

21ST



PGDIS CONFERENCE



6-8 May 2024
Kuala Lumpur
Malaysia

**PGT and
BEYOND...**

A randomized double blinded controlled
trial of non-invasive PGT-A:
laboratory optimization prior to
commencement of the trial

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7th May 2024

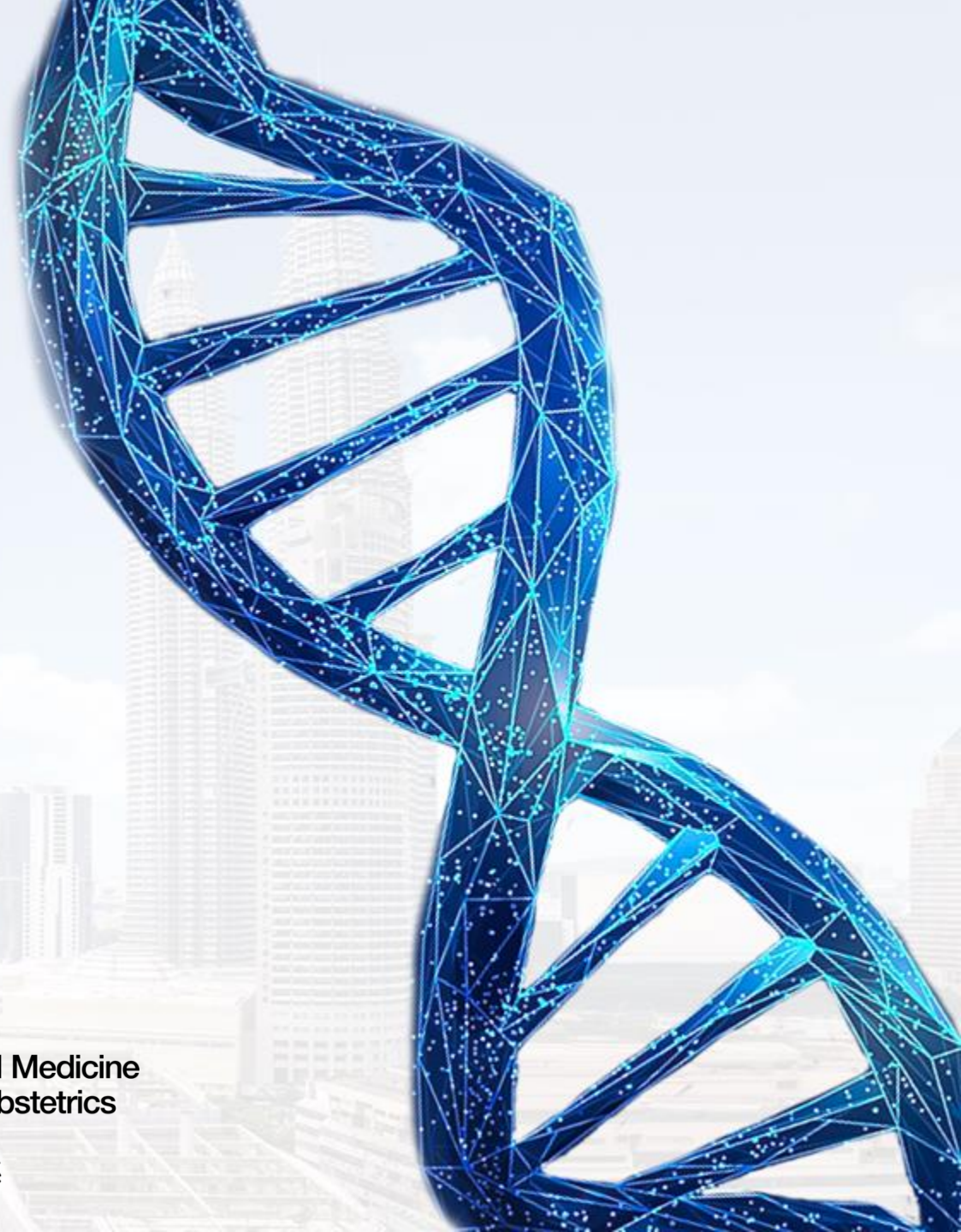


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Background

- ❑ the success rate of IVF treatment for couples with infertility remain low
- ❑ aneuploidy rate of embryos increases exponentially with advancing maternal age
- ❑ recent randomized trials found that PGT-A only improved live-birth rates in women >35 years, but not in the general population
- ❑ trophectoderm (TE) biopsy is an invasive procedure which may reduce implantation potential of embryos

Munne et al., Fertil Steril 2019;112:1071-9

Yan et al. The New England journal of medicine. 2021;385(22):2047-58.



