Zanjan University of Medical Sciences

Performance indicators for clinical practice in ART

شاخص های عملکرد بالینی در تکنیک های کمک باروری

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ESHRE PAGES

The Maribor consensus: report of an expert meeting on the development of performance indicators for clinical practice in ART†

ESHRE Clinic PI Working Group, Veljko Vlaisavljevic[1], Susanna Apter[2], Antonio Capalbo[3,4], Arianna D'Angelo[5], Luca Gianaroli[6], Georg Griesinger[7], Efstratios M. Kolibianakis[8], George Lainas[9], Tonko Mardesic[10], Tatjana Motrenko[11], Sari Pelkonen[12], Daniela Romualdi[13,14], Nathalie Vermeulen[15], and Kelly Tilleman[16,*]

Human Reproduction Open, pp. 1–17, 2017
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The Vienna consensus: report of an expert meeting on the development of art laboratory performance indicators†,‡

ESHRE Special Interest Group of Embryology[1,*] and Alpha Scientists in Reproductive Medicine[2,*]

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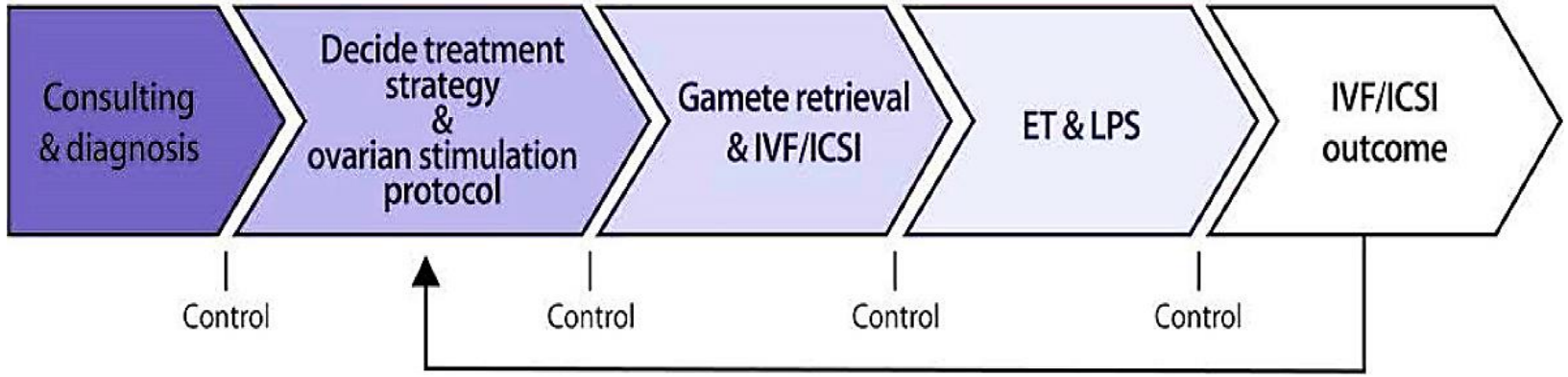
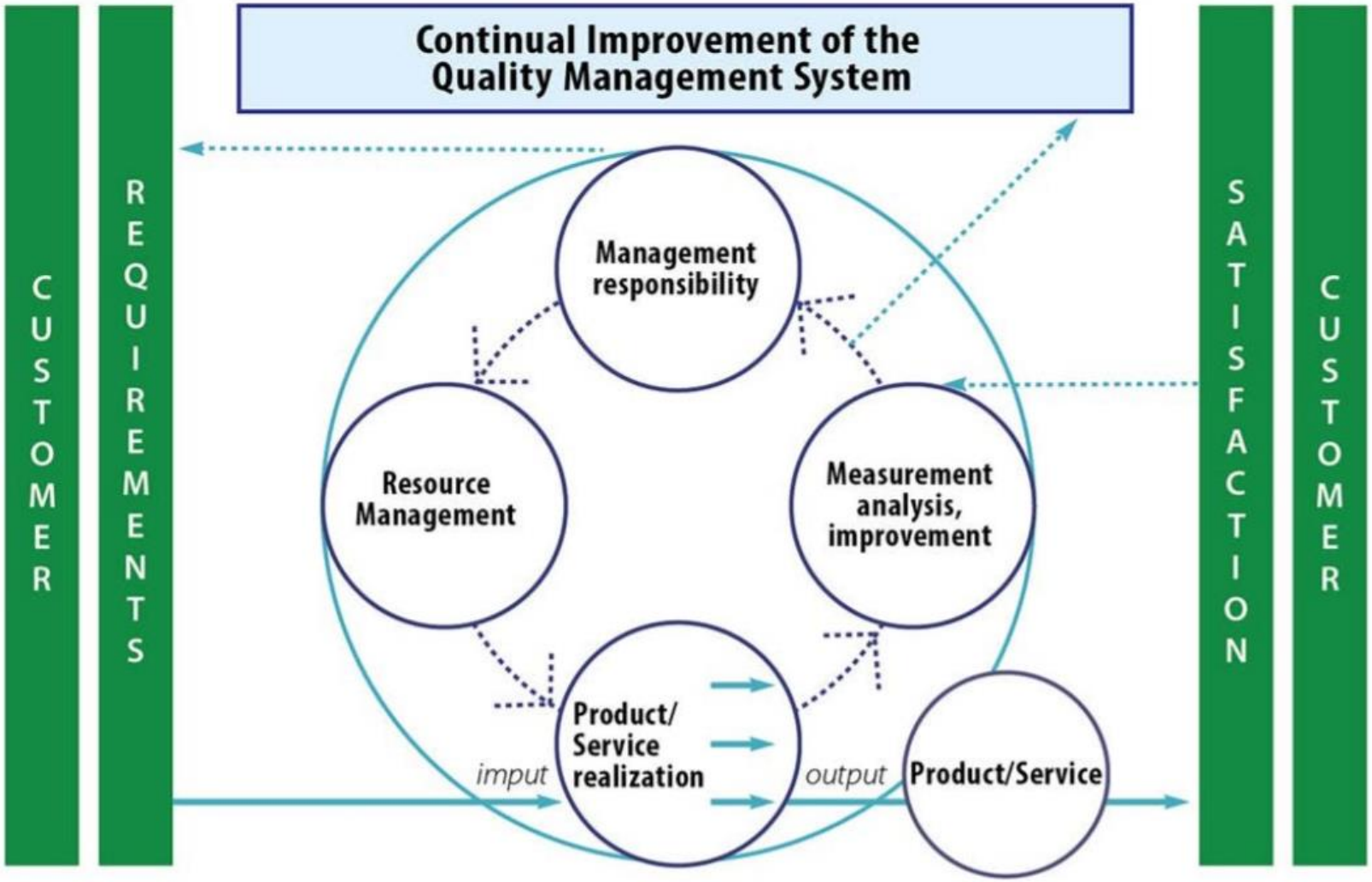
You can’t manage what you can’t measure

