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ESHRE guideline: number of embryos to transfer during IVF/ICSI†

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ABSTRACT

STUDY QUESTION: Which clinical and embryological factors should be considered to apply double embryo transfer (DET) instead of elective single embryo transfer (eSET)?

SUMMARY ANSWER: No clinical or embryological factor *per se* justifies a recommendation of DET instead of eSET in IVF/ICSI.

WHAT IS KNOWN ALREADY: DET is correlated with a higher rate of multiple pregnancy, leading to a subsequent increase in complications for both mother and babies. These complications include preterm birth, low birthweight, and other perinatal adverse outcomes. To mitigate the risks associated with multiple pregnancy, eSET is recommended by international and national professional organizations as the preferred approach in ART.

STUDY DESIGN, SIZE, DURATION: The guideline was developed according to the structured methodology for development and update of ESHRE guidelines. Literature searches were performed in PUBMED/MEDLINE and Cochrane databases, and relevant papers published up to May 2023, written in English, were included. Live birth rate, cumulative live birth rate, and multiple pregnancy rate were considered as critical outcomes.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Based on the collected evidence, recommendations were discussed until a consensus was reached within the Guideline Development Group (GDG). A stakeholder review was organized after the guideline draft was finalized. The final version was approved by the GDG and the ESHRE Executive Committee.

MAIN RESULTS AND THE ROLE OF CHANCE: The guideline provides 35 recommendations on the medical and non-medical risks associated with multiple pregnancies and on the clinical and embryological factors to be considered when deciding on the number of embryos to transfer. These recommendations include 25 evidence-based recommendations, of which 24 were formulated as strong recommendations and one as conditional, and 10 good practice points. Of the evidence-based recommendations, seven (28%) were supported by moderate-quality evidence. The remaining recommendations were supported by low (three recommendations; 12%), or very low-quality evidence (15 recommendations; 60%). Owing to the lack of evidence-based research, the guideline also clearly mentions recommendations for future studies.

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LIMITATIONS, REASONS FOR CAUTION: The guideline assessed different factors one by one based on existing evidence. However, in real life, clinicians' decisions are based on several prognostic factors related to each patient's case. Furthermore, the evidence from randomized controlled trials is too scarce to formulate high-quality evidence-based recommendations.

WIDER IMPLICATIONS OF THE FINDINGS: The guideline provides health professionals with clear advice on best practice in the decision-making process during IVF/ICSI, based on the best evidence currently available, and recommendations on relevant information that should be communicated to patients. In addition, a list of research recommendations is provided to stimulate further studies in the field.

STUDY FUNDING/COMPETING INTEREST(S): The guideline was developed and funded by ESHRE, covering expenses associated with the guideline meetings, the literature searches, and the dissemination of the guideline. The guideline group members did not receive payment. DPB declared receiving honoraria for lectures from Merck, Ferring, and Gedeon Richter. She is a member of ESHRE EXCO, and the Mediterranean Society for reproductive medicine and the president of the Croatian Society for Gynaecological Endocrinology and Reproductive Medicine. CDG is the past Chair of the ESHRE EIM Consortium and a paid deputy member of the Editorial board of Human Reproduction. IR declared receiving reimbursement from ESHRE and EDCD for attending meetings. She holds an unpaid leadership role in OBBCSSR, ECDC Sohonet, and AER. KAR-W declared receiving grants for clinical researchers and funding provision to the institution from the Swedish Cancer Society (200170F), the Senior Clinical Investigator Award, Radiumhemmets Forskningsfonder (Dnr: 201313), Stockholm County Council FoU (FoUI-953912) and Karolinska Institutet (Dnr 2020-01963), NovoNordisk, Merck and Ferring Pharmaceuticals. She received consulting fees from the Swedish Ministry of Health and Welfare. She received honoraria from Roche, Pfizer, and Organon for chairmanship and lectures. She received support from Organon for attending meetings. She participated in advisory boards for Merck, Nordic countries, and Ferring. She declared receiving time-lapse equipment and grants with payment to institution for pre-clinical research from Merck pharmaceuticals and from Ferring. SS-R received research funding from Roche Diagnostics, Organon/MSD, Theramex, and Gedeo-Richter. He received consulting fees from Organon/MSD, Ferring Pharmaceuticals, and Merck Serono. He declared receiving honoraria for lectures from Ferring Pharmaceuticals, Besins, Organon/MSD, Theramex, and Gedeon Richter. He received support for attending Gedeon Richter meetings and participated in the Data Safety Monitoring Board of the T-TRANSPORT trial. He is the Deputy of ESHRE SQART special interest group. He holds stock options in IVI Lisboa and received equipment and other services from Roche Diagnostics and Ferring Pharmaceuticals. KT declared receiving payment for honoraria for giving lectures from Merck Serono and Organon. She is member of the safety advisory board of EDQM. She holds a leadership role in the ICCBBA board of directors. ZV received reimbursement from ESHRE for attending meetings. She also received research grants from ESHRE and Juhani Aaltonen Foundation. She is the coordinator of EHSRE SQART special interest group. The other authors have no conflicts of interest to declare.

