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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# 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,*]**


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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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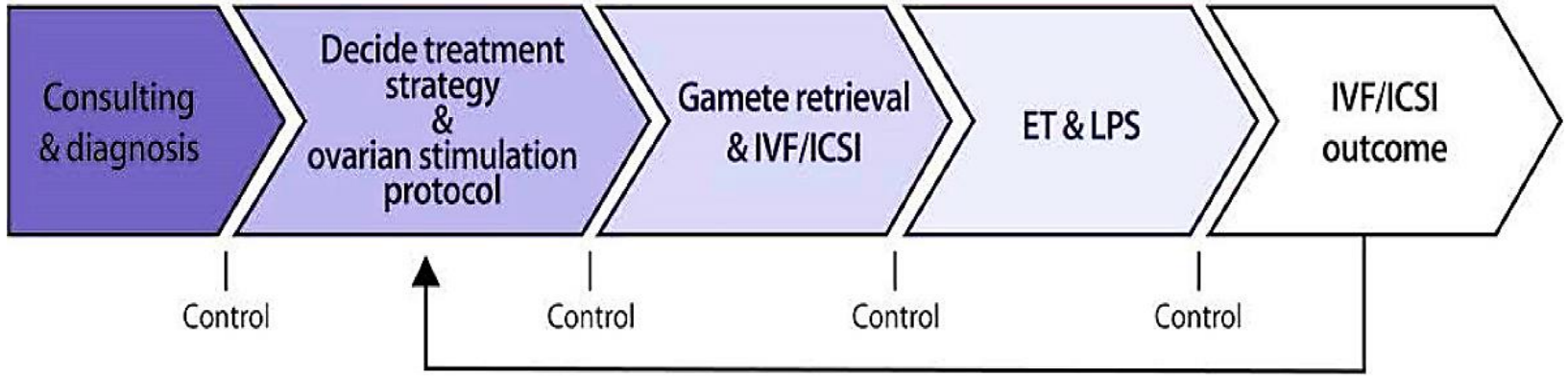
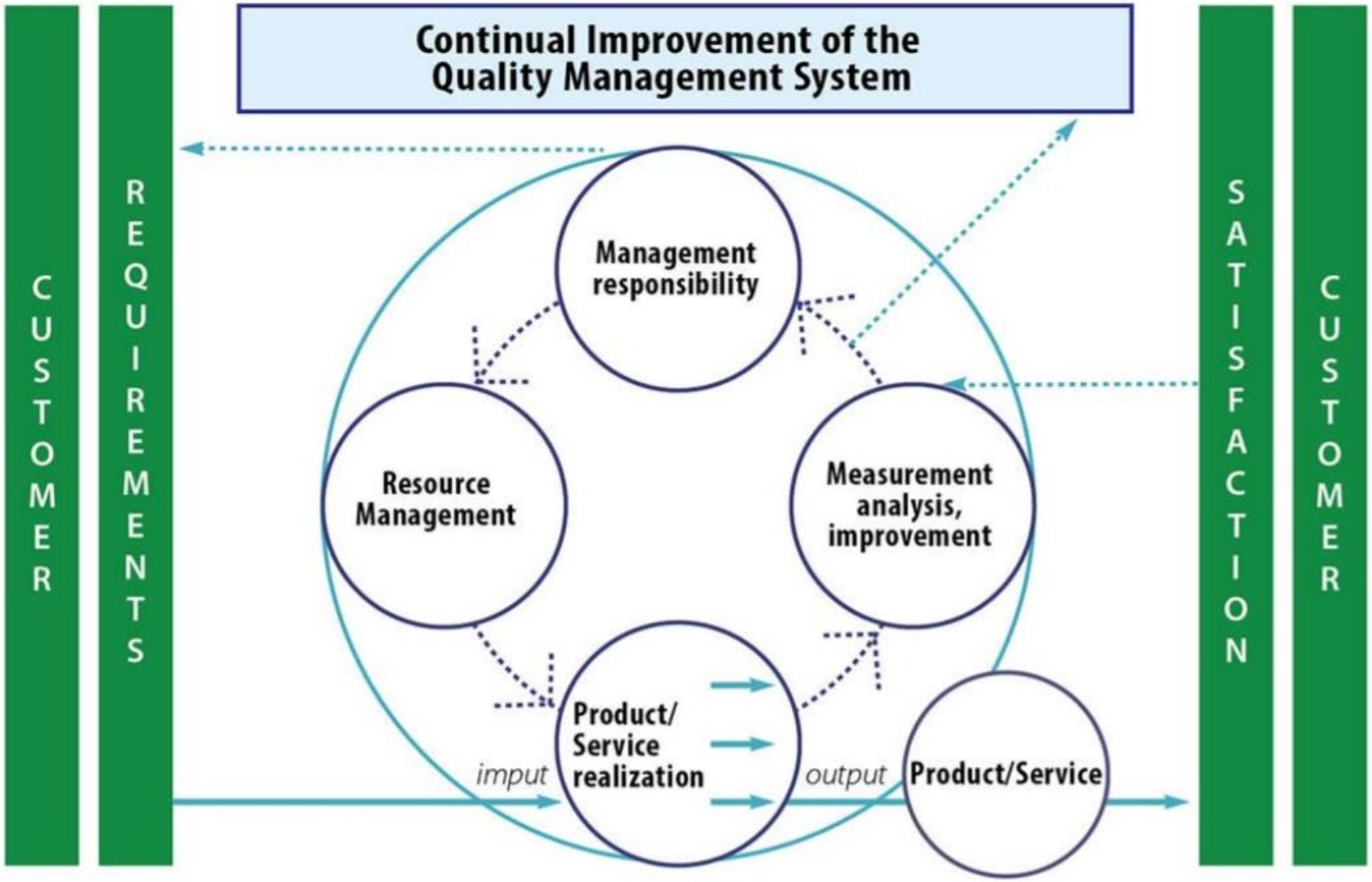
# You can’t manage what you can’t measure