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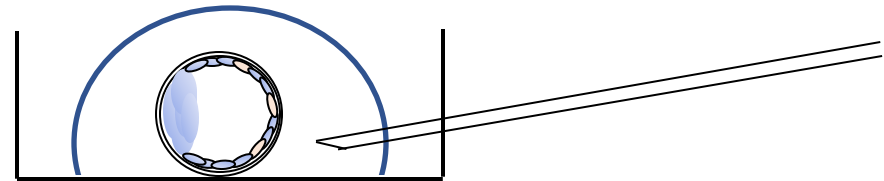


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Spent culture media (SCM)

- ❑ non-invasive approach for PGT-A (niPGT-A) is desirable
- ❑ cell free embryonic DNA in SCM provides a source of DNA for niPGT-A



Randomized double-blind controlled trial of ni-PGT

- ❑ two tertiary assisted reproduction centres
- ❑ A total of 500 infertile women recruited
- ❑ randomised on day 6 into 2 groups
- ❑ intervention group: using embryo morphology and niPGT-A
- ❑ control group: embryo morphology alone

Cheng et al., BMJ Open. 2023;13(7):e072557 Trial registration number NCT04474522



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Maternal contamination in early window of culture

	Day 3	Day6
Amplification rate	81.8% (9/11)	100% (11/11)
Informative result	100% (9/9)	81.8% (9/11)
Total concordance with same sex	22.2% (2/9)	66.7% (6/9)
SCM shows 46,XX	100% (9/9)	22.2% (2/9)

Origin and composition of cfDNA

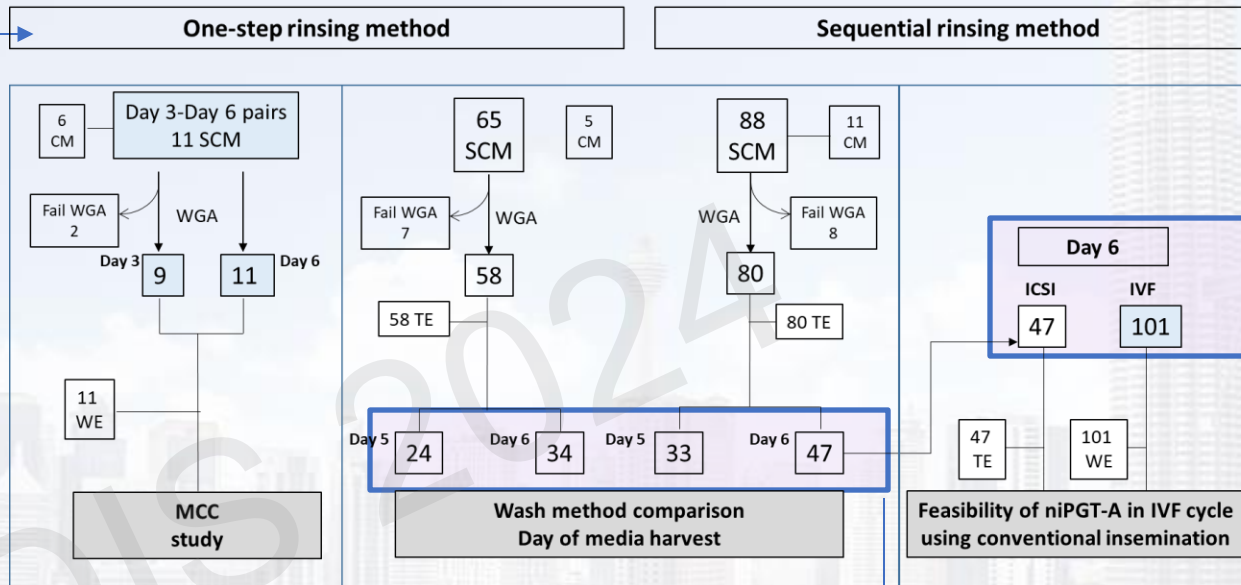
- ❑ Significantly higher quantity of cfDNA in SCM vs control media
- ❑ Ploidy concordance (n=56): D5 SCM vs TE biopsy (30.4%)
- ❑ SNP sequencing indicated maternal contamination (n=35)

