



Programmi transnazionali di ovodonazione

Nuove strategie per la preparazione dell'endometrio

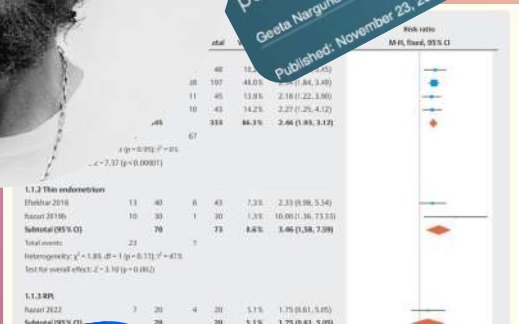
Dr. Antonio Forgiarini



maximizing live birth rates cannot be the only key performance indicator of IVF

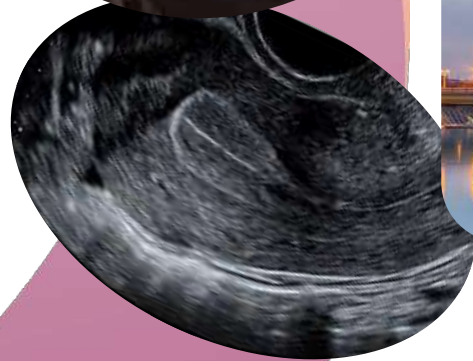
Published: November 29, 2021 • DOI: <https://doi.org/10.1016/j.rbmo.2021.11.011>

Geeta Nargund • Adhija Kumar Datta



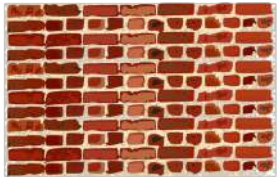
Preparation of the endometrium for frozen embryo transfer: an update on clinical practices

Xiao Fu, Jinlong Ma, Gao





1961



PAPERS AND SHORT REPORTS

Pregnancy established in an infertile patient after transfer of a donated embryo fertilised in vitro

ALAN TROUNSON, JOHN LEETON, MANDY BESANKO, CARL WOOD, ANGELO CONTI



1978

PRELIMINARY COMMUNICATION | VOLUME 327, ISSUE 8486, P884-886, APRIL 19, 1986

PREGNANCY AFTER HUMAN OOCYTE CRYOPRESERVATION

Christopher Chen

Published: April 19, 1986 • DOI: [https://doi.org/10.1016/S0140-6736\(86\)90989-X](https://doi.org/10.1016/S0140-6736(86)90989-X)

