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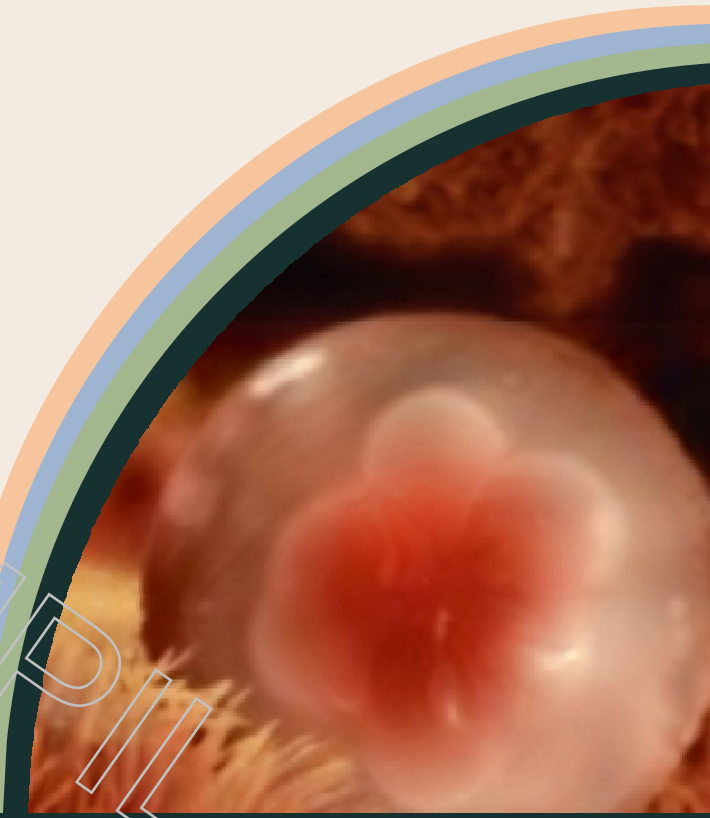
LABORATOIRE DE RECHERCHE & D'INNOVATION

RESULTS OF A RANDOMISED CONTROLLED TRIAL

optimizing success rates in assisted reproductive technology with personalized care based on the endometrial immune profiling



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SINCE 2012

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SAMPIL, 29 Avril 2025

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OBJECTIVE OF THE RCT

Does endometrial immune profiling combined with precision therapy improve the performance of IVF treatment ?

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STUDY DESIGN

INCLUSION CRITERIA:

GOOD PROGNOSIS PATIENTS

Infertile patient with planned fresh or frozen ET
Younger than 38 years
Range of oocyte pick-up with ET <3
No ovarian insufficiency (AMH>1.5 pg/ml; AFC>6)
No azoospermia