Keywords: IVF / ICSI / embryo transfer / single embryo transfer / double embryo transfer / live birth rate / multiple pregnancies / medical risks

Introduction

Elective single embryo transfer (eSET) is considered the preferable approach towards safe and effective ART. Currently, this is recommended by several international and national professional organizations (De los Santos *et al.*, 2016; ASRM, 2021). In Europe, the recommendations led to a decrease in the proportion of double embryo transfer (DET) and an increase of the elective transfer of only one embryo at a time (Kupka *et al.*, 2014; Wyns *et al.*, 2021, 2022). However, the data show that there is still a considerable difference in the practice of eSET and the recommendations are not equally followed in all countries, as evident in annual reviews (Sunderam *et al.*, 2022; Wyns *et al.*, 2022).

With the aim of providing the healthcare professionals and patients with the best available evidence, ESHRE has developed a guideline on the number of embryos to transfer during IVF/ICSI. This guideline assesses the medical and non-medical factors that are to be taken into consideration when deciding on the number of embryos to transfer.

Materials and methods

The guideline was developed following a well-documented methodology that is universally used for ESHRE guidelines (Vermeulen *et al.*, 2019). In summary, the Guideline Development Group (GDG) formulated 22 questions structured in PICO format (Patient, Intervention, Comparison, Outcome). Literature searches were conducted in databases (PUBMED/MEDLINE and the Cochrane library) from inception to May 2023, with a limitation to studies written in English. The critical outcomes considered in this guideline are the efficacy in terms of cumulative live birth rate (CLBR) per started cycle and LBR per started cycle, as well as multiple pregnancy rate. A total of 17 700 papers were screened, and relevant studies were selected based on the PICO questions, assessed for quality, and summarized in evidence tables and summary of findings tables. Three relevant papers published after May 2023 were selected by the GDG members and added where appropriate. During the GDG meetings, the evidence and draft recommendations were presented and discussed until consensus was reached within the group. Each recommendation was classified as strong or conditional (Fig. 1), and a grade was assigned (Andrews *et al.*, 2013) based on the strength of the supporting evidence (High ⊕⊕⊕⊕—Moderate ⊕⊕⊕◯—Low ⊕⊕◯◯—Very low ⊕◯◯◯). In the absence of evidence, the GDG formulated no recommendation, or a good practice point (GPP) based on clinical expertise. The draft of the guideline and an invitation for stakeholder review were published on the ESHRE website. Personal invitations