1983

1986



1989





Passato: tutto in fresco

Ovociti in fresco



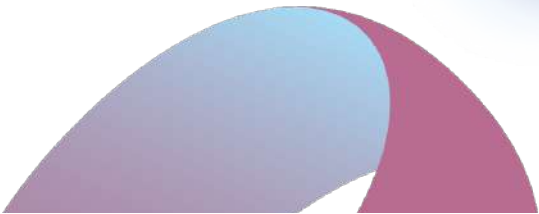
FIV o ICSI



Spermatozoi in fresco



Transfer embrionario in fresco

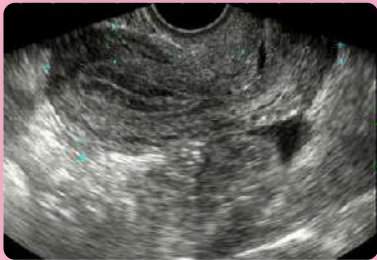


Passato: tutto sincronizzato



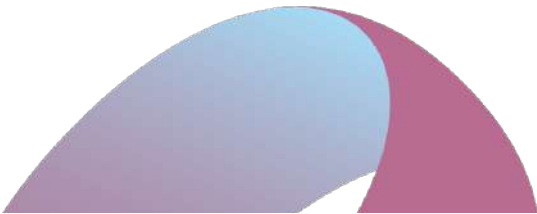
Donatrice

- Sincronizzazione con la ricettrice
- Disponibilità a donare



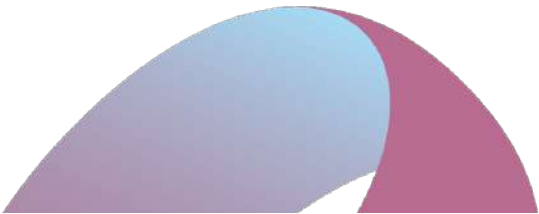
Ricettrice

- Sincronizzazione con la donatrice
- Transfer in fresco

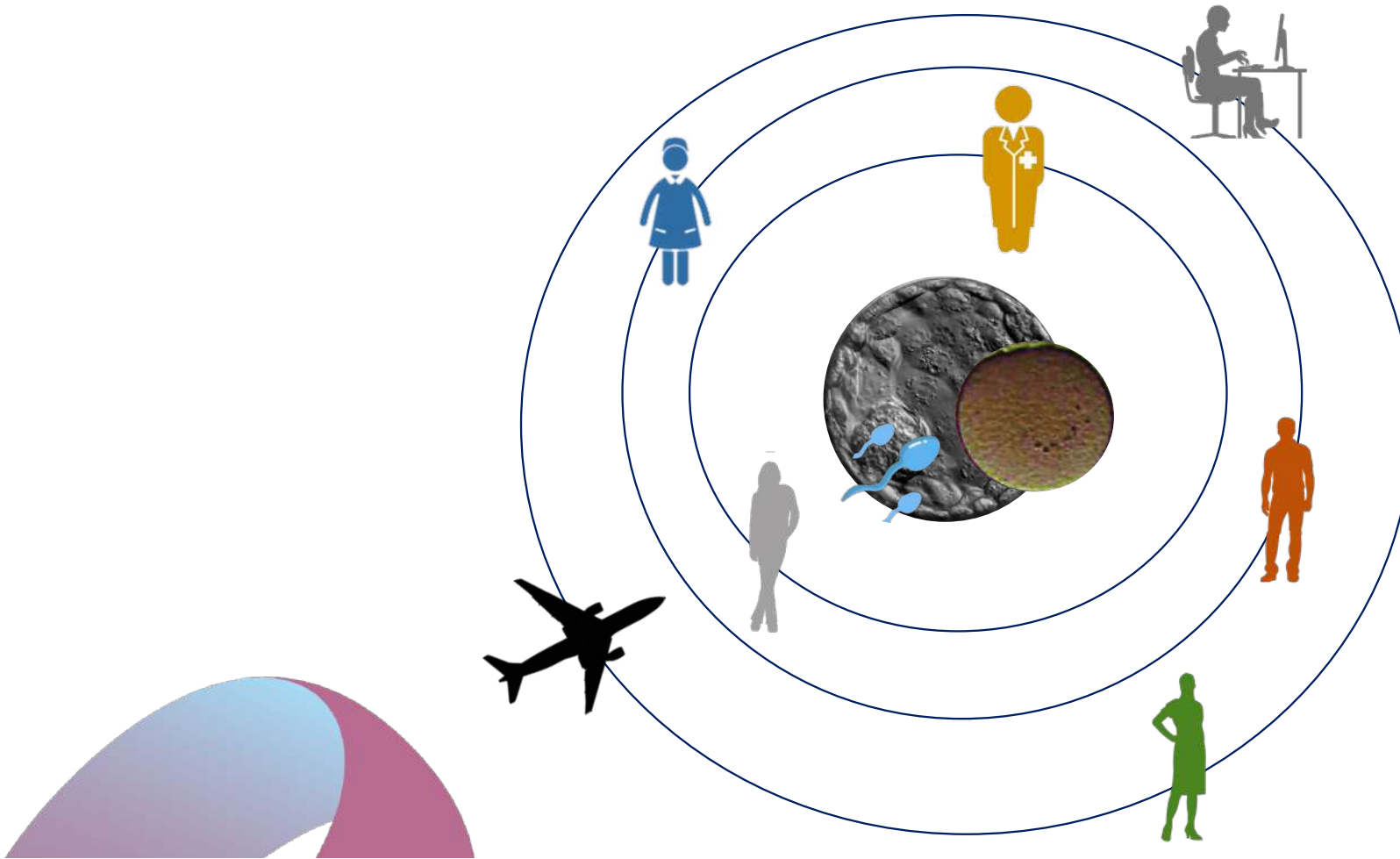


Inconvenienti

- Sincronizzare la mestruazione della donatrice e della ricettrice
- Preparazione endometriale inadeguata
- Risposta della donatrice inadeguata
- Viaggi prenotati all'ultimo momento
- Lunghe liste d'attesa



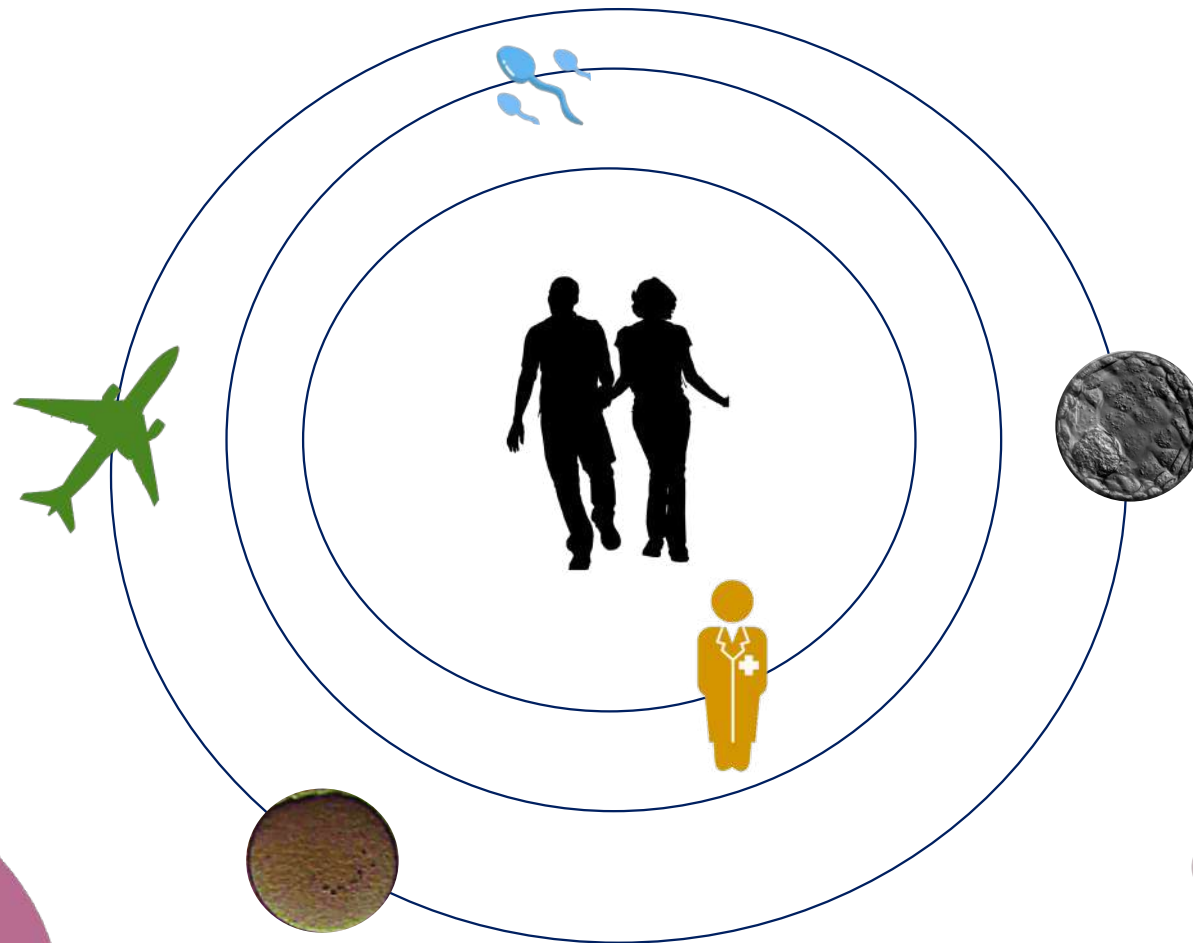
Gameti ed embrioni non viaggiavano



Telefonami tra vent'anni [Lucio Dalla]



Presente: paziente al centro



Randomized Controlled Trial > Fertil Steril. 2008 Jun;89(6):1657-64.
doi: 10.1016/j.fertnstert.2007.05.050. Epub 2007 Sep 24.

