PRE-CONGRESS COURSE 12

Total quality management (TQM) in an IVF Centre.

Task Force Management of Fertility Units in conjunction with the Special Interest Groups Andrology / Embryology / Reproductive Surgery & Safety and Quality in ART

London - UK, 7 July 2013

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SCIENCE MOVING
PEOPLE
MOVING SCIENCE

Total quality management (TQM) in an IVF Centre

London, United Kingdom
7 July 2013

Organised by
The Task Force Management of Fertility Units in conjunction with the Special Interest Groups Andrology/Embryology/Reproductive Surgery & Safety and Quality in ART

Contents

Course coordinators

Paul Devroey (Belgium) and Luca Gianaroli (Italy)

Course description

Total quality management or TQM is an integrative philosophy of management for continuously improving the quality of services and processes. Through the years, this concept has become fundamental in Healthcare, a field in which a high standard of treatment should constantly be pursued. This Course focuses on all processes performed within Fertility Units and how they can be influenced and improved by TQM in order to provide patients with the best and most safe treatments and procedures available. The course will also investigate how TQM can be a useful tool to improve efficacy and efficiency, also with reference to financial and administrative aspects.

Target audience

- Clinicians
- Embryologists
- Professionals involved in Quality Control and Total Quality Management
- Managers of Fertility Units and public and academic hospitals

Scientific programme

08:45 - 09:00 Introduction: What is TQM? *Luca Gianaroli - Italy*

Part I: Impact of total quality management in:
Chairman: Luca Gianaroli - Italy

09:00 - 09:30 Andrology lab
David Mortimer - Canada
09:30 - 09:45 Discussion
09:45 - 10:15 Embryology
Arne Sunde - Norway
10:15 - 10:30 Discussion

10:30 - 11:00 Coffee break

Chairman: Paul Devroey - Belgium

11:00 - 11:30 Reproductive surgery
Rudi L. Campo - Belgium
11:30 - 11:45 Discussion
11:45 - 12:15 Complications related to ART
Jan Gerris - Belgium
12:15 - 12:30 Discussion

12:30 - 13:30 Lunch

Part II: The cycle of TQM
Chairman: Amparo Ruiz Jorro - Spain

13:30 - 14:00 Patient pathway and patient satisfaction
Bart C.J.M. Fauser - The Netherlands
14:00 - 14:15 Discussion
14:15 - 14:45 How to implement TQM
Tonko Mardesic - Czech Republic
14:45 - 15:00 Discussion

15:00 - 15:30 Coffee break

Chairman: Timur Gürgan - Turkey

15:30 - 16:00 The cost of quality: Example of the IVI approach to the continuous improvement
Carlos Blanes - Spain
16:00 - 16:15 Discussion
16:15 - 16:45 The role of the European Tissue Directive on TQM
Edgar Vasile Mocanu - Ireland
16:45 - 17:00 Discussion
17:00 - 17:15 Closing remarks
Veljko Vlaisavljevic - Slovenia

What is Total Quality Management (TQM)?

L. Gianaroli, S. Sgargi, D. Barnabé

S.I.S.Me.R. Reproductive Medicine Unit, Bologna (Italy)

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Management - Definition

Management in all business and organizational activities is the act of getting people together to accomplish desired goals and objectives using available resources efficiently and effectively. Management comprises planning, organizing, staffing, leading or directing, and controlling an organization (a group of one or more people or entities) or effort for the purpose of accomplishing a goal. Resourcing encompasses the deployment and manipulation of human resources, financial resources, technological resources and natural resources.

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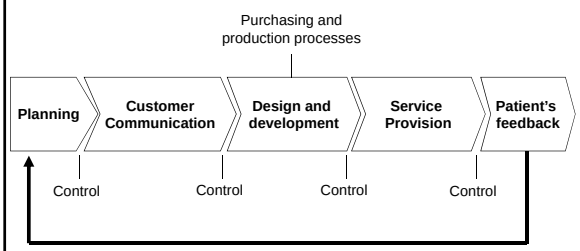
Service Realization



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Management of an IVF Unit

Characteristics of healthcare practices:

- Consumers = patients
- Product = specialized health services
- Staff = varied educational and experience backgrounds
- Owner = usually a Physician

Peculiar characteristics of IVF practices:

- Patient population usually knowledgeable about treatments
- Patient population highly motivated
- Success rates important in the choice of practice and clinician
- Patients have high expectations as they cover the majority of treatment expenses

S. Gerson et al. *Fertility and Sterility*, 2004

Management of an IVF Unit

Management of Human Resources

Management of ITC and planning tools

Financial planning

Communication

Insurance cover

TQM

Integrated management of corporate activities

Company - Organization
Management activities

Quality	**Environment**	**Safety**	**Other activities**
Continuous quality improvement	Compliance with Laws and continuous improvement	Compliance with Laws and continuous improvement	Gains, market shares, personnel, processes, communication,
ISO 9001	**ISO 14001**	**OHSAS 18001**	**ETHICS**

TOTAL QUALITY MANAGEMENT
Total control of all corporate activities
High corporate performance
Customer and personnel satisfaction

Total Quality Management

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Total Quality Management
Performance management

Performance management includes activities that endure that goals are consistently being met in an effective and efficient manner.

Can focus on the performance of an organization, a department, a team, an employee.

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Management – Quality Principles

1) Customer oriented approach

2) Leadership

3) Personnel involvement

4) Process approach

5) Systems approach to corporate management

6) Continuous improvement

7) Evidence-based decision making

8) Reciprocal beneficiary relationship with suppliers

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Risk management

No organization is immune from a crisis so all must do their best to prepare for one.

Crisis – any situation that is threatening or could threaten to harm people or property, seriously interrupt business, damage reputation or negatively impact share value.

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Risk management

Crisis management is a critical organizational function.

Failure to manage crisis can result in serious harm to partners/stakeholders, losses for an organization or end its very existence

If not properly managed, a disruptive event can escalate to an emergency, a crisis or even a disaster.

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Risk management

It includes strategies that allow to face possible damages limiting their consequences as much as possible

- DIRECT DAMAGES
Costs deriving from this kind of damage are immediate and quantifiable

- INDIRECT DAMAGES
They include al damages occurring between the prejudicial event and its solution

- CONSEQUENTIAL DAMAGES
They occur after the prejudicial event and they prolong themselves in time

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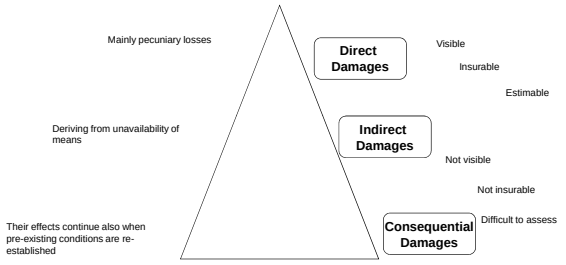
Damages



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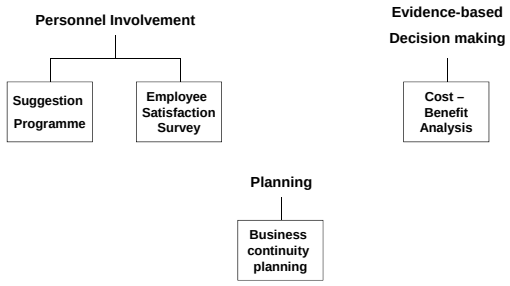
Total Quality Management - Tools



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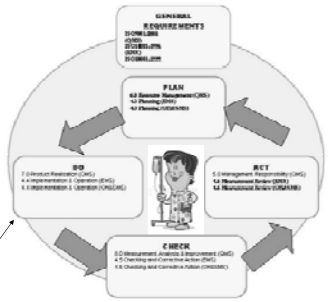
Take home message

TQM = management philosophy and company practices that aim to harness the human and material resources of an organization in the most effective way to achieve the objectives of the organization and to pursue customer satisfaction

TQM in Healthcare = rigorous set of processes and techniques to measure, improve, and control the quality of care and service based on what is important to the patient

QUALITY OF ORGANIZATION
=
QUALITY OF CARE
(Patients satisfaction + better outcome)



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IMPACT OF TQM IN THE ANDROLOGY LAB

Dr David Mortimer, PhD
Oozoa Biomedical Inc, Vancouver, Canada

Learning Objectives

1. To recognize that TQM is fundamental to the efficient and effective operation of the andrology laboratory.
2. To understand how the principles of TQM influence the selection and implementation of technical methodology for semen analysis.
3. To recognize that the principles of TQM require proper operator training and verification of competence.
4. To understand how embracing TQM will lead to semen analysis results that are more accurate and precise, and hence more likely to have clinical relevance.

Commercial Conflicts of Interest Disclosure

David Mortimer has undertaken consulting work since 1986, and has been a full-time freelance consultant since October 1999.

He is currently President and co-owner of Oozoa Biomedical Inc, a Vancouver-based international consulting company providing services in the reproductive biomedicine field since March 2000.

He has performed work, on either commercial or a pro bono basis, for many clients and groups including: assisted conception clinics and sperm banks; biotechnology, pharmaceutical and ART products companies; academic institutions; researchers; government agencies; non-government organizations; professional associations and other bodies.

No commercial or financial interest has influenced the statements made in this presentation.

Keeping the Andrology Lab In Control

- QC and QA are essential and must be routine
- Environmental monitoring: temperature, ventilation, oxygen depletion, air filtration (particulates, micro-organisms, VOCs), infection control
- Tolerance limits for quantitative technical procedures
- Monitoring of in-process controls
- Monitoring reagents and supplies, includes traceability of contact materials for therapeutic procedures as per EUTCD
- Monitoring of lab operational performance (e.g. via KPIs)
- Inspections and audits
- Protocol qualifications, verifications and validations
- Dealing with misconduct

TQM in the Andrology Lab

- Scope of Activity: Diagnostics, cryobanking, therapeutics
- Regulatory: Regulatory compliance / licensing (EUTCD), accreditation (e.g. ISO 15189)
- Physical Facility: Space size, layout, HVAC, cleaning, security
- Equipment: Suitability for use, Installation Qualification, Operational Qualification (also after repair), Performance Qualification (QC)
- Human Resources: Education, experience, aptitude, training, competence, CPD, adequate for peak workload
- Management: Policies, systems and process management, scheduling, efficiency, audits, QI (PDCA cycle), non-conformity ("incident") reporting
- Methodology: Suitability for purpose, SOPs, QC, QA, EQAP
- Data & records: Data entry verification, confidentiality, storage, security (access & backups), retention

Key Service Quality Requirements

- Safety of the patients, specimens and staff
- Patient identification, specimen labelling (2 unique identifiers), witnessing (human / *Witness* / *Matcher*)
- Diagnostics: – accuracy and precision of assessments
  – timeliness of reporting
- Cryobanking: – efficacy, safety and security of storage
- Therapeutics: – timeliness, respecting the physiology
  – avoiding iatrogenic damage
  – efficacy (quality of outcome)
- Ability to cope with the workload without compromise to safety, quality of service, or outcomes
- Customer satisfaction (patients and referrers)

Uncertainty of Measurement

ISO Guide to the Expression of Uncertainty in Measurement (1993)

- Every measurement has an error associated with it, and without a quantitative statement of the error a measurement lacks worth, even credibility.
- The parameter that specifies the boundaries of the error of a measurement is the "uncertainty of measurement".
- An uncertainty statement must have an associated confidence level, most usually a 95% confidence interval, i.e. effectively 2x the combined uncertainty.

Quality of Sperm Assessments

EXPECTATIONS OF ACCURACY AND PRECISION

Traditional manual/visual methods (ESHRE, WHO)

- **Establishment of method:** **≤5% between replicates (precision)**
- **Training of new staff:** **≤5% for 95% range of discrepancy**
- **Ongoing quality control:** **≤10% for 95% range of discrepancy**

CASA methodology

- **Precision:** **≤5% between replicates**
- **Accuracy:** **≤10% for 95% range of discrepancy**
  ***c.f.* reference method**

ISO Guide: Sources of Uncertainty

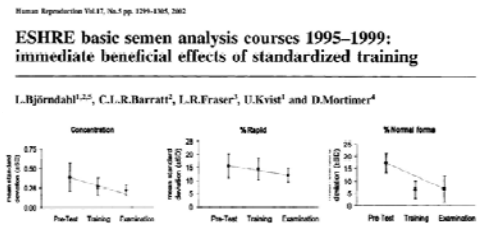
1. Incomplete definition of the measurand.
2. Incomplete realization of the definition of the measurand.
3. Non-representative sampling.
4. Inadequate knowledge of the effects of environmental conditions on the measurand (or imperfect measurement of those conditions).
5. Personal bias in reading analog instruments – or making subjective assessments!
6. Finite instrument resolution or discrimination threshold.
7. Inexact values of measurement standards and reference materials.
8. Inexact values of constants and other parameters obtained from external sources.
9. Approximations and assumptions incorporated in the measurement method and procedure.
10. Variations in repeated observations of the measurand under apparently identical conditions ("repeatability").

SOPs are Key to Operator Competence

1. Define the exact methodology that has been selected
2. Method must be able to achieve the required accuracy and precision
3. A method must include elements to control (minimize) all sources of error and bias within practical limits
4. The SOP provides step-by-step instructions so that all operators will perform the technique exactly as required
5. Operators are trained in the method before using it, and their competence (ideally objectively defined) is verified
6. Internal QC, and effective participation in an External QA programme (which includes QI functionality), are essential

Goal-Orientated Training

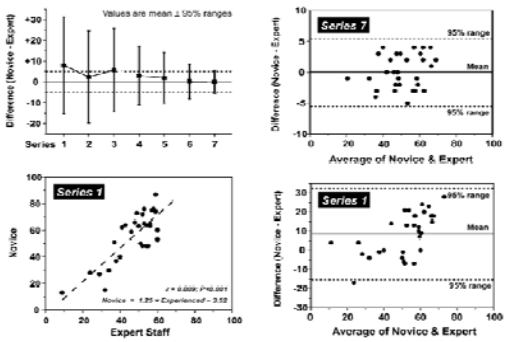
- Originally elaborated in Calgary during the 1980s to facilitate the training of new staff
- Subsequently applied in Sydney, London, Stockholm, Boston, Bangkok, Vancouver, Halifax



ESHRE basic semen analysis courses 1995–1999: immediate beneficial effects of standardized training

L.Björndahl[1,2,5], C.L.R.Barratt[3], L.R.Fraser[3], U.Kvist[1] and D.Mortimer[4]

Goal-Orientated Training – Example



ESHRE SIG-A Basic Semen Analysis Course

Human Reproduction, Vol.26, No.0 pp. 0-0, 2011
Advanced Access publication
human reproduction ORIGINAL ARTICLE ESHRE pages

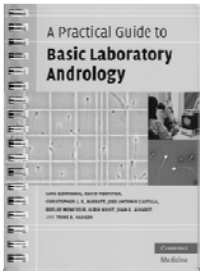
The ESHRE Special Interest Group for Andrology Basic Semen Analysis Course: A continued focus on accuracy, quality, efficiency and clinical relevance

Christopher L.R. Barratt, Lars Björndahl, Roelof Menkveld, and David Mortimer

- The revised course (first held in Stockholm, June 2011) is not WHO5-compliant, but it will educate participants on where there are differences, and why they exist.
- Text book for the course: Björndahl *et al.*, 2010.