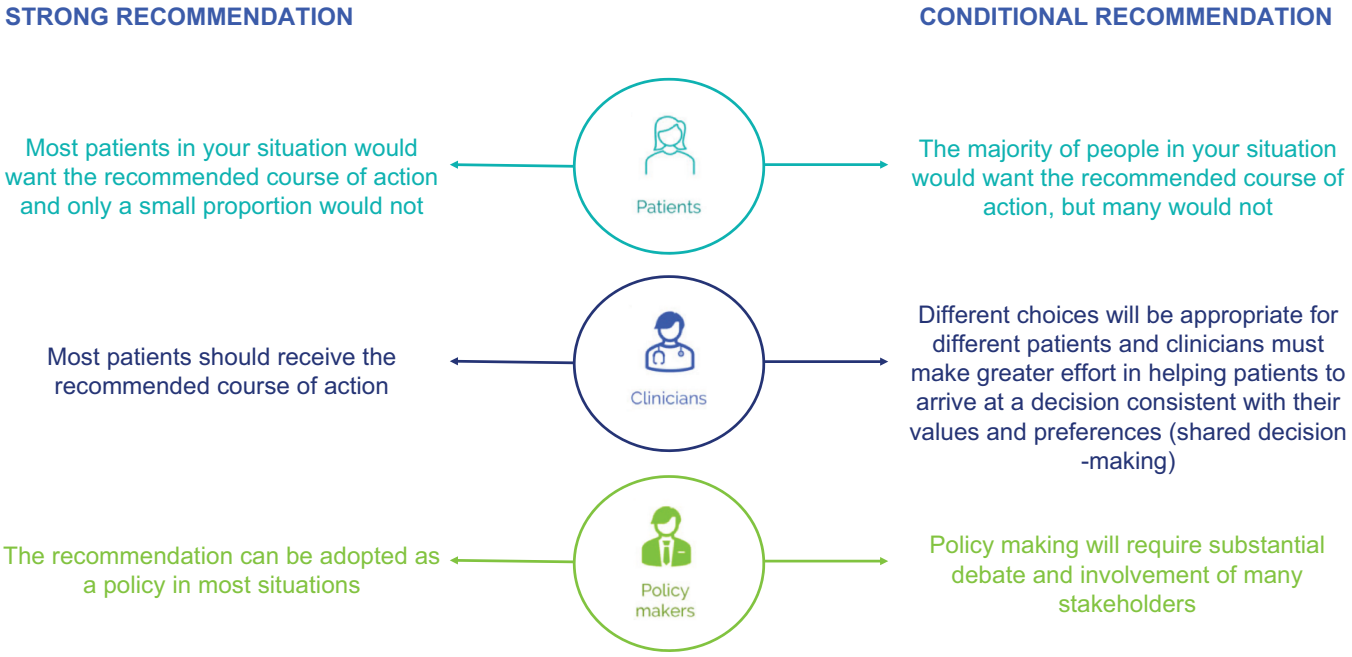

Figure 1. Interpreting strong and conditional recommendations. Suggested interpretation of strong and conditional recommendations from the perspectives of patients (upper panel), clinicians (middle panel), and healthcare policymakers (lower panel).

to review were sent to all relevant stakeholders, and a total of 71 comments were received from 19 reviewers representing 15 countries, including two national societies (Commission of the Spanish Society of Clinical Chemistry (SEQC) and Kazakhstan Association of the Reproductive Medicine (KARM)). All comments were processed by the GDG, either by adapting the content of the guideline or by providing responses to the reviewers. The review process is summarized in the review report, which is published on the ESHRE website (www.eshre.eu/Guidelines-and-Legal/Guidelines/Embryo-transfer). This guideline will be considered for an update 4 years after publication, with an intermediate assessment of the need for updating 2 years after publication.

Results

Key questions and recommendations

The ESHRE guideline on the numbers of embryos to transfer during IVF/ICSI provides 25 recommendations and 10 GPPs answering 22 key questions regarding clinical, embryological, and other factors to be considered in the decision-making process (The ESHRE Guideline Group on the Number of Embryos to Transfer During IVF/ICSI, 2023).