Comparison of concomitant outcome achieved with fresh and cryopreserved donor oocytes vitrified by the Cryotop method

Ana Cobo¹, Masashigue Kuwayama, Sonia Pérez, Amparo Ruiz, Antonio Pellicer, José Remohí

Meta-Analysis > Hum Reprod Update. 2019 Jan 1;25(1):2-14. doi: 10.1093/humupd/dmy033.

Fresh versus elective frozen embryo transfer in IVF/ICSI cycles: a systematic review and meta-analysis of reproductive outcomes

Matheus Roque^{1 2}, Thor Haahr³, Selmo Geber^{2 4}, Sandro C Esteves^{3 5 6},
Peter Humaidan^{3 5}

Meta-Analysis > Cochrane Database Syst Rev. 2021 Feb 4;2(2):CD011184.

doi: 10.1002/14651858.CD011184.pub3.

Fresh versus frozen embryo transfers in assisted reproduction

Tjitske Zaat¹, Miriam Zagers¹, Femke Mol¹, Mariëtte Goddijn¹, Madelon van Wely¹,
Sebastiaan Mastenbroek¹



Presente

Vetrificare ovociti



Congelare spermatozoi



Vetrificare embrioni



Transfer embrionario in fresco o differito



International Multicenter Egg Donation (IMEDO)

Article in *Current Trends in Clinical Embriology* · January 2017

DOI: 10.11138/cce/2017.4.2.045

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 Gabriella Zito ²
 Alba Burguera ¹
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 Massimo Manno ⁵
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⁵ Centro di Medicina San Donà di Piave, Venezia, Italy

⁶ GynePro Medical Centers, Bologna, Italy

Table 1 - Results by total oocytes.

	Oocytes	%
Total	3,679	
Survived	3,120	84.8
Fertilized	2,358	75.6
Total embryos	2,202	
Transferred embryos	832	

Table 2 - Results by oocytes batches.

	Batches	%	Oocytes
Thawing failure	17	3.1	116
Fertilization failure	6	1.1	39
Poor quality embryos	6	1.1	42
Successful transfer	512	94.6	3,482
Total	541		3,679

Table 3 - Results by subjects. PR: pregnancy rate; IR: implantation rate; MR: miscarriage rate.

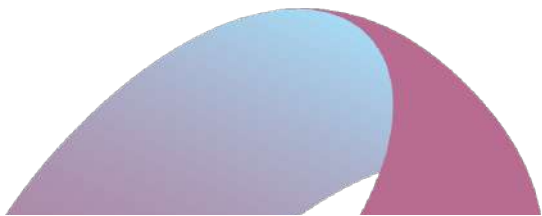
	n	%
Transfer	512	
PR	304	59.3
Single	241	79.3
Multiple	63	20.7
IR	367	44.1
MR	63	20.7

Table 4 - Results by shipping. PR: pregnancy rate. *p<0.05.

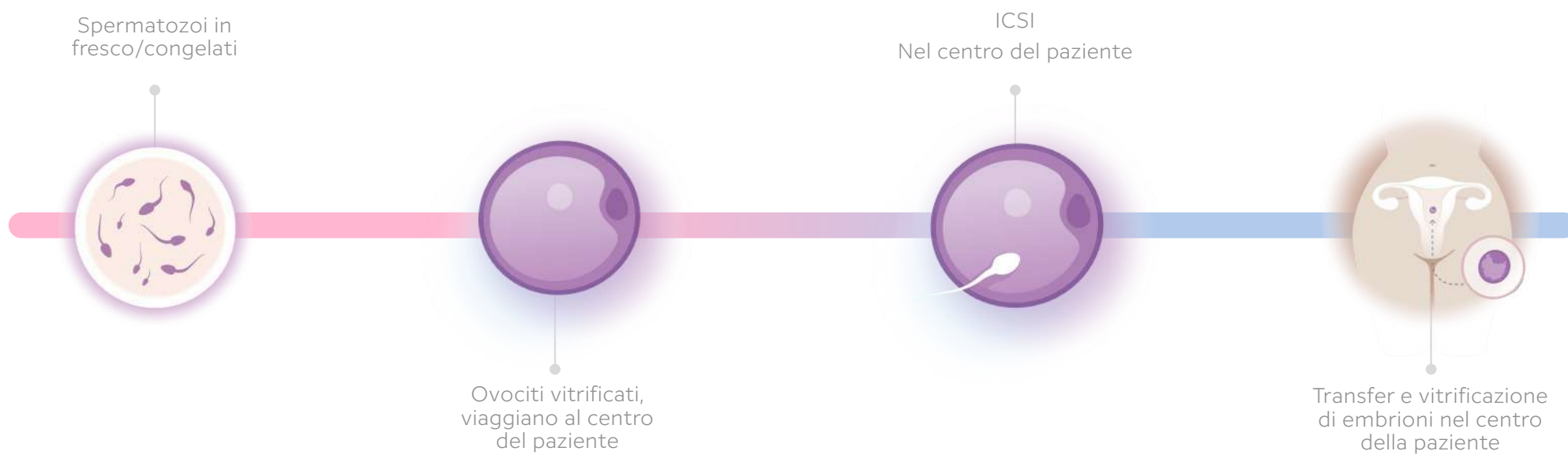
	Land shipping	Air shipping
Oocytes batches	105	40
Total oocytes	697	270
Survival rate*	81.1%	67.4%
Fertilization rate	73.4%	73.6%
Transfers	102	39
PR/transfer*	50%	25.6%