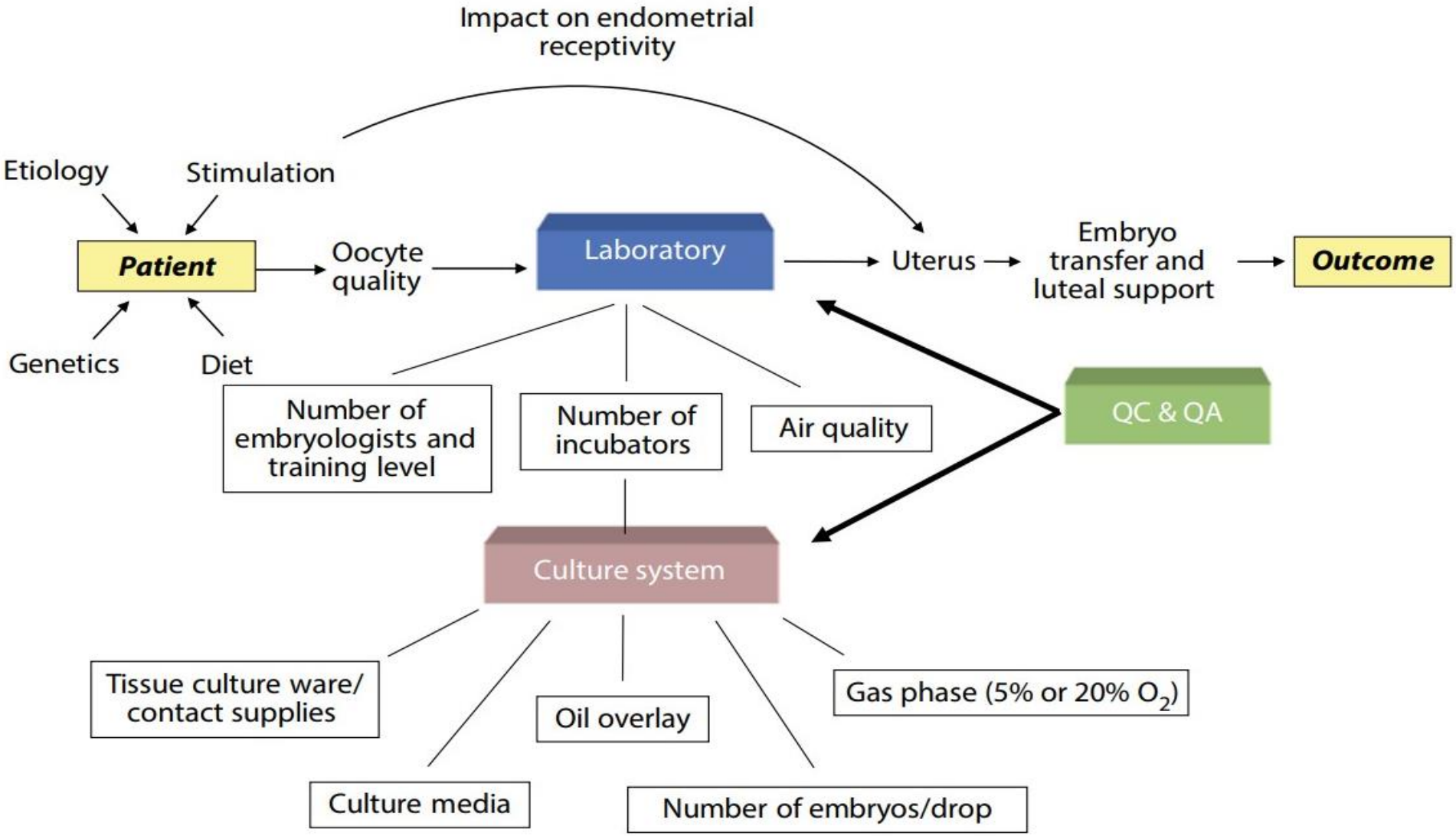
Performance indicators (PIs): a valid way to check that the healthcare provided is high in quality and operates within acceptable limits



