switzerland	NR	458 men; 468 women	Pre
Lanzendorf <i>et al.</i> (2010)	Jan 02–Jul 07	USA	University hospital	149 patients	Post
Lyerly <i>et al.</i> (2010)	Jun 06–Jan 07	USA	Private clinic	795 women; 225 men	Pre
Hill and Freeman (2011)	Jan 98–Dec 08	USA	Private clinic	364 patients	Post
Lyerly <i>et al.</i> (2011)	Jun 06–Jan 07	USA	Private clinic	786 women; 219 men	Pre
Provoost <i>et al.</i> (2011)	NR	Belgium	University hospital	326 couples	Pre/post
Sharma <i>et al.</i> (2011)	May 08–Apr 09	USA	University hospital	400 patients	Post
Provoost <i>et al.</i> (2012a)	NR	Belgium	University hospital	200 women	Post
Provoost <i>et al.</i> (2012b)	NR	Belgium	University hospital	326 couples	Pre/post
Provoost <i>et al.</i> (2012c)	1992–2006	Belgium	University hospital	2334 couples	Pre/post
Qualitative studies					
Lyerly <i>et al.</i> (2004)	NR	USA	University hospital	31 women; 7 couples	Pre
Lyerly <i>et al.</i> (2006)	Sept 02 – May 04	USA	University hospital	31 women; 8 men; 7 couples	Pre
Parry (2006)	Jun 01	UK	Fertility clinic	50 participants <sup>a</sup>	Pre
Fuscaldo and Gillam (2007)	Apr–Sept 04	Australia	Mixed	11 men; 31 women	Pre
Haimes and Taylor (2009)	2005–2006	UK	Private clinic	30 couples	Post
Kufner <i>et al.</i> (2009)	2005	Germany	University hospital	9 women; 9 men	Pre
Melamed <i>et al.</i> (2009)	NR	Brazil	Private clinic	50 couples	Pre
Peddie <i>et al.</i> (2009)	Aug 07–Jan 08	UK	University Hospital	15 couples	Pre/post
Provoost <i>et al.</i> (2009)	May–Jul 06	Belgium	University hospital	7 couples; 11 women	Pre
Mitzkat <i>et al.</i> (2010)	NR	China	Private clinic	5 women	Post
Nachtigall <i>et al.</i> (2010)	NR	USA	Private clinic	110 women; 74 men	Post
Provoost <i>et al.</i> (2010)	NR	Belgium	University hospital	7 couples; 11 women	Pre
Frith <i>et al.</i> (2011)	Sept 08–Dec 09	USA	NR	18 couples; 7 women	Post
Kato and Sleeboom-Faulkn (2011)	2006–2008	Japan	NR	40 women; 18 men	Pre
Takahashi <i>et al.</i> (2012)	NR	Japan	University hospital	10 women	Pre/post
Mixed-methods studies					
Laruelle and Englert (1995)	NR	Belgium	University hospital	200 couples	Post
Zweifel <i>et al.</i> (2007)	Aug 04–May 05	USA	University hospital	45 couples	Post
Jin <i>et al.</i> (2013)	Jan–Apr 12	China	University hospital	363 couples	Pre

NR, not referenced.

<sup>a</sup>This study included five focus groups and seven interviews, in a total of 50 participants. Data were retrieved from the focus groups with fertility support groups.



the 39 papers, samples were composed mostly of couples ( $n = 17$ ), followed by samples of both women and men ( $n = 8$ ), couples and women/men ( $n = 6$ ), and only women ( $n = 3$ ). In five studies, the gender of the participants is not specified.

Time of assessment

Almost half of the studies ( $n = 18$ ) used pre-decision information, 15 studies used post-decision information and 6 studies combined pre- and post-decision information. The majority of studies ( $n = 36$ ) were cross-sectional. Studies by Lornage et al. (1995), Newton et al. (2007) and Provoost et al. (2012c) evaluated more than one moment in time.

Proportion of IVF patients who agreed to donate embryos for research

Figure 2 presents the proportions of IVF patients who donated embryos for research retrieved from the 8 quantitative studies which assessed the proportion of donation through a dichotomic answer (yes or no to donation for research). In these studies, proportions of donation to research varied from 10% in a study conducted in the USA between 1998 and 2008 (Hill and Freeman, 2011) to 73% in a Swiss study based on data collected in 2004 (Mohler-Kuo et al., 2009). Proportions varied among studies conducted in the same country and published in the same or contiguous years in the cases of the USA and Australia. In the USA, the studies published in 2010 and 2011 presented proportions between 10% (Hill and Freeman, 2011) and 50% (Lyerly et al., 2011). In Australia, two papers published in 2003 and 2004 presented proportions from 27% (Burton and Sanders, 2004) to 44% (McMahon et al., 2003).

Figure 3 presents the proportions of IVF patients who donated embryos for research retrieved from 12 quantitative studies where these proportions were assessed through the hierarquization of the

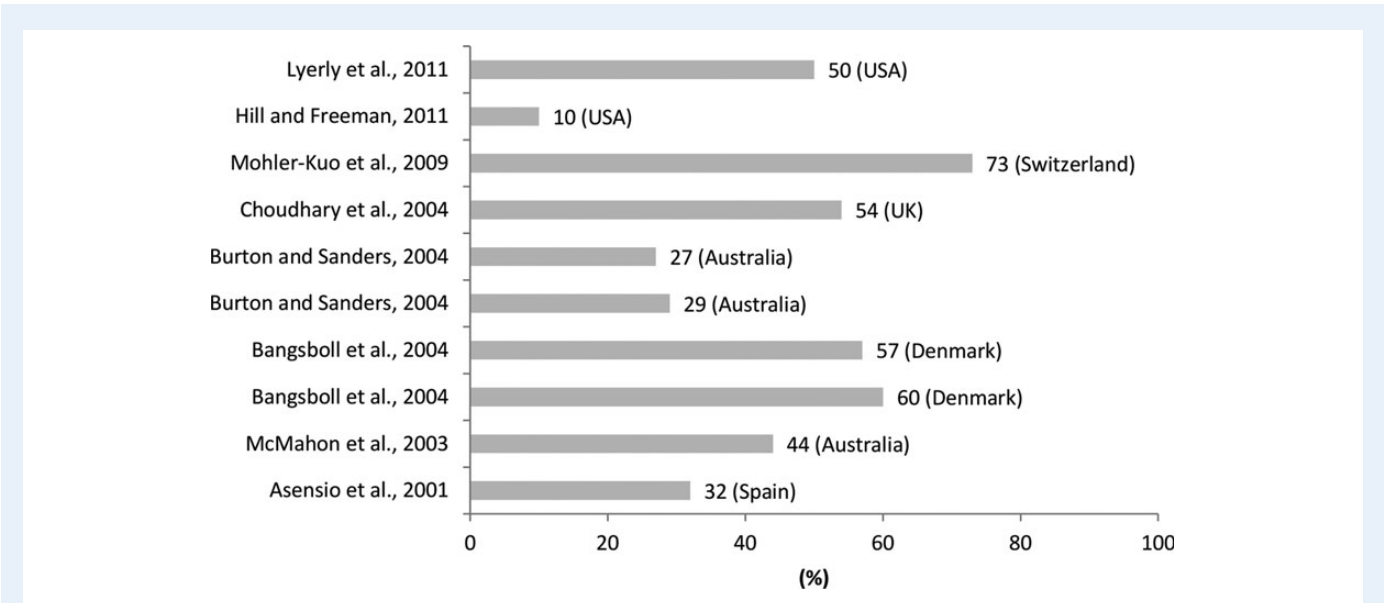
available options for embryo disposition. Proportions of donation to research in these studies varied from 7% in a study conducted in France between 1987 and 1992 (Lornage et al., 1995) to 59% in a study developed in the USA from 2002 to 2007 (Lanzendorf et al., 2010). Two studies conducted in Belgium, both published in 2012, presented proportions of 26% in a study collecting information about embryo disposition over 15 years (Provoost et al., 2012c) and 51% in a study best described as cross-sectional (Provoost et al., 2012a).