Next Fertility 2022

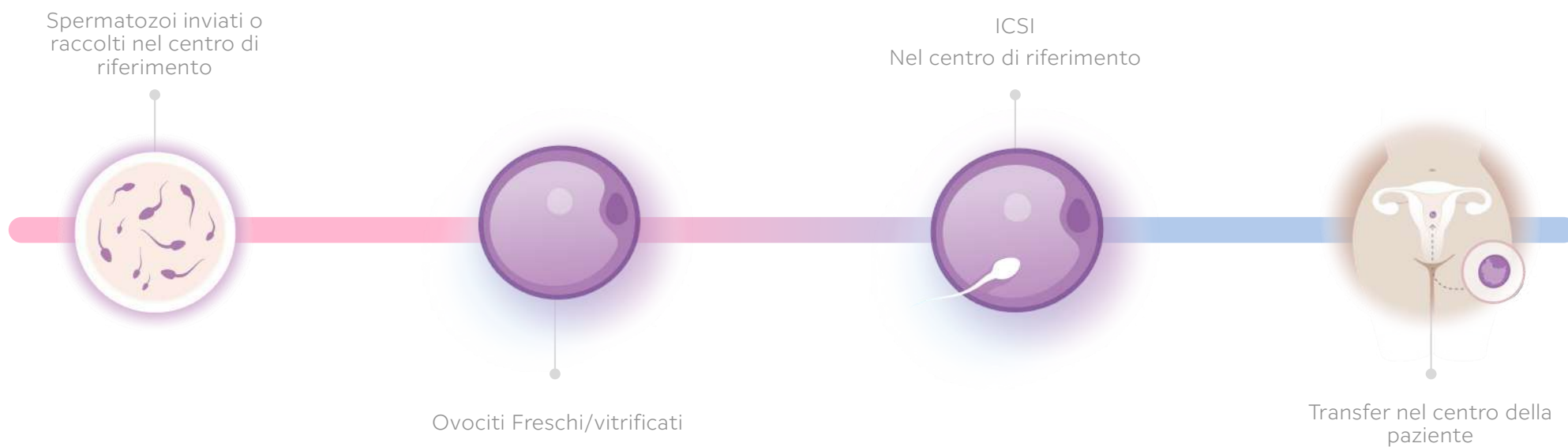
	Ovociti freschi	Ovociti vetrificati
Totale	1134	810
% Fertilizzazione	72,1 %	73,5 %
% Blastocisto	59,8 %	58,3 %
Ovociti per blastocisto	2,3	2,3



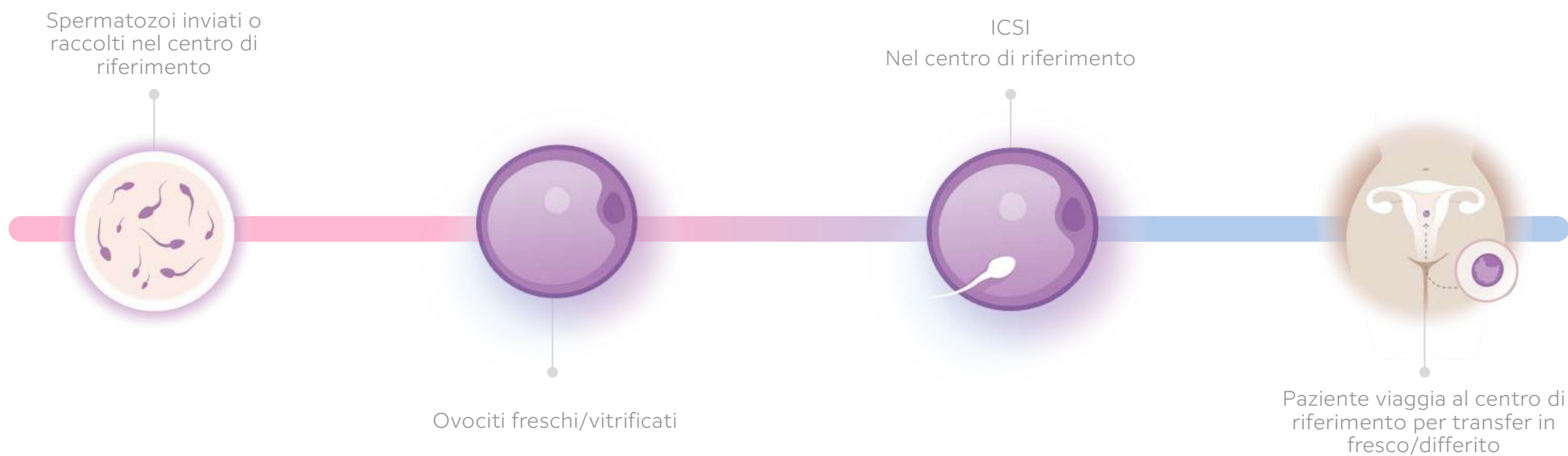
Ovociti in viaggio



Embrioni in viaggio



Pazienti in viaggio



Modello migliore?

	Ovociti viaggiano	Blastocisti viaggiano
% sopravvivenza	84,7 %	99 %
% impianto	49,1 %	50,9 %
% gravidanza	62,3 %	61,2 %
% aborto	16,3 %	16,8 %