Conceptual model of QMS



Complex and interdependent nature of IVF treatment

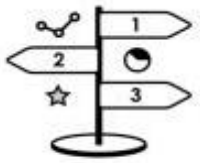


The aim of consensus papers on PIs

Is to speak a ‘common language’ and analyze the same indicators using the same formulas.

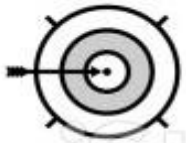
To determine a set of PIs for clinical work in ART

To determine clear definitions of PIs with limits of acceptable competence levels to be used in the quality management system of each ART center



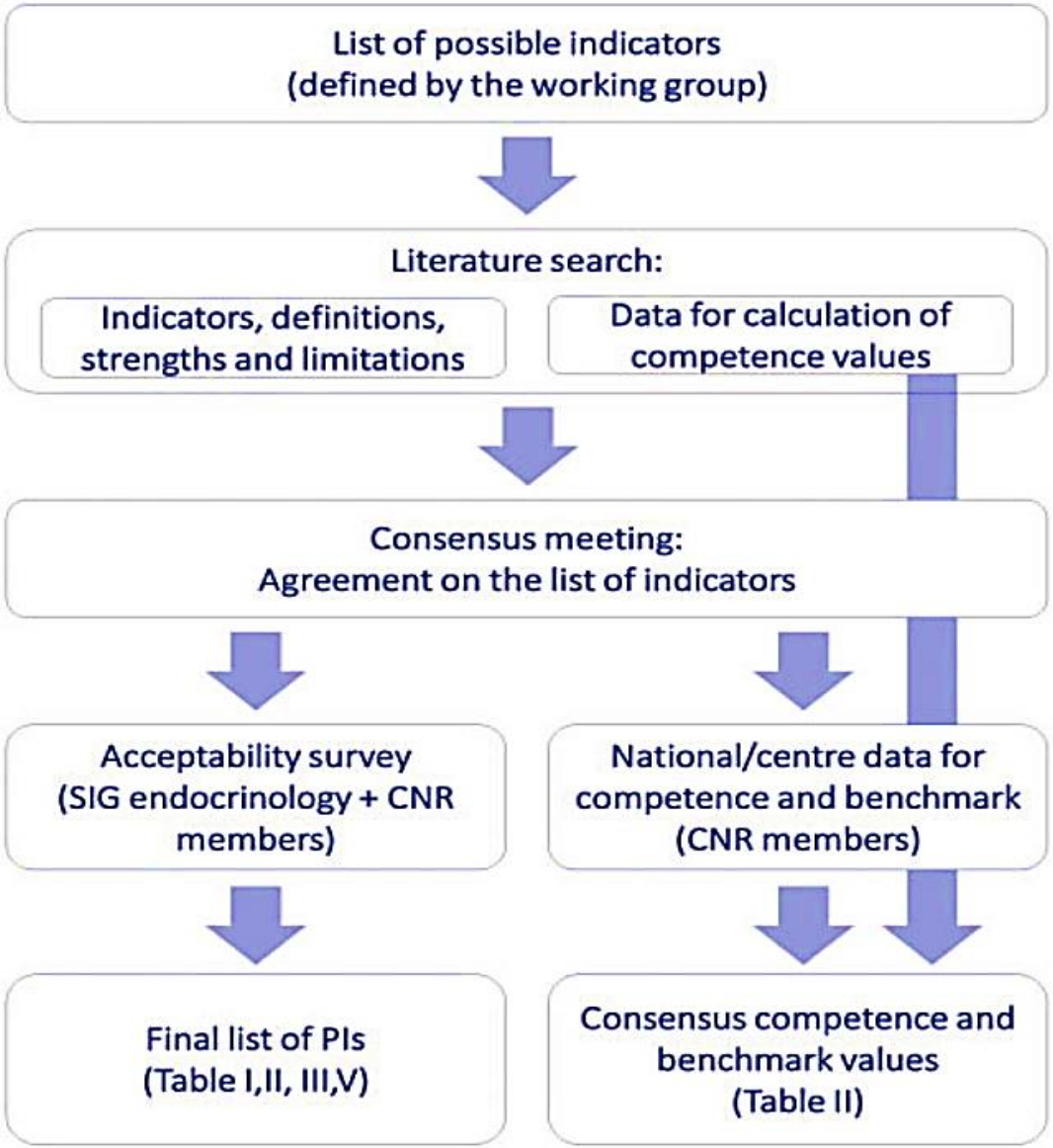
Indicators


Evaluation


Objective


Performance

Methodology for the development of performance indicators



PIs in four steps of a standard ART process

A standard ART process:

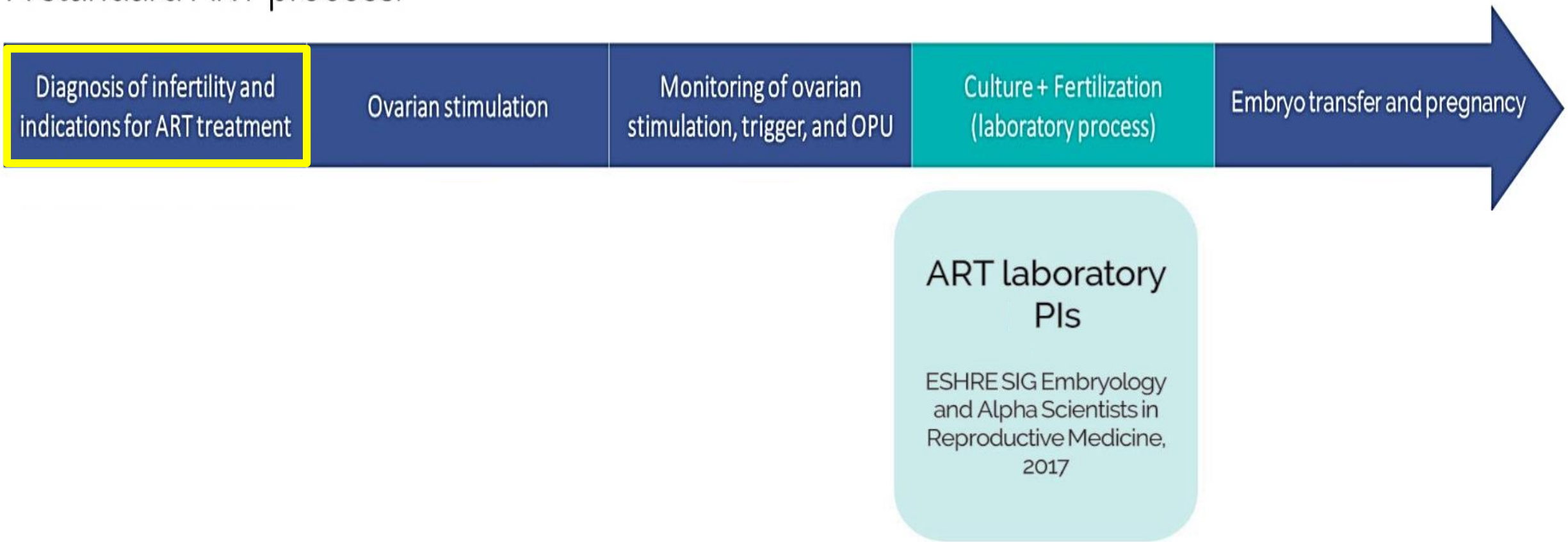
The survey, which consisted of a total of 31 statements and formulas on PIs described for each step of the ART process

ART laboratory PIs

ESHRE SIG Embryology and Alpha Scientists in Reproductive Medicine, 2017

PIs in four steps of a standard ART process

A standard ART process:



Established indications for ART

- Tubal damage or blockage
- Severe male factor infertility
- Unexplained infertility (selected cases)
- Severe endometriosis
- Genetic disorders indicating PGT
- Medical conditions requiring oocyte or embryo donation
- Use of a gestational carrier (surrogacy)
- Medical indications for fertility preservation (male and female)
- Infertility or subfertility related to pathologies with an immunologic origin
- Low ovarian reserve or advanced female age

(ESHRE guideline group on female fertility preservation et al., 2020)