ESHRE BSA Course Reference Textbook

- Detailed, logical, unambiguous SOP-type methods designed to minimize technical errors, avoid unnecessary effort and facilitate quality control

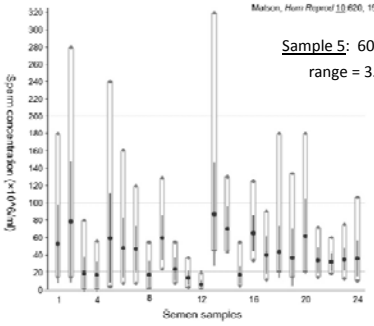


- Includes chapters on quality and risk management and accreditation principles
- Reference values section:
  - Defines prerequisites for interpretation
  - Provides cautionary notes regarding each characteristic
  - Considers the in-vivo and in-vitro significance of each characteristic separately

Sperm Concentration Determination

- Sample aliquot representative of ejaculate?
  - semen homogeneous (mixed)?
  - accurate sample aliquot (beware viscosity)?
  - duplicate aliquot?
- Accurate dilution
  - volumes of sample aliquot and diluent?
  - storage (airtight) / sperm bind to vial?
- Secondary sampling
  - mixing of diluted aliquot?
  - duplicate aliquots?
- Preparation of counting chambers
  - good chamber design/manufacture?
  - chamber loaded correctly &/or cover glass placed correctly?
  - adequate minimum number of cells?
  - repeatability of duplicate counts?
- Calculations correct?
- Precision of results?
- Uncertainty of measurement known?

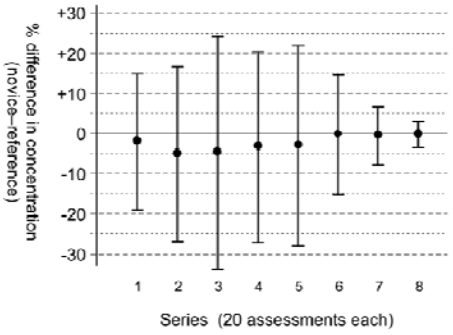
EQA for Sperm Concentration



Sample 5: 60.1 ± 51.3 M/ml
range = 3.6 – 240.0

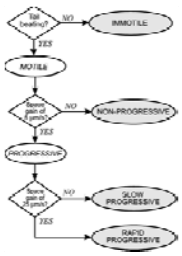
Values are:
mean ± SD (red)
range (orange diamonds, yellow rectangles)
for 20 labs

Sperm Concentration Training



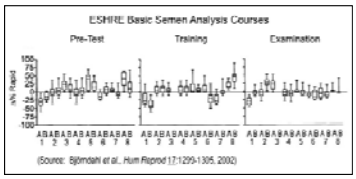
Sperm Motility Assessments

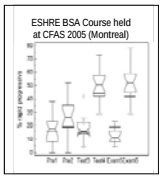
- Are assessments performed at ~37°C?
- Have the definitions been implemented correctly?
- Are staff trained to classify progression?
- Effect of temperature:
  - % motile (a+b+c) = minimal
  - % progressive (a+b) = slight
  - % rapid (a) = very large
- Representative sample aliquots?
- Duplicate assessments?
- Adequate number of sperm counted?
- Repeatability of replicate counts?
- Calculations performed correctly?
- Precision of results?
- Uncertainty of results?
- Internal quality control?
- External quality assurance / proficiency testing?



WHO5 Abandons Grade “a” Motility

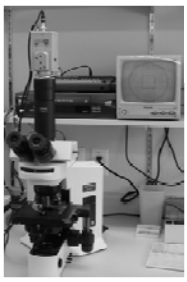
- It is too subjective and cannot be assessed reliably by eye
  (e.g. Yeung et al., *Fertil Steril* 67:1156, 1997; Handelsman & Cooper, *Asian J Androl* 12:118, 2010)
- But the quality of sperm motility is a prime factor to be considered in semen analysis. Achievement of intra- and inter-observer standardization is essential in any method used to assess sperm motility, and observers must be properly trained (MacLeod & Gold, *Fertil Steril* 2:187-204, 1951).

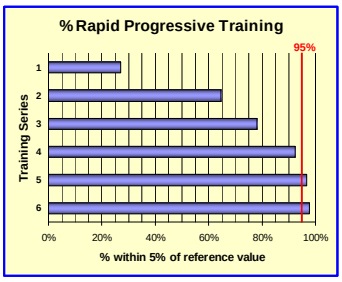




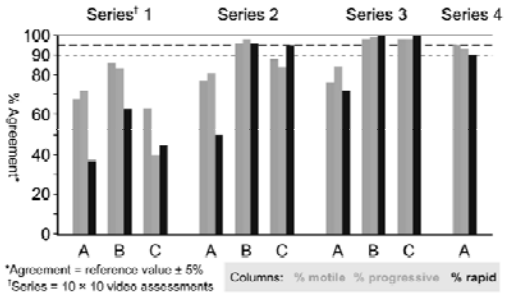
Training To Assess Grade “a” Motility

- Use reference video recordings and a calibrated overlay
- Goal-orientated iterative training





Motility Assessment Training



Internal QC in Semen Analysis

Mean ± SD% differences between 4 trained andrology scientists using WHO manual/visual semen analysis methods on 60 determinations (Calgary Diagnostic Semen Lab, *ca* 1990)

	Concentration	Total motility	Prog motility
A	-2.3 ± 7.4	+0.3 ± 3.0	+0.4 ± 2.6
B	-1.7 ± 4.9	-0.8 ± 3.1	-0.8 ± 2.9
C	+4.5 ± 7.3	-1.0 ± 3.3	-0.6 ± 3.3
D	-0.5 ± 7.0	+1.6 ± 2.9	+1.0 ± 2.8

A, B = experienced semen analysis technicians
C = lab supervisor
D = most recent trainee

Quality of Semen Analysis Results

Human Reproduction, Vol.28, No.1 pp. 10–16, 2013
Advanced Access publication on October 9, 2012 doi:10.1093/humrep/des355

human reproduction ORIGINAL ARTICLE Andrology

Proposal of guidelines for the appraisal of SEMen QUAlity studies (SEMQUA)

M.C. Sánchez-Pozo[1,*], J. Mendiola[2], M. Serrano[3], J. Mozas[3], L. Björndahl[4,5], R. Menkveld[6], S.E.M. Lewis[7], D. Mortimer[8], N. Jørgensen[9], C.L.R. Barratt[10], M.F. Fernández[11,12,13] and J.A. Castilla[3,14,15], on behalf of the Special Interest Group in Andrology (SIGA) of the European Society of Human Reproduction and Embriology

- Checklist includes:
  - Items #8–#11 concerning analytical methods
  - Item 16 concerning measurement uncertainty

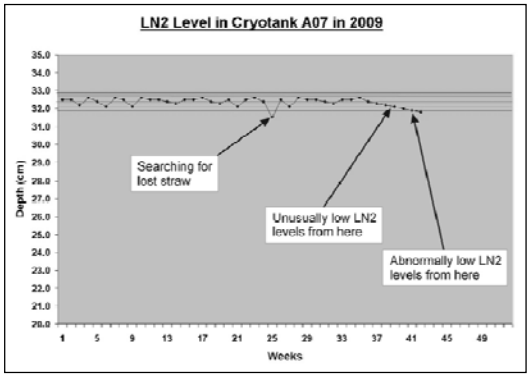
Monitoring Andrology Lab Equipment

- Design Qualification: suitability for intended purpose or use
- Installation Qualification for new equipment [engineer]
- Preventive maintenance / servicing / calibration [users or engineers as appropriate]
- Operational Qualification [engineer] verifies key aspects of instrument performance without any contributory effects that could be introduced by a method
- Performance Qualification [user] ascertains that an instrument or process consistently performs according to specification under routine conditions

TQM for Cryotanks

- Regular cryotank filling (e.g. weekly):
  - Measure LN2 levels before re-filling
  - Document and plot on a control chart
- Low level / temperature alarms:
  - Connect to a dial-out alarm or
  - Real-time monitoring system
- Cleaning / sanitization?
- Quarantine / isolation tanks *vs* effective biocontainment packaging?
- Oxygen depletion sensor and alarms with extraction ventilation for the cryobank

Monitoring Cryotank LN2 Levels



Conclusions – Take Home Messages

- TQM (embracing quality management, risk management and process management) creates the environment for effective and efficient lab operations, including "quality results" (i.e. accurate, precise, low uncertainty).
- Quality must be inherent in every aspect of the laboratory's operation, it must be integral – it cannot be "added on" like a coat of paint.
- Results lacking in quality are meaningless, and hence clinically useless – perhaps even misleading or even dangerous.
- How much of the "poor clinical relevance" of andrology lab results might be due to their poor quality?
- How useful might more accurate results be in future clinical andrology practice?

References

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Impact of total quality management in Embryology

Arne Sunde

Fertility Clinic, St. Olav's University Hospital
Norwegian University Of Science and Technology
Trondheim, Norway

Commercial relationships

- Own shares in CellCura of Norway

My background in ART

- Head of a fertility clinic that is ISO 9001:2008 certified
  - Certified by DNV (Det Norske Veritas)
- Laboratory manager from 1983 to 2006
- I am a "believer" in quality management.
  - It is worth the efforts!

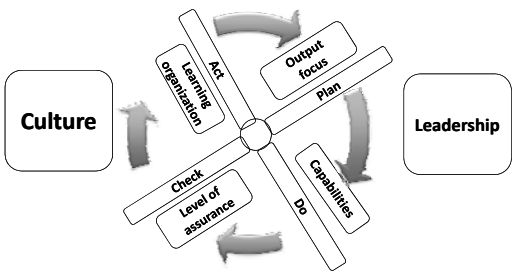
Why ISO certified?

- Experience from other organizations that are certified
  - Even Hot-Dog stands are certified
- The EU-Tissue Directive requires implementation of professional quality management in the ART lab
  - why don't use an established standard?
- We're still the only clinical unit in our hospital that is ISO-certified.

Total quality management

- **Two important aspects**
- **Technicalities**
  - Standard operating procedures
  - Documentation, traceability..etc.
- **Culture**
  - Quality management culture is part of the group identity

The Quality Circle



Building a Quality Culture

- This is the most important goal
  - Technicalities is a tool
- If you succeed in building a quality culture, the rest is downhill
  - Involve everyone
  - Listen to everyone
  - Show that you listen
- Act accordingly

Quality management of a human IVF-embryology laboratory

- Building a quality culture takes time and can be exhausting..
- It is easier to talk about technicalities, but don't forget that these are just a tools
  - ..not the goal

ISO 9001:2008 Quality management systems — Basic Requirements

- *Control of Documents*
  - A system for tracking documents
  - SOPs, letters, patient information, …
- *Control of Records*
  - Clinical record must be complete
  - Procedures, date/time, operator, utensils, consumables
  - Assessments and decisions…

Quality management in IVF-laboratory

- Standard operating procedures (SOP) for ”everything”
  - Easily available
  - Must be updated
  - Systems for checking that the correct version is used
  - Removal of old version
  - Document tracking and control
- This is the easy part.. ☺

ISO 9001:2008 Quality management systems — Basic Requirements

- *Internal Audits*
- Very important to get going
  - Train people in the lab to be auditors
  - Do audits at regular intervals
    - Dates and signatures
    - Serology documented
    - Documentation of equipment variables
    - Decisions according to SOP?

ISO 9001:2008 Quality management systems — Basic Requirements

- *Control of Nonconforming Product / Service*
- This is essential..one of the core elements
- Two aspects again:
- Operational
  - Identify errors, flaws, mistakes, suboptimal SOPs..
- Culture
  - Quality focus
  - Every employee can contribute..and be seen

ISO 9001:2008 Quality management systems — Basic Requirements

- Corrective Action
  - Correct mistakes and errors that has happened
- Preventive Action
  - Change of SOPs, routines to prevent mistakes and errors to happen

Building a Quality Culture

- Positively reinforce focus on errors and deviation
- It is OK that someone tells you that you done a substandard job
  - It is a success when the youngest technician can tell the senior doctor
    - ..well yesterday you…. and it had the following consequence..
    - And the senior MD says.. you're right.. thank you..
  - It is success when you're criticised by a patient and you turn around and say:
    - "Thank you for bringing that up…we have focus on quality and your comment will help us in achieving that"

Quality management in IVF-laboratory

- Standardized training programs
  - New employees
    - Training log
  - Employees that have been out of the lab for a while
    - Read all SOP's, train manual skills
- Continuous education program for everybody
  - Minimum reguirements

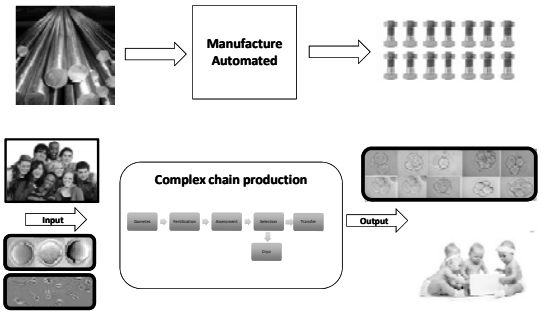
Quality management in IVF-laboratory

- Traceability
  - All consumables and utensils
  - Events, time points, operators
- Validation
  - Procedures
  - Equipment
- Quality control
  - Ingoing material
  - Equipment
  - Production
  - Output

Quality management in Embryology

- **Equipment**
  - Validated for embryology?
    - Specifications, design, References
  - Validated in you lab
    - Testing before use
  - Continuous monitoring of critical variables during use
    - Temperature, CO_2/O_2
  - All this documented
- **Ingoing materials**
  - Validated for embryology?
  - CE-mark?
  - References
- In-house testing of ingoing materials?
- Monitoring
  - Fertilization, Implantation..
  - Lot numbers, QC -certificates
- All this documented

Quality management of a human IVF-embryology laboratory



Quality management of a human IVF-embryology laboratory

- Biological variation in..
  - means biological variation out…
- Choose your quality control parameters with care
- Don't select parameters that will hurt your patients

Quality management of a human IVF-embryology laboratory

- What's your important quality parameters for production control?
  - Fertilization rate?
  - "Good embryo" rate?
  - Implantation rate?
  - Pregnancy rate?
  - Delivery rate?
  - Multiple delivery rate?
  - Cumulative delivery rate (fresh + frozen)?
  - Healthy Children?