Proportions were extracted by using as the denominator all the participants who answered the question about embryo disposition in each study. Two proportions were retrieved from the studies that presented results regarding the donation of embryos for research stratified by 'research to improve techniques' and 'stem-cell research' (Burton and Sanders, 2004) and 'infertility research' and 'stem cell research' (Bangsboll et al., 2004).

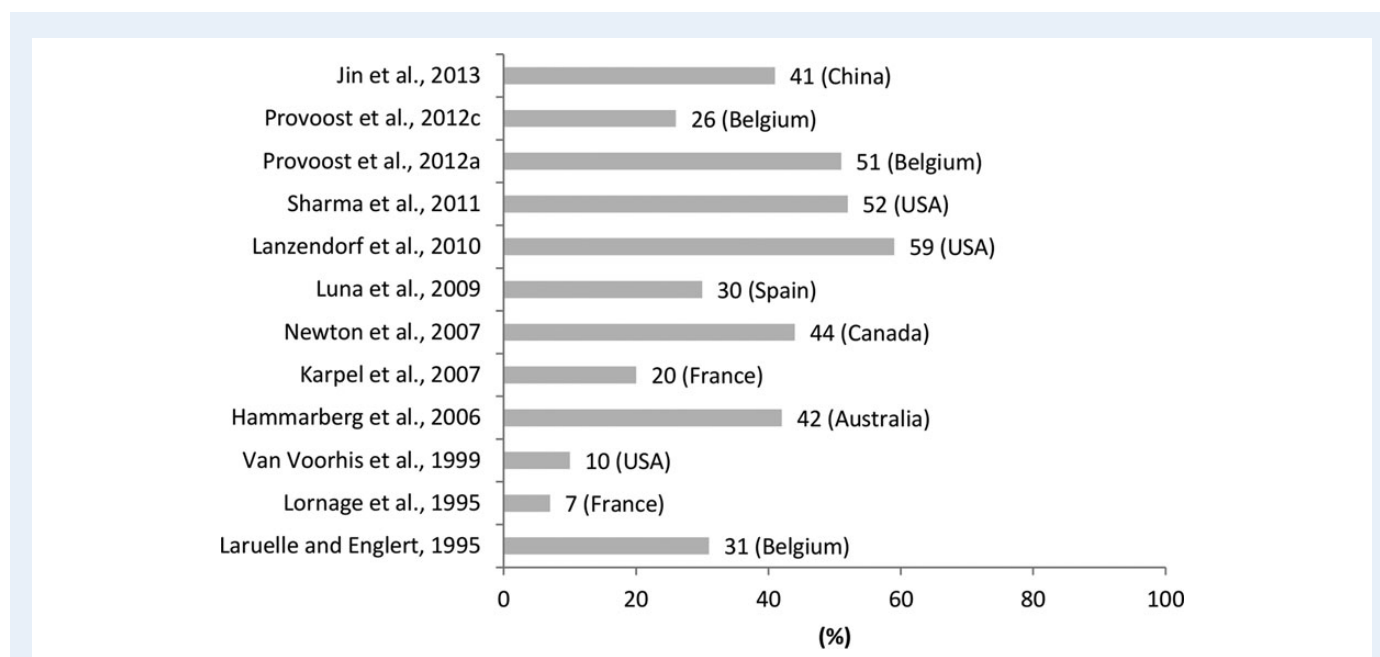
The sum of all proportions is presented when the response options included mutually exclusive categories regarding donation of embryos for research: 'a possible decision' and 'a likely decision' (McMahon et al., 2003); 'yes, in principle' and 'yes, with some restrictions' (Mohler-Kuo et al., 2009); 'donation and experimentation' and 'experimentation' (Laruelle and Englert, 1995). Because of the fact that articles by Lyerly et al. (2010, 2011) and Provoost et al. (2011, 2012a, b) were based on the same sample, only the overall proportion of non-stratified results was extracted from one paper (Lyerly et al., 2011; Provoost et al., 2012a).

Factors associated with the donation and non-donation of embryos for research

The quantitative synthesis of the factors associated with the decision to donate or not to donate embryos for research is presented in Table II.



**Figure 2** Proportion of IVF patients who agreed to donate embryos for research, in the studies where the proportion was estimated through a dichotomic answer (yes/no to donation for research). Notes: Two proportions were retrieved from the studies that presented results stratified by 'donation to research to improve techniques' (29%) and 'stem-cell research' (27%) (Burton and Sanders, 2004) and 'infertility research' (60%) and 'stem cell research' (57%) (Bangsboll et al., 2004). The proportion of donation to research, in Hill and Freeman (2011), was calculated by adding the absolute frequencies of participants who agreed to donate to research in two groups of patients: 'patients using autologous oocytes' (41 out of 364) and 'donor oocyte recipients' (6 out of 110), which was divided by the total number of participants ( $n = 474$ ). Proportions are rounded to units.



**Figure 3** Proportion of IVF patients who agreed to donate embryos for research, in the studies where the proportion was assessed through the hierarchization of the possible options for embryo disposition. Note: Proportions are rounded to units.