- ❑ Later, with modified embryo rinsing method
- ❑ Ploidy concordance (n=115): D5/D6/D7 vs TE biopsy (78.7%)
- ❑ Embryos with both TE & SCM are euploid showed 3-fold higher in implantation rate vs those with only TE is euploid

Vera-Rodriguez, M et al., 2018. Human reproduction (Oxford), 33(4), pp.745–756.
Rubio, Carmen et al., 2019. Fertility and sterility, 112(3), pp.510–519.

Optimization of niPGT-A protocol

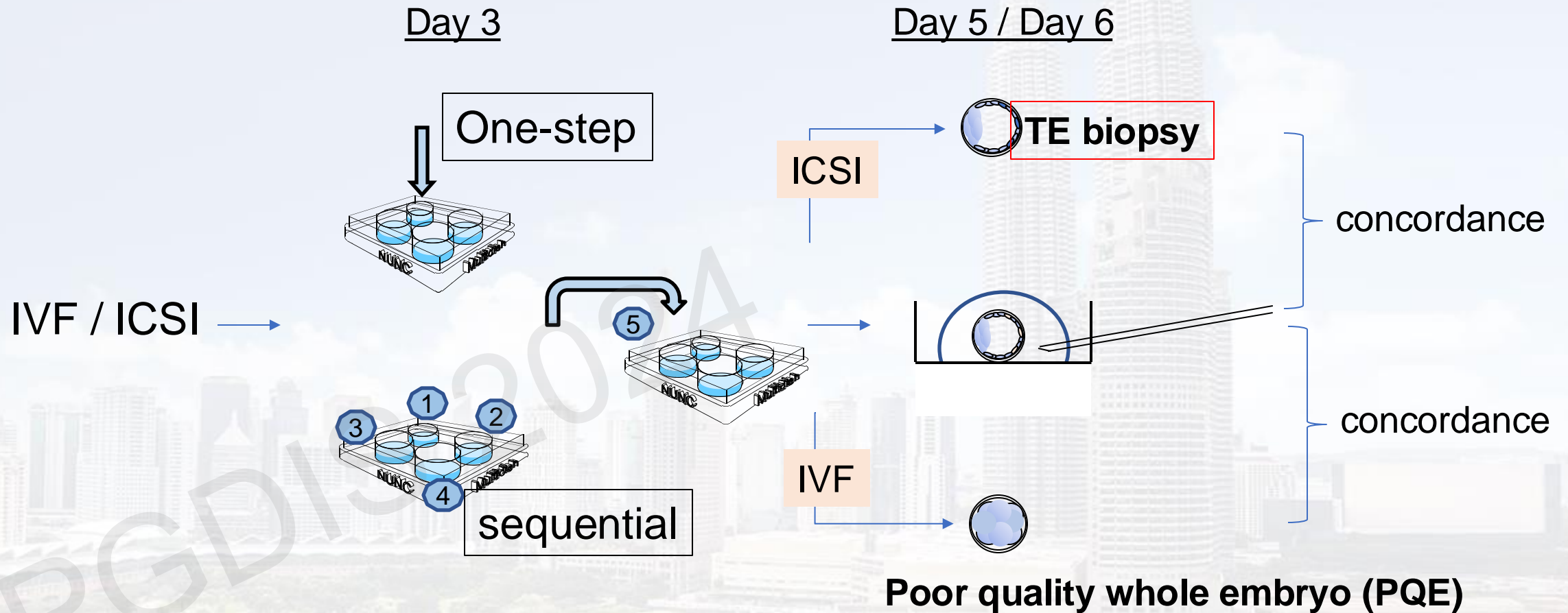
Embryo rinsing
Methods
N= 65 vs 88



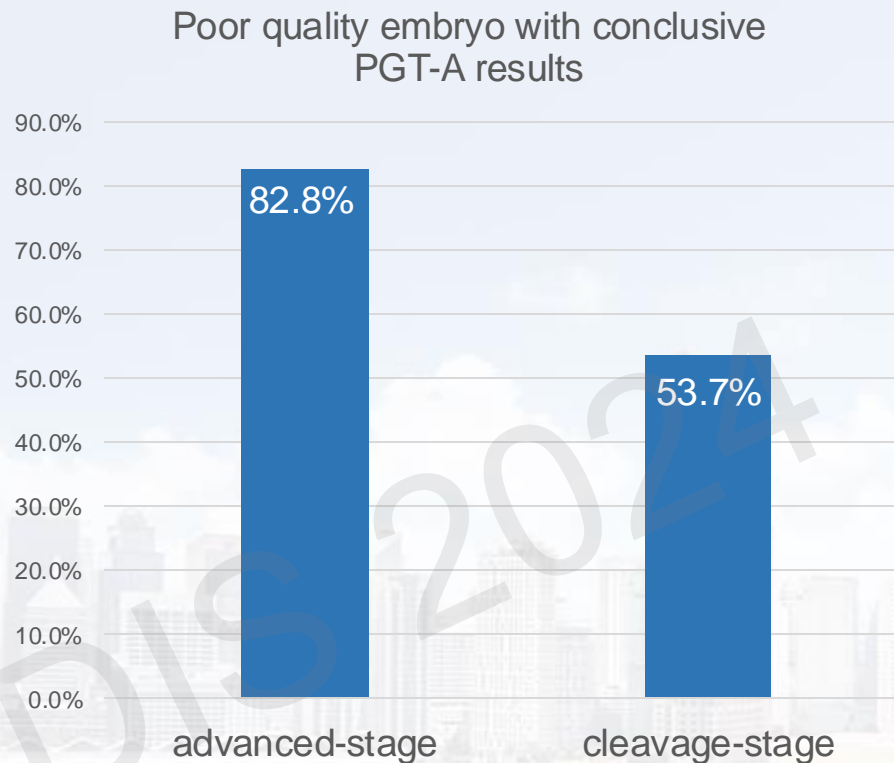
ICSI vs IVF
N= 47 vs 101

Day of media harvest (day 5 n=57, day 6 n=81)