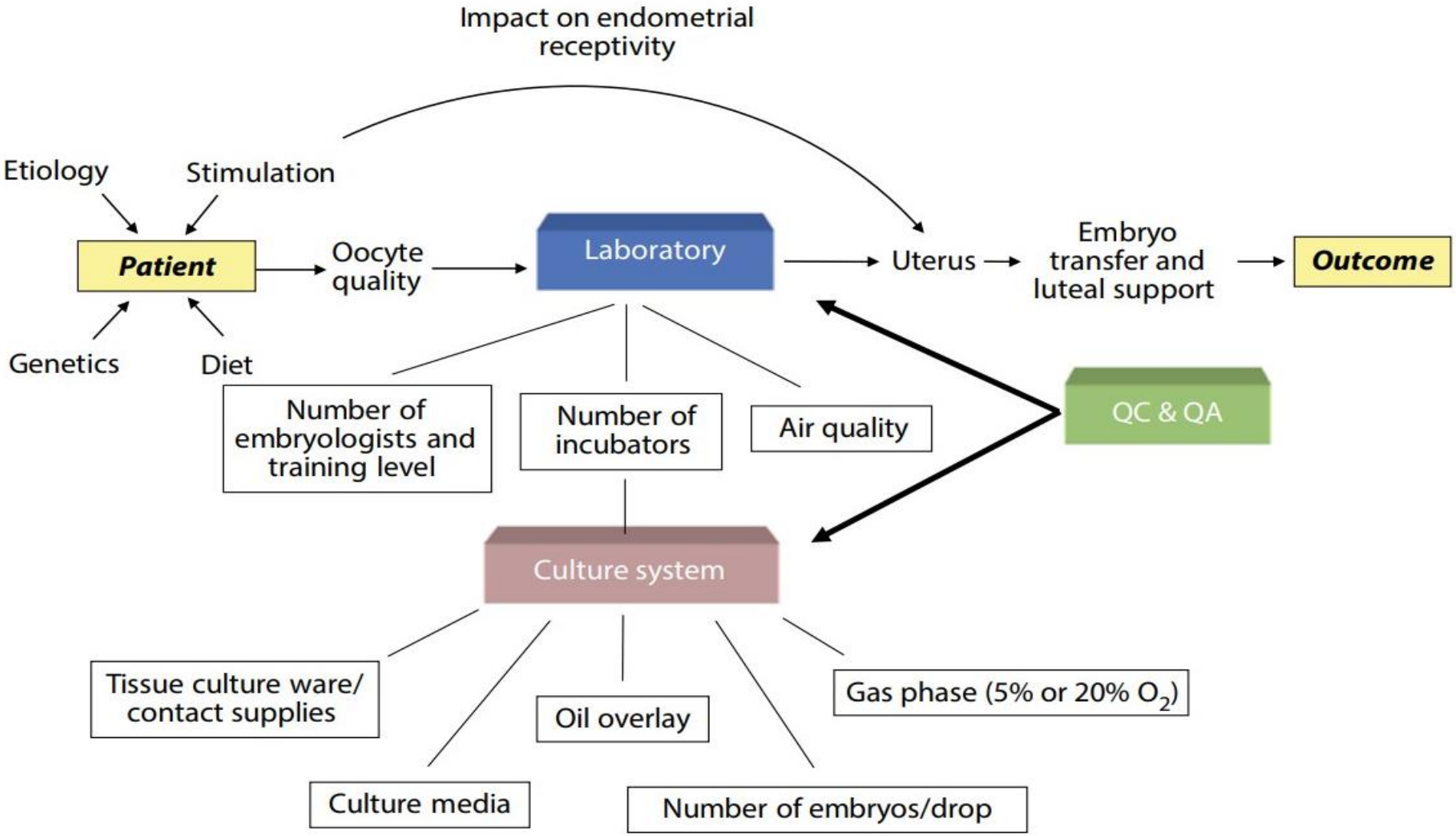
**Performance indicators (PIs):** a valid way to check that the healthcare provided is high in quality and operates within acceptable limits