Overview of the results of the survey

Statement	Nr of replies	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	JUDGEMENT
Diagnosis and indications for ART treatment							
Fertility work up should aim at establishing a prognosis of the residual chance of spontaneous conception, causal factors for infertility and the individual prognosis and risks for treatment and pregnancy.	221	66.97	31.22	1.36	0.45	0.00	ACCEPTED
Treatments other than by ART should be considered, when feasible, for patients with certain disorders amenable to other treatments.	222	55.41	38.74	5.86	0.00	0.00	ACCEPTED
When indicating ART, four treatment dimensions should be considered: burden, effectiveness, safety and costs (Dancet, 2014).	221	60.63	33.03	5.43	0.90	0.00	ACCEPTED
Expected benefits should be weighed against risks and burden of treatment, also taking the health of the subsequent pregnancy and the child into account.	220	60.45	33.64	3.64	1.36	0.91	ACCEPTED
ART should only be considered for cases with no alternative treatment of less invasiveness, burden, risks and costs.	219	31.05	38.36	16.44	12.33	1.83	DEBATABLE

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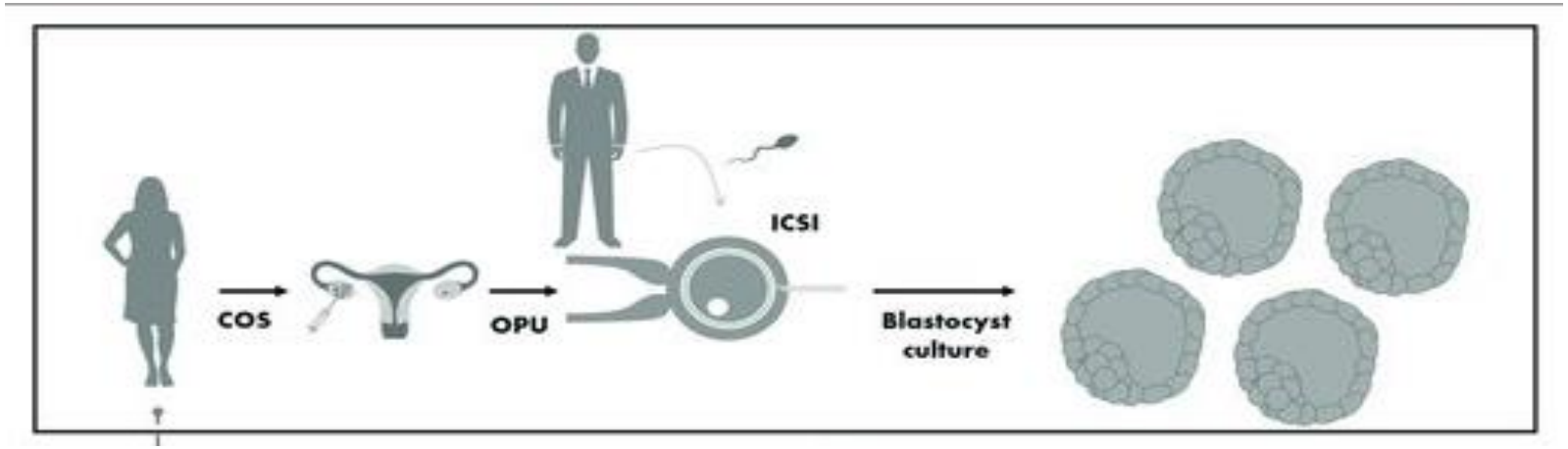
Cancellation of an ART cycle can occur prior to or after OPU

Cycle cancellation after OPU may result from

- Zero oocytes identified after oocyte retrieval
- Failed fertilization
- Poor embryo development



Cycle cancellation between OPU and ET is not considered a good indicator for clinical work

- related to biological factors (such as failure of sperm to fertilize)
- factors related to the capacity of the oocyte to be activated and fertilized
- factors associated with the clinic's ET strategy (such as blastocyst transfer regardless of the number of oocytes or embryos available)

Cancellation between OPU and ET related to laboratory performance can be monitored by other PIs (e.g. failed fertilization rate, embryo development rate)

Cycle cancellation before OPU can be attributed to

- Poor response to ovarian stimulation
- Premature ovulation
- Errors in taking medications
- Local reimbursement policy
- Patient preferences

Overview of the results of the survey

Ovarian stimulation							
Cycle cancellation rate (before oocyte pick-up [OPU]) is a relevant parameter to measure performance in ovarian stimulation.	206	26.21	45.63	17.48	8.25	2.43	ACCEPTED
Cycle cancellation rate (before OPU) should be calculated as the number of cycles cancelled before OPU over the number of started cycles.	205	44.88	44.88	7.32	1.46	1.46	ACCEPTED
Cycle cancellation rate (before OPU) should be calculated separately for poor responders, normal responders and high responders.	205	36.59	37.56	12.68	9.27	3.90	ACCEPTED
Rate of cycles **with moderate/severe ovarian hyperstimulation syndrome [OHSS]** is a relevant parameter to measure performance in ovarian stimulation.	206	36.89	45.63	10.68	4.85	1.94	ACCEPTED
Rate of cycles with **moderate/ severe OHSS** should be calculated as the number of cycles with moderate to severe OHSS over the number of started cycles.	204	37.75	50.98	8.82	1.96	0.49	ACCEPTED
Rate of cycles with moderate/severe OHSS should be calculated separately for **agonist** and **antagonist** cycles.	205	31.71	40.98	14.63	7.80	4.88	ACCEPTED
Rate of cycles with moderate/severe OHSS should be calculated separately for poor responders, normal responders and high responders.	206	22.33	34.47	21.84	15.53	5.83	DEBATABLE