"**A I want have very good results**" - clinic This is a real example

- The clinics quality parameters:
  - Implantation rate per embryo above 30%
  - Monitor for every 50 transfer
    - Cause for attention: below 25%
    - Full overhaul: below 20%

- This happened too often
  - Likely cause each time was to many low prognosis patients
- Solution: include only good prognosis patients

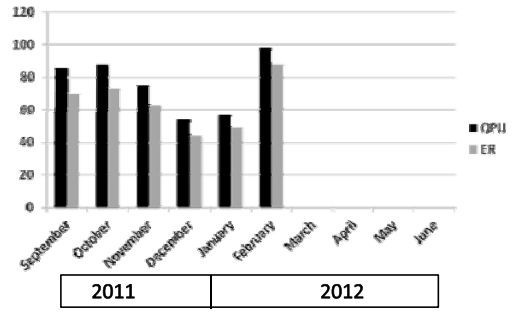
"**A I want have very good results**" clinic

- Alternative solutions:
- Change observation period
  - Less prone to random effects
- Choose and index population of good prognosis patients
  - Age, infertility diagnosis, BMI?

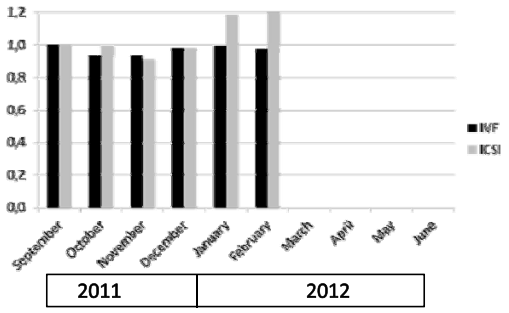
A real world example

- The value of traceability of all materials used that may come in contact with gametes and embryos ("critical use")

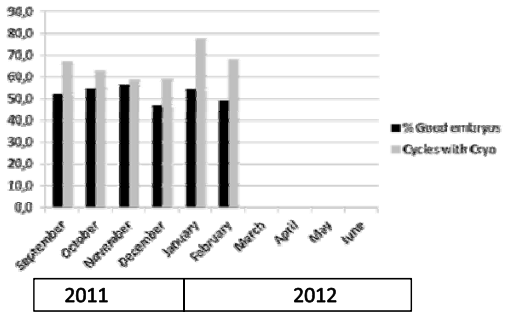
Number of oocyte recoveries and embryo replacements monthly
IVF/ICSI



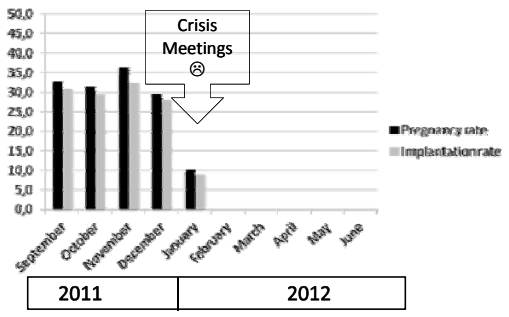
Fertilization rate IVF and ICSI
Relative to the rate in September-11



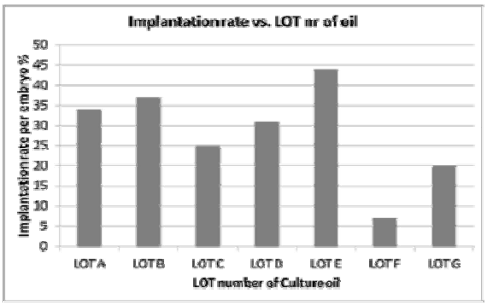
Embryos replaced and/or cryopreserved (”good embryos) /2PN%
Treatment Cycles with Cryopreservation of embryos%



Monthly pregnancy rate and implantation rates
IVF/ICSI 85% single embryo transfer



Any relationship with materials used ?



The culture oil problem

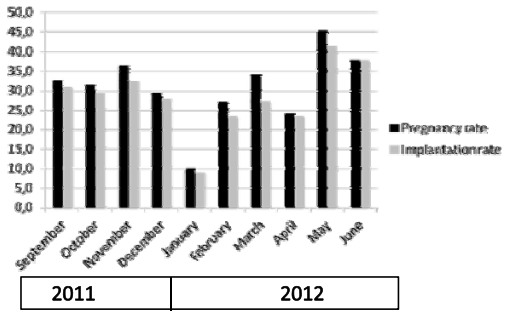
- **Cause**
  - Substances in the oil that will generate peroxides in the presence of hSA
    - oil-medium interphase
  - Was NOT picket up by the MEA during manufacture QC
  - Clinics reported problems
    - Blastocyst rate down
  - Indications of within-batch variations(?)

- **TQM in an oil-crisis**
  - Monitoring
    - Implantation rate below action level
  - Action
    - Internal audit
  - Finding
    - Substandard ingoing material
  - Alarm other TQM clinics
    - Do they see the same thing?

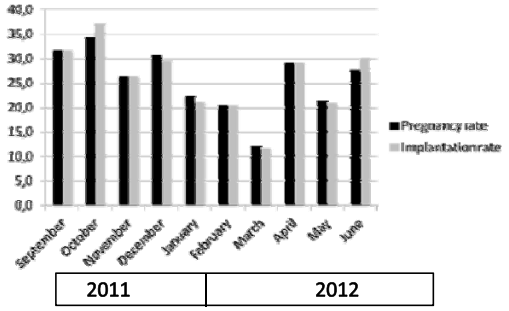
Action

- The recalled batches of oil were already used☹
- All frozen embryos which have been in contact with the recalled oil was discarded
- Patients that were treated when we used batches of oil that was recalled, were offered a new treatment cycle free of charge
- New supplier of culture oil

Monthly pregnancy rate and implantation rates 85% single embryo transfer



Frozen embryo replacements Data by month (24-56 FER/month)



Certification or Accreditation?

- Certification according to ISO 9001:2008
  - You do what you say you should do
    - ..and you control and document it
  - The ISO standard does not specify how good you should be in pregnancy rates or implantation rates
    - You need to specify that yourself..
  - You can be certified
    - ..and have lousy results..
    - as long as that is what you aim for..☺

Certification or accreditation?

- **Accreditation standards**
  - **ISO 17025** *General requirements for the competence of testing and calibration laboratories*
  - ***ISO 15189*** *Medical laboratories — Particular requirements for quality and competence*
  - ISO 9000 requirements are generic and are intended to be applicable to any type of organization
  - ISO 17025/15189 requirements are more specific to testing and calibration laboratories.

Certification or accreditation?

- Medical biochemistry laboratories are often
  - ISO 9001 certified in general
    - AND
  - have accreditation for some of the tests they offer
  - External validation, ring testing…
    - You document that you are live up to the industry standard (target value, variance…)
- Some andrology laboratories are accredited

Certification or accreditation?

- What about the IVF-lab?
  - Human clinical embryology
  - Certified for sure..
- I'm not that convinced that the current accreditation standards are useful for clinical embryology..
  - Relevant universal performance standards that are independent of biological input?
  - No general agreement on success criteria in ART!
  - Performance and success criteria should be relevant to the patients

Quality management

- **Useful- worth the efforts?**
  - It takes time and efforts
- **On a clinic level..**
  - Definitively
  - I have asked cleaning ladies, secretaries, nurses, MDs, lab technicians and embryologists in our unit:
  - Shall we skip the ISO and go back to our previous management model?

–Clear response..NO!!

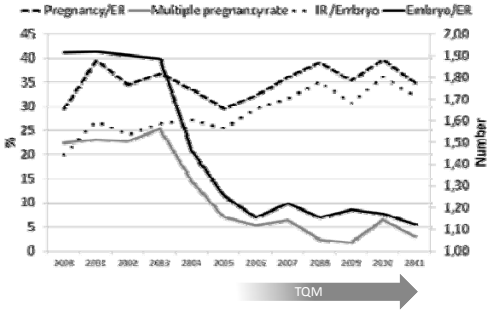
Quality management

- **Useful- worth the efforts?**
  - It takes time and efforts
- What about the IVF-laboratory - embryology
  - Results better?
  - Consistency in results better?
  - **Physical lab parameters better?**
  - **Information flow better?**
  - **Documentation better?**
  - **Traceability better?**
  - **Deviations and mistakes/errors identified more often?**
  - **Corrective actions more swift and relevant?**
  - **Training of new staff better ?**
  - …

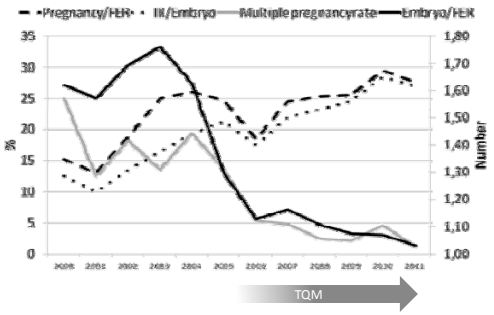
Quality management in Embryology

- A lot of nice words…
  - but did help in terms of pregnancy rates..?

IVF/ICSI



Frozen embryo replacement



Quality management in the IVF-laboratory

- **Implementation of TQM takes time and efforts**
  - It does not come easily and you are never finished
- **It is a tool**
  - not a goal in itself
- **Quality culture makes our Lab more dynamic, flexible and adaptable**
  - Not the opposite…
- **In times of crisis**
  - it is very useful to have "full traceability and documentation"
- **No guarantee that you clinical results will improve**
  - You have to define your success criteria and quality parameters yourself
  - TQM is a tool to get there…

ESGE European Society for Gynaecological Endoscopy

STAY IN SCOPE... WWW.ESGE.COM

Gynaecological Endoscopic Surgical Education and Assessment

GESEA Program

STAY IN SCOPE... WWW.ESGE.ORG ESGE

Patient Safety study in The Netherlands

Because of inacceptable amount of serious (lethal) complications in common laparoscopic procedures within general surgery and gynaecology in the Netherlands the ministry of health performed a major inspection regarding patient safety with a report published in November 2007

To deal with the assurance of patient safety, it seems obvious, but not yet implemented , that **future Laparoscopic surgeons should possess objective measurable theoretical knowledge and practical skills**, prior to enter in a one to one clinical training – teaching program.

Ref: http://www.igz.nl/publicaties/rapporten/2007/mic

STAY IN SCOPE... WWW.ESGE.ORG ESGE

Study in Belgium – May 18th, 2013

Opleiding specialisten voldoet niet

Dominance of the apprentice-tutor model

Self-management philosophy of educational portfolio

European or National Governement cannot interfere as the healthcare environment is by definition independent

Medical Education and surgical Quality control in Europe is a young 'science'

CME principles introduced since 1995 in some European countries on a voluntary basis

EEACME (European Accreditation Councel for CME) started in 1999, unifying the accreditation and recognition

EEACME and AMA recognition signed in 2000

CPD (Continuous Professional Development) declared in 2001, structuring the application of the medical knowledge, skills and attitude.

Objectives of ESGE's Testimonium (Diplomat) Program

The main objective of the introduction of a testimonium scheme for endoscopic surgical competence is to:

- Classify the available educational programs and offers (courses, classes, conferences, programs, seminars, lectures, …) in a staged framework
- Structure an educational curriculum for mastering endoscopic surgery

Influences of ESGE's Testimonium (Diplomat) Program

Facilitates Training Centers and educational initiatives to position the courses and programs for a target audience and to define the required access level

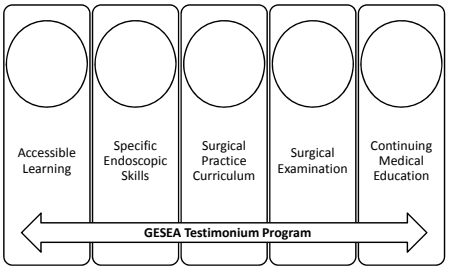
Encourages the physician to improve proficiency and skills on the educational path

GESEA Program's foundation principles

The program is founded on 5 specific domains or pillars of surgical professional competence available in Europe and as such being recognized by the EBCOG.
(European Board and College of the Obstetrics and Gynaecology)

Each of the 5 pillars has a recognized and documented educational or training route and appropriate stages for assessment.
(in different phases of development)

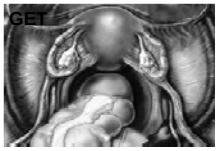
5 Pilars of Surgical Professional Competence



1. Accessible learning

- Is offered through an e-learning platform covering all surgical disciplines with tutorials on techniques, pathology, experts' opinions.
- Each level has a series of subjects instructed through lectures and video material.
- For each subject item, one needs to succeed in a five (random) question test before the next subject is made accessible.
- Access to the e-learning/e-testing platform is free, only profile registration is required

E learning program in laparoscopic surgery



WWW.WINNERSPROJECT.COM

2. Specific Endoscopic Skills

LASTT®: Laparoscopic Skills Training and Testing Method

A practical validated test to measure the competence level of an individual in the basic laparoscopic psychomotor skills like camera handling, hand-eye coordination and bimanual handling in the pelvic environment.

SUTT®:Suturing Skills Training and Testing Method

practical test on fine psychomotor skills related to stitching and knotting operations.

HYSTT®: Hystersocopic Skills Training and Testing Method

practical validated test to measure the competence level of an individual in basic hysteroscopic psychomotor skills like camera handling, hand-eye coordination and bi-manual handling in the specific uterus environment.

A Gynaecological endoscopic surgeon needs 2 specific practical skills.

Gynaecological Endoscopic Surgeon

⇧ ⇧

EPS
Endoscopic Psychomotor Skills

ESS
Endoscopic Surgical Skills

Laparoscopic Instrument handling including the fine psychomotor skills to perform suturing and fine surgical acts. ⇨ Surgical skills with knowledge of anatomy, pathology, treatment options, etc

A Gynaecological endoscopic surgeon needs
2 specific practical skills.

EPS Endoscopic Psychomotor Skills	**ESS** Endoscopic Surgical Skills
Computer game skills to learn in a skill lab No skiled tutor necessary	One to one teaching Minimal LPS necessary to enter the training Skilled tutor necessary
Learning proces similar to swimming or biking	Learning proces similar to learning a language

Psychomotor Skills

- Are the practical skills for correct camera handling to deal with the depth appreciation from 2D screen, remote handling of instruments without tactile feedback, hands-eyes coordination, working with long instruments, the fulcrum effect and more difficult and fine psychomotor skills are necessary for surgical acts like stitching and knotting.
- Scientific evidence gathered by +he academy has defined exercises on simple, cost friendly and reproducible inanimate models to train and test the LPS of an individual.

Individual certification of Laparoscopic practical skills

Laparoscopic Skill Training and Testing method (LASTT®)

AIM: measuring the individual proficiency to deal with typical laparoscopic psychomotor skills

Positive test result should grant for perfect laparoscopic instrument handling capabilities.