Factors related with reproductive and gynaecological history and socio-demographic characteristics were more frequently addressed, followed by other factors such as storage length and perception of embryo status.

The donation of embryos for research was consistently less frequent among IVF patients who conceptualized embryos in terms of personhood, a life or as having a high moral status, or among those who viewed embryos as a symbol of the relationship of the couple. The donation of embryos for research was also associated with: the country of birth (being an Asian born inside the USA versus an Asian born outside the USA); giving a high importance to altruism in the decision about embryo disposition; a higher decisional conflict; a joint decision by partners; and having an interest in participating in clinical research. There were no statistically significant associations between the decision to donate or not to donate embryos for research and the duration of infertility, numbers of previous cycles, types of treatment, parity, types of funding, concerns about family/finances, or consultation with someone other than the partner regarding the decision.

Results about the decision to donate or not donate with regard to having children or not, the number of embryos, the use of homologous/heterologous techniques, unsuccessful cycles, age, education levels, religion beliefs, ethnicity and embryo storage lengths were contradictory.

However, 14 out of 22 variables were assessed once or twice, resulting in inconclusive data. Additionally, most of the quantitative studies were descriptive, which does not allow conclusions to be reached about the isolated effect of a specific variable in the decision about embryo donation or non-donation for research. Odds ratios and respective 95% confidence intervals (OR, 95% CI) for the associations between factors and the decision to donate or not to donate embryos for research were presented in four studies (Bangsbo et al., 2004; Mohler-Kuo et al., 2009; Lyerly et al., 2010, 2011). Three of them clearly stated that adjusted ORs (OR<sub>adj</sub>) were calculated, i.e. the observed associations had been adjusted for multiple confounders

(Bangsbo et al., 2004; Mohler-Kuo et al., 2009; Lyerly et al., 2011). Considering that the variables analysed with ORs were not measured in a standardized way and that the same outcome was assessed in a maximum of two studies, a meta-analysis was not conducted.

#### *Reproductive and gynaecological history*

Having children after an IVF treatment (versus no children) was predictive of donating embryos for stem cell research (OR<sub>adj</sub> = 3.80, 95% CI: 1.40–10.20) (Bangsbo et al., 2004), while having children conceived naturally was associated with donating less often for research in one study, compared with those having children from IVF or Intracytoplasmic Sperm Injection (ICSI) (OR<sub>adj</sub> = 0.60, 95% CI: 0.40–0.90) (Mohler-Kuo et al., 2009). Having had a live birth was associated with donating less frequently for research than discarding (30 versus 52%;  $P = 0.05$ ) (Newton et al., 2007). No association between the decision to donate and having (or not) IVF children was found by Choudhary et al. (2004), Hammarberg and Tinney (2006) and Lanzendorf et al. (2010). Also the decision to donate embryos for research was not influenced by whether the patients had children, regardless of being or not conceived by IVF (Burton and Sanders, 2004; Lyerly et al., 2010; Sharma et al., 2011) or being children of only one of the members of the couple (Sharma et al., 2011).

Results regarding the impact of the number of embryos were contradictory. Choudhary et al. (2004) showed that those with a higher number of embryos donate more frequently to research ( $7.25 \pm 4.91$  versus  $5.73 \pm 3.98$ ;  $P = 0.004$ ), but Provoost et al. (2012c) found the opposite association, with those with a lower number of embryos donating more (4.08 versus 4.51;  $P = 0.020$ ). No association between these variables was found by Hammarberg and Tinney (2006) and Newton et al. (2007).

Couples who used their own gametes (versus donor gametes) were more willing to donate embryos for research in one study (56.9 versus 42.9%;  $P < 0.05$ ) (Luna et al., 2009). However, another study showed that couples treated with donor (versus the husband's) sperm are

**Table II** Main findings on the factors associated with the donation of embryos for research, identified on the quantitative and mixed-methods studies ( $n = 18$ ).