Embryo rinsing methods



Selection of PQE as reference



N=157 vs 190
P<0.00001

Advanced-stage: Morula or later

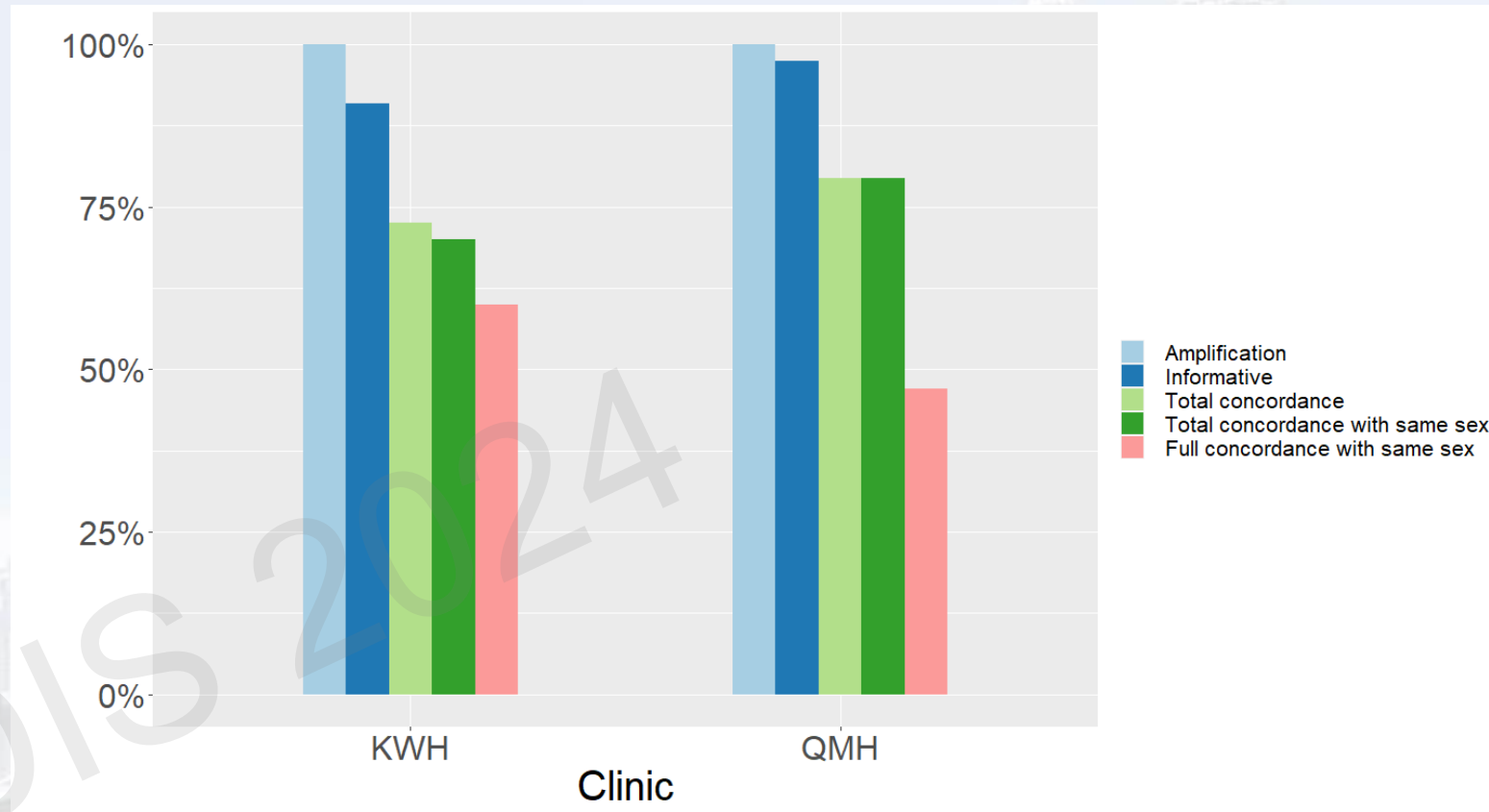
Rinsing methods and Day of medium collection

	A			B				
	One-step	Sequential	P value	One-step		Sequential		P value
				Day 5	Day 6	Day 5	Day 6	
Total concordance	68.0%	75.4%	0.38	73.7%	64.5% ^b	60.0% ^a	85.0% ^{ab}	^a <u>0.0228</u> ^b <u>0.0449</u>
Total concordance with same sex	50.0%	61.5%	0.22	42.1%	54.8% ^b	28.0% ^a	82.5% ^{ab}	^a <u><0.0001</u> ^b <u>0.0113</u>
Full concordance with same sex	24.0%	47.7%	0.0092	21.1%	25.8% ^b	24.0% ^a	62.5% ^{ab}	^a <u>0.0025</u> ^b <u>0.0021</u>

SCM collected in ICSI and conventional insemination (IVF) cycle

	ICSI	IVF	<i>P</i> value
Amplification rate	95.9% (47/49)	100% (101/101)	
Informative result	85.1% (40/47)	94.1% (95/101)	0.0732
Total concordance	85.0% (34/40)	74.7% (71/95)	0.1902
Total concordance with same sex	82.5% (33/40)	71.6% (68/95)	0.1819
Full concordance with same sex	62.5% (25/40)	61.1% (58/95)	0.8746

niPGT-A results between two IVF centres



Conclusion

- ❑ sequential rinsing outperforms one-step rinsing
- ❑ day 6 SCM gives higher concordance rate than day 5 SCM
- ❑ comparable results between SCM in IVF and ICSI cycles
- ❑ with well-defined protocol, consistent results between centres

THANK YOU

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