The current document summarizes all the key questions and the recommendations from the guideline. Further background information and the supporting evidence for each recommendation can be found in the full version of the guideline available at www.eshre.eu/Guidelines-and-Legal/Guidelines/Embryo-transfer.

Which pregnancy-related risks and issues should be considered before the transfer of more than one embryo?

Medical risks related to multiple pregnancy/birth

Medical risks that should be considered before the transfer of more than one embryo are the higher rates of maternal, foetal, and neonatal complications (D'Souza *et al.*, 1997; Makhseed *et al.*, 1998; Pinborg *et al.*, 2004; van Heesch *et al.*, 2014; Li *et al.*, 2015; Perkins *et al.*, 2015; Bu *et al.*, 2016; Santos-Ribeiro *et al.*, 2016; Eapen *et al.*, 2020; Gupta *et al.*, 2020; Sites *et al.*, 2020; Luke *et al.*, 2021; Anzhel *et al.*, 2022; Cirillo *et al.*, 2022; Wang *et al.*, 2022; Rodriguez-Wallberg *et al.*, 2023).	Strong ⊕⊕⊕◯
The GDG recommends that whenever the transfer of >1 embryo is considered, the patient should be provided with clear information about the higher risk of pregnancy loss, ectopic pregnancy, pre-eclampsia, gestational diabetes, antepartum and postpartum haemorrhage, Caesarean section, stillbirth, preterm birth, low birthweight, neonatal intensive care admission, and neonatal death associated with multiple pregnancies. The GDG also recommends that the patients sign an additional consent form if >1 embryo is transferred.	GPP

Financial issues of multiple pregnancy/birth

It is recommended to consider the increased direct costs related to obstetric care of multiple pregnancies and paediatric care of twins and triplets (Gerris et al., 2004; Koivurova et al., 2004, 2007; Lukassen et al., 2004, 2005; Motohashi et al., 2004; Fiddelers et al., 2006; Kjellberg et al., 2006; Veleva et al., 2009; Chambers et al., 2014; Velez et al., 2014; Hernandez Torres et al., 2015; van Heesch et al., 2015; Carpinello et al., 2016).	Strong ⊕⊕⊕◯
It is recommended to consider increased indirect costs with multiple pregnancies due to sick leave days, over-the-counter medication, and loss of productivity because of an ill child (Fiddelers et al., 2006; Kjellberg et al., 2006; Stillman et al., 2009).	Strong ⊕⊕◯◯
The GDG recommends that cost-related information should be provided and discussed with the patient(s) at the treatment planning stage.	GPP

Psychological issues of multiple pregnancy/birth

Clinicians should consider the possible complications of multiple pregnancies with regards to mental health postpartum, emotional distress, and possible marital problems, as well as the influence of personality characteristics, sociodemographic factors, and family functioning, on the mental health of parents and offspring regardless of the number of children born (Boivin et al., 2005; Golombok et al., 2007; Spinelli et al., 2013; Noy et al., 2014; Wenze et al., 2015; van den Akker et al., 2016; Anderson et al., 2017; De Roose et al., 2018; Porat-Zyman et al., 2018).	Strong ⊕⊕◯◯
The GDG recommends that information on possible psychosocial complications should be provided to patients at the treatment planning stage.	GPP

Which personal, regulatory, and reimbursement factors are expected to affect the decision for the number of embryos to transfer?

Patient preferences, regulatory factors, and reimbursement policies have an impact on embryo transfer practices.

Social, legislative, and economic factors

The GDG encourages legislative and health insurance policies that promote the practice of eSET.	GPP

Which clinical criteria should be considered as factors when deciding to apply DET instead of (E) SET for couples/individuals undergoing ART?