Il miglior modello é rispondere alle necessità dei pazienti

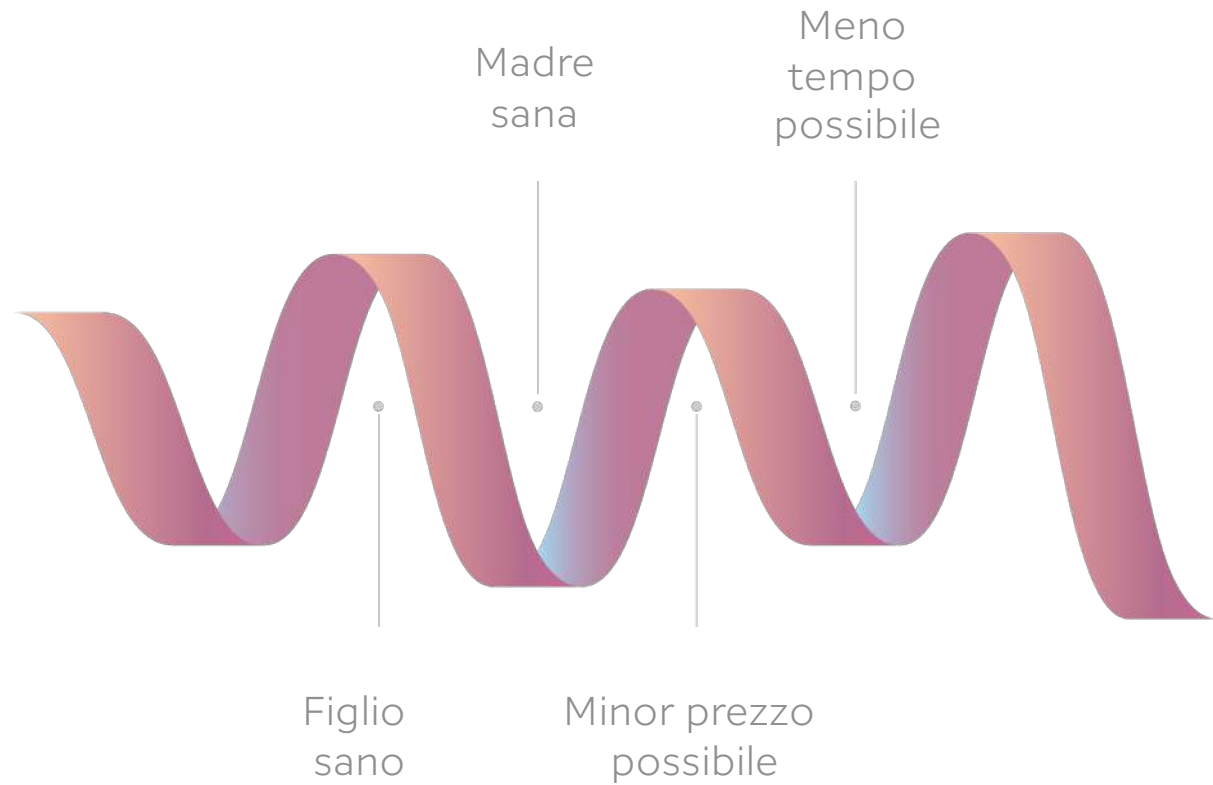
RBMO
REPRODUCTIVE BIOMEDICINE ONLINE

COUNTERCURRENT | VOLUME 44, ISSUE 4, P587-589, APRIL 01, 2022

Maximizing live birth rates cannot be the only key performance indicator of IVF

Geeta Nargund   Adrija Kumar Datta

Published: November 23, 2021 • DOI: <https://doi.org/10.1016/j.rbmo.2021.11.011>



Programma Due Paesi Due Centri

- **Sicuro:** mantiene i risultati
- **Efficace:** permette lo scambio di grandi quantità di materiale biologico
- **Patient friendly:** si adatta alle necessità dei pazienti





REVIEW

Open Access

Preparation of the endometrium for frozen embryo transfer: an update on clinical practices

Yiting Zhang^{1,2,3,4,5,6}, Xiao Fu^{1,2,3,4,5,6}, Shuli Gao^{1,2,3,4,5,6}, Shuzhe Gao^{1,2,3,4,5,6}, Shanshan Gao^{1,2,3,4,5,6*}, Jinlong Ma^{1,2,3,4,5,6} and Zi-Jiang Chen^{1,2,3,4,5,6,7,8}



Cycle regimens for frozen-thawed embryo transfer

Tarek Ghobara, Tarek A Gelbaya, Reuben Olugbenga Ayeleke Authors' declarations of interest

Version published: 05 July 2017 Version history

<https://doi.org/10.1002/14651858.CD003414.pub3>

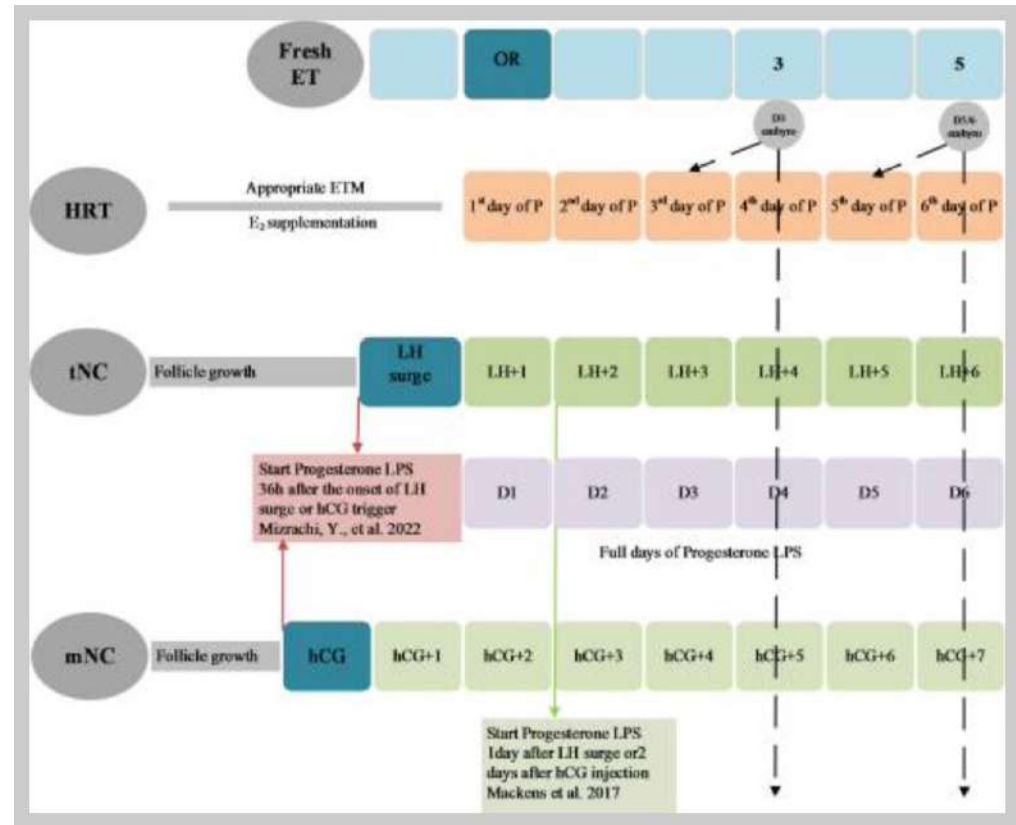


Front Endocrinol (Lausanne). 2023; 14: 1250847.
 Published online 2023 Aug 29. doi: [10.3389/fendo.2023.1250847](https://doi.org/10.3389/fendo.2023.1250847)