How to PI calculation

Performance indicator		Calculation	
Cycle cancellation rate (before OPU)	%CCR	Nr of cycles cancelled before OPU x 100 / Nr of started cycles	
Rate of cycles with moderate/ severe OHSS	% mosOHSS	Nr of cycles with moderate to severe OHSS x 100 / Nr of started cycles	Antagonist protocol Agonist protocol

GnRH agonists: moderate/severe OHSS is 6.43% and 10.61%

GnRH antagonists : 2.94% and 2.14%

replacing hCG with GnRH agonist and not performing a fresh transfer, has been reported

PIs in four steps of a standard ART process

A standard ART process:

ART laboratory PIs

ESHRE SIG Embryology and Alpha Scientists in Reproductive Medicine, 2017

Overview of the results of the survey

Monitoring of ovarian stimulation, trigger and oocyte pick-up							
Oocyte retrieval rate is a relevant parameter to measure performance in monitoring of ovarian stimulation, trigger and OPU.	192	37.50	45.83	9.38	3.65	3.65	ACCEPTED
Oocyte retrieval rate should be calculated as the number of oocytes retrieved over the number of follicles (>10mm) on the day of trigger.	193	22.28	40.93	12.44	20.21	4.15	DEBATABLE
Number of mature (MII) oocytes per number of follicles (≥ 16mm) is a relevant parameter to measure performance in monitoring of ovarian stimulation, trigger and OPU.	193	37.31	43.52	9.84	6.22	3.11	ACCEPTED
Number of mature (MII) oocytes per number of follicles (≥ 16mm) should be calculated as the number of MII oocytes at ICSI over the number of follicles (≥16mm) on the day of trigger.	192	23.44	50.00	13.54	8.33	4.69	ACCEPTED
✓ **The oocyte maturation rate** should be defined as the number of MII oocytes at ICSI over the number of cumulus-oocyte complexes retrieved (as in the Vienna consensus)	193	44.04	40.93	10.36	3.63	1.04	ACCEPTED
Complication rate after OPU is a relevant parameter to measure performance in monitoring of ovarian stimulation, trigger and OPU.	193	32.12	39.38	16.58	10.36	1.55	ACCEPTED
Complication rate after OPU should be calculated as the number of complications (any) that require an (additional) medical intervention or hospital admission (apart from OHSS) over the number of OPUs performed.	193	42.49	43.52	11.40	2.07	0.52	ACCEPTED

How to PI calculation

Performance indicator		Calculation
Proportion of MII oocytes at ICSI	%MII	$\frac{\text{Nr of MII oocytes at ICSI} \times 100}{\text{Nr of cumulus-oocyte complexes retrieved}}$
Complication rate after OPU	%CoOPU	$\frac{\text{Nr of complications (any) that require an (additional) medical intervention or hospital admission (apart from OHSS)} \times 100}{\text{Nr of OPUs performed}}$

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Overview of the results of the survey

ET and Pregnancy

Clinical pregnancy rate is a relevant parameter to measure performance in embryo transfer (ET) and pregnancy.	186	51.08	36.02	5.38	6.45	1.08	ACCEPTED
Clinical pregnancy rate should be calculated as the number of pregnancies (diagnosed by ultrasonographic visualization of one or more gestational sacs or definitive clinical signs of pregnancy) over the number of ET cycles.	186	47.31	38.71	5.38	6.45	2.15	ACCEPTED
Multiple pregnancy rate is a relevant parameter to measure performance in ET and pregnancy.	186	46.77	27.42	12.90	9.68	3.23	ACCEPTED
Multiple pregnancy rate should be calculated as the number of pregnancies with more than one embryo or fetus over the number of pregnancies.	186	52.15	40.86	3.23	2.15	1.61	ACCEPTED
Ectopic pregnancy rate is a relevant parameter to measure performance in ET and pregnancy.	186	18.82	26.34	21.51	25.81	7.53	DEBATABLE
Ectopic pregnancy rate should be calculated as the number of pregnancies outside the uterine cavity over the number of pregnancies.	185	44.32	47.03	4.86	2.70	1.08	ACCEPTED
✓ Benchmark and competence values for clinical pregnancy rate should be set for a specific local context	186	27.42	50.00	13.98	5.38	3.23	ACCEPTED
✓ Benchmark and competence values for multiple pregnancy rate should be set for a specific local context	185	28.65	45.95	13.51	8.65	3.24	ACCEPTED
✓ Should clinical pregnancy rate be measured per ET or per OPU?	185	69.19% preferred *per ET* with an additional 4.32% suggested calculating *per ET* and *per OPU*. Other suggested denominators included *per OPU* (10.27%), *per started cycle* (8.65 %), *per embryo transferred* (2.70%), *per patient* (1.08%) and other replies (3.78%)					na