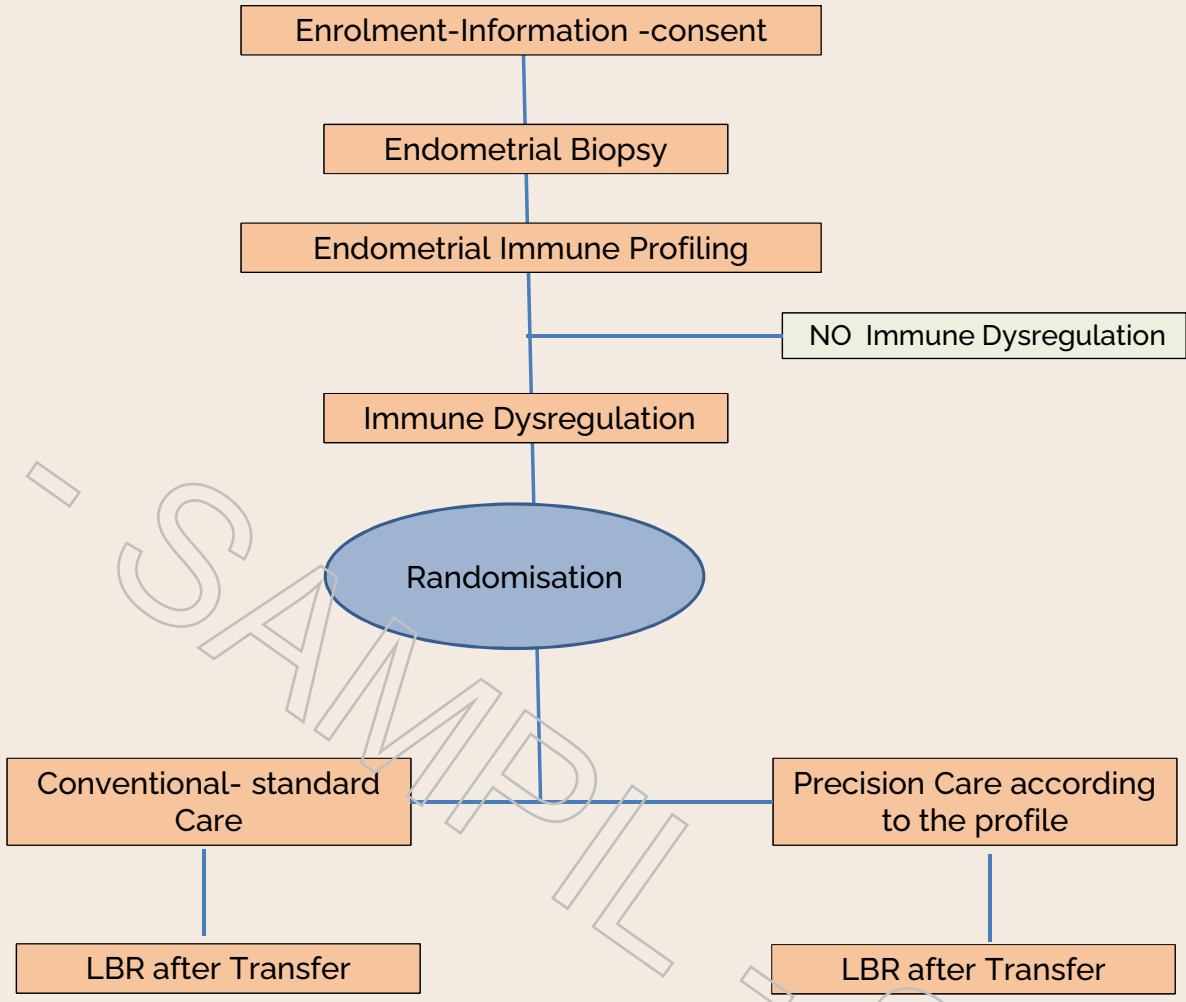
METHOLOGY:

THE PRIMARY ANALYSIS:

Focus on demonstrating the superiority of precision care using the modified intent-to-treat (mITT) population, excluding patients without ET

THE PRIMARY ENDPOINT: Live birth rate (LBR) per transfer

HYPOTHESIS: A relative increase of 40% of LBR



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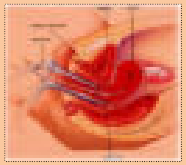
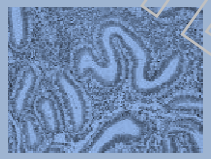
THE UTERINE IMMUNE PROFILING (UTIMPRO) PROCESS

- The uterine immune profiling through the quantification of the RNA expression of predefined targets aims to document this very particular immune environment
- All process respect the norm **QMS 13485**



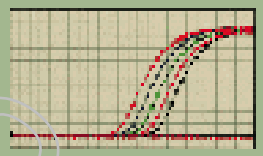
SAMPLE COLLECTION

- An endometrial biopsy at mid-luteal phase
- The sample is sent to us laboratory



PRE- ANALYSIS

- Mid luteal phase
- RNA extraction
- RNA integrity



ANALYSIS

Cytokine expression (MLI) :
- Reverse transcription
- Real time PCR
- Patented ranges and methods of interpretation

IL-18 TWEAK IL-15 Fn-14 CD56

MEDICAL REPORT

Diagnosis of Ut. Immune profile

Precision therapy plan:
- Targeted strategy
- Targeted treatments

UNDER IMMUNE ACTIVATION

TARGETED STRATEGY :