PMCID: PMC10497870
 PMID: 37711892

Finding of the optimal preparation and timing of endometrium in frozen-thawed embryo transfer: a literature review of clinical evidence

Ya-Wen Hsueh,¹ Chien-Chu Huang,¹ Shuo-Wen Hung,² Chia-Wei Chang,¹ Hsi-Chen Hsu,¹ Tung-Chuan Yang,¹ Wu-Chou Lin,¹ Shan-Yu Su,² and Hsun-Ming Chang^{2,1,*}



Preparazione endometriale

Ciclo

Naturale
Naturale modificato
Mild stim
Sostituito

Agonista GnRH

Ecografia

Trilaminare
Spessore
Compattazione

Estrogeni

Orali
Vaginali
Transdermici
Sottocute
Intramuscolo

Compresse
Cerotti
Gel

Dose fissa
Ascendente

10-36 giorni

Analisi

Estradiolo
Progesterone
LH

Progesterone

Orale
Vaginale
Sottocute
Intramuscolo

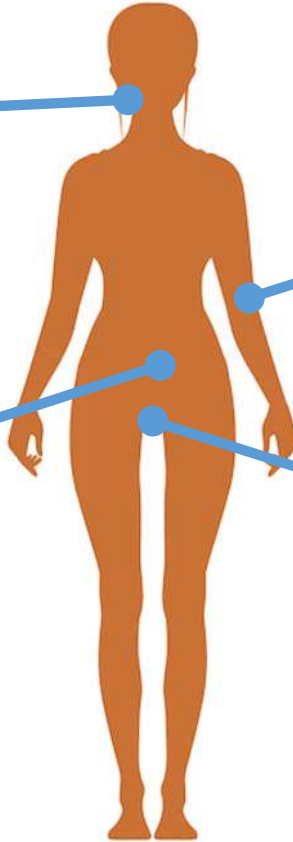
IM
SC
Vaginale + IM
Vaginale + SC
Vaginale + sostegno

Preparazione con estrogeni

- 10-36 giorni

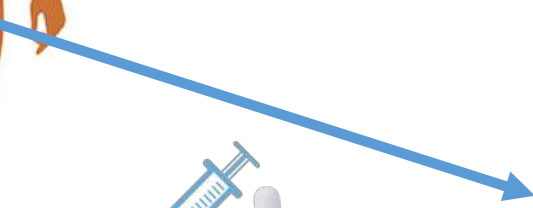
Ecografía

- Endometrio >7mm



Livelli ormonali

- $P < 1$ ng/ml
- $P > 9-10$ ng/ml



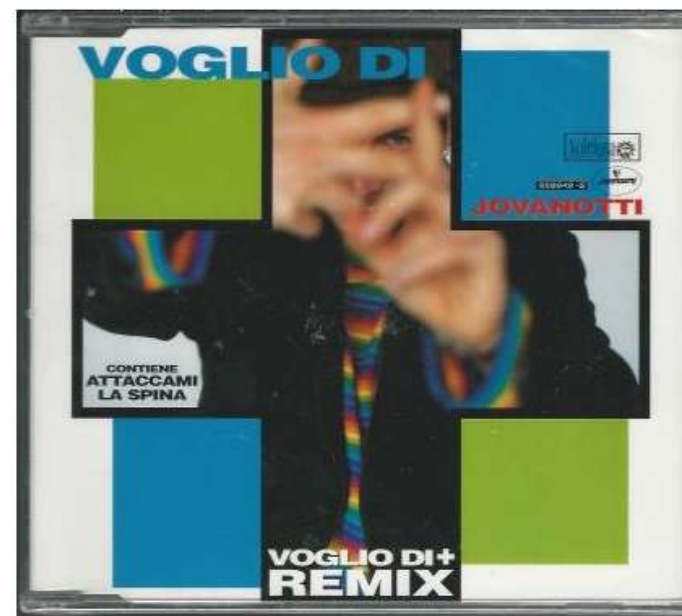
Progesterone

- IM
- SC 50 mg
- VAG con sostegno



*Tu... tu... non mi
basti mai*

**Voglio di piú!
E non mi
basta mai!**



ENDOMETRIO

REFRATTARIO

- **Aumento/cambio estrogeni**
- **Vasodilatatori**
 - Sildenafil
 - Tocoferolo
 - Pentossifillina
 - Arginina
- **Scratching endometriale**
- **GM-CSF**
- **PRP**
- **Cellule staminali**
 - Midollo osseo
 - Tessuto adiposo
 - Mestruazioni
 - Esosomi



Contents

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- 2. Pathophysiol
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- (NMES)
- array (ERA)

Review

The thin endometrium in assisted reproductive technology: An ongoing challenge

Maryam Eftekhari^a, Nasim Tabibnejad^a

VIEWES AND REVIEWS | VOLUME 112, ISSUE 6, P987-993, DECEMBER 2019

In vitro fertilization add-ons for the endometrium: it doesn't add-up

Sarah Lensen, Ph.D. • Norman Shreeve, B.M.B.S. • Kurt T. Barnhart, M.D., M.S.C.E. •
 Ahmed Gibreel, M.D. • Ernest Hung Yu Ng, M.D. • Ashley Moffett, M.D.

..... go implantation
 with lower possibility of
 applied to improve endometrial
 controversial. Large randomized trials should be
 ge, timing of administration and outcomes of these

RBMO



REVIEW

Management of thin endometrium in assisted reproduction: a clinical practice guideline from the Canadian Fertility and Andrology Society



BIOGRAPHY

Dr Kimberly Liu is an infertility specialist practising at Mount Sinai Fertility, Toronto, Canada, and an Assistant Professor at the University of Toronto. She is the Program Director for the University of Toronto Gynecologic Reproductive Endocrinology and Infertility Fellowship Program. She is the author of numerous research publications and several national guidelines for fertility and ART practice in Canada.

Kimberly E. Liu^{1,*}, Michael Hartman², Alex Hartman³.