How to PI calculation

Performance indicator		Calculation
Clinical pregnancy rate	%CPR	$\frac{\text{Nr of pregnancies (diagnosed by US of one or more gestational sacs or definitive clinical signs of pregnancy) x 100}}{\text{Nr of embryo transfer cycles}}$
Multiple pregnancy rate	%MPR	$\frac{\text{Nr of pregnancies with more than one embryo or foetus x 100}}{\text{Nr of pregnancies}}$

Reference population

Female patients <40 years old, using own fresh oocytes, ejaculated spermatozoa (fresh or frozen), any insemination method (i.e. routine IVF and ICSI, and no preimplantation genetic testing (PGT).

Where relevant: stratified according to ovarian response (poor (PR), normal (NR), and high responders (HR))

Poor response

≥ 3 follicles on day of oocyte maturation trigger and/or 3 oocytes obtained characterize a low response (Ferraretti et al., 2011; Zegers-Hochschild et al., 2017)

High response

more than 18 follicles 11 mm in size on day of oocyte maturation trigger and/or 18 oocytes collected
(The ESHRE Guideline Group on Ovarian Stimulation et al., 2020)

Performance indicator		Calculation	
Cycle cancellation rate (before OPU)	%CCR	Nr of cycles cancelled before OPU x 100 / Nr of started cycles	
Rate of cycles with moderate/ severe OHSS	% mosOHSS	Nr of cycles with moderate to severe OHSS x 100 / Nr of started cycles	Antagonist protocol / Agonist protocol
Proportion of MII oocytes at ICSI	%MII	Nr of MII oocytes at ICSI x 100 / Nr of cumulus-oocyte complexes retrieved	
Complication rate after OPU	%CoOPU	Nr of complications (any) that require an (additional) medical intervention or hospital admission (apart from OHSS) x 100 / Nr of OPUs performed	
Clinical pregnancy rate	%CPR	Nr of pregnancies (diagnosed by US of one or more gestational sacs or definitive clinical signs of pregnancy) x 100 / Nr of embryo transfer cycles	
Multiple pregnancy rate	%MPR	Nr of pregnancies with more than one embryo or foetus x 100 / Nr of pregnancies	

Competence and benchmark values for the performance indicators

Performance indicator		Competence value[1] (%)					Benchmark value[1] (%)		
		Calculated from published data		Calculated from data reported by CNR members		Consensus value	Calculated from data reported by CNR members		Consensus value
	POPULATION	Mean	95% CI	Mean	95% CI		Mean	95% CI	
Cycle cancellation rate (before OPU) (%CCR)	Reference population	5	4–6	6.29	4.55–8.03	6	3.75	2.88–4.62	3.5
	Poor responders	40	30–49	28.86	14.51–43.21	40	20.00	10.04–29.96	20
	Normal responders	20	11–29	11.83	3.56–20.11	20	6.93	2.55–11.30	7
	High responders	3	1–4	2.50	1.93–3.07	3	1.50	−0.03 to 3.03	1.5
Rate of cycles with moderate/severe OHSS (with antagonist protocol) (%mosOHSS)	Reference population			1.52	0.42–2.62	1.5	0.61	0.17–1.06	0.5
	Normal responders	3	1–5	1.44	0.44–2.44	3	0.44	0.04–0.85	0.5
	High responders	2	0–5	2.89	1.03–4.74	3	1.64	−0.06 to 3.35	1.5
Rate of cycles with moderate/severe OHSS (with agonist protocol) (%mosOHSS)	Reference population			2.59	−0.51 to 5.68	2.5	1.13	0.12–2.13	1
	Normal responders	6	3–11	3.70	0.87–6.52	6	2.08	0.31–3.85	2
	High responders	11	4–20	7.63	3.66–11.61	11	5.83	2.23–9.43	5.5

Competence and benchmark values for the performance indicators

Performance indicator		Competence value[1] (%)					Benchmark value[1] (%)		
		Calculated from published data		Calculated from data reported by CNR members		Consensus value	Calculated from data reported by CNR members		Consensus value
	POPULATION	Mean	95% CI	Mean	95% CI		Mean	95% CI	
Proportion of MII oocytes at ICSI (%MII)	Reference population			74.13	67.51–81.24	74	81.25	72.67–89.83	75–90[2]
Complication rate after OPU (%CoOPU)	Reference population	0.2		0.36	0.10–0.62	0.5	0.19	–0.09 to 0.46	0.1
Clinical pregnancy rate (%CPR)	Reference population			32.24	29.27–35.21	na[3]	35.50	26.32–51.35	na[3]
Multiple pregnancy rate (%MPR)	Reference population			12.82	8.36–17.28	13	7.71	2.69–12.74	7.5

Relevance and challenges of using different denominators in the definition of **clinical pregnancy rate**