Previous unsuccessful ART treatments

The decision to perform DET instead of eSET should not be based on the number of previous unsuccessful ART treatments (Monteleone et al., 2016).	Strong ⊕◯◯◯

Duration of infertility

The decision to perform DET instead of eSET should not be based on the duration of infertility (Yilmaz et al., 2013; Monteleone et al., 2016).	Strong ⊕◯◯◯

Previous pregnancy/live birth

The decision to perform DET instead of eSET should not be based on previous pregnancies or live births from ART (Luke et al., 2015).	Strong ⊕◯◯◯

Female age

The decision to perform DET instead of eSET should not be based on female age.	Strong ⊕⊕◯◯
Women aged less than 38 years should receive eSET (Veleva et al., 2006; Lawlor and Nelson, 2012; Niinimaki et al., 2013; Mancuso et al., 2016; Tannus et al., 2017; Arab et al., 2020; Ma et al., 2022).	Strong ⊕⊕⊕◯
Women aged 38 years or more should receive eSET (Veleva et al., 2006; Niinimaki et al., 2013; Tannus et al., 2017; Mejia et al., 2021).	Strong ⊕◯◯◯

Ovarian response

For normal responders, eSET is recommended (Moustafa et al., 2008).	Strong ⊕◯◯◯
The GDG recommends eSET in patients with low or high ovarian response.	GPP

Criteria related to the endometrium

The decision to perform DET instead of eSET in fresh embryo transfer cycles should not be based on endometrial characteristics (Huang et al., 2020).	Strong ⊕◯◯◯
The decision to perform DET instead of eSET in frozen embryo transfer cycles should not be based on endometrial characteristics (El-Toukhy et al., 2008).	Strong ⊕◯◯◯

Treatments with donor oocytes and donated embryos

Only eSET should be practised for patients undergoing ART with donor oocytes (Clua et al., 2015; Acharya et al., 2016; Jeve et al., 2016; Fishel et al., 2017; Mersereau et al., 2017; Arab et al., 2020).	Strong ⊕⊕⊕◯
Only eSET should be practised for patients undergoing ART with donated embryos (Peigné et al., 2023).	Strong ⊕◯◯◯

Gestational carriers

Only eSET should be practised for gestational carriers (Wang et al., 2016; Namath et al., 2021).	Strong ⊕◯◯◯
The GDG recommends that both gestational carriers and intended parents be counselled that DET is associated with greater risk of pregnancy and perinatal complications in surrogate pregnancies.	GPP

Which embryo-related criteria should be considered as factors in deciding to apply DET instead of (E)SET for couples/individuals undergoing ART?

Fresh embryo transfer cycles

Cleavage stage

In fresh cleavage-stage embryo transfer, the decision to perform DET instead of eSET should not be based on embryo criteria (Martikainen et al., 2001; Thurin et al., 2004; Le Lannou et al., 2006; Fauque et al., 2010; Hatörnaz et al., 2016; Aldemir et al., 2020).	Strong ⊕⊕⊕◯

Blastocyst stage

In fresh blastocyst transfer cycles, the decision to perform DET instead of eSET should not be based on blastocyst morphology/quality (Abuzeid *et al.*, 2017; Aldemir *et al.*, 2020; Hill *et al.*, 2020; Theodorou *et al.*, 2021).	Strong ⊕⊕⊕◯

Frozen embryo transfer cycles

When reporting research on vitrified-warmed treatments, the GDG recommends including details on the minimal embryo criteria for vitrification and/or transfer as well as on the selection of devices or embryos for thawing and warming (e.g. randomly picked or according to quality criteria as choosing the first embryos with the best quality).	GPP
The GDG recommends cryopreserving one embryo per device in order to facilitate the practice of SET and for traceability purposes.	GPP

Cryopreserved-warmed cleavage stage

In cryopreserved-warmed cleavage-stage embryo transfer cycles, the decision to perform DET instead of SET should not be based on embryo criteria (Thurin *et al.*, 2004; Hydén-Granskog *et al.*, 2005; Le Lannou *et al.*, 2006; Salumets *et al.*, 2006; Moustafa *et al.*, 2008; López Regalado *et al.*, 2014; Racca *et al.*, 2020; Zhu *et al.*, 2020).	Strong ⊕⊕⊕◯