Intervention	Benefits versus harms (efficacy versus safety)	Level of evidence for efficacy (LBR/CPR) ¹	Level of evidence for safety ¹	Considerations	Recommendation	
Platelet-rich plasma	Intrauterine PRP administration	⊕○○○	⊕○○○	Current studies include a small sample size and heterogeneous study population in addition to different procedures of PRP	Intrauterine administration of platelet-rich plasma is not recommended .	
	Intraovarian PRP administration	No data	No data		Intraovarian administration of platelet-rich plasma is not recommended .	
Duostim	No data of benefit on LBR or miscarriage rate. Harms are expected to be similar to standard OS	No data	No data	An RCT comparing duostim with two conventional stimulations has not been performed to date	Duostim is currently not recommended for routine clinical use .	
Adjuncts during ovarian stimulation	Conflicting evidence on LBR. Safety concerns	⊕⊕○○	⊕⊕○○	/	Adjuncts (metformin, growth hormone, testosterone, DHEA, aspirin, indomethacin, and sildenafil) before or during ovarian stimulation are not recommended .	
Intravaginal and intrauterine culture device	Intravaginal culture device	No evidence of a benefit on LBR. No data on harms	⊕○○○	No data	An embryologist and an IVF lab are still required	Intravaginal or intrauterine culture devices are currently not recommended for routine clinical use .
	Intrauterine culture device	One small study showing no benefit on LBR. No data on harms	⊕○○○	No data		
Additions to transfer media (HA)	With a high dose of HA, a benefit on LBR and reduced risk of miscarriage was found. Complications: increased multiple pregnancy rate	⊕⊕⊕○	⊕⊕⊕○	The use of HA should be combined with a single embryo transfer policy	Hyaluronic acid addition to transfer media is recommended . Monitoring of the multiple pregnancy rate is still advisable.	
Endometrial scratching	Inconclusive data of benefit on LBR, with no effect on miscarriage rate. Complications: moderate pain, bleeding, risk of infection	⊕⊕⊕○	⊕⊕⊕○	Timing of scratch and methodology of the procedure differed between studies.	Endometrial scratching is currently not recommended for routine clinical use .	
Flushing of the uterus	Intrauterine administration of hCG	Some benefit for cleavage stage (not blastocyst) transfer at >500 IU. No evidence of harm	⊕⊕⊕○	⊕○○○	Timing of administration, dosage of hCG and timing of embryo transfer differed between studies.	Intrauterine administration of hCG is not recommended .
	Intrauterine administration of G-CSF	RIF. No evidence of benefit on LBR. Thin endometrium may improve LBR (1 RCT). Very few side effects reported	⊕⊕○○	⊕○○○	/	Intrauterine administration of granulocyte colony-stimulating factor is not recommended .
	Endometrial administration of embryo culture supernatant	No evidence of benefit on LBR or miscarriage rate. No evidence of harm	⊕○○○	⊕○○○	In several studies, it was unclear how the culture media were administered, by injection or as a uterine infusion.	Endometrial administration of embryo culture supernatant is not recommended .

Intervention	Benefits versus harms (efficacy versus safety)	Level of evidence for efficacy (LBR/CPR) ¹	Level of evidence for safety ¹	Considerations	Recommendation	
Endometrial exposure to seminal plasma	No evidence of a benefit on LBR or miscarriage rate. Complications: no evidence of an effect on multiple pregnancy rate, potential risk of allergic reaction	⊕⊕○○	⊕⊕○○	Available evidence is very heterogeneous with regards to the inclusion/exclusion criteria of patients, and the interventions	Endometrial exposure to seminal plasma is not recommended .	
Stem cell mobilization	Stem cell therapy for POI or DOR	Available evidence comes from case reports and uncontrolled studies with very little information on the actual procedures and long-term follow-up is lacking	No data	No data	/	Stem cell therapy for premature ovarian insufficiency, diminished/poor ovarian reserve or thin endometrium is not recommended .
	Stem cell therapy for thin endometrium		No data	No data		

Good practice recommendations on add-ons in reproductive medicine[†]

ESHRE Add-ons working group: K. Lundin¹, J.G. Bentzen², G. Bozdag³, T. Ebner⁴, J. Harper⁵, N. Le Clef⁶, A. Moffett⁷, S. Norcross⁸, N.P. Polyzos⁹, S. Rautakallio-Hokkanen¹⁰, I. Sfontouris¹¹, K. Sermon¹², N. Vermeulen¹³, and A. Pinborg¹⁴*

Effects of Intrauterine Infusion of Autologous Platelet-Rich Plasma in Women Undergoing Treatment with Assisted Reproductive Technology: a Meta-Analysis of Randomized Controlled Trials

Shifu Hu ¹, Zhishan Jin ¹, Qianqian Tang ¹

The studies were included if they

1. were RCTs;
2. included patients undergoing treatment with ARTs, including in vitro fertilization (IVF) or intracytoplasmic sperm injection;
3. were already published;
4. compared intrauterine infusion of autologous PRP with no injection/placebo; and
5. included at least one of the following reported outcomes: chemical pregnancy rate, clinical pregnancy rate, and miscarriage rate.

The studies were excluded if they

1. were review articles, commentaries, letters, or observational studies;
2. were non-clinical trials;
3. were not RCTs; and
4. reported inability to extract data from the literature.