" Trigger the mobilisation and activation of immune cells "

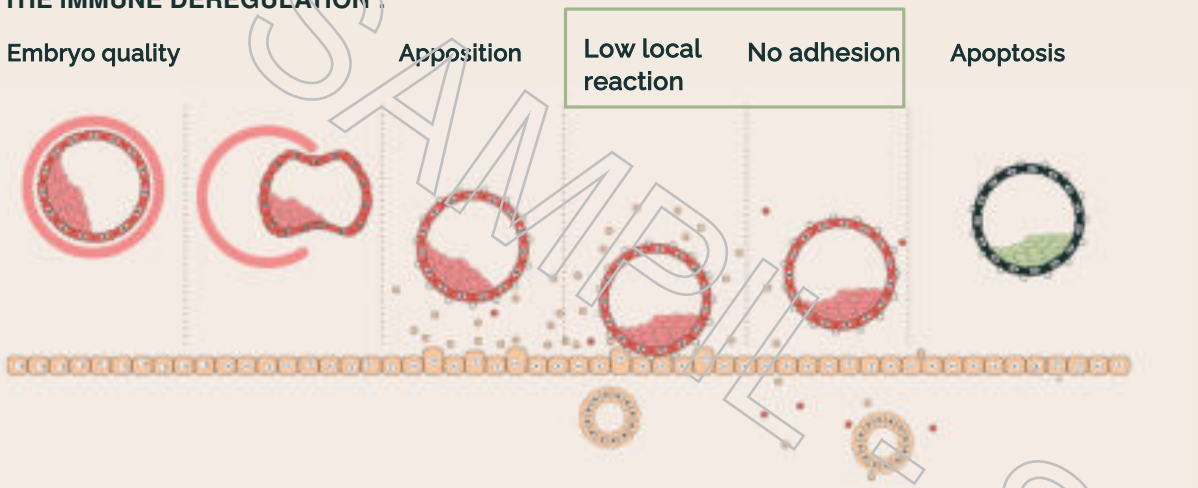
TARGETED TREATMENTS :

- Scratching mid-luteal phase prior ET
- HCG supplementation luteal phase of ET cycle
- Sexual intercourse after ET
- Double sequential embryo transfer (D3-D5) if relevant

DIAGNOSIS OF UTERINE IMMUNE PROFILING :

- No Th-2 angiogenic cytokines (IL-18)
- Immature uNK cells (IL-15)
- Absence of uNK mobilisation

THE IMMUNE DEREGULATION :



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OVER IMMUNE ACTIVATION

TARGETED STRATEGY :

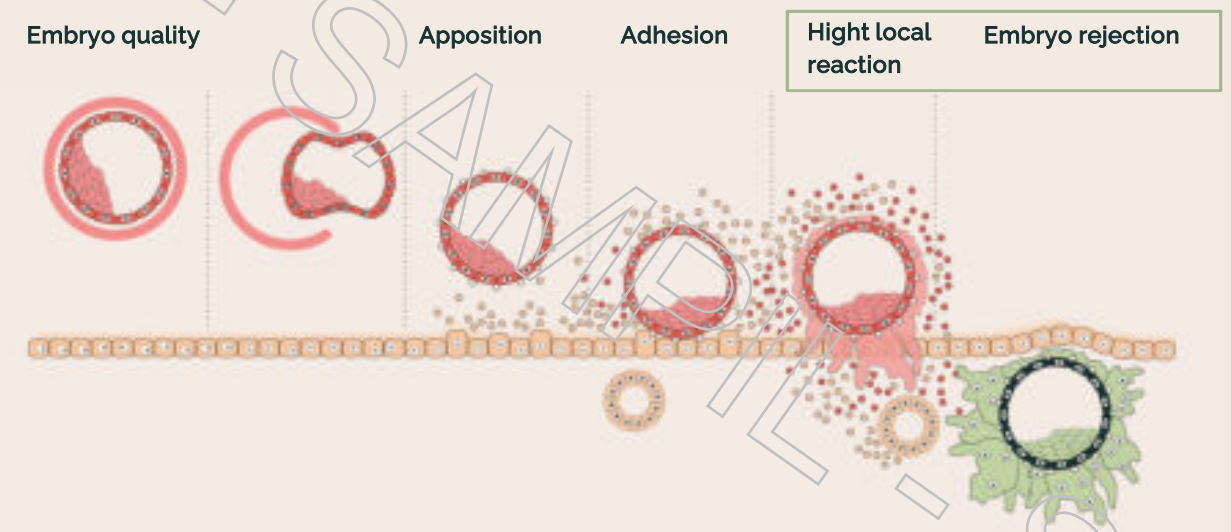
" To control the activation of immune cells "