Suturing Skill Training and Testing method (SUTT ®)

AIM: measuring the ability of fine and complex motor skills by performing correct stitches and correct intracorporeal knots.

Positive test result should result in perfect ability of laparoscopic needle handling and intracorporeal knotting.

LAST+T

LAparoscopic Skills Training and Testing model .

Training of 3 essential exercises to acquire the laparoscopic psychomotor skills.

Exercise 1 : Camera navigation
Exercise 2 : Hand eyes coordination
Exercise 3 : Bimanual coordination

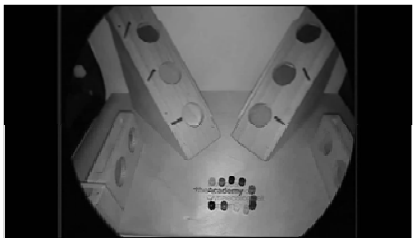
Test proficiency should grant for perfect laparoscopic instrument handling capabilities.

LASTT exercise 1 : Camera navigation

ORIGINAL ARTICLE

Feasibility and construct validity of a novel laparoscopic skills testing and training model

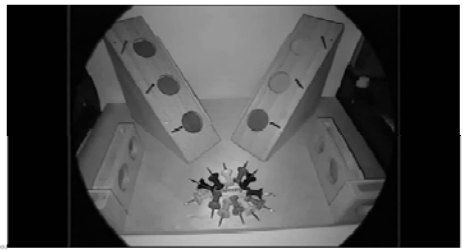
LASTT exercise 2 : Hand eye coordination



ORIGINAL ARTICLE

A valid model for testing and training laparoscopic psychomotor skills

LASTT exercise 3 : Bimanual coordination

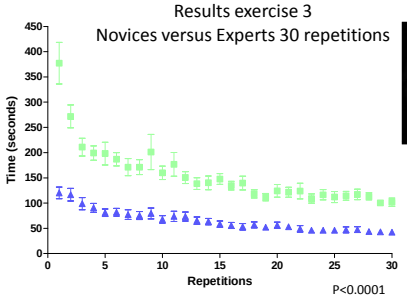


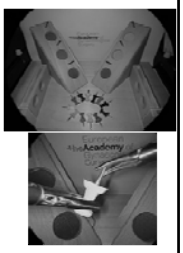
ORIGINAL ARTICLE

Defining a structured training program for acquiring basic and advanced laparoscopic psychomotor skills in a simulator

Carlos Roger Molinas · Rudi Campo

Results exercise 3
Novices versus Experts 30 repetitions

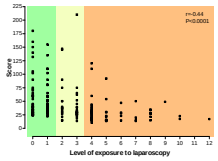


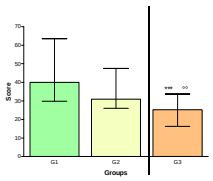


P<0.0001

Correlation exposure to laparoscopy and E3 score

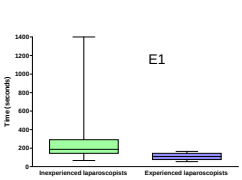
199 gynaecologists classified in three groups according to their exposure to laparoscopy
G1: no/little GREEN , G2: intermediate YELLOW , G3: large ORANGE.

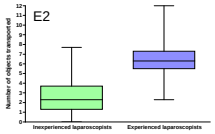


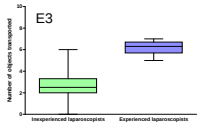


*** P<0.001 (G1 vs. G3); °° P<0.01 (G2 vs. G3)

Construct validity testing of E 1-3 on 283 Individuals







P<0.0001

Content validity

Results 60 first year residents pre and post course

pre-course

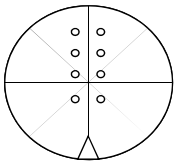
LASTT score		
excellent	intermediate	minimal
0%	69.2%	30.8%

post-course

LASTT score		
excellent	intermediate	minimal
69.2%	30.8%	0%

SUTT 1 : Greek running suture

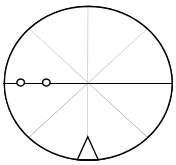
- Start at red dot performing stitch
- Needle should correctly be positioned in the dots.
- Change hand after each stitch
- Be careful with tread transport not to perform trauma
- Time for the exercise is 15 min.



SUTT 2 : Right hand dominant

- Precise positioning of stitch on the predefined entry (red dot) and exit point (black dot)
- 15 cm 2-0, V-20 ½ 26 mm needle.
- 1 Intra-corporeal knot with flat knot, 1st locking sequence and 2nd locking sequence

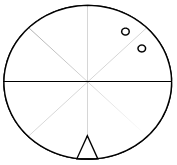
The exercise is being timed till the participant releases the thread at both ends at the end of the knotting movements.



SUTT 3 : Left hand

- Precise positioning of stitch on the predefined entry (red dot) and exit point (black dot)
- 15 cm 2-0, V-20 ½ 26 mm needle.
- 1 Intra-corporeal knot with flat knot, 1st locking sequence and 2nd locking sequence

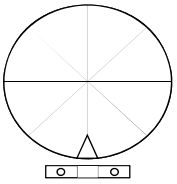
The exercise is being timed till the participant releases the thread at both ends at the end of the knotting movements.



SUTT 4 : Tissue approximation

- Precise positioning of stitch on the predefined entry and exit point with 15 cm 2-0 Caprosyn V-20 ½ 26 mm with dominant hand.
- Correct approximation of tissue by performing one Intra-corporeal flat knot with 2 locking sequences.

The exercise is being timed till the participant releases the thread at both ends at the end of the knotting movements.



Structured program in laparoscopic skills

The scientific work performed in the last years has put forward following evidence to take into acount for a structured training program.

1 Training of only suturing exercises does not provide full proficiency in the laparoscopic psychomotor skills.

2. Full acquisition of all 3 LASTT exercises facilitates the acquisition of more complex laparoscopic tasks (SUTT).

3. The psychomotor skills remains in time proving the similarity with swimming or biking skills.

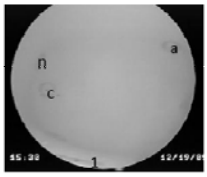
4. The presence and assistance of a tutor is less important than repetition (training) of excercises to acquire the LPS skills.

HYST+T tm

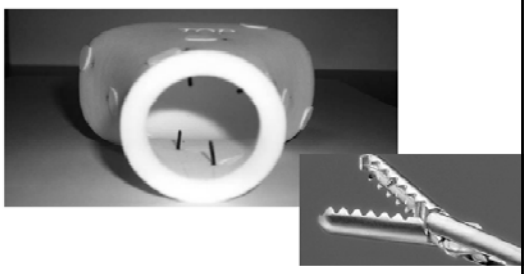
Hystersocopic Skills Training and Testing Method

Practical test to measure the competence level of an individual in basic hysteroscopic psychomotor skills like camera handling, hand-eye coordination and bi-manual handling in the specific uterus environment.

HYST+T tm



HYST+T™



3. Surgical Practice Curriculum

The frequency of practical exposure to endoscopic procedures is recognized being a criterion for the assessment of the professional level.

The grading is defined as:

Level 1: exposure to 50 defined case of laparoscopy and/or hysteroscopy and having participated (with certification) to an ESGE recognized suturing workshop.

For Level 2: exposure, as first surgeon, to 50 procedures ESGE Class 3 in laparoscopy and/or ESGE Class 2 in hysteroscopy, within a period of max 5 years

For Level 3: exposure, as first surgeon, to 50 procedures ESGE Class 4 in laparoscopy and/or ESGE Class 3 in hysteroscopy, within a period of max 5 years

ESGE Procedure Classification

ESGE Laparoscopic Procedure Classification

First level (basic)

- Diagnostic Laparoscopy
- Tubal Sterilization
- Cyst Aspiration
- Biopsies

Second level (intermediate)

- Salpingotomy / salpingectomy
- Salpingo-oophorectomy
- Cystectomy
- Moderated Adhesiolysis
- Minimal/mild Endometriosis

Third level (advance)

- Hysterectomy
- Myomectomy
- Urinary Incontinence
- Extensive Adhesiolysis
- Severe Endometriosis
- Bowel or bladder lesions reparation

Fourth level

- Pelvic floor disorders
- Oncology (Lymphadenectomy, radical hysterectomy, axilloscopy)
- Recto-vaginal endometriosis

ESGE HYSTEROSCOPIC PROCEDURES CLASSIFICATION

First level (basic)

- Diagnostic hysteroscopy
- Simple procedures (excluding the use of laser or electro-surgery):
  - Target biopsies
  - Removal of IUCD
  - Minor intrauterine adhesions

Second level (intermediate)

- Polypresection
- Resection of type 0 myoma
- Endometrial ablation
- Treatment of uterine septum
- Tubal canulation

Third level (advanced)

- Resection of type 1 and 2 myoma
- Major Asherman's syndrome

4. Surgical Examination

For level 1 : theoretical exam only

TESTT®:

validated test on theoretical knowledge on endoscopic anatomy, endoscopic instrumentation and hardware, OR organization, and complication management.

4. Surgical Examination

Predefined surgical procedures have to be performed in a OR (or equivalent) environment for level 2 and level 3 of the program

Model	Disadvantages	Advantages
Animal Models	- ethical problems - facilities - costs - validation animal model for reproductive surgery	- Allows an immediate assessment of surgical skills
Video	- objectivation - time consuming - possibility of cheating	- assessment of surgical skills - costs
Simulator	- initial investment - only skills assessment	- hardware lasts for a long time - easily updatable
Electronic assessment	- software preparation	- objective - cheap - comparable - fast
Live surgery	- time consuming - costs - unrealistic in case of a high number of applicants	- assessment and validation of surgical skills - extremely realistic - ACS (Anti Cheating System)

5. Continuing Medical Education

The Standing Committee on CME/CPD (SCCPD) of the EBCOG is responsible in Europe for establishing the guidelines on European targets in Gynaecological Endoscopy. The working group is currently in charge of preparing a proposal for the GESEA program.

Reporting and certification will be managed through the CME procedures of the UEMS.

Introducing 3 distinghuised levels of surgical skills with different diplomas

1. Bachelor in Endoscopy
   (entrance to the training curriculum for Endoscopic Surgeon)
2. Gynaecological Laparoscopic surgeon.
   Hysteroscopic surgeon
   Reproductive surgeon
3. Laparoscopic Pelvic Surgeon

GESEA Testimonium Program						
LEVEL	Accessible learning	Specific Endoscopic Skills	Surgical Practice Curriculum	Surgical Examination	Continuing Medical Education	Diploma
1	Winners Bachelor First *		Exposure to 50 cases + Suturing workshop	TESTT®	EBCOG Project Definition	**Bachelor in Endoscopy**
2	Winners GLS Second **		First Surgeon 50 ESGE Class 3	Under Validation ESHRE	EBCOG Project Definition	**Gynaecological Laparoscopic Hysteroscopic Reproductive Surgeon**
3	Winners EPS Third ***		First Surgeon 50 ESGE Class 4	Under Validation	EBCOG Project Definition	**Laparoscopic Pelvic Surgeon**

Testimonium Management

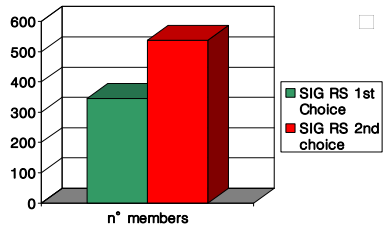
1. The Certification of the Specific Endoscopic Skills (LASTT / HYSTT / SUTT / TESTT) will be supervised by an official certification body **CERTENDO**, in process of creation and application for NBN EN ISO/IEC 17024 accreditation aligned to the NANDO European Act and open to recognition under the MRA (Mutual Recognition Agreements) procedure with other countries (Australia, Canada, Switzerland, United States, Japan, …) (or equivalent)
2. The GESEA Testimonium **Public Registry** lists individual surgeons who have successfully completed one of the three levels of the Program and the corresponding certification program, the type of diploma and certificate issue date; certificate and their respective validity.

Rationale reproductive surgeon

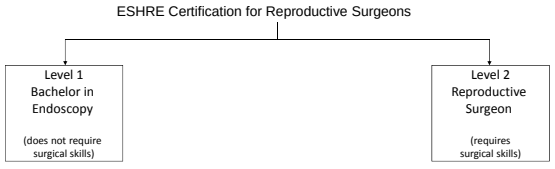
Reproductive Surgery (RS) is crucial for Reproductive Medicine. In the last 10 years, there have been tremendous improvements in the infrastructure (settings and instrumentation) as well as in the developed capabilities of individuals and groups, in treating infertile women to become pregnant spontaneously and also increasing ART pregnancy rates.

There is enough experience and evidence based data that RS undertaken by well trained and experienced clinicians significantly improves and preserves fertility results, alleviates patients from pain and improves their quality of life. In addition, surgery performed by competent gynaecologists contributes to patients' safety and secures the profession's good reputation.

ESHRE SIG Reproductive Surgery



Ways of examination – Practical and theoretical skills



Surgical training

Bachelor Certification

Applicants for bachelor certification will have to be exposed to 50 Hysteroscopies (25 Diagnostic Hysteroscopies + 25 Major or minor Hysteroscopies), to 20 diagnostic laparoscopies and to 30 operative laparoscopies

Reproductive Surgeon Certification

Applicants for reproductive surgeon certification will have to perform 50 hysteroscopies (of which at least 20 major ones) and 50 laparoscopies (of which at least 20 operative ones) as first operators within a time frame of 3 years.

Surgical Exam – Only for reproductive surgeons

It will be composed of a theoretical part and of a practical part.

The theoretical test will be the first part of the exam and it will be composed of multiple choice questions. The Committee will define the names of the clinicians in charge of preparing the questions, selected according to the criteria previously described.

As far as the practical test is concerned, the working group dedicated a large amount of energy to a careful analysis of different models available, summarizing the pros and cons of each one of them.

The practical test was deemed necessary considering the characteristics of the Certification.

Surgical Exam – Exam model

After a long discussion, the WG unanimously agreed that the best option would be to **combine Video and Electronic Assessment**.

The ESHRE WG will draft a document including the number of videos to be submitted by applicants and the number of videos to be examined in a random way, plus some potential extra questions to be asked to applicants.

The WG will also elaborate a first draft of the electronic document of the test.

The group agreed that in case of failure, applicants for certification will be entitled to request a site visit for a live surgery session for fee.

ESHRE –
Reproductive Surgery Accreditation Program and Certification
(ERSAPC)

ESGE European Society for Gynaecological Endoscopy

STAY IN SCOPE... WWW.ESGE.COM

Gynaecological Endoscopic Surgical Education and Assessment

GESEA Program

Complications related to ART

ESHRE Pre-Congress Course
"Total Quality Management (TQM) in an IVF Centre"
London July 7th 2013

Jan M.R. Gerris, MD, PhD
Centre for Reproductive Medicine,
Dept. Ob-Gyn,
Ghent University - Belgium

This presentation is completely independent.