Vitrified-warmed blastocyst stage

In vitrified-warmed blastocyst transfer cycles, SET should be applied regardless of the quality of the vitrified blastocyst (Van Landuyt *et al.*, 2011; Liu *et al.*, 2014; Dobson *et al.*, 2018; Park *et al.*, 2019; Arab *et al.*, 2020; Chen *et al.*, 2020; Wang *et al.*, 2020; Zhu *et al.*, 2020).	Strong ⊕◯◯◯

Can time-lapse morphokinetics or preimplantation genetic testing outcomes be considered factors in decising to apply DET instead of (E)SET for couples/individuals undergoing ART?

Time-lapse morphokinetics

Time-lapse imaging-derived parameters for embryo selection should not be considered a factor to perform DET instead of eSET (Fishel *et al.*, 2017).	Strong ⊕◯◯◯

Preimplantation genetic testing

Outcomes of preimplantation genetic testing for aneuploidies should not be considered when deciding to perform DET instead of eSET.	Strong ⊕◯◯◯

In any patient undergoing ART, should the transfer of more than two embryos be applied considering the risks of the higher order pregnancies?

Transfer of more than two embryos

Transfer of more than two embryos is not recommended (Salha *et al.*, 2000; Ng *et al.*, 2001; Combelles *et al.*, 2005; Elizur *et al.*, 2005; Setti *et al.*, 2005; Heijnen *et al.*, 2006; Clayton *et al.*, 2007; Berin *et al.*, 2010; Sun *et al.*, 2012; Li *et al.*, 2015; Perkins *et al.*, 2015; Bu *et al.*, 2016; Richter *et al.*, 2016; Ruhlmann *et al.*, 2017; Pi *et al.*, 2020; Anzhel *et al.*, 2022; Cirillo *et al.*, 2022).	Strong ⊕◯◯◯

In any patient undergoing ART, should the transfer of more than two embryos with embryo reduction after implantation be applied considering the risks of the procedure?

Foetal reduction

In patients who conceived higher-order multiples (HOM) following multiple embryo transfer, foetal reduction can be considered to reduce the risk of maternal complications (Groutz *et al.*, 1996; Anthoulakis *et al.*, 2017; Zipori *et al.*, 2017; Liu *et al.*, 2019; Jin *et al.*, 2020).	Conditional ⊕◯◯◯
The transfer of two or more embryos with the intention of performing foetal reduction in case of multiple embryo implantation instead of (e)SET is not recommended (van de Mheen *et al.*, 2015; Kristensen *et al.*, 2022; Wang *et al.*, 2022; Yimin *et al.*, 2022).	Strong ⊕◯◯◯
The GDG recommends against the transfer of more than two embryos with foetal reduction after multiple embryo implantation considering the high risks of the procedure.	GPP

Which issues are crucial for decision-making regarding the number of embryos to transfer and how should they be discussed with the patients?

Patient counselling

The GDG strongly recommends that healthcare professionals discuss with the patient a number of issues related to the number of embryos to transfer. Main topics include: • Medical, economic, social, and psychological consequences of transferring >1 embryo. • Patient wishes regarding family building. • Clinical, science-based recommendations for the specific patient case.	GPP
Key elements for the discussion, and the decision-making process regarding the number of embryos to transfer are the following: • Patient involvement, which ensures a decision that reflects both healthcare professionals' good clinical judgement and the patients' values and personal context. • - Involvement of both members of the patient couple.	