TARGETED TREATMENTS :

- No local injury (over)/ scratching (Mixed)
- High dose of progesterone
- Glucocorticoids or Intralipids (test under therapy)

UTERINE IMMUNE PROFILING :

Excess of Th-1 cytokines
No local immunoregulation
Excessive uNK cells mobilisation



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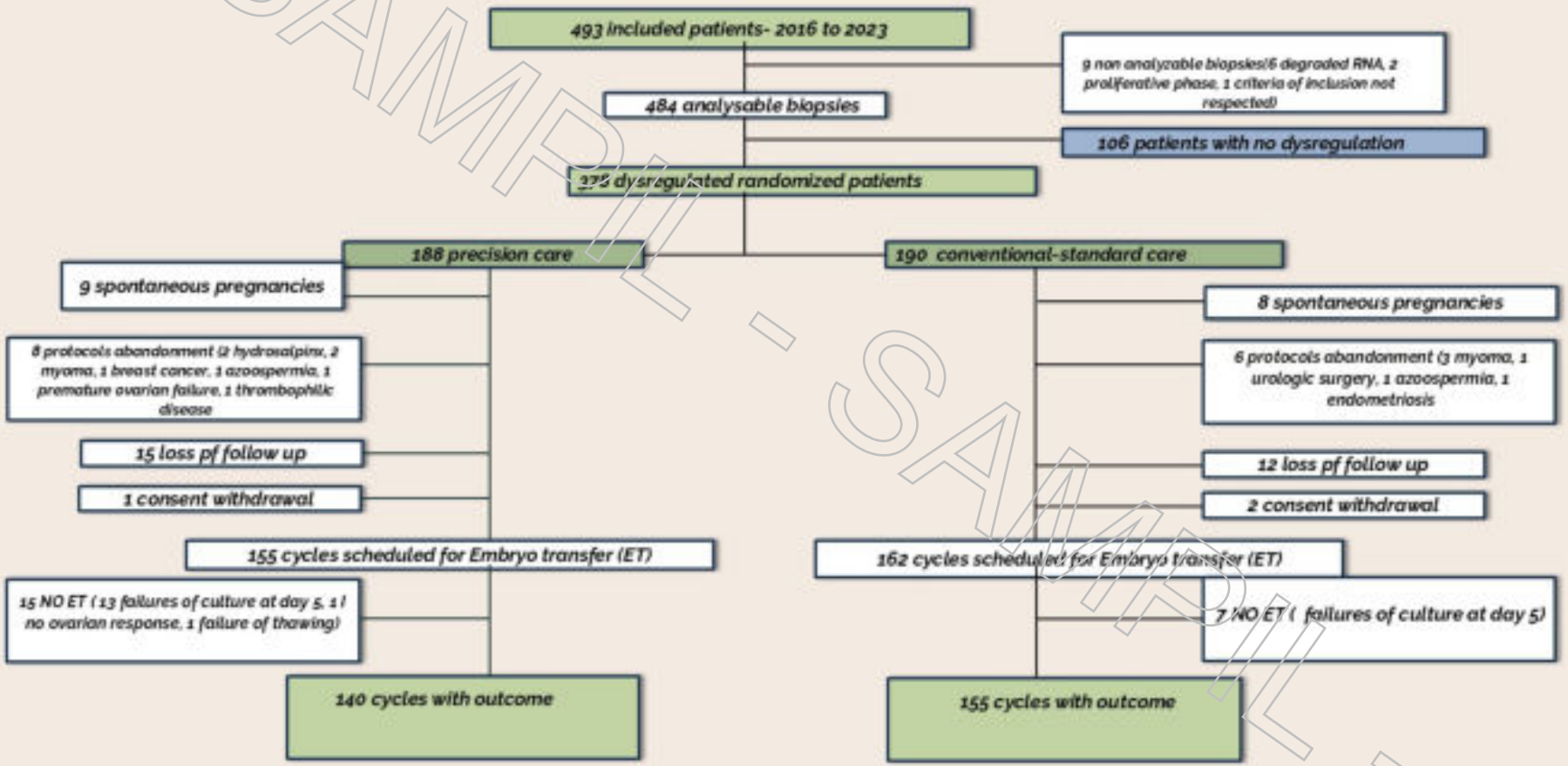
FLOW CHART OF THE STUDY