I have no commercial relationships with any company.

Objectives of this presentation

At the end of this presentation, participants will have a better understanding of (risks and) complications (R&C) of fertility enhancing treatments by

- knowing what *are* the *clinically* most relevant R&C before, during and after treatment;
- understanding a rational *approach* towards prevention, minimizing their effects on treatment outcome;
- understanding the complementarity between personal responsability in the clinic and the role of guidelines
- understanding where future meaningful action is lying.

World Health Organization (WHO)
Definition of Health

Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity

Safety is state of continuous technical, human and organizational proficiency resulting in the absence of incidents and accidents

Classification of R&C

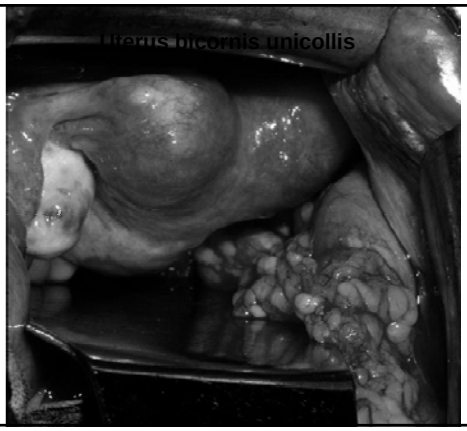
- Pre-treatment R&C
  - Poor selection
  - Pre-existing risks
- Treatment R&C
  - Stimulation
  - Oocyte retrieval
  - Laboratory phase
  - Embryo transfer
  - Luteal phase
- Post-treatment R&C
  - Pregnancy
  - Late complications in non-pregnant patients
  - Long-term risks and complications

What *are* the R & C's?

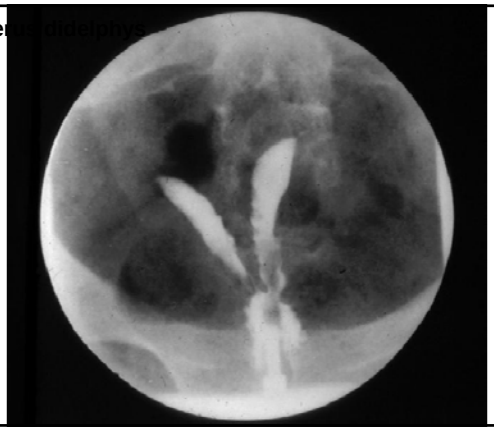
Pre-treatment R&C

Pre-existing risks

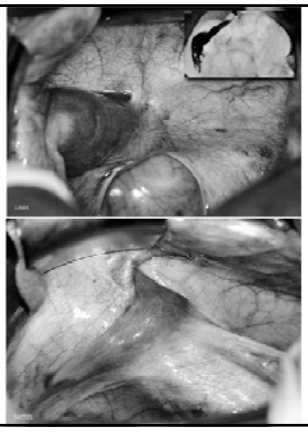
- **SYSTEMIC DISEASE**
  - IDDM
  - Obesity/metabolic syndrome
  - Hyper- and hypothyreosis
  - Liver- and kidneydisease
  - Thrombophilia or previous DVT
  - Auto-immune diseases
  - …
- **GYNECOLOGICAL PRECONDITIONS**
  - Uterine myomatosis (embolize or remove if cavitary)
  - Congenital anomalies of the uterus (mSET)
  - Previous prematurity
  - Isthmic insufficiency
  - (Substantial)LLETZ
  - Turner patient (2% rupture of aortic aneurysm)
  - Age of both partners
  - …

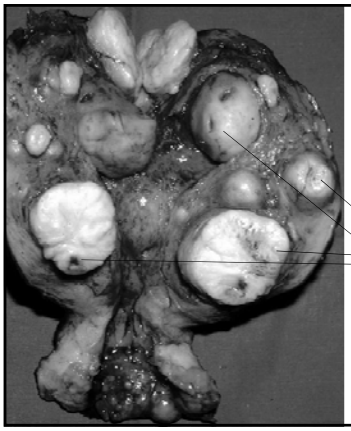


Uterus didelphys



Uterus unicornis





Multiple myomatosis

Pearl white hard myoma tissue

Influence of myomas on reproductive function: <u>all locations</u>

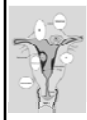
Effect of fibroids on fertility: all locations.

Outcome	Number of studies/substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	18	0.849	0.734–0.983	P=.029
Implantation rate	14	0.821	0.722–0.932	P=.002
Ongoing pregnancy/live birth rate	17	0.697	0.583–0.826	P<.001
Spontaneous abortion rate	18	1.678	1.373–2.051	P<.001
Preterm delivery rate	3	1.357	0.807–3.036	Not significant

- <u>Expected:</u> lower pregnancy rate (PR), more miscarriages
- <u>Evidence:</u>
  - Significantly lower PR, IR, LBR and higher MCR
  - No difference in verschil in Preterm Delivery Rate

Pritts EA et al. Fibroids and infertility: an updated systematic review of the evidence.*Fertil Steril 2009*; **91:1215-1223.**

Influence of myomas on reproductive function: <u>intracavitary distorsion</u>



Effect of fibroids on fertility: submucous fibroids.

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	4	0.363	0.179–0.737	P=.005
Implantation rate	2	0.283	0.123–0.649	P=.003
Ongoing pregnancy/live birth rate	2	0.319	0.119–0.850	P<.001
Spontaneous abortion rate	2	1.678	1.373–2.051	P=.022
Preterm delivery rate	0	—	—	—

- <u>Expected:</u> clear influence on PR, ….
- <u>Evidence:</u>
  - Significantly lower PR, IR, LBR, higher MCR
  - No studies on PDR

Pritts EA et al. Fibroids and infertility: an updated systematic review of the evidence.*Fertil Steril 2009*; **91:1215-1223.**

Influence of myomas on reproductive function: <u>no intracavitary distorsion (IM and SS)</u>

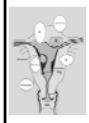
Effect of fibroids on fertility: no intracavitary involvement.

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	24	0.897	0.800–1.004	Not significant
Implantation rate	14	0.792	0.696–0.901	P<.001
Ongoing pregnancy/live birth rate	16	0.780	0.690–0.883	P<.001
Spontaneous abortion rate	16	1.891	1.473–2.428	P<.001
Preterm delivery rate	2	2.767	0.797–9.608	Not significant

- <u>Expected:</u> no/little influence on PR, ….
- <u>Evidence:</u>
  - No difference in PR
  - Significantly lower IR, LBR and higher MCR
  - No difference in PDR (2 studies)

Pritts EA et al. Fibroids and infertility: an updated systematic review of the evidence.*Fertil Steril 2009*; **91:1215-1223.**

Influnce of myomas on reproductive function: SS



- Expected: no/little effect on PR, ….
- Evidence:
  - No effect op PR, IR, LBR, AR en PDR!

Pritts EA et al. Fibroids and infertility: an updated systematic review of the evidence.*Fertil Steril 2009*; **91:1215-1223.**

Influence of *myomectomy* on reproductive function: SM (controls: myoma in situ)

Effect of myomectomy on fertility: submucosal fibroids.

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
A. Controls: fibroids in situ (no myomectomy)				
Clinical pregnancy rate	2	2.034	1.081–3.826	P=.028
Implantation rate	0	–	–	–
Ongoing pregnancy/live birth rate	1	2.654	0.920–7.658	Not significant
Spontaneous abortion rate	1	0.771	0.359–1.658	Not significant
Preterm delivery rate	0	–	–	–

- Expected: better resultats after myomectomy
- Indeed significantly higher PR
- No difference LBR and MCR (both just one study, near significance- LBR!)
- No studies on IR and PDR

Pritts EA et al. Fibroids and infertility: an updated systematic review of the evidence.*Fertil Steril 2009*; **91:1215-1223.**

Influence of *myomectomy* on reproductive function: SM (controls: no myoma)

Effect of myomectomy on fertility: submucosal fibroids.

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
B. Controls: infertile women with no fibroids				
Clinical pregnancy rate	2	1.545	0.998–2.391	Not significant
Implantation rate	2	1.116	0.906–1.373	Not significant
Ongoing pregnancy/live birth rate	3	1.128	0.939–1.326	Not significant
Spontaneous abortion rate	2	1.241	0.475–3.242	Not significant
Preterm delivery rate	0	–	–	–

- Expected: equal results after myomectomy
- Indeed equal results ~ PR, IR, LBR én AR
- No studies on PDR

Pritts EA et al. Fibroids and infertility: an updated systematic review of the evidence.*Fertil Steril 2009*; **91:1215-1223.**

Influence of *myomectomy* on reproductive function: IM (controls: myoma in situ)

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	2	3.765	0.470–30.136	Not significant
Implantation rate	0	—	—	—
Ongoing pregnancy/live birth rate	1	1.071	0.750–3.723	Not significant
Spontaneous abortion rate	1	0.758	0.296–1.043	Not significant
Preterm delivery rate	0	—	—	—

- Expected: ? (depending on presence or absence of distorsion at hysteroscopy)
- No difference in PR, LBR and MCR (pos trends)
- No studies on IR en PDR

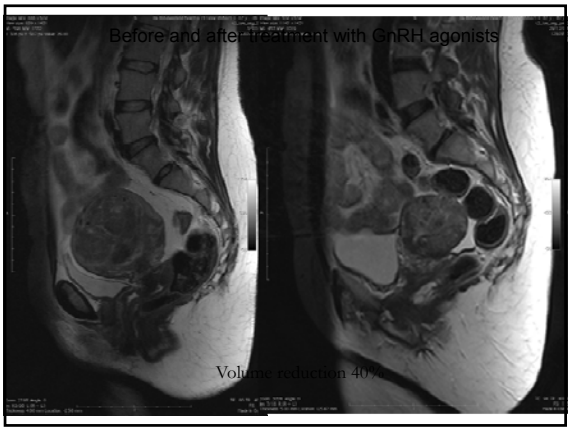
Pritts EA et al. Fibroids and infertility: an updated systematic review of the evidence.*Fertil Steril 2009*; **91:1215-1223.**

Guidelines concerning myomas in women with subfertility (1)

- Subserosal myomas: remove only if symptomatic
- Submucous (=intracavitary) myomen (type 0 and 1):
  - ≤4 cm: hysteroscopic resection (if needed in several times)
  - >4 cm:
    - Pretreatment with GnRH-analogues, then hysteroscopic resection
    - Quid embolisation? Not in patients with subfertility

Guidelines concerning myomas in women with subfertility (2)

- Intramural myomas: perform voer hysteroscopy (and/or HyFoSy) when slightest doubt regarding submucous component and/or distorsion of the cavity
  - If present: consider myomectomy, certainly if
    - myoma > 3 cm
    - Pt with repeated failures
  - If absent: no myomectomy



Other concomittant diseases

- Anemia
  - Iron deficiency
  - Sickle cell
  - Hemoglobinopathias
- HIV infection
- Malaria
- Treponematosis
- Tuberculosis
- Undernutrition
- Other tropical diseases or issues

The older patient

The decrease in (live born) MFR relative to the MFR of women aged 20-30 years

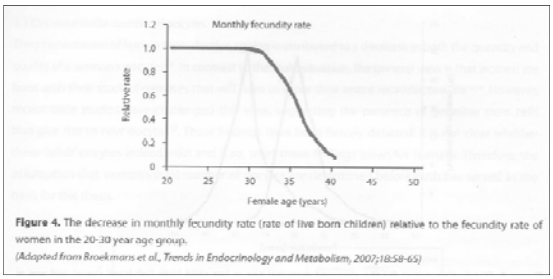
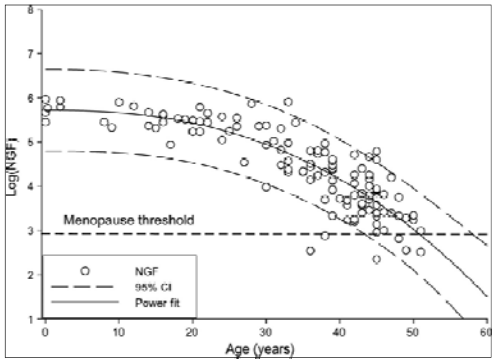


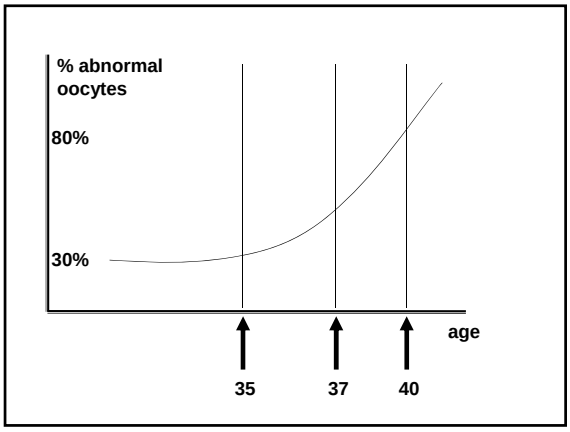
Figure 4. The decrease in monthly fecundity rate (rate of live born children) relative to the fecundity rate of women in the 20-30 year age group.
(Adapted from Broekmans et al., Trends in Endocrinology and Metabolism, 2007;18:58-65)

Haadsma et al., 2010

Model of ovarian non-growing follicle (NGF) decay



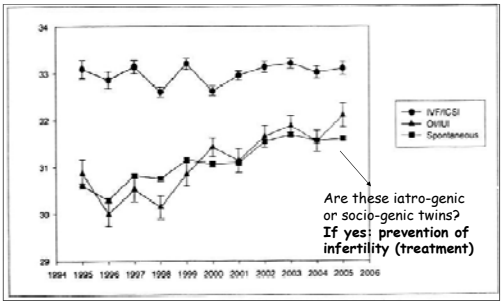
Hansen, K. R. et al. Hum. Reprod. 2008 23:699-708



Clinical conclusion

- Increasing age is an objective basis to consider multiple embryo transfer.
- This does not contradict the need for eSET in young women in first attempts

Evolution of maternal age in dizygotic twins in The Netherlands 1995 - 2006

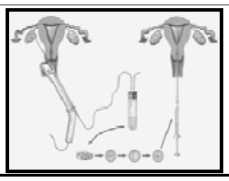


Lambalk, 2007

Male partner: one clinical suggestion ~risks and complications

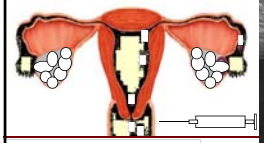
- Amniocentesis from the age of 50 years onwards because
  - Increase in Down syndrome
  - Increase in some monogenic dominant anomalies