Factors (number of papers)	Main findings
Reproductive and gynaecological history	
Having children ( $n = 9$ )	<p>Children after IVF treatment (versus no children): predictive of agreement to embryo donation for stem cell research (ORadj = 3.80, 95% CI: 1.40–10.20) (Bangsbo et al., 2004<sup>a</sup>)</p> <p>Children conceived naturally (versus children from IVF/ICSI): less likely to donate (ORadj = 0.60, 95% CI: 0.40–0.90) (Mohler-Kuo et al., 2009<sup>b</sup>)</p> <p>Live birth: 52% discard versus 30% donate for research (<math>P = 0.05</math>) (Newton et al., 2007)</p> <p>No association with having (or not) IVF children (Choudhary et al., 2004; Hammarberg and Tinney, 2006; Lanzendorf et al., 2010)</p> <p>No association with having (or not) previous children (Burton and Sanders, 2004; Lyerly et al., 2010; Sharma et al., 2011)</p>
Number of embryos ( $n = 4$ )	<p>Higher number of embryos: more likely to donate (<math>7.25 \pm 4.91</math> versus <math>5.73 \pm 3.98</math>; <math>P = 0.004</math>) (Choudhary et al., 2004)</p> <p>Lower number of embryos: more likely to donate (4.08 versus 4.51; <math>P = 0.020</math>) (Provoost et al., 2012c)</p> <p>No association (Hammarberg and Tinney, 2006; Newton et al., 2007)</p>
Homologous/heterologous techniques ( $n = 3$ )	<p>Couples treated with donor (versus husband sperm): more likely to donate to infertility research (OR = 1.30, 95% CI: 1.20–1.50) (Bangsbo et al., 2004<sup>a</sup>)</p> <p>Couple's own gametes (versus donor gametes): more likely to donate (56.9% versus 42.9%; <math>P &lt; 0.05</math>) (Luna et al., 2009)</p> <p>No association with donation for stem cell research (Bangsbo et al., 2004<sup>a</sup>; Sharma et al., 2011)</p>
Unsuccessful cycle ( $n = 2$ )	<p>Previous failed fertilization: less likely to donate (<math>P = 0.009</math>) (Choudhary et al., 2004)</p> <p>No association (Sharma et al., 2011)</p>
Duration of infertility ( $n = 2$ )	No association (Bangsbo et al., 2004 <sup>a</sup> ; Choudhary et al., 2004)
Number of previous cycles ( $n = 2$ )	No association (Choudhary et al., 2004; Sharma et al., 2011)
Type of treatment ( $n = 2$ )	No association (Bangsbo et al., 2004 <sup>a</sup> ; Choudhary et al., 2004)
Parity ( $n = 1$ )	No association (Sharma et al., 2011)
Sociodemographic characteristics	
Age ( $n = 8$ )	<p>Older (<math>&gt;40</math> versus <math>\leq 40</math> years old): more likely to donate to medical research (ORadj = 1.80, 95% CI: 1.10–3.00) (Mohler-Kuo et al., 2009<sup>b</sup>)</p> <p>No association (Asensio et al., 2001; Burton and Sanders, 2004; Choudhary et al., 2004; Hammarberg and Tinney, 2006; Lanzendorf et al., 2010; Sharma et al., 2011; Provoost et al., 2012c)</p>
Education level ( $n = 3$ )	<p>College and University education and Vocational School + 2 years versus mandatory/vocational school): more likely to donate (ORadj = 1.80, 95% CI: 1.10–3.00 and ORadj = 2.00, 95% CI: 1.20–3.40, respectively) (Mohler-Kuo et al., 2009<sup>b</sup>)</p> <p>No association (Hammarberg and Tinney, 2006; Jin et al., 2013)</p>
Religion beliefs ( $n = 3$ )	<p>Moderate to strong beliefs (versus not very strong beliefs): less likely to donate in both women (20 versus 42%; <math>P = 0.008</math>) and men (18 versus 41%; <math>P = 0.01</math>) (Burton and Sanders, 2004)</p> <p>Perceived (high) importance of religious principles on attitude toward reproductive medicine: less likely to donate (ORadj = 0.40, 95% CI: 0.20–0.60) (Mohler-Kuo et al., 2009<sup>b</sup>)</p> <p>No association: commitment to religion (versus non-religious) (McMahon et al., 2003)</p>
Ethnicity ( $n = 2$ )	<p>Caucasian (versus Asian): donate more (56 versus 27%; <math>P = 0.022</math>) (Choudhary et al., 2004)</p> <p>Caucasian (versus Asian): donate more (41.6 versus 57%; <math>P &lt; 0.001</math>) (Sharma et al., 2011)</p> <p>No association (Lyerly et al., 2010)</p>
Country of birth ( $n = 1$ )	Asians born outside the USA (versus Asians born inside the USA): less likely to donate (37.9 versus 57.6%; $P = 0.001$ ) (Sharma et al., 2011)
Other factors	
Storage length ( $n = 6$ )	<p>Longer periods of storage: more likely to donate (35.7% among 5–10 years, 34.9% among <math>&gt; 10</math> years versus 19.1% among <math>\leq 4</math> years; <math>P &lt; 0.05</math>) (Luna et al., 2009)</p> <p>No association (Asensio et al., 2001; Hammarberg and Tinney, 2006; Newton et al., 2007; Lanzendorf et al., 2010; Lyerly et al., 2010)</p>
Embryo status ( $n = 5$ )	<p>View of the moral status of the embryo as a cluster of cells versus life, potential child: 86.2 versus 13.6% donate to medical research and therapy (<math>P &lt; 0.05</math>) (Jin et al., 2013)</p> <p>Lower moral status to human embryos (versus higher): more likely to donate (OR = 0.69, 95% CI: 0.60–0.79) (Lyerly et al., 2010)</p> <p>Strong agree/agree with embryo as a human being (versus strong disagree/disagree): less likely to donate (ORadj = 0.30, 95% CI: 0.20–0.50) (Mohler-Kuo et al., 2009<sup>b</sup>)</p>

Continued



**Table II** *Continued*

Factors (number of papers)	Main findings
	Embryo as a child (versus others): less likely to donate (16 versus 36%; $P < 0.05$ ) (Laruelle and Englert, 1995)
Type of funding ( $n = 2$ )	Patients without the Symbol of One's Relationship (SOR) view <sup>c</sup> (versus patients with the SOR view): more willing to donate (87.2 versus 65.1%; $P = 0.018$ ) (Provoost <i>et al.</i> , 2012b)
Altruism ( $n = 1$ )	No association (Choudhary <i>et al.</i> , 2004; Sharma <i>et al.</i> , 2011)
Concerns about family/finances ( $n = 1$ )	High importance of altruism in the decision about the fate of embryos (versus less importance): more likely to donate than to discard (OR = 1.65, 95% CI: 1.47–1.85) (Lylerly <i>et al.</i> , 2010)
Consultation of others regarding the decision ( $n = 1$ )	No association (Lylerly <i>et al.</i> , 2010)
Decisional conflict <sup>d</sup> ( $n = 1$ )	No association (Provoost <i>et al.</i> , 2012a)
Joint decision ( $n = 1$ )	Higher decisional conflict (versus lower): more likely to donate embryos for research (ORadj = 1.66, 95% CI: 1.12–3.46) (Lylerly <i>et al.</i> , 2011)
Research interest ( $n = 1$ )	Joint decision made by partners (comparing with decision by woman alone/by woman after consulting man or by man after consulting woman): more often in couples who donated for science (87.9% versus 12.1%; $P = 0.014$ ) (Provoost <i>et al.</i> , 2012a)
	Interest in participating in clinical research (versus no interest): more proportion of donation (62.5% versus 31.8%; $P < 0.008$ ) (Sharma <i>et al.</i> , 2011)

OR, odds ratios; CI, confidence interval.

<sup>a</sup>Only factors associated with donation to infertility research or stem cell research were retrieved.

<sup>b</sup>Only factors associated with donation to medical research were retrieved.

<sup>c</sup>Couples were asked to take a position on the statement: 'Embryo is a symbol of the relationship between me and my partner', being the answers 'yes' or 'no/neutral'.

<sup>d</sup>Defined as 'The extent to which patients with cryopreserved embryos reported personal uncertainty about disposition decisions and related deficits in knowledge and values clarity'.

more likely to donate to fertility research (OR = 1.30, 95% CI: 1.20–1.50) (Bangsboll *et al.*, 2004). No association was found concerning donation for stem cell research (Bangsboll *et al.*, 2004; Sharma *et al.*, 2011).

A previous failed fertilization was associated with donating less frequently for research ( $P = 0.009$ ) (Choudhary *et al.*, 2004), but Sharma *et al.* (2011) found no association between unsuccessful cycles and the donation for research.

The number of previous cycles (Choudhary *et al.*, 2004; Sharma *et al.*, 2011), the duration of infertility (Bangsboll *et al.*, 2004; Choudhary *et al.*, 2004), the type of treatment (Bangsboll *et al.*, 2004; Choudhary *et al.*, 2004), and parity (Sharma *et al.*, 2011) were not significantly associated with the decision to donate embryos for research.