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Descriptive clinical data of randomised patients

	Total N=295	Precision care N=140	Conventional care N=155
Age, years (Median, Q1-Q3)	33.4 (31.1;36.0)	33.7 (31.5;36.1)	33.4 (31.0;36.1)
AMH, ng/ml (Median, Q1-Q3)	3.16 (2.27;4.70)	3.30 (2.40;4.49)	2.95 (2.21;4.86)
Number of previous oocyte pick-ups (Median, Q1-Q3)	1 (0;1)	1 (0;1)	1 (0;1)
Number of previous embryos transferred (Median, Q1-Q3)	1 (0;2)	1 (0;2)	1 (0;2)
Previous ET failure, three levels — no. (%)			
Two or more transfers failed	133 (45.1%)	69 (49.3%)	64 (41.3%)
One transfer failed	64 (21.7%)	26 (18.6%)	38 (24.5%)
No previous ET	98 (33.2%)	45 (32.1%)	53 (34.2%)
Type of Embryo transfer — no. (%)			
Fresh	222/290(76.6%)	103/138(74.6%)	119/153(77.8%)
Freezed-thawed	68/290(23.4%)	35/138(25.4%)	34/153(22.2%)
Number of embryos transferred (Median, Q1-Q3)	1 (1;2)	1 (1;2)	1 (1;1)

RESULTS OF ANALYSIS

Patients with a history of repeated failed implantations has exactly the same repartition

"We are not documenting endometrial pathology, we are documenting a physiological imbalance"

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PATIENTS INCLUDED IN THE RANDOMISED CONTROLLED TRIAL (RCT)

78 %

DYSREGULATED PROFILE

30 %

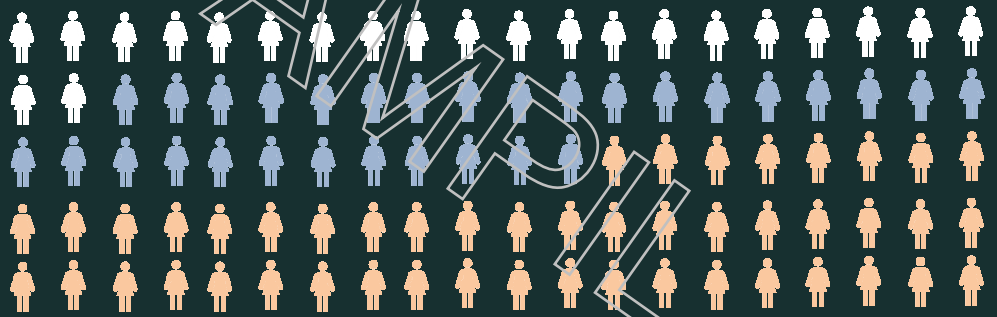
UNDER-ACTIVE PROFILE

48 %

OVER-ACTIVE & MIXED PROFILE

22 %

REGULATED PROFILE



PRIMARY END-POINT OF THE mITT ANALYSIS

AND SECONDARY END –POINT OF THE MODIFIED INTENTION TO TREAT (MITT)