Treatment R&C

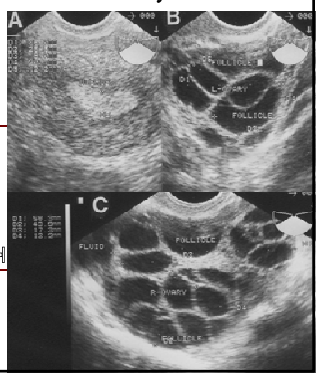


Ovarian hyperstimulation syndrome

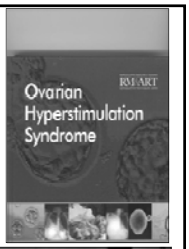
Powerful drugs lead sometimes to excessive stimulation…



… development of several tens of ovarian follicles



OHSS
Prevention

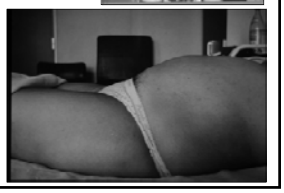


The best prevention method is

1) To *detect* patients at risk

2)To *adapt* the selected stimulation

3) To closely *monitor* the patient



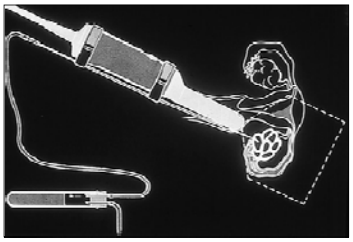
OHSS
Risk factors

- Young age
- Low body weight
- PCO or PCO-like patients
- High number of resting follicles (« necklace sign »)
- History of OHSS

OHSS
Prevention methods

- Withholding hCG
- Coasting
- IV albumin / macromolecules
- Antagonists + GnRH-a
- Total embryo freezing & segmentation

Miscellaneous complications



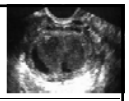
Literature data on complication rates after ART

	Baber	Bergh	Roest	Serour	Govaerts
N cycles	600	10,125	2,495	3,500	1,500
OHSS + hosp	-	0.7%	0.7%	1.7%	1.8%
Bleeding	1.3%	0.7%	-	0.1%	0.2%
Adnex torsion	-	-	0.1%	-	0.1%
Infection	0.5%	0.3%	0.3%	0.3%	0.4%
Total	**1.8%**	**1.7%**	**1.1%**	**2.1%**	**2.5%**

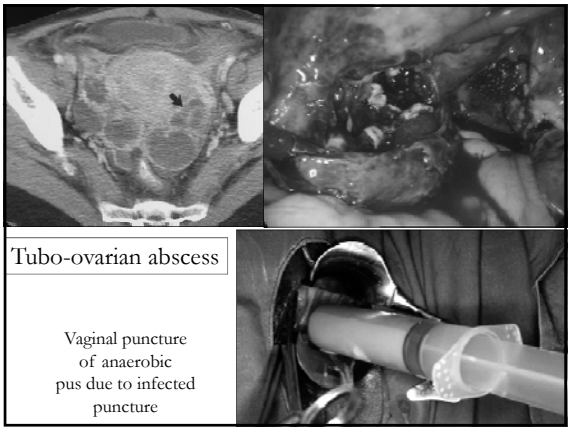
Bleeding following pick-up

- Vaginal hemorrhage in 5-10%
- Significant (>100 ml) blood loss in 0.8% of all TV/US OPU
- Very serious bleeding in 0.1% (retroperitoneal ovarian, sacral / iliacal vessels), leading to laparoscopy /-tomy
- Blood loss after 24h normally ~230 ml (Dessole '01):
  - a drop in Hct of 5% or of Hb of 1.6 g% = normal
  - if blood loss is "normal", any postoperative acute abdomen must be infectious in origin
- Prevention:
  - limit vaginal puncture sites to two
  - leave risky follicles untouched

Infections after egg retrieval

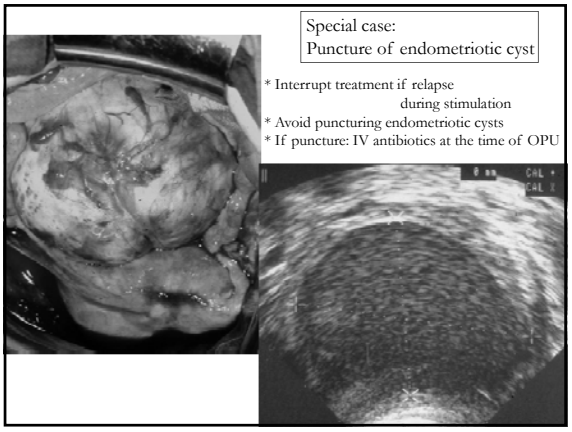


- Incidence: 0.6%, sometimes with abscess formation
- abscesses: often asymptomatic, late diagnosis (until six weeks later or even later)
- culture: E. Coli, B. fragilis or Enterococcus sp. in mixed cultures, often negative
- Rare cases of infections after OPU: appendicitis, vertebral osteomyelitis



Tubo-ovarian abscess

Vaginal puncture of anaerobic pus due to infected puncture



Special case:
Puncture of endometriotic cyst

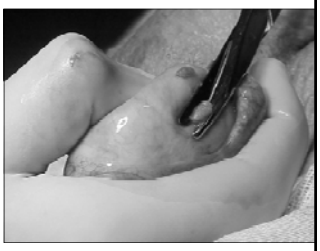
* Interrupt treatment if relapse during stimulation
* Avoid puncturing endometriotic cysts
* If puncture: IV antibiotics at the time of OPU

Infections after egg retrieval

- DO NOT puncture endometriotic cysts (consider laparoscopic OPU), pseudocysts or hydrosalpinges on purpose
- DO NOT administer routinely antibiotics prophylactically (?); only when (suspicion of) inadvertent puncture > fluoroquinolones/tetracyclins
- DO NOT desinfect vagina (Betadin: 17.2% vs 30.3% PR (Van Os, '92) but cleanse with physiological water

Complications after TESE

- Bleeding (scrotal hematoma)
- Infection
- Pain and dysfunction
- Androgen deficiency?

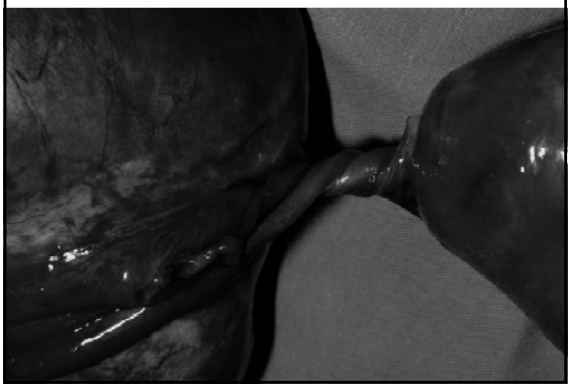


Adnexal (sub)torsion

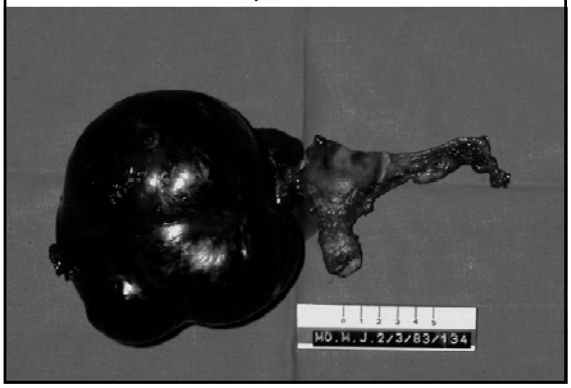
- Typical of stimulated cycles
- Incidence 0.1% of all ART cycles.
- If pregnant 1/162
- If OHSS 7.5%
- R/ laparoscopic untwisting (even after ischemia, no removal !) optionally after puncturing
- R/ transvaginal puncture

Torsion of hyperstimulated ovary without necrosis

Torsion of hyperstimulated ovary with reversible necrosis



Torsion of ovarian cyst with irreversible necrosis

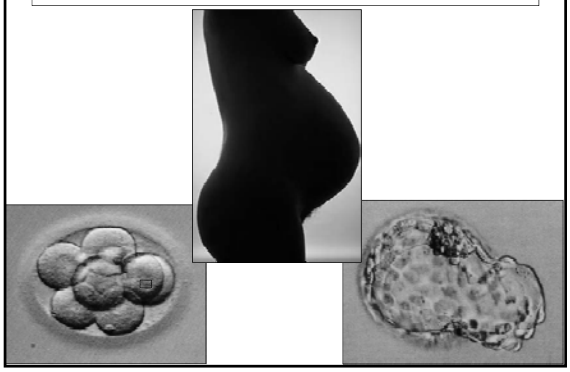


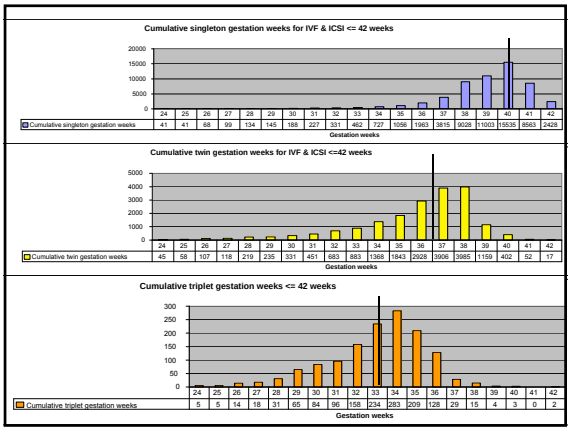
Thrombotic complications related to the ovarian stimulation (without OHSS)

- Thrombosis < hypercoagulability in all stimulated women (due to E2-rise)
- A (underreported) number of severe cases of DVT have been described in hyperstimulated women
- Family / personal history taking and heparin prophylaxis if indicated
- Do not pretreat patients at risk with estrogen containing COC (either natural cycle or post-POP start)

Post-treatment R&C

Multiple pregnancy





TWINS

- « A nice chance to have 2 babies at once ! »
- « …to make up for lost time »

BUT

- **Maternal mortality** **X 2 or 3**
- **Transfer in ICU** **X 15.5**
- **Severe prematurity** **X 4**
- **SFGA** **X 4**
- **Infant mortality** **X 5**
- **Cerebral Palsy** **X 5 to 10**

Maternal Morbidity

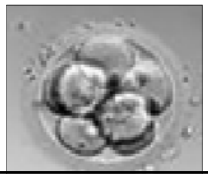
Multiple (n=44,674) vs singleton pregnancy (n=165,188)

	RR (95% CI)
Pre-eclampsia	2.8 (2.7-2.9)
Gestational diabetes	1.1 (1.9-1.2)
Myocardial infarction	**3.7 (2.3-5.8)**
Heart failure	**12.9 (2.7-62.3)**
Venous thromboembolism	**2.7 (2.0-3.5)**
Pulmonary edema	**7.1 (4.5-11.3)**
Post partum haemorrhage	1.9 (1.8-1.9)
Caesarean delivery	2.2 (2.1-2.2)
Hysterectomy	2.3 (1.7-3.2)

The clinical tools …

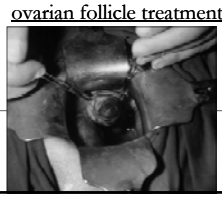
in IVF: SET

- Judicious single embryo transfer
- Both for near-elimination of triplets and for drastic reduction of twins



in non-IVF: SOFT

- **Judicious use of ovulation**
- induction for single ovarian follicle treatment



BELGIAN REIMBURSEMENT REGULATION

- Six IVF/ICSI cycles (= oocyte harvests) reimbursed in a life-time
- 1182€ per cycle for laboratory costs (gamete procurement and handling)
- Including cryocycles
- Up to the age of 43 years

Linked to a rational transfer strategy

≤ 36 years

1st trial ever or 1st trial after previous IVF/ICSI-delivery: always one fresh embryo;

2nd trial: one embryo if of sufficient quality; two if of insufficient quality;

≥3rd trial: maximum 2 embryos.

>36 – ≤39 years

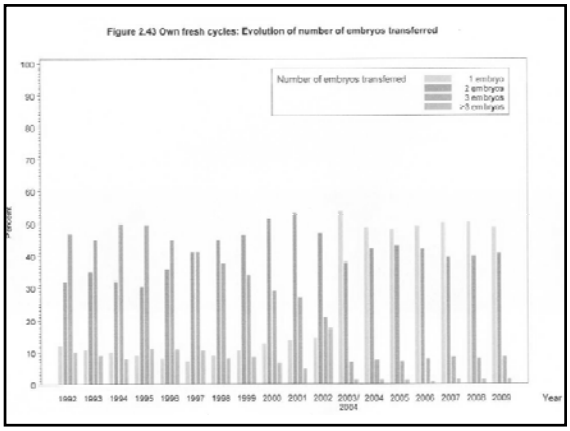
1st and 2nd trial: maximum 2 embryos;

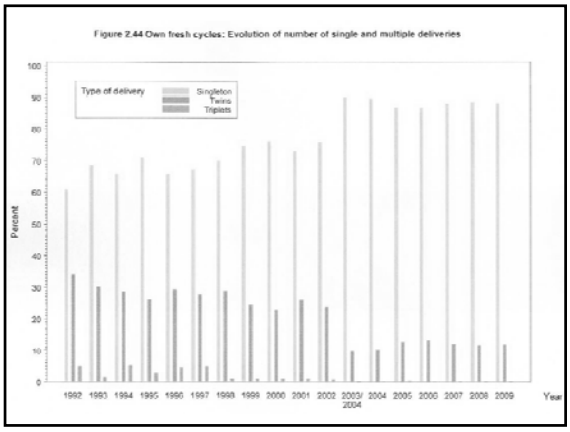
≥3rd trials: maximum 3 embryos.