#### Sociodemographic characteristics

Age was assessed in eight studies. While Mohler-Kuo *et al.* (2009) observed that the prevalence of embryo donation to medical research was significantly higher among those older than 40 years (ORadj = 1.80, 95% CI: 1.10–3.00), none of the other seven studies observed any effect of age on the decision to donate embryos for research, regarding either the women's age (Lanzendorf *et al.*, 2010; Provoost *et al.*, 2012c) and the women's and men's ages (Asensio *et al.*, 2001; Burton and Sanders, 2004; Choudhary *et al.*, 2004; Hammarberg and Tinney, 2006; Sharma *et al.*, 2011).

One study showed that participants with higher educational levels were more likely to donate embryos for research than those with lower educational levels (Mohler-Kuo *et al.*, 2009). Those with college and university studies and those with vocational school plus 2 years were more likely to donate than those with mandatory/vocational school (ORadj = 1.80, 95% CI: 1.10–3.00 and ORadj = 2.00, 95% CI: 1.20–3.40, respectively) (Mohler-Kuo *et al.*, 2009). Two other studies found no association between these variables (Hammarberg and Tinney, 2006; Jin *et al.*, 2013).

Religious beliefs were assessed in three studies (McMahon *et al.*, 2003; Burton and Sanders, 2004; Mohler-Kuo *et al.*, 2009). Both women and men with moderate to strong religious beliefs were less likely to donate embryos for research, compared with those with not very strong beliefs (20 versus 42%;  $P = 0.008$  and 18 versus 41%;  $P = 0.01$ , respectively) (Burton and Sanders, 2004). Those who attributed a higher importance to religious principles in their attitudes toward reproductive medicine were less likely to donate embryos for research (ORadj = 0.40, 95% CI: 0.20–0.60) (Mohler-Kuo *et al.*, 2009). In the study of McMahon *et al.* (2003), having commitment to religion (religious affiliation/moderate or high commitment), in comparison with a non-religious commitment (no religious affiliation/religious affiliation but slight or no commitment), was not shown to be associated with the decision to donate/not to donate embryos for research.

Concerning ethnicity, two studies showed that Caucasians donate embryos for research more often than Asians: 56 versus 27%;  $P = 0.022$  (Choudhary *et al.*, 2004) and 57 versus 42%;  $P < 0.001$  (Sharma *et al.*, 2011). One study found no association between the decision and being 'white' or 'non-white' (Asian, African American and Other) (Lylerly *et al.*, 2010).

Only one study evaluated country of birth (Sharma *et al.*, 2011), concluding that Asians born outside the USA (versus Asians born in the USA) were less likely to agree with embryo donation for research (37.9 versus 57.6%;  $P = 0.001$ ).

#### Other factors

The association between the storage period of cryopreserved embryos and their donation for research was quantified in six studies. While Luna *et al.* (2009) found that couples with older cryopreserved embryos were more likely to donate (35.7% among 5–10 years and 34.9% among > 10 years versus 19.1% among ≤ 4 years;  $P < 0.05$ ), the other five studies

found no association between such variables (Asensio et al., 2001; Hammarberg and Tinney, 2006; Newton et al., 2007; Lanzendorf et al., 2010; Lyerly et al., 2010).

The five studies that quantitatively assessed embryo status evaluated it by different means: by measuring the perception of their moral status, from low to high (Lyerly et al., 2010) or a cluster of cells versus life/potential child (Jin et al., 2013), or by agreement with the statement that an embryo is a human being (Mohler-Kuo et al., 2009), a child (Laruelle and Englert, 1995), or a 'Symbol of One's Relationship' (Provoost et al., 2012b). Couples were less likely to donate embryos for medical research (OR = 0.30, 95% CI: 0.20–0.50) when they perceived embryos as human beings (Mohler-Kuo et al., 2009), as life/potential child (versus as a cluster of cells: 86.2 versus 13.6%;  $P < 0.05$ ) (Jin et al., 2013), or as children (versus other perceptions: 16 versus 36%;  $P < 0.05$ ) (Laruelle and Englert, 1995), as well as when they attributed a higher moral status to human embryos, in comparison with those who attributed a lower moral status (OR = 0.69, 95% CI: 0.60–0.79) (Lyerly et al., 2010). Patients who did not classify embryos as a symbol of the relationship (versus those who did) were more likely to donate embryos for research (87.2 versus 65.1%;  $P = 0.018$ ) (Provoost et al., 2012b).

The type of funding (Choudhary et al., 2004; Sharma et al., 2011), having concerns about family/finances (Lyerly et al., 2010), and consulting someone other than the partner to make the decision about embryo disposition (Provoost et al., 2012a) were not associated with the decision to donate or not to donate embryos for research.

The interest in participating in clinical research (Sharma et al., 2011) and altruism (Lyerly et al., 2010) were significantly associated with the decision to donate embryos for research. Those who reported an interest in participating in clinical research, comparing to those who declared no interest, were more likely to donate embryos for research (62.5 versus 31.8%;  $P < 0.008$ ) (Sharma et al., 2011). Those who agreed with donating also more frequently attributed a high importance to altruism in the underlying decision-making process than those who did not donate embryos for research (OR = 1.65, 95% CI: 1.47–1.85) (Lyerly et al., 2010).

One quantitative study mentioned decisional conflict as influencing the non-donation of embryos for research, being described as the extent to which patients with cryopreserved embryos reported personal uncertainty about disposition decisions and related deficits in knowledge and values clarity (Lyerly et al., 2011). Couples with a higher decisional conflict were more likely to donate embryos for research, compared with those with lower decisional conflict (OR = 1.66, 95% CI: 1.12–3.46) (Lyerly et al., 2011). Couples who donated for science significantly more often made a joint decision (compared with cases where the decision is made by the woman alone, by the woman after consulting the man or by the man after consulting the woman) (87.9 versus 12.1%;  $P = 0.014$ ) (Provoost et al., 2012a).

## Reasons for donating and not donating embryos for research

The qualitative synthesis of the reasons for donating and not donating embryos for research is presented in Table III. The donation of embryos for research is rooted in reasons related to the individual's contribution to society (helping others or improving health and IVF treatments and research), the perception of such a decision as better than the destruction of embryos, and in positive views about research and

the medical system. The conceptualization of cryopreserved embryos in terms of personhood, the perception of risks, and the lack of information about research projects proved to have the highest relevance as motives for not donating embryos for research.