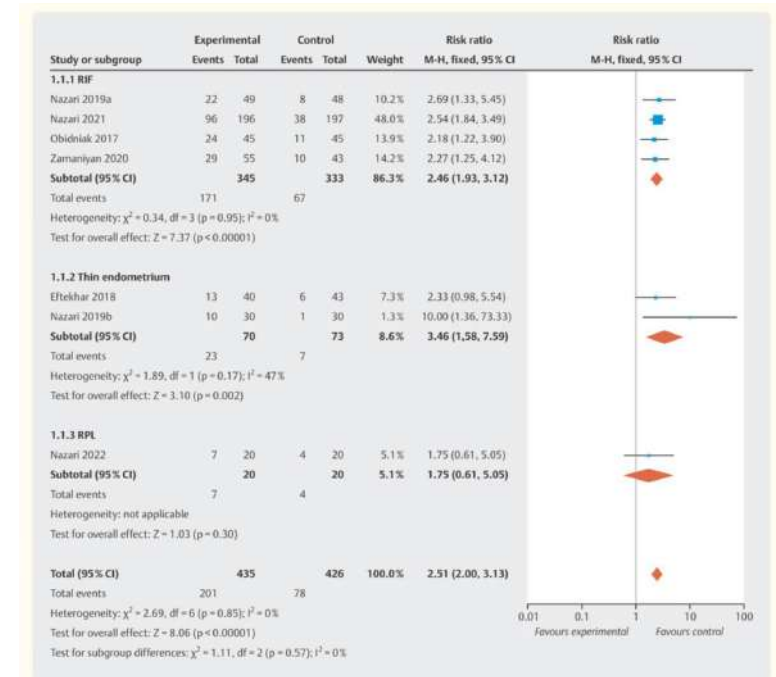
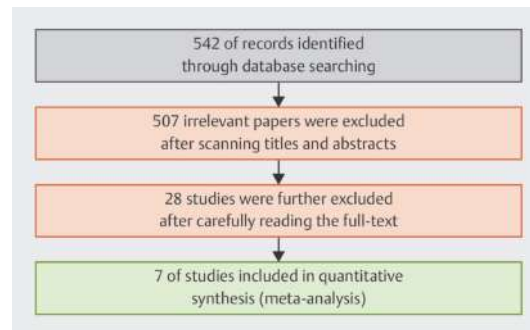


Fig. 2

Forest plot diagram showing the clinical pregnancy rate in women who received intrauterine platelet-rich plasma versus controls regarding population type (recurrent implantation failure (RIF), recurrent pregnancy loss (RPL) and thin endometrium). CI = confidence intervals.

Platelet-Rich Plasma Intrauterine Infusion as Assisted Reproduction Technology (ART) to Combat Repeated Implantation Failure (RIF): A Systematic Review and Meta-Analysis

Chunling Huang, Xiaohui Ye, Lifang Ye, Lunyuan Lu, and Fengxiang Liu^{✉*}

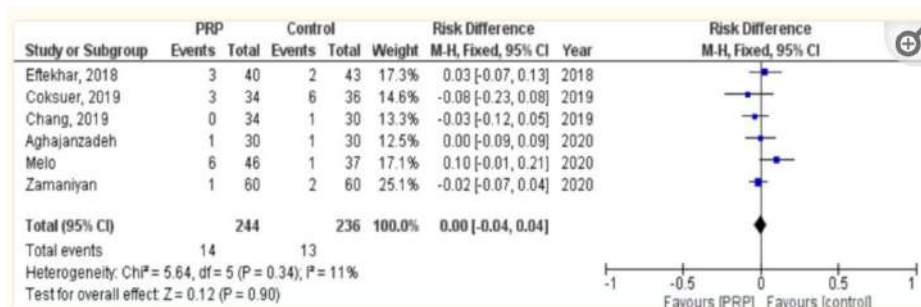


Fig. 5:

Forest plot showing individual and combined effect size estimates and 95% CI in studies that evaluated the risk of miscarriage in women who received intrauterine platelet rich plasma versus control

Iran J Public Health. 2023 Aug; 52(8): 1542–1554.

doi: [10.18502/ijph.v52i8.13394](https://doi.org/10.18502/ijph.v52i8.13394)

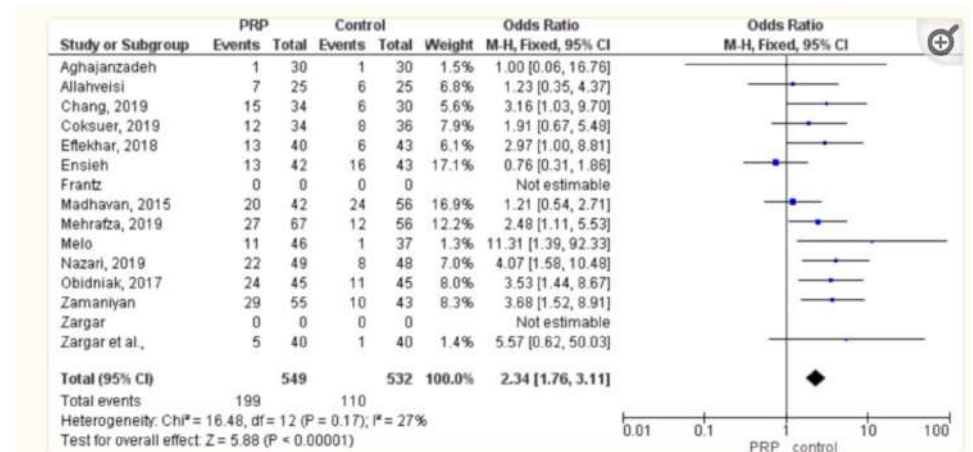
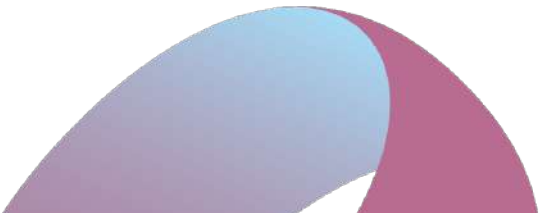


Fig. 2:

Forest plot detailed odds ratio and 95% CI for clinical pregnancy

Interpretazione PRP

- Volume
- Concentrazione piastrine
- Concentrazione fattori di crescita
- Attivazione
- Metodo di instillazione



Preparazione endometriale

Ciclo

Naturale
Naturale modificato
Mild stim
Sostituito

Agonista GnRH

Ecografia

Trilaminare
Spessore
Compattazione

Estrogeni

Orali
Vaginali
Transdermici
Sottocute
Intramuscolo

Compresse
Cerotti
Gel

Dose fissa
Ascendente

10-36 giorni

Análisis

Estradiolo
Progesterone
LH

Progesterone

Orale
Vaginale
Sottocute
Intramuscolo

IM
SC
Vaginale + IM
Vaginale + SC
Vaginale + sostegno

- Aumento/cambio estrogeni
- Vasodilatatori
 - Sildenafil
 - Tocoferolo
 - Pentossifillina
 - Arginina
- Scratching endometriale
- GM-CSF
- PRP
- Cellule staminali
 - Midollo osseo
 - Tessuto adiposo
 - Mestruazioni
 - Esosomi

Grazie per
l'attenzione



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