Discussion

The current paper summarizes the 35 recommendations (25 evidence-based recommendations and 10 GPPs) on the factors to consider when deciding on the number of embryos to transfer during IVF/ICSI, as developed in the ESHRE guideline on the number of embryos to transfer during IVF/ICSI. As a basis for the current guideline, a broad and formal literature review was conducted according to the ESHRE guidelines methodology (Vermeulen *et al.*, 2019). The GDG identified a limited number of randomized controlled trials (12 RCTs across various key questions), with evidence for most interventions deriving from cohort studies.

The effects of different prognostic factors were revised one by one to facilitate a more tailored evidence-based decision-making process towards a successful pregnancy with minimal potential risks of complications. No clear indication in any single factor to favour DET over eSET was found.

DET should be avoided at all costs for treatments with donor oocytes, donated embryos or in gestational carriers because of clearly increased pregnancy complications risks. Instead, eSET is strongly recommended for these cases.

Blastocysts should also be transferred in a SET because of the higher monozygotic twin potential of blastocysts (Hviid *et al.*, 2018) and because of the high risk of multiple pregnancy and complications after the transfer of two blastocysts, regardless of the developmental stage of the embryo at the time of cryopreservation or its quality (Van Landuyt *et al.*, 2011; Liu *et al.*, 2014; Abuzeid *et al.*, 2017; Dobson *et al.*, 2018; Park *et al.*, 2019; Aldemir *et al.*, 2020; Arab *et al.*, 2020; Chen *et al.*, 2020; Hill *et al.*, 2020; Wang *et al.*, 2020; Zhu *et al.*, 2020; Theodorou *et al.*, 2021).

The practical recommendation for all other treatments is a more nuanced one because, in real life, patient cases present as a combination of factors associated with either good or poor prognosis. However, the clinical reality is not well represented in scientific research and, currently, there are few studies comparing DET and eSET outcomes in the setting of a truly multivariate regression analysis. Moreover, complex settings frequently encountered in everyday clinical practice cannot be separated from clinic treatment policies, making multivariate studies susceptible to bias regarding ovarian stimulation, embryo selection for transfer, and preparation for frozen embryo transfer.

The number of previously failed treatments has long been recognized as a prognostic factor of poor outcomes (Templeton *et al.*, 1996; Roberts *et al.*, 2010). Each unsuccessful ART cycle has been shown to decrease the odds of ongoing implantation (Thurin *et al.*, 2005). Two previous unsuccessful IVF treatments have been associated with lower chance for live birth when compared with no previous IVF (Strandell *et al.*, 2000; McLernon *et al.*, 2016).

The evidence indicated that DET is not associated with a higher cumulative live birth in poor prognosis patients when considering each factor separately. However, transferring two embryos to patients is sometimes opted for in those marginal cases where patients present several poor prognostic factors, including advanced age, poor-quality embryos, and a lack of live birth from previous ART cycles. Nevertheless, patients for whom DET is considered should be counselled not only regarding the chances their treatment will be successful, but also regarding short- and long-term medical risks, social and economic factors. This should preferably be done as part of shared decision-making.

Apart from the counselling regarding the risks of pregnancy complications with the transfer of more than one embryo, and resulting multiple gestations, patients for whom DET is considered should be aware that the risk of ectopic pregnancy increases along with the number of embryos transferred, up to about 20-fold (Li *et al.*, 2015; Perkins *et al.*, 2015; Bu *et al.*, 2016; Santos-Ribeiro *et al.*, 2016; Pi *et al.*, 2020; Anzhel *et al.*, 2022; Cirillo *et al.*, 2022). The risk of extrauterine pregnancy is elevated after the transfer of two versus one embryo, regardless of development stage or freezing status (Santos-Ribeiro *et al.*, 2016; Anzhel *et al.*, 2022). The rate of ectopic pregnancy is higher after the transfer of non-top-quality embryos (Anzhel *et al.*, 2022). Furthermore, even if a singleton pregnancy develops after DET, it is associated with an overall higher risk of neonatal death and a higher risk of

Figure 2. **The benefits of transferring only one embryo at a time.**

low birthweight in frozen embryo transfer, compared with singleton pregnancies after SET (Rodriguez-Wallberg *et al.*, 2023).