## Sociotechnical context

Patients who agreed to donate embryos for research reported 'a sense of gratitude to reproductive medicine' (Mitzkat et al., 2010), a feeling of reciprocity for being able to 'give back' (Lyerly et al., 2006) or being able 'to give a little to take a little' (Provoost et al., 2010), as well as a sensation of 'obligation in terms of returning the favour' (Fuscaldo and Gillam, 2007), which is the opportunity afforded to them of having a child of their own, which is offered by science and technology, in six studies (Lyerly et al., 2006; Parry, 2006; Fuscaldo and Gillam, 2007; Karpel et al., 2007; Mitzkat et al., 2010; Provoost et al., 2010). This decision was also framed in a context where the desire of the medical team or the need of scientists regarding the use of embryos for scientific purposes were presented as reasons to donate embryos for research, as described by Fuscaldo and Gillam (2007), Haimes and Taylor (2009), Lyerly et al. (2006), McMahon et al. (2003), Parry (2006), Provoost et al. (2010) and Zweifel et al. (2007).

In eleven studies, the participants who did not donate embryos for research justified their decision with the perception of risks related to research, like 'the fear that someone needed an embryo and they would give it to somebody, or they would mix it up' (Lyerly et al., 2006) or that 'researchers would allow the embryo to go on developing' (Provoost et al., 2010) (see also Choudhary et al., 2004; Parry, 2006; Fuscaldo and Gillam, 2007; Kufner et al., 2009; Provoost et al., 2009; Mitzkat et al., 2010; Nachtigall et al., 2010; Takahashi et al., 2012; Jin et al., 2013). Issues linked with the lack of information concerning the objectives of the research projects requiring embryos were highlighted in eight studies (McMahon et al., 2003; Lyerly et al., 2006; Parry, 2006; Fuscaldo and Gillam, 2007; Mitzkat et al., 2010; Nachtigall et al., 2010; Provoost et al., 2010; Jin et al., 2013), while the need for regulation which guarantees that research remains 'within a defined [legal] frame' was referred to in two studies (Kufner et al., 2009; Melamed et al., 2009).

## Views about embryos

The moral status of the embryo emerged as a key explanation for not donating embryos for research in thirteen studies, being described in different perspectives: embryo as 'a child'/'children' (McMahon et al., 2003; Kufner et al., 2009; Provoost et al., 2009, 2010; Frith et al., 2011; Kato and Sleeboom-Faulkn, 2011; Takahashi et al., 2012); 'life' (Lyerly et al., 2004, 2006; Provoost et al., 2009, Takahashi et al., 2012); 'a early life' (Hammarberg and Tinney, 2006); 'not just a bunch of cells' (Provoost et al., 2009); 'a potential person', 'potential life' or 'potential children' (McMahon et al., 2003; Parry, 2006; Provoost et al., 2010; Frith et al., 2011; Jin et al., 2013); 'a baby' (Fuscaldo and Gillam, 2007; Provoost et al., 2009); or 'brothers and sisters' of the daughters who are already born (Kato and Sleeboom-Faulkn, 2011). The preference for donating embryos to other couples was described in six studies as a reason for not donating embryos for research (McMahon et al., 2003; Hammarberg and Tinney, 2006; Parry, 2006; Fuscaldo and Gillam, 2007; Provoost et al., 2010; Frith et al., 2011), while their use for the 'sole purpose' of having a baby was reported in three studies (Parry, 2006; Haimes and Taylor, 2009; Kato and Sleeboom-Faulkn, 2011).

**Table III** Qualitative synthesis of the main reasons for donating and not donating embryos for research (n = 22).

	Donate (n)	Not donate (n)
Sociotechnical context		
A sense of gratitude to reproductive medicine	6 (Parry, 2006; Lyerly et al., 2006; Fuscaldo and Gillam, 2007; Karpel et al., 2007; Mitzkat et al., 2010; Provoost et al., 2010)	
If you [medical team] really want it [cryopreserved embryos], then take it	4 (Lyerly et al., 2006; Fuscaldo and Gillam, 2007; Haimes and Taylor, 2009; Provoost et al., 2010)	
Research has to be done	4 (Zweifel et al., 2007; McMahon et al., 2003; Parry, 2006; Provoost et al., 2010)	
Have that irrational fear (...) that they would mix it up		11 (Choudhary et al., 2004; Lyerly et al., 2006; Parry, 2006; Fuscaldo and Gillam, 2007; Kufner et al., 2009; Provoost et al., 2009; Mitzkat et al., 2010; Nachtigall et al., 2010; Provoost et al., 2010; Takahashi et al., 2012; Jin et al., 2013)
You have no idea what kind of research will be done with them		8 (McMahon et al., 2003; Lyerly et al., 2006; Parry, 2006; Fuscaldo and Gillam, 2007; Mitzkat et al., 2010; Provoost et al., 2010; Nachtigall et al., 2010; Jin et al., 2013)
It [embryo research] has to stay within a defined [legal] frame		2 (Kufner et al., 2009; Melamed et al., 2009)
Views about embryos		
If people are only going to destroy embryos, I can't see why research isn't a good way of using them	14 (McMahon et al., 2003; Lyerly et al., 2004; Hammarberg and Tinney, 2006; Fuscaldo and Gillam, 2007; Karpel et al., 2007; Haimes and Taylor, 2009; Kufner et al., 2009; Peddie et al., 2009; Provoost et al., 2009; Lyerly et al., 2010; Provoost et al., 2010; Kato and Sleeboom-Faulkn, 2011; Takahashi et al., 2012; Jin et al., 2013)	
Embryos with bad quality: They [embryos] wouldn't have progressed anyway (...)	4 (Parry, 2006; Haimes and Taylor, 2009; Peddie et al., 2009; Mitzkat et al., 2010)	
That's not just a bunch of cells, right? That's life you know		13 (Lyerly et al., 2004; Hammarberg and Tinney, 2006; Lyerly et al., 2006; Parry, 2006; Fuscaldo and Gillam, 2007; Kufner et al., 2009; Provoost et al., 2009; Provoost et al., 2010; Frith et al., 2011; Kato and Sleeboom-Faulkn, 2011; Takahashi et al., 2012; Jin et al., 2013)
I'd rather give someone a chance of having a baby than giving some to research		6 (Frith et al., 2011; Fuscaldo and Gillam, 2007; Hammarberg and Tinney, 2006; McMahon et al., 2003; Parry, 2006; Provoost et al., 2010)
[Our] 'sole purpose' is to have a baby		3 (Parry, 2006; Haimes and Taylor, 2009; Kato and Sleeboom-Faulkn, 2011)
Societal benefits		
We will be happy that they [cryopreserved embryos] could help others	12 (McMahon et al., 2003; Lyerly et al., 2006; Lyerly et al., 2004; Zweifel et al., 2007; Haimes and Taylor, 2009; Kufner et al., 2009; Provoost et al., 2009; Mitzkat et al., 2010; Provoost et al., 2010; Kato and Sleeboom-Faulkn, 2011; Takahashi et al., 2012; Jin et al., 2013)	
I did contribute to make this world a healthier place	10 (Hammarberg and Tinney, 2006; Lyerly et al., 2006; Fuscaldo and Gillam, 2007; Zweifel et al., 2007; Kufner et al., 2009; Peddie et al., 2009; Provoost et al., 2009; Mitzkat et al., 2010; Provoost et al., 2010; Takahashi et al., 2012)	
Maybe advance the technology and knowledge about IVF treatment	4 (Lyerly et al., 2006; Parry, 2006; Mitzkat et al., 2010; Provoost et al., 2010)	
I did not do all this [hard work and expensive treatment] for the benefit of others		1 (Kato and Sleeboom-Faulkn, 2011)