> 39 years

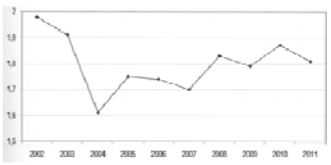
No maximum number of embryos to transfer is dictated

CRYOCYCLES: 1 or 2 embryos

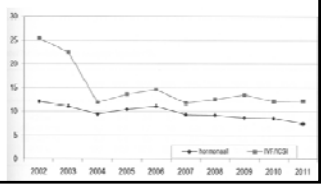




Evolution of the number of twin pregnancies (as % of total deliveries) in Flanders

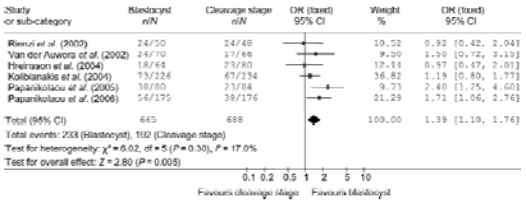


Evolution of the % of twin pregancies after ART treatment before and after the legal arrangement of July 2003



Live birth rate per randomized couple comparing cleavage stage with day 5 embryos

(Papanikolaou et al., *Hum. Reprod. (2008) 23 (1): 91-99***).**



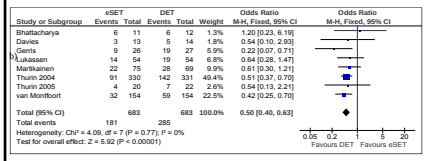
Papanikolaou E G et al. Hum. Reprod. 2008;23:91-99

human reproduction

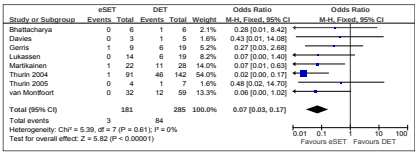
Forrest plots showing the odds ratios of eSET versus DET for the separate trials and the pooled odds ratios for

Live birth

Mc Lernon et al., Lancet, 2010



Multiple Live birth



Single vs Double embryo transfer:
Individual patient data meta-analysis of randomised trials

Meta-Analysis Group for Elective Single Embryo Transfer
International Collaboration (Magestic)
Collaborative Group

Kirsten Harrild,Christina Bergh, Michael Davies, Diana De Neubourg, John Dumoulin, Jan Gerris, Kirsten Harrild, Jan Kremer, Hannu Martikainen, Ben Mol, Robert Norman, Ann Thurin-Kjellberg, Aafke van Montfoort, Arno Van Peperstraten, Eric Van Royen, Siladitya Bhattacharya,

Acknowledgement: David McLernon

Fresh cycle eSET vs DET: live birth

	eSET N = 677	DET N = 676	OR (95% CI)	P-value
Live birth	**27%**	**42%**	**0.50 (0.40, 0.63)**	**< 0.001**
			0.46 (0.36, 0.58)*	< 0.001*
Multiple live birth	**2%**	**29%**	**0.04 (0.01, 0.13)**	**< 0.001**

* Adjusted for duration & cause of infertility, female's age, BMI, & parity, use of ICSI, no. of embryos available for transfer, & day of transfer

All 8 trials included

Fresh & frozen eSET vs fresh DET: livebirth

	eSET N = 350	DET N = 353	OR (95% CI)	P-value
Live birth	**38%**	**42%**	**0.83 (0.61, 1.12)**	**0.22**
			0.85 (0.62, 1.15)*	0.29*
Multiple live birth	**1%**	**32%**	**0.02 (0.00, 0.13)**	**< 0.001**

* Adjusted for duration & cause of infertility, female's age, BMI, & parity, use of ICSI, no. of embryos available for transfer, & day of transfer

2 trials included

Two fresh eSET versus fresh DET

	eSET N = 54	DET N = 54	OR (95% CI)	P-value
Live birth	**41%**	**35%**	**1.27 (0.58, 2.76)**	**0.55**
			0.43 (0.13, 1.42)*	0.17*
Multiple live birth	**2%**	**32%**	-	**< 0.01**

* Adjusted for duration & cause of infertility, female's age, BMI, & parity, use of ICSI, & no. of embryos available for transfer

1 trial included

Conclusion

- Live birth rate lower with eSET in fresh cycle
- Fewer twins and fewer preterm deliveries
- Similar term singleton rate
- Comparable live birth with additional fresh/frozen SET
- Multiple live birth rate following eSET similar to natural rate
- Results in fresh cycle hold true for sub-groups (age and embryo quality)
- High live birth rates in younger women

DET > eSET

unless one adds the cryocycles

OR

is it not so much a question of how many embryos but which embryo?

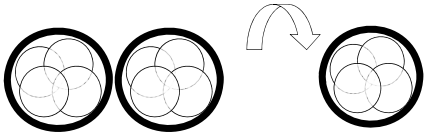
Prerequisites for a particular centre to implement esET

- 1. Excellent results (the better the centre, the higher the % of eSET)
- 2. Willingness to decrease a very high MP rate
- 3. Willingness to invest in optimization of a freeze/thaw programme
- 4. eSET must be compatible with specific societal circumstances in which the centre works

Five pillars for eSET

- Creating awareness
- International agreement on patient and embryo characteristics prior to SET
- Marketing the idea
- In-depth counseling
- Appropriate funding

Reducing the number of twin births: **1st step**

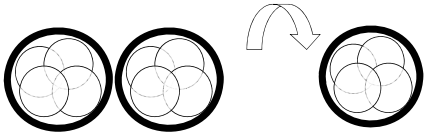


Single embryo transfer in selected cases

Twin-prone patient selection

Embryo selection

Reducing the number of twin births: 2nd step



Single embryo transfer in all cases except

In patients with poor prognosis

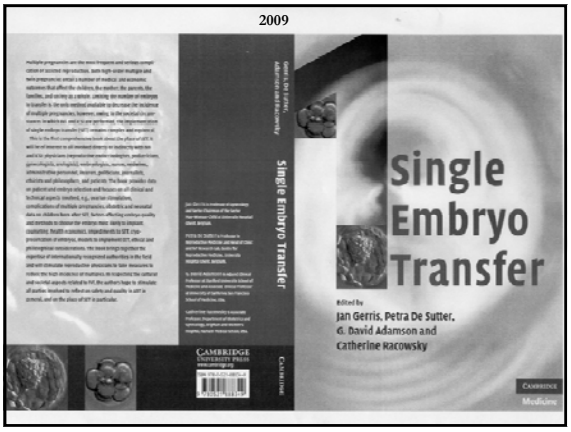
If only poor quality embryos are available

Take home message

The ideal candidate for SET:

1. Young woman (<35 years old)
2. First or second attempt
3. With a choice of embryos to transfer/freeze (producing big oranges)
4. Blastocyst

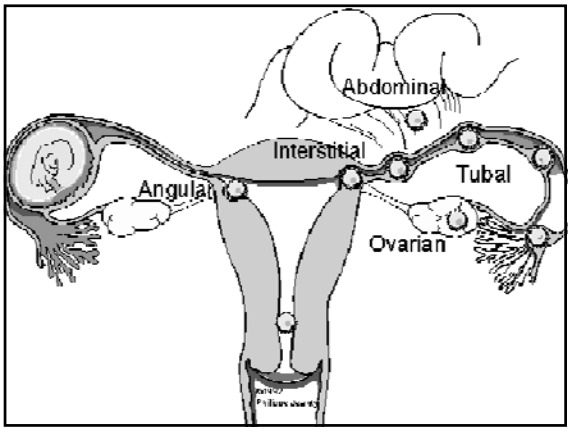
2009

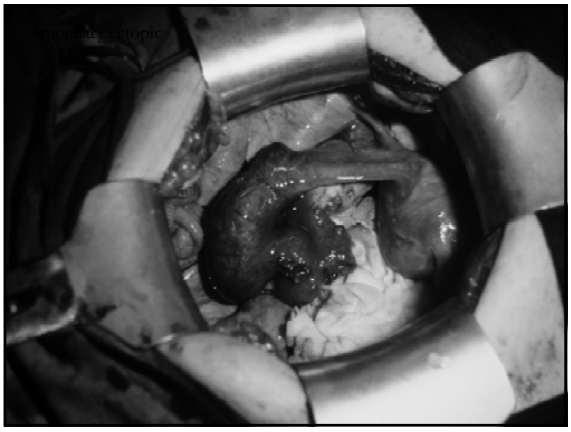


Extrauterine pregnancy

Ectopic Pregnancy

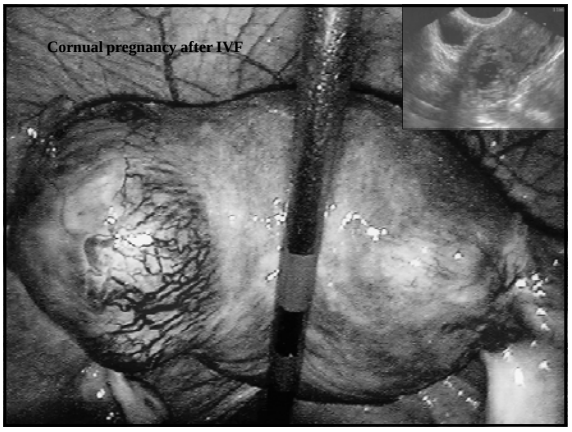
- ~ 4% of all ART pregnancies
- risk factors:
  - damaged tubes
  - previous myomectomy (uterine contractility ?)
- OR for E.P. after difficult transfer = 3.91 (1.49-10.23)

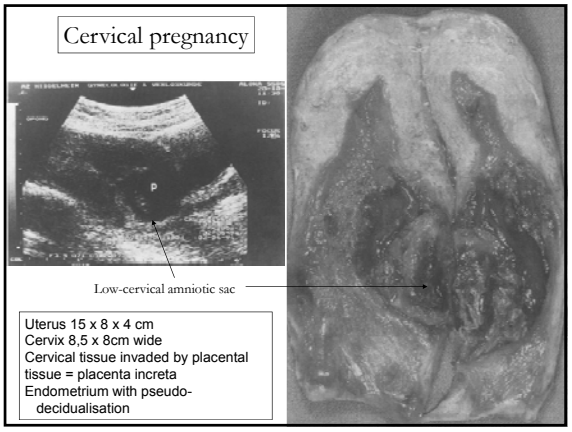




Interstitial / Cornual Pregnancy

- 2 to 6% of all ectopic localizations, may be combined with intrauterine pregnancy
- difficult diagnosis, often late
- beware: rupturing, acute hemorrhage and shock (even leading to hysterectomy !)
- typical after salpingectomy (rupturing later in pregnancy possible in these patients)

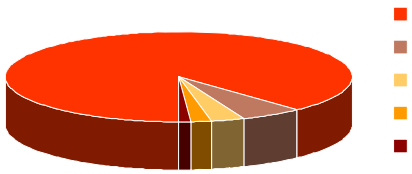




Heterotopic Pregnancy

- 1-3% of all ART pregnancies
- risk factors: same as for ectopics + number of transferred embryos
- diagnosis: often late (think heterotopic !)
- symptoms: abdominal pain, bleeding, shock at rupture -> surgery
- 72.5% of intrauterine pregnancies : live birth

Heterotopic Pregnancy: localization



Pregnancy of Unknown Location

PUL

Transient rise in HCG without clinical nor sonographic indication of localisation of implantation:

- Diagnostic dilemma: academic
  (tubal abortion or tubal miscarriage)
- Therapeutic dilemma: by clinical symptoms; do not overtreat

"Look beyond the most obvious diagnosis and always expect the unexpected"

Think ectopic, think heterotopic !

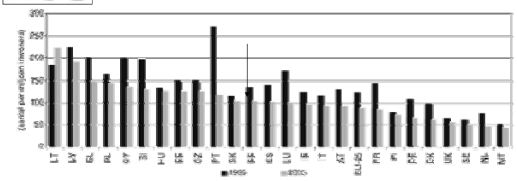
What should we *do* about the R & C's?

Safety = "zero tolerance"?

- Total absence of an undesired phenomenon
- Can/should we maintain it in (reproductive) medicine?
- "Do-no-harm" instead of "Zero-tolerance" because there is a benefit (most of the time)?

Principles

Number of deaths by traffic accidents in the EU-25 1996-2005



Belgium:

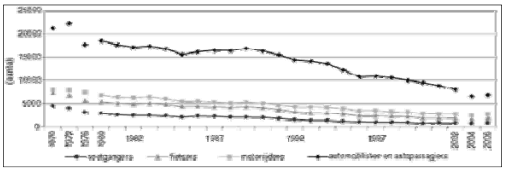
1996 ~1400 deaths

2005 ~1020 deaths

2009 ~ 750 deaths (1/3 of all ART children)

Let's go for "ZERO"

Number of deaths and heavy injured by traffic accidents in Belgium 1970-2006



"Let's go for zero!" High cost due to:

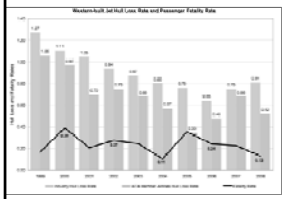
* police actions
* automatic speed control by road cameras (n=?)
* citizens paying a fortune in fines
* increased insurance contracts

…

But nobody says: stop the traffic!

Air traffic

2008



502 deaths in 109 accidents
= 1 death/1,3 million flights
= 1 death/7,7 million passengers

Yet, nobody says:
Stop flying!


GULF NEWS

Prognosis grim, say U.K. officials

Airlines begin slow return to normality

BACKLOG CAUSED BY ASH CLOUD WILL TAKE TIME TO CLEAR

WORLD MUSIC

Charter flight brings in Womad artists

Festival in Abu Dhabi goes ahead as planned

Except… Ash cloud over Europe deepens travel chaos

Because of "concern with PAX safety"?

- In fact: because fear for *more risk than usual* when flying (annual mortality = extremely low)
- As long as no "absolute" safety guarantee could be given, no airline dared to fly for fear of public perception not to care for the PAX safety
- Up to the point that …


UAE airlines resume flights to Europe as airspace clears

DISRUPTION FROM ASH CLOUD COST CARRIERS $1.7B IN LOST REVENUE

Long wait

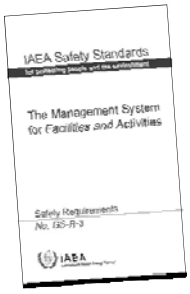
!

• **AIR TRAFFIC**	• **ART**
"Absolute" safety comes with a price …	In ART too safety has a price…
When the price rises too high, safety concerns laxen …	When the price rises too high, risks are taken (multiples)…
People WANT to fly …	People WANT children…
There appears to be a balance	There is a trade-off between desired outcome and risks
Zero – tolerance is impossible: nobody says stop flying!	Zero-tolerance is theoretical: nobody says stop ART!

The Columbia Accident Investigation Board

"In our view, the NASA <u>organizational culture</u> had as much to do with this accident as the foam. Organizational culture refers to the basic values, norms, beliefs, and practices that characterize the functioning of an institution. At the most basic level, it defines the assumptions that employees make as they carry out their work. It is a powerful force that can persist through reorganizations and the change of key personnel."

Nuclear Safety



Nevertheless
11-12/03/2011
Earthquake &
tsunami in Japan

Conclusion

In sectors where we expect zero-tolerance, e.g. international space flight and nuclear energy production, we still see major “risks and complications”, e.g. Columbia/Tsjernobyl/Fukushima

My questions to you

- In (reproductive) medicine, is the goal “zero-tolerance” or minimal risk?
- What level of safety (quantitative) do you want in reproductive medicine?
- What kind of experiences do you really learn from?
- How can we foster a prevention culture?
- How can you change cultures?
- How can ESHRE contribute to the safety of *your* work?