# Conceptual model of QMS




# Complex and interdependent nature of IVF treatment



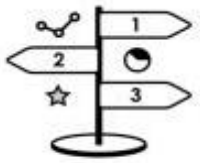
# The aim of consensus papers on PIs



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

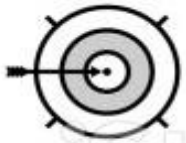
To determine a set of PIs for clinical work in ART

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



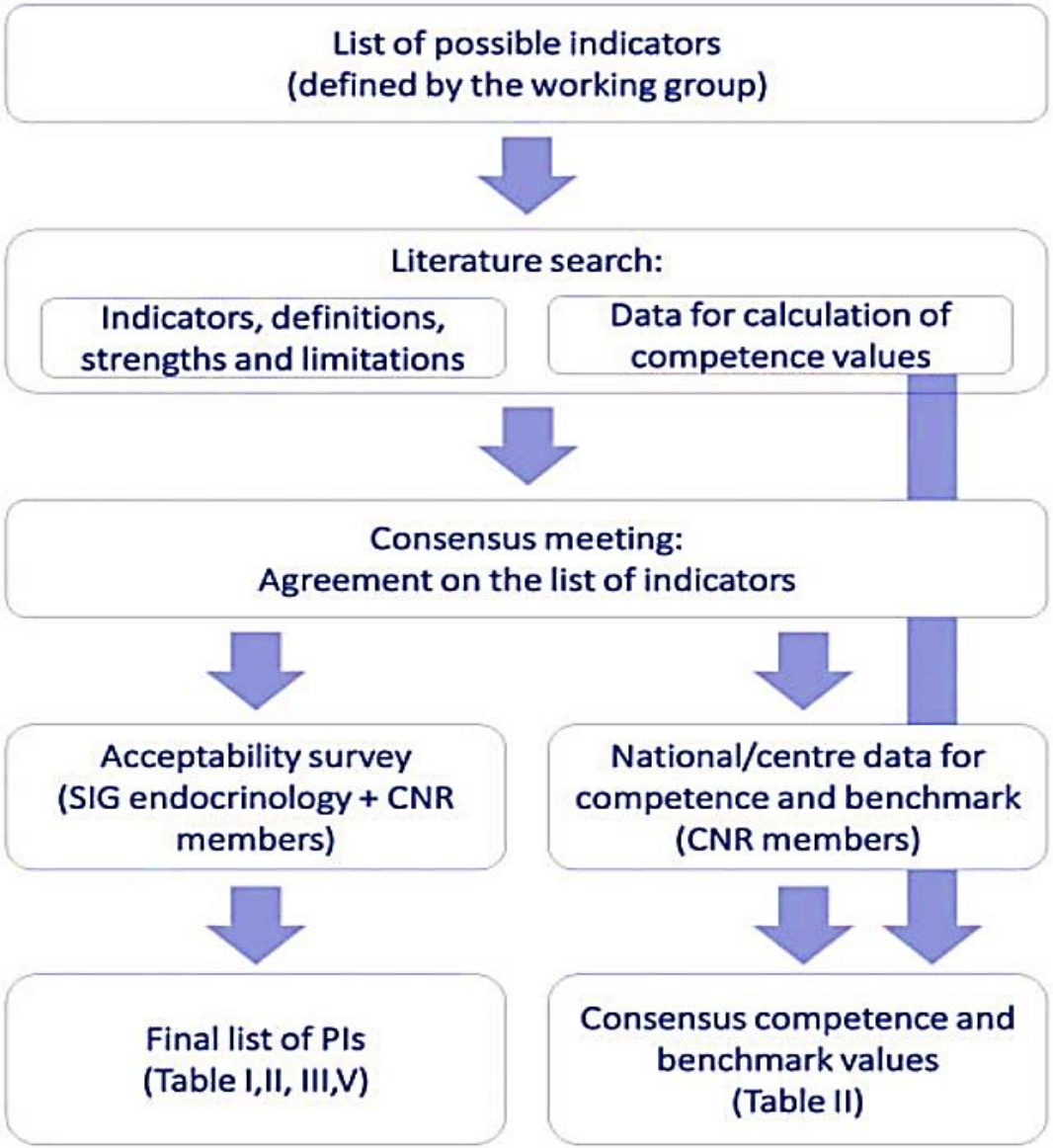
Indicators


Evaluation


Objective


Performance

# Methodology for the development of performance indicators



# PIs in four steps of a standard ART process

A standard ART process:

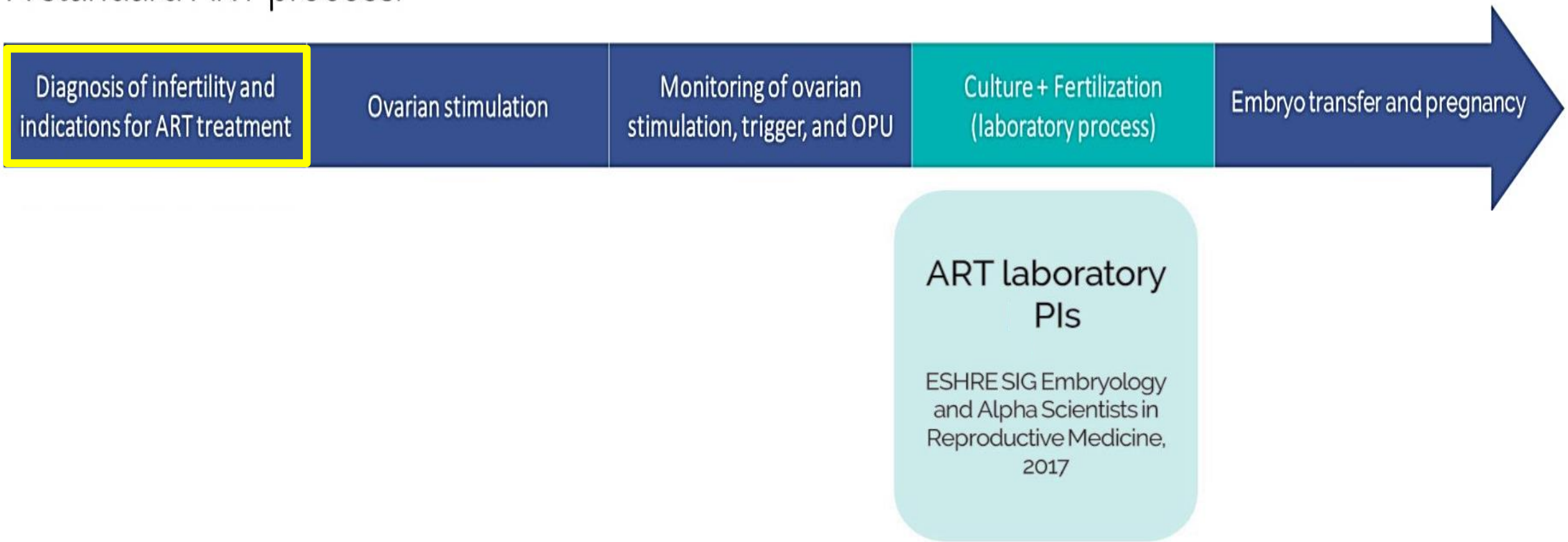

The survey, which consisted of a total of 31 statements and formulas on PIs described for each step of the ART process

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 |

# PIs in four steps of a standard ART process

A standard ART process:


## ART laboratory PIs

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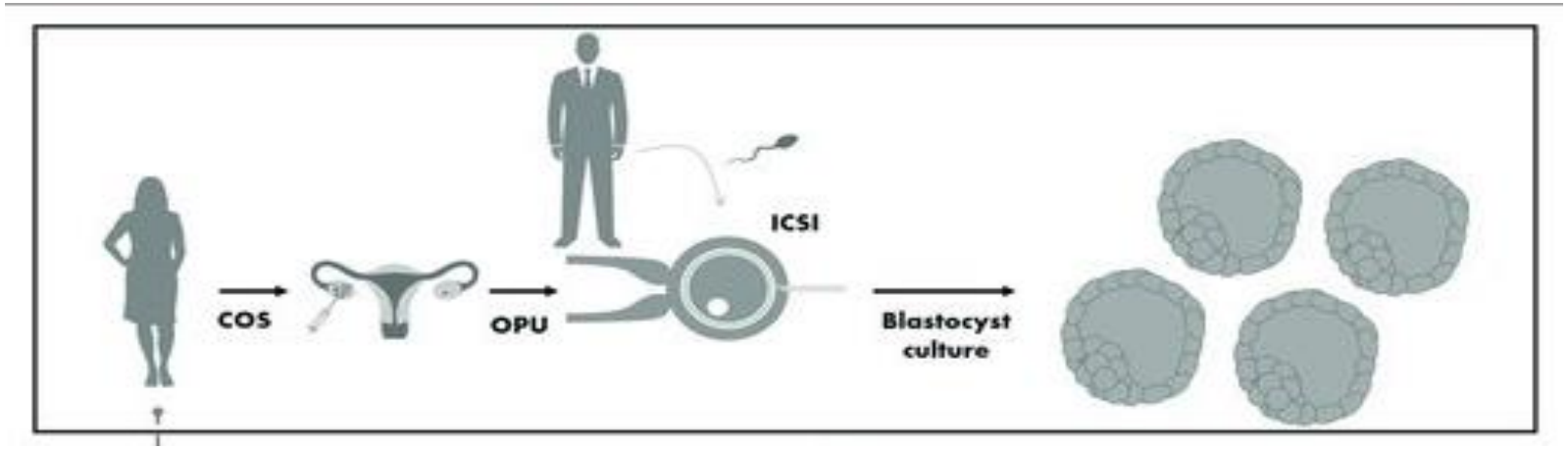
# Cancellation of an ART cycle can occur prior to or after OPU

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<br>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

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# 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 | $\frac{\text{Nr of complications (any) that require an (additional) medical intervention or hospital admission (apart from OHSS)} \times 100}{\text{Nr of OPUs performed}}$ |

# 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



## 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% |

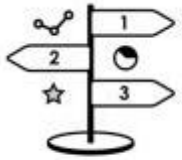
# PIs for the ART laboratory



| 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

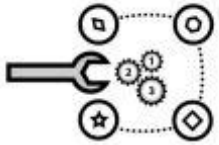
Evaluation

Objective

Performance

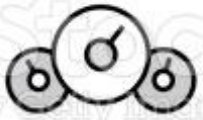
# PI

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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