	Total	Precision Care	Conventional Care	Precision Care vs. Conventional care			
	N=295	N=140	N=155				
				Odds Ratio* (95% CI)	p-value£	Odds Ratio** (95% CI)	p-value£
LIVE BIRTH RATE	35.3% (104/295)	**41.4% (58/140)**	**29.7% (46/155)**	**1.68** (1.04; 2.73)[b]	0.036	1.75 (1.04; 2.92)[b]	0.030
Ongoing pregnancy rate	35.6% (105/295)	41.4% (58/140)	30.3% (47/155)	1.63 (1.01; 2.65)[b]	0.048	1.68 (1.00; 2.81)[b]	0.043
Clinical pregnancy rate	44.7% (132/295)	50.7% (71/140)	39.4% (61/155)	1.59 (1.00; 2.52)[b]	0.052	1.66 (0.99; 2.70)[b]	0.041
Early miscarriage rate	20.3 % (27/133)	18.3% (13/71)	22.6% (14/62)	0.77 (0.31; 1.87)[b]	0.543	0.80 (0.31; 2.04)[b]	0.608

* Unadjusted Odds Ratio. Adjusted Odds Ratio for Age class, embryo quality, embryo transfer and Uterine immune profile

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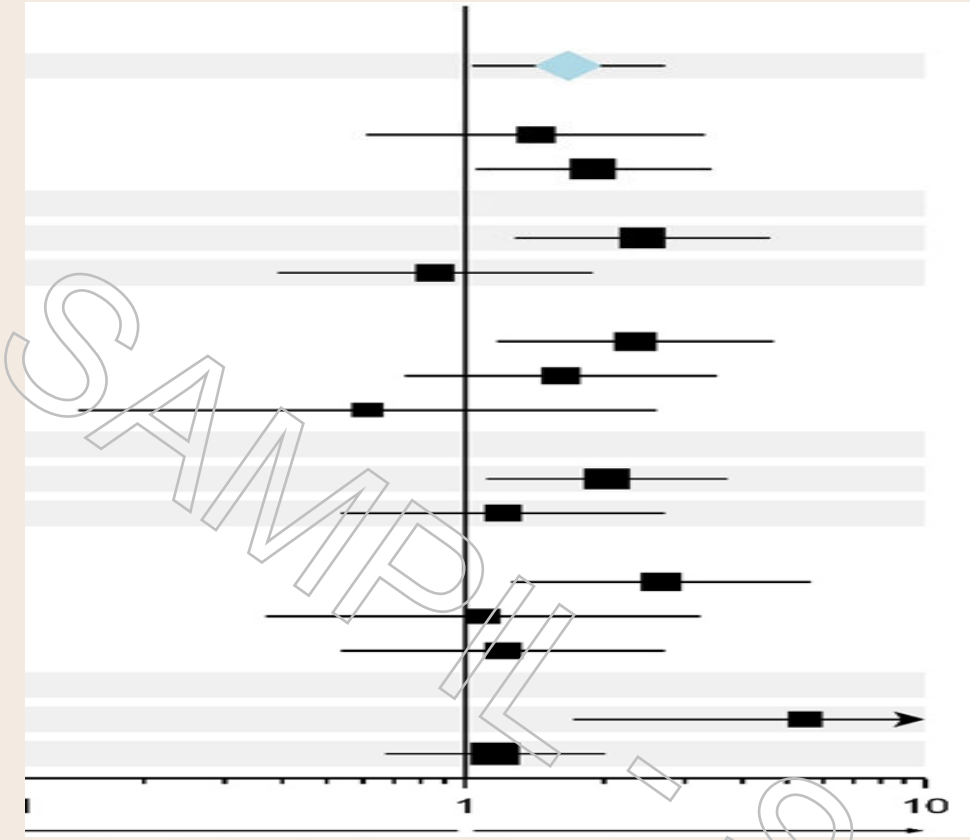
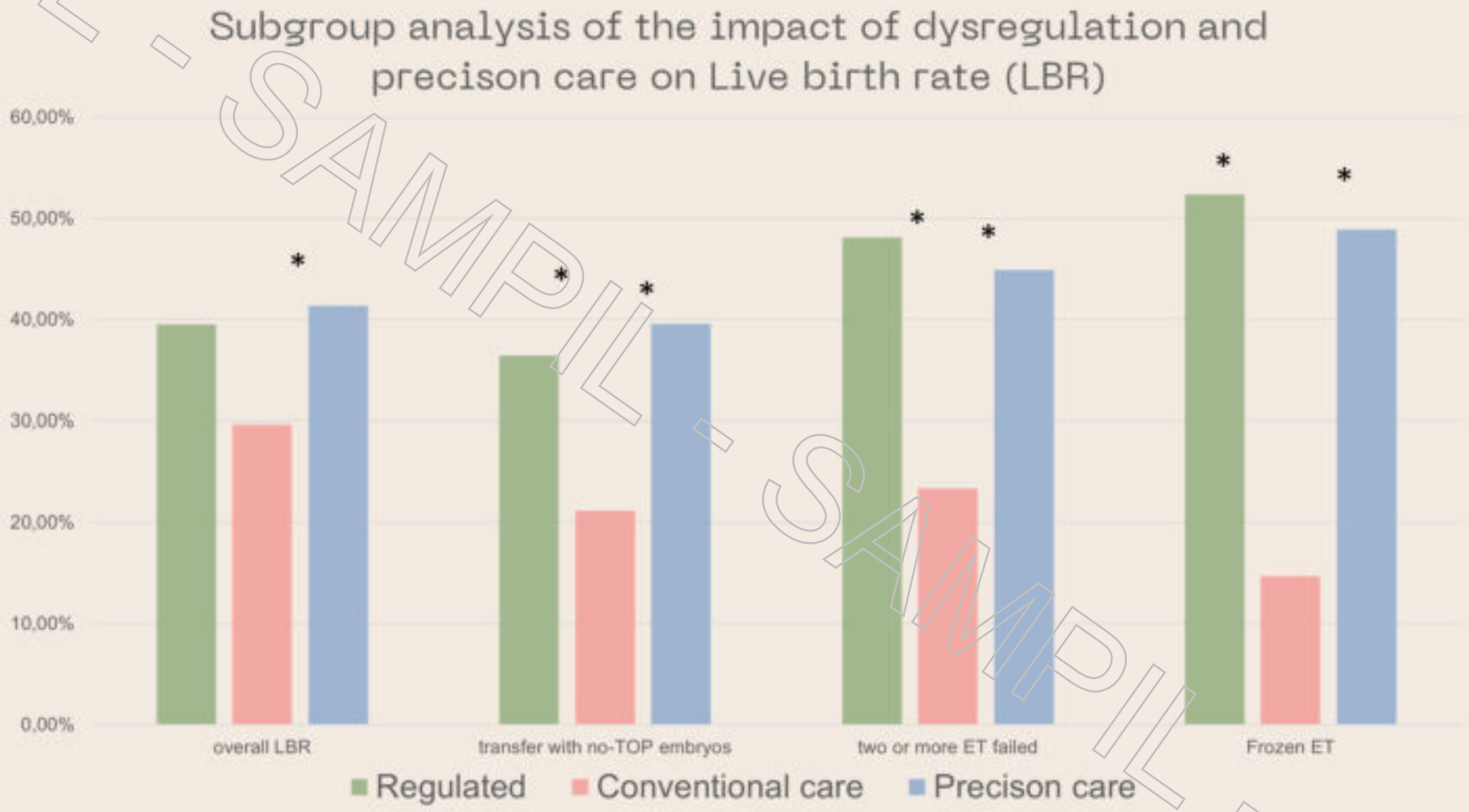
FOREST PLOT: ODDS OF LIVE BIRTH OUTCOMES