n, number of papers.

Otherwise, the belief that donating embryos for research is better than their destruction was mentioned in fourteen studies as a motive for donating embryos for that purpose (McMahon et al., 2003; Lyerly et al., 2004, 2010; Hammarberg and Tinney, 2006; Fuscaldo and Gillam, 2007; Karpel et al., 2007; Haimes and Taylor, 2009; Kufner et al., 2009; Peddie et al., 2009; Provoost et al., 2009, 2010; Kato and

Sleeboom-Faulkn, 2011; Takahashi et al., 2012; Jin et al., 2013). Additionally, having embryos considered to be of poor quality was reported in four studies as an explanation for donating embryos for research, because they would not develop into an eventual pregnancy (Parry, 2006; Haimes and Taylor, 2009; Peddie et al., 2009; Mitzkat et al., 2010).

### Societal benefits

Societal benefits constituted the first group of reasons cited by those who agreed to donate embryos for research. These motives were presented in three forms: (i) answers like 'We will be happy that they [cryopreserved embryos] could help others' (Jin et al., 2013) proved to have the highest relevance, and were described in twelve studies (McMahon et al., 2003; Lyerly et al., 2004, 2006; Zweifel et al., 2007; Haimes and Taylor, 2009; Kufner et al., 2009; Provoost et al., 2009, 2010; Mitzkat et al., 2010; Kato and Sleeboom-Faulkn, 2011; Takahashi et al., 2012; Jin et al., 2013); (ii) in ten studies, there was a reference to the opportunity of contributing to make this world a healthier place (Hammarberg and Tinney, 2006; Lyerly et al., 2006; Fuscaldo and Gillam, 2007; Zweifel et al., 2007; Kufner et al., 2009; Peddie et al., 2009; Provoost et al., 2009, 2010; Mitzkat et al., 2010; Takahashi et al., 2012); and (iii) the perception that the donation of embryos for research may advance the technology and knowledge about IVF treatment was cited in four studies (Lyerly et al., 2006; Parry, 2006; Mitzkat et al., 2010; Provoost et al., 2010).

The avoidance of benefiting others was indicated in one study as a motive for not donating embryos for research: 'I did not do all this [hard work and expensive treatment] for the benefit of others' (Kato and Sleeboom-Faulkn, 2011).

## Discussion

### Current state of research and future direction

The aim of this systematic review was to synthesize the current body of knowledge about IVF patients' motivations to donate or not to donate embryos for research, based on quantitative and qualitative studies. It suggested that IVF patients' decision-making process about embryo donation for research is influenced by several factors from individual, social and structural levels. Three main iterative and dynamic dimensions emerged: (i) hierarquization of the possible options regarding embryo disposition, framed on patients' beliefs about what should be done or their representations regarding the moral and social status of embryos; (ii) patients' understanding of expectations and risks of the research on human embryos; (iii) and patients' experiences of information exchange and levels of trust in the medical-scientific institutions.

Qualitative studies reported consistent data about the influence of the sociotechnical context, which included the IVF patients' understanding of science and medicine and the leading values in the doctor-patient relationship, and of the perception of the societal benefits of research on human embryos for the society, for IVF patients, and for individuals. Qualitative synthesis showed that those who donate embryos for research reported feelings of reciprocity towards science and medicine, revealed a positive vision of research and high levels of trust in the medical system. Additionally, they described such a decision as an opportunity to help others, by contributing to a healthier world and to the improvement of IVF treatments. Those who do not donate embryos for research perceive the embryo as a potential life or person or intended

to use embryos for reproductive purposes, including donation to other couples. They also revealed low levels of confidence in science and a lack of information concerning the specific research projects in which embryos will be used, reporting the need for a clear legal framework.

Quantitative papers were based on specific sets of variables, mainly about sociodemographic characteristics and reproductive and gynaecological history, for which the assessment varied among studies. Furthermore, 14 out of 22 variables were analysed in very few studies (a maximum of two papers), resulting in inconclusive data. Contradictory results were reported concerning seven of the eight remaining variables: having children, number of embryos, use of homologous/heterologous techniques, age, education level, religion beliefs and the storage length.

The influence of the views about embryos was simultaneously assessed in quantitative and qualitative studies. The perception of embryos in terms of personhood with a moral and social status is a factor influencing the non-donation of embryos for research, while viewing the embryo as an entity with a high instrumental value was positively linked with donation for science (Provoost et al., 2009). Attributing the status of person to one's embryos was not linked with an absolute objection to any action that leads to the destruction of the embryo (Frith et al., 2011; Provoost et al., 2010). At the same time, results coherently revealed that heterogeneous classifications were attributed to cryopreserved embryos by IVF users, reinforcing the idea that embryos are not universal and fixed entities (Haimes et al., 2008). For example, embryos were classified in terms of the level of their moral status, from low to high (Lyerly et al., 2010). In other studies, embryos were defined as a cluster of cells (Jin et al., 2013), as life/potential child (Frith et al., 2011; McMahon et al., 2003; Lyerly et al., 2004, 2006; Hammarberg and Tinney, 2006; Parry 2006; Provoost et al., 2009, 2010; Takahashi et al., 2012; Jin et al., 2013), as a human being (Kufner et al., 2009; Mohler-Kuo et al., 2009; Provoost et al., 2009), as a child (Laruelle and Englert, 1995; McMahon et al., 2003; Fuscaldo and Gillam, 2007; Kufner et al., 2009; Provoost et al., 2009, 2010; Frith et al., 2011; Kato and Sleeboom-Faulkn, 2011; Takahashi et al., 2012), or as a 'Symbol of One's Relationship' (Provoost et al., 2012b). Embryos were thus simultaneously perceived as epistemic or medical objects for research and clinical practices, and ontological objects for reproduction.