Denominator	Relevance	Challenges	Comments with regards to data collection	Comments with regards to PI calculations
Per initiated cycle	It assesses the probability of a successful ART procedure. The estimation is often made on the basis of the group of all patients starting treatment (intention-to-treat principle).	It cannot be used in cases of segmented cycles when all oocytes or embryos are cryopreserved for use and ET is performed in one of the future cycles.	Many registers do not record the start of the controlled ovarian stimulation (COS), and only report on cycles where COS ends with OPU.	Overlap with the PI—cycle cancellation rate (prior to OPU)
Per OPU (i.e. per aspirated cycle)	It assesses the probability of a successful ART procedure.	It cannot be used in cases of segmented cycles when all oocytes or embryos are cryopreserved for use and ET is performed in one of the future cycles.		
Per embryo transfer	It assesses the probability of a successful ET	The analysis lacks all cycles without ET, which consequently results in a seemingly higher effectiveness of ART.	It omits all (unsuccessful) cycles with no ET. The result is especially high when pregnancy, rather than live birth, is the numerator.	Important for calculation of individual PIs for clinicians.

Frequency of reporting

Performance indicator	Suggested frequency of analysis/reporting
Cycle cancellation rate (before OPU) (%CCR)	Calculate every 6 months, or per 100 cycles, whichever comes first.
Rate of cycles with moderate/severe OHSS (%mosOHSS)	
Proportion of MII oocytes at ICSI (%MII)	
Complication rate after OPU (%CoOPU)	
Clinical pregnancy rate (%CPR)	Calculate every 3 months, or per 50 cycles, whichever comes first.
Multiple pregnancy rate (%MPR)	

Number of procedures to be completed for training

Procedure	Number of procedures to be completed for training (*within a period of 2 years*)
Ovarian stimulation and trigger	100 cycles*
Oocyte collection/OPU	75*
Embryo transfer	75*

*The numbers are those proposed by the working group, and should be applied in consideration that they were challenged in the survey.

PIs for the ART laboratory

A standard ART process:

ART laboratory PIs

ESHRE SIG Embryology and Alpha Scientists in Reproductive Medicine, 2017

RIs for identifying performance of the ART laboratory

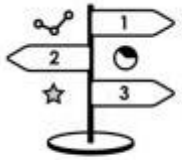
RI	Calculation	Benchmark ialue
Proportion of oocy[illegible]ecovered (stimulated cycles)	[illegible] oocytes retrieved / no. follicles on day of trigger × 100	80–95% of [illegible]icles measured
Proportion of MII oocytes at ICSI	no. MII oocytes at ICSI / no. COCs retrieved × 100	75–90%

PIs for the ART laboratory

PI	Calculation	Competency value (%)	Benchmark value (%)
Sperm motility post-preparation (for IVF and IUI)	$\frac{\text{progressively motile sperm}}{\text{all sperm counted}} \times 100$	90	≥95
IVF polyspermy rate	$\frac{\text{no. fertilized oocytes with} > 2\text{PN}}{\text{no. COCs inseminated}} \times 100$	<6	
1 PN rate (IVF)	$\frac{\text{no. 1PN oocytes}}{\text{no. COCs inseminated}} \times 100$	<5	
1 PN rate (ICSI)	$\frac{\text{no. 1PN oocytes}}{\text{no. MII oocytes injected}} \times 100$	<3	
Good blastocyst development rate	$\frac{\text{no. good quality blastocysts on Day 5}}{\text{no. 2PN/2PB oocytes on Day 1}} \times 100$	≥30	≥40

PN, pronucleus; PI, performance indicator; PB, polar body.

What does this mean for patients?



Indicators

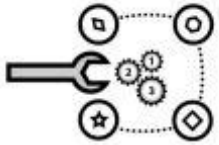
Evaluation

Objective

Performance

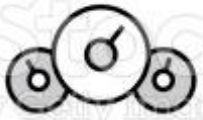
PI

Strategy



Optimization

Data Visualization



Measurement

Consensuses:

Reproductive BioMedicine Online (2011) 22, 632–646

ARTICLE

Istanbul consensus workshop on embryo assessment: proceedings of an expert meeting☆

Alpha Scientists in Reproductive Medicine and ESHRE Special Interest Group Embryology [1,*]

Reproductive BioMedicine Online (2012) 25, 146–167

ARTICLE

The Alpha consensus meeting on cryopreservation key performance indicators and benchmarks: proceedings of an expert meeting

Alpha Scientists in Reproductive Medicine [1,*]

Reproductive BioMedicine Online (2015) 30, 451–461

REVIEW

The Alpha Consensus Meeting on the professional status of the clinical embryologist: proceedings of an expert meeting

Alpha Scientists in Reproductive Medicine [1,*]

RBM ONLINE

ELSEVIER

Review

The Vienna consensus: report of an expert meeting on the development of ART laboratory performance indicators

ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine [a,b,*]

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