COMPARING CONVENTIONAL VS. PRECISION CARE APPROACHES

Subgroup	Precision care event/total (%)	Conventional-Standard care event/total (%)	OR (95%) CI
Overall	58/140 (41.4%)	46/155 (29.7%)	1.68 (1.04 to 2.71)
Age, class			
≥ 35	18/54 (33.3%)	13/50 (26.0%)	1.42 (0.61 to 3.32)
< 35	40/86 (46.5%)	33/105 (31.4%)	1.90 (1.05 to 3.43)
Embryos quality			
No Top	36/91 (39.6%)	21/99 (21.2%)	2.43 (1.28 to 4.61)
Top	20/47 (42.6%)	25/54 (46.3%)	0.86 (0.39 to 1.89)
Uterine immune profile			
Over activation	33/71 (46.5%)	20/74 (27.0%)	2.34 (1.17 to 4.69)
Under activation	20/46 (43.5%)	21/65 (32.3%)	1.61 (0.74 to 3.52)
Mixt	5/23 (21.7%)	5/16 (31.3%)	0.61 (0.14 to 2.60)
Previous ET failure, two levels			
At least 1 ET failure	39/95 (41.1%)	26/102 (25.5%)	2.04 (1.11 to 3.73)
No previous ET	19/45 (42.2%)	20/53 (37.7%)	1.21 (0.54 to 2.71)
Previous ET failure, three levels			
Two or more transfer failed	31/69 (44.9%)	15/64 (23.4%)	2.66 (1.26 to 5.63)
One transfer failed	8/26 (30.8%)	11/38 (28.9%)	1.09 (0.37 to 3.24)
No previous ET	19/45 (42.2%)	20/53 (37.7%)	1.21 (0.54 to 2.71)
Type of Embryo transfer			
Frozed-thawed	17/35 (48.6%)	5/34 (14.7%)	5.48 (1.72 to 17.43)
Fresh	39/103 (37.9%)	41/119 (34.5%)	1.16 (0.67 to 2.01)





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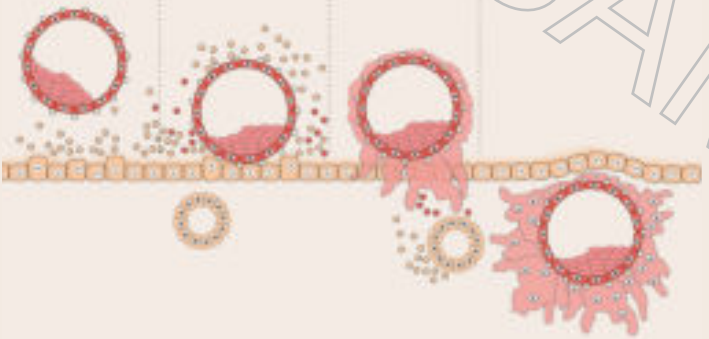
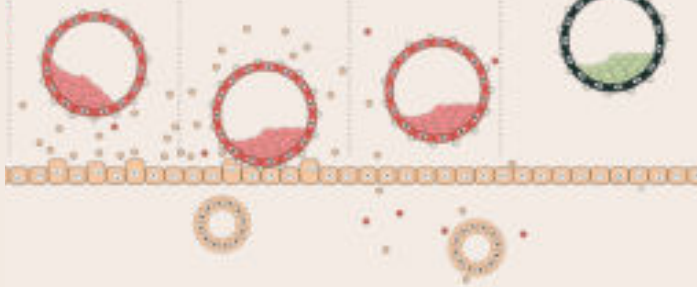
BALANCED IMMUNE ACTIVATION



OVER IMMUNE ACTIVATION

UNDER IMMUNE ACTIVATION



CONCLUSION

The immune environment of the uterus appears as a fundamental and crucial parameter

This RCT indirectly establishes that pregnancy results from a very early balanced immune dialogue between the embryo and the endometrium.

Its rebalancing **can help 75-80%** of infertile patients, even at the beginning of their ART treatment

Precision therapy significantly increased LBR after embryo transfer.

Personalization is particularly **useful** for those with **sub-optimal embryo quality; patients** with **history** of only two ET **failures and frozen ET**.

FUTURE DIRECTION

- The generalizability and robustness of our findings depend on the replication of our RCT by independent research teams, potentially incorporating optimal embryo by using PGT-A for example.
- It is essential to clarify how restoring the endometrial immune balance can support the development of certain embryos.

REPLICATE	CLARIFY	GENERALIZE

TEAM & PARTNER

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