Although for many citizens, embryos were described as potential lives, this did not override their views about the preference of 'using' embryos rather than discarding them, as found by de Lacey et al. (2012). Additionally, embryos were perceived as having both an intrinsic moral and social status and an instrumental value for IVF patients (Provoost et al., 2009). How these dimensions intertwine varies according to historical and geographical contexts and the social position of those who classified embryos (Lyerly et al., 2006; Haimes and Taylor, 2009; Silva and Machado, 2010a).

This review also highlights the relevance of the balance between expectations and fears about research with human embryos on IVF patients' motivations to donate or not donate embryos for such a purpose, which involves issues of trust, hope, power, knowledge and responsibilities, both of medical and scientific institutions, and citizens (Silva and Machado, 2011). These results are particularly relevant in a context where embryo donation for research has become increasingly popular during the last two decades, as the positive trend on the proportion of users donating embryos for this purpose illustrates (Provoost et al., 2012c).



This may have implications on the patients' motivation and choice regarding embryo disposition, in three complementary ways. Firstly, attention should be drawn to the responsibility of scientific and medical institutions, health professionals and researchers that shape the choices of IVF users, namely by providing accurate and timely information, in accordance with patients' needs. For raising information and confidence, it is essential to use routine medical practices with the intention to carefully deal with ethically sensitive decisions (Gerrits *et al.*, 2013). Informed consent should include accurate information about all the available options on embryo disposition, with detailed data being provided about the research projects aiming to use human embryos (de Lacey, 2007). Secondly, referencing risks and their implications in the actions of social and/or professional groups, including IVF patients and researchers, should be central topics in the debates of biomedicine in a broader sense and in the local ethics of clinical research and doctor-patient relationships (Silva and Machado, 2010b). Finally, the increased popularity of the donation of embryos for research may be reconfigured as a new morality that presses IVF patients to donate embryos for research as a contribution to a healthier society (Rose and Novas, 2005; Burns, 2009).

Some psychosocial factors generally associated with patients' experiences of IVF treatments are absent from most of the studies included in this systematic review, in particular those associated with the couples' relationship (Peterson *et al.*, 2008), the meanings of parenthood (Fisher and Hammarberg, 2012) and social support (Martins *et al.*, 2011), as well as personal well-being and psychopathological symptoms (Hammarberg and Tinney, 2006; Boivin *et al.*, 2011). Evidence produced by studies on the cognitive dimension underlying the decision-making process regarding the fate of embryos reveals feelings of conflict, often between the members of the couple, with psychological implications, such as anguish and anxiety (de Lacey, 2005; Hammarberg and Tinney, 2006). In a decision where the couple is most frequently the key element, the incorporation of these variables must be taken into account.

An analytic tool could serve as a basis for comparative intercultural studies covering different regulatory, economic and political contexts. It would be relevant for the definition of patient-centred policies on hESC research, as well as for ethics in clinical practice. It could also allow the comparison of the real-world decisions among different cultural, economic and political contexts that influence access, care and decision-making in reproductive medicine.

## Methodological features

There are some methodological limitations in the studies included in this systematic review that should be taken into account when interpreting the results. Although 11 out of the 39 papers were found through reference tracking, all of the relevant studies were identified. It is important to stress the need to include the MeSH term 'embryo disposition' in papers published about the utilization or disposal of an embryo that is fertilized but not immediately transplanted and resulting course of action.

A relatively small number of empirical studies conducted in few countries and specific settings are available. White Western countries are over-represented in this review sample, although research with hESCs is allowed in many countries worldwide. National regulations and guidelines vary widely in issues as the access criteria to infertility treatments, the available options for embryo disposition and the policies concerning funding or the governance of hESC research (ESHRE, 2013; European Science Foundation, 2013; International Federation of Fertility Societies

(IFFS), 2013). Some countries included in this review have legislations which permit research only on surplus IVF embryos, prohibiting the creation of embryos solely for research purposes. This is the case in Brazil, Denmark, France, Spain, the UK and the USA. The retrieved proportions of donation for research can be affected by the varied legislations of the countries but can also be biased by the different measures used to assess it (dichotomic answers versus hierarquization of the possible options for embryo disposition).

Taking into account the sensitive nature of the decision under analysis and its dependence on national or local policies on hESC research, more information on regulation and policies concerning counselling processes and the available options on embryo disposition is required to contextualize the assessment of the outcome in the studies. In fact, the evidence cannot be generalized as the conditions of social policy or clinical practice may vary significantly between countries, in states within countries, or even in individual clinics (de Lacey, 2007).

Additionally, more detailed information about the sampling and time of assessment within IVF treatments' stage should be provided, in order to increase reliability and to allow data comparison and weighing of the studies, which was not possible in this systematic review.

Finally, a dynamic analysis of the interactions between qualitative and quantitative data calls for the development of more mixed-methods studies, which represented only a small portion of the studies included in this review (3/39). This methodology would lead to a wider understanding of the decision-making process, taking into account the factors influencing the donation and non-donation of embryos for research.

## Conclusion

The aim of this study was to synthesize the current body of knowledge about the motivations of IVF patients to donate or not donate embryos for research, based on quantitative and qualitative studies. Three iterative and dynamic dimensions of the decision-making on embryo donation emerged from this review: the hierarquization of the possible options regarding embryo disposition, according to the moral, social and instrumental status attributed to embryos; the patients' understanding of expectations and risks of the research on human embryos; and the patients' experiences of information exchange and levels of trust in the medical-scientific institutions. Results relating to the influence of sociodemographic characteristics and reproductive and gynaecological history were mostly inconclusive. Further research is needed for the development of a theoretical framework, contributing to a deeper understanding of real-world decisions about embryo disposition. An analytical tool could serve as a basis for the definition of patient-centred policies on hESCs research, benefiting informed relational ethics in clinical practice.

## Supplementary data

Supplementary data are available at <http://humupd.oxfordjournals.org/>.

## Authors' roles

C.S. and S.S. contributed significantly to all stages of the preparation of this manuscript. C.S. and M.P. did the data extraction. H.M. and B.F. provided important intellectual content in the design and analysis. All authors approved the final version of this manuscript.



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## Conflict of interest

The authors declare no financial or commercial conflicts of interest in this study.

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