The guideline recommendations emphasize that eSET is the best practice for achieving a healthy pregnancy and minimizing the risk of multiple pregnancies (Fig. 2).

Conclusion

As there is no evidence showing that CLBR in eSET is inferior to that in DET, and as published data clearly demonstrate that the multiple birth rate after DET significantly exceeds that after (e)SET, the GDG recommends eSET as the standard procedure whenever more than one embryo is available.

Data availability

This article conducts a literature review of existing research records, and no new data were generated or analysed in support of this manuscript. A full literature search report can be found on the ESHRE website (https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Embryo-transfer).

Acknowledgements

The Guideline Development Group acknowledges the help of 19 reviewers who provided feedback on the content of the guideline and submitted helpful comments to the draft version. A detailed list of all the reviewers can be found in the ESHRE guideline on the number of embryos to transfer on ESHRE website: www.eshre.eu/Guidelines-and-Legal/Guidelines/Embryo-transfer

Authors' roles

Z.V. chaired the guideline development group and hence fulfilled a leading role in collecting the new evidence, rewriting the updated chapters, and dealing with reviewer comments. S.M. as methodological expert, performed all literature searches update for the guideline, provided methodological support and coordinated the guideline development. All other authors, listed in alphabetical order, as guideline group members, contributed equally to the article, by synthesizing the evidence, writing the guideline, and discussing the recommendations until consensus within the group was reached.

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Conflict of interest

D.P.B. declared receiving honoraria for lectures from Merck, Ferring, and Gedeon Richter. She is a member of ESHRE EXCO, and the Mediterranean Society for reproductive medicine and the president of the Croatian Society for Gynaecological Endocrinology and Reproductive Medicine. C.D.G. is the past Chair of the ESHRE EIM Consortium and a paid deputy member of the Editorial board of *Human Reproduction*. I.R. declared receiving reimbursement from ESHRE and EDCD for attending meetings. She holds an unpaid leadership role in OBBCSSR, ECDC Sohonet, and AER. K.A.R.-W. declared receiving grants for clinical researchers and funding provision to the institution from the Swedish Cancer Society (200170F), the Senior Clinical Investigator Award, Radiumhemmets Forskningsfonder (Dnr: 201313), Stockholm County Council FoU (FoUI-953912) and Karolinska Institutet (Dnr 2020-01963), NovoNordisk, Merck and Ferring Pharmaceuticals. She received consulting fees from the Swedish Ministry of Health and Welfare. She received honoraria from Roche, Pfizer, and Organon for chairmanship and lectures. She received support from Organon for attending meetings. She participated in advisory boards for Merck, Nordic countries, and Ferring. She declared receiving time-lapse equipment and grants with payment to institution for pre-clinical research from Merck pharmaceuticals and from Ferring. S.S.-R. received research funding from Roche Diagnostics, Organon/MSD, Theramex, and Gedeo-Richter. He received consulting fees from Organon/MSD, Ferring Pharmaceuticals, and Merck Serono. He declared receiving honoraria for lectures from Ferring Pharmaceuticals, Besins, Organon/MSD, Theramex, and Gedeon Richter. He received support for attending Gedeon Richter meetings and participated in the Data Safety Monitoring Board of the T-TRANSPORT trial. He is the Deputy of ESHRE SQART special interest group. He holds stock options in IVI Lisboa and received equipment and other services from Roche Diagnostics and Ferring Pharmaceuticals. K. T. declared receiving payment for honoraria for giving lectures from Merck Serono and Organon. She is member of the safety advisory board of EDQM. She holds a leadership role in the ICCBBA board of directors. Z.V. received reimbursement from ESHRE for attending meetings. She also received research grants from ESHRE and Juhani Aaltonen Foundation. She is the coordinator of ESHRE SQART special interest group. The other authors have no conflicts of interest to declare.

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