Let us state ourselves what we rationally consider as “safe”

Safety issue	Zero tolerance level (ZTL)	Realistic lowest tolerance level (RLTL)
Multiple pregnancies Monozygotic MPs		
OHSS (severe)		
Bleeding at OPU		
Infection after OPU		
Congenital anomalies		
Cytogenetic abnormalities		
Effects of freezing & vitrification		
Epigenetic effects (media)		
Oncological effects		
Maternal deaths		
Fetal reduction		
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”

Safety issue	Zero tolerance level	Realistic lowest tolerance level
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)		
Bleeding at OPU		
Infection after OPU		
Congenital anomalies		
Cytogenetic abnormalities		
Effects of freezing & vitrification		
Epigenetic effects (media)		
Oncological effects		
Maternal deaths		
Fetal reduction		
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”

Safety issue	Zero tolerance level	Realistic lowest tolerance level (?)
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)	0.0%	<0.5%
Bleeding at OPU		
Infection after OPU		
Congenital anomalies		
Cytogenetic abnormalities		
Effects of freezing & vitrification		
Epigenetic effects (media)		
Oncological effects		
Maternal deaths		
Fetal reduction		
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Infection after OPU		
Congenital anomalies		
Cytogenetic abnormalities		
Effects of freezing & vitrification		
Epigenetic effects (media)		
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OHSS (severe)	0.0%	<0.5%
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Infection after OPU	0.0%	?
Congenital anomalies		
Cytogenetic abnormalities		
Effects of freezing & vitrification		
Epigenetic effects (media)		
Oncological effects		
Maternal deaths		
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Laboratory errors		

Let us state ourselves what we rationally consider as “safe”

Safety issue	Zero tolerance level	Realistic lowest tolerance level
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)	0.0%	<0.5%
Bleeding at OPU	0.0%	?
Infection after OPU	0/0%	?
Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities		
Effects of freezing & vitrification		
Epigenetic effects (media)		
Oncological effects		
Maternal deaths		
Fetal reduction		
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”

Safety issue	Zero tolerance level	Realistic lowest tolerance level
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)	0.0%	<0.5%
Bleeding at OPU	0.0%	?
Infection after OPU	0/0%	?
Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification		
Epigenetic effects (media)		
Oncological effects		
Maternal deaths		
Fetal reduction		
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”		
Safety issue	Zero tolerance level	Realistic lowest tolerance level
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)	0.0%	<0.5%
Bleeding at OPU	0.0%	?
Infection after OPU	0/0%	?
Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification	None	?
Epigenetic effects (media)		
Oncological effects		
Maternal deaths		
Fetal reduction		
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”		
Safety issue	Zero tolerance level	Realistic lowest tolerance level
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)	0.0%	<0.5%
Bleeding at OPU	0.0%	?
Infection after OPU	0/0%	?
Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification	None	?
Epigenetic effects (media)	None	?
Oncological effects		
Maternal deaths		
Fetal reduction		
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”		
Safety issue	Zero tolerance level	Realistic lowest tolerance level
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)	0.0%	<0.5%
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Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification	None	?
Epigenetic effects (media)	None	?
Oncological effects	None	probably none
Maternal deaths		
Fetal reduction		
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”		
Safety issue	Zero tolerance level	Realistic lowest tolerance level
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OHSS (severe)	0.0%	<0.5%
Bleeding at OPU	0.0%	?
Infection after OPU	0/0%	?
Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification	None	?
Epigenetic effects (media)	None	?
Oncological effects	None	probably none
Maternal deaths	None	unrelated to ART
Fetal reduction		
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”		
Safety issue	Zero tolerance level	Realistic lowest tolerance level
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Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification	None	?
Epigenetic effects (media)	None	?
Oncological effects	None	probably none
Maternal deaths	None	unrelated to ART
Fetal reduction	None	?
Psychosocial effects		
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”		
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OHSS (severe)	0.0%	<0.5%
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Infection after OPU	0/0%	?
Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification	None	?
Epigenetic effects (media)	None	?
Oncological effects	None	probably none
Maternal deaths	None	unrelated to ART
Fetal reduction	None	?
Psychosocial effects	None	limited
Future fertility of ART-children		
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”

Safety issue	Zero tolerance level	Realistic lowest tolerance level
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)	0.0%	<0.5%
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Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification	None	?
Epigenetic effects (media)	None	?
Oncological effects	None	probably none
Maternal deaths	None	unrelated to ART
Fetal reduction	None	?
Psychosocial effects	None	limited
Future fertility of ART-children	None	??
Laboratory errors		

Let us state ourselves what we rationally consider as “safe”

Safety issue	Zero tolerance level	Realistic lowest tolerance level
Multiple pregnancies Monozygotic MPs	0.9% 0.3%	<10% <1%
OHSS (severe)	0.0%	<0.5%
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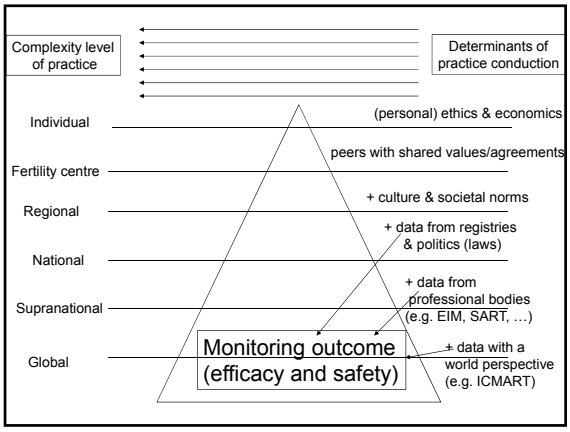
Congenital anomalies	~ natural conception (3-4%)	~ natural conception (3-4%)
Cytogenetic abnormalities	~ natural conception (5-6%)	~ natural conception (5-6%)
Effects of freezing & vitrification	None	?
Epigenetic effects (media)	None	?
Oncological effects	None	probably none
Maternal deaths	None	unrelated to ART
Fetal reduction	None	?
Psychosocial effects	None	limited
Future fertility of ART-children	None	??
Laboratory errors	None	≠ 0

Practice



EUROPE

Assisted reproductive technology in Europe, 1997-2006: results generated from European registers by ESHRE by *The European IVF-monitoring (EIM) Consortium*

Main CPI's reflecting safety in fresh IVF + ICSI 1997-2006

Multiple pregnancies

eshrc European Society of Human Reproduction and Embryology

Main CPI's for fresh IVF + ICSI 1997-2008

IVF/ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries		x2	+50%	-50%	1/7		-20%	1/3	IVF	ICSI	IVF	ICSI
2008 N=36	**315.287**	**22.4**	**53.2**	22.3	2.1	**73.024**	**20.7**	1.0	28.5	28.7	32.5	31.9
2007 N=33	264022	21.4	53.4	22.7	2.5	72493	21.3	1.0	**29.1**	28.6	**32.8**	**33.0**
2006 N=32	222354	22.1	57.3	**19.0**	**1.6**	58725	20.8	0.9	29.0	**29.9**	32.4	**33.0**
2005 N=30	236480	20.0	56.1	21.5	2.3	47966	21.0	**0.8**	26.9	28.5	30.3	30.9
2004 N=29	225480	19.2	55.3	22.1	3.3	45128	21.7	1.0	26.6	27.1	30.1	29.8
2003 N=28	234142	15.7	55.9	24.9	3.5	47212	22.0	1.1	26.1	26.5	29.6	28.7
2002 N=25	203877	13.7	54.8	26.9	4.7	42827	23.2	1.3	26.0	27.2	29.5	29.4
2001 N=23	189549	12.0	51.7	30.8	5.5	37467	24.0	1.5	25.1	26.2	29.0	28.3
2000 N=22	171301	12.1	46.7	33.3	6.8	36066	24.4	2.0	24.7	26.6	28.4	28.7
1999 N=22	132979	11.9	39.2	39.6	9.3	25085	24.0	2.2	24.2	26.1	27.7	27.9
1998 N=18	141251	11.5	37.2	42.0	9.4	22859	23.9	2.3	23.2	24.8	27.0	26.8
1997 N=18	103125	11.5	35.9	38.3	14.2	24516	25.6	3.3	NA	NA	26.1	26.4

Main CPI's for fresh IVF + ICSI 1997-2006												
IVF+ ICSI	nETs					nDEL			CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
2005 N=30	236480					47966						
2004 N=29	225480					45128						
2003 N=28	234142					47212						
2002 N=25	203877					42827						
2001 N=23	189549					37467						
2000 N=22	171301					36066						
1999 N=22	132979					25085						
1998 N=18	141251					22859						
1997 N=18	103125					24516						

Main CPI's for fresh IVF + ICSI 1997-2006												
IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
2005 N=30	236480					47966						
2004 N=29	225480					45128						
2003 N=28	234142					47212						
2002 N=25	203877					42827						
2001 N=23	189549					37467						
2000 N=22	171301					36066						
1999 N=22	132979					25085						
1998 N=18	141251					22859						
1997 N=18	103125					24516						

Main CPI's for fresh IVF + ICSI 1997-2006												
IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
2005 N=30	236480					47966						
2004 N=29	225480					45128						
2003 N=28	234142					47212						
2002 N=25	203877					42827						
2001 N=23	189549					37467						
2000 N=22	171301					36066						
1999 N=22	132979					25085						
1998 N=18	141251					22859						
1997 N=18	103125	11.5	35.9	38.3	**14.2**	24516	**25.6**	**3.3**	NA	NA	26.1	26.4

Main CPI's for fresh IVF + ICSI 1997-2006												
IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
2005 N=30	236480					47966						
2004 N=29	225480					45128						
2003 N=28	234142					47212						
2002 N=25	203877					42827						
2001 N=23	189549					37467						
2000 N=22	171301					36066						
1999 N=22	132979					25085						
1998 N=18	141251	11.5	37.2	42.0	9.4	22859	23.9	2.3	23.2	24.8	27.0	26.8
1997 N=18	103125	11.5	35.9	38.3	**14.2**	24516	**25.6**	**3.3**	NA	NA	26.1	26.4

Main CPI's for fresh IVF + ICSI 1997-2006												
IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
2005 N=30	236480					47966						
2004 N=29	225480					45128						
2003 N=28	234142					47212						
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2001 N=23	189549					37467						
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Main CPI's for fresh IVF + ICSI 1997-2006												
IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
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IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
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2004 N=29	225480					45128						
2003 N=28	234142					47212						
2002 N=25	203877					42827						
2001 N=23	189549	12.0	51.7	30.8	5.5	37467	24.0	1.5	25.1	26.2	29.0	28.3
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N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
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2004 N=29	225480					45128						
2003 N=28	234142					47212						
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IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2006 N=32	222354					58725						
2005 N=30	236480	20.0	56.1	21.5	2.3	47966	21.0	0.8	26.9	28.5	30.3	30.9
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Main CPI's for fresh IVF + ICSI 1997-2006												
IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
										+20%		
N countries		x2	+50%	-50%	1/10		-20%	1/3	IVF	ICSI	IVF	ICSI
2006 N=32	222354	**22.1**	57.3	19.0	1.6	58725	**19.9**	**0.9**	29.0	29.9	32.4	33.0
2005 N=30	236480	20.0	56.1	21.5	2.3	47966	21.0	0.8	26.9	28.5	30.3	30.9
2004 N=29	225480	19.2	55.3	22.1	3.3	45128	21.7	1.0	26.6	27.1	30.1	29.8
2003 N=28	234142	15.7	55.9	24.9	3.5	47212	22.0	1.1	26.1	26.5	29.6	28.7
2002 N=25	203877	13.7	54.8	26.9	4.7	42827	23.2	1.3	26.0	27.2	29.5	29.4
2001 N=23	189549	12.0	51.7	30.8	5.5	37467	24.0	1.5	25.1	26.2	29.0	28.3
2000 N=22	171301	12.1	46.7	**33.3**	6.8	36066	24.4	2.0	24.7	26.6	28.4	28.7
1999 N=22	132979	11.9	39.2	39.6	9.3	25085	24.0	2.2	24.2	26.1	27.7	27.9
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1997 N=18	103125	11.5	35.9	38.3	**14.2**	24516	**25.6**	**3.3**	NA	NA	26.1	26.4

Main CPI's for fresh IVF + ICSI 1997-2008

IVF/ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries		x2	+50%	-50%	1/7		-20%	1/3	IVF	ICSI	IVF	ICSI
2008 N=36	**315.287**	**22.4**	**53.2**	22.3	2.1	**73.024**	**20.7**	1.0	28.5	28.7	32.5	31.9
2007 N=33	264022	21.4	53.4	22.7	2.5	72493	21.3	1.0	**29.1**	28.6	**32.8**	**33.0**
2006 N=32	222354	22.1	57.3	**19.0**	**1.6**	58725	20.8	0.9	29.0	**29.9**	32.4	**33.0**
2005 N=30	236480	20.0	56.1	21.5	2.3	47966	21.0	**0.8**	26.9	28.5	30.3	30.9
2004 N=29	225480	19.2	55.3	22.1	3.3	45128	21.7	1.0	26.6	27.1	30.1	29.8
2003 N=28	234142	15.7	55.9	24.9	3.5	47212	22.0	1.1	26.1	26.5	29.6	28.7
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2000 N=22	171301	12.1	46.7	33.3	6.8	36066	24.4	2.0	24.7	26.6	28.4	28.7
1999 N=22	132979	11.9	39.2	39.6	9.3	25085	24.0	2.2	24.2	26.1	27.7	27.9
1998 N=18	141251	11.5	37.2	42.0	9.4	22859	23.9	2.3	23.2	24.8	27.0	26.8
1997 N=18	103125	11.5	35.9	38.3	14.2	24516	25.6	3.3	NA	NA	26.1	26.4

Main CPI's for fresh IVF + ICSI 1997-2015

Where are we heading?

IVF+ ICSI	nETs	%1e	%2e	%3e	%≥4e	nDEL	%twin	%trip	CPR/OPU		CPR/ET	
N countries									IVF	ICSI	IVF	ICSI
2015 N=max		**50**	35	14	1		**<10? <5?**	**0.1**	~32	~33	~34	~35
2010 N=?												
2011 N=?												
2008 N=36		**22.4**	53.2	22.3	2.1		**20.7**	**1.0**	28.5	28.7	32.5	31.9

This is work in progress to which we all contribute

Complications at OPU 2000-2008 in ESHRE (N=36)

Year	Total cycles	OHSS	All compl. to OPU	Bleeding	Infection	Maternal death	Fetal reduction
2008	525640	2947 (0.6%)	976 (0.19%)	652 (0.12%)	49 (0.09%0)	1	394
2007	492442	2470 (0.5%)	991	574	64	3	364
2006	459170	2753 (0.8%)	938	544	42	0	466
2005	418111	3347 (1.2%)	1048	523	207	0	436
2004	367066	2858 (0.8%)	1125	520	362	4	526
2003	365103	2646 (0.7%)	NA	799	135	2	480
2002	324238	2148 (0.7%)	1156	622	227	2	461
2001	289690	1851 (0.6%)	569	395	0	0	397
2000	279267	1586 (0.6%)	652 (0.23%)	388 (0.14%)	36 (0.13%0)	0	256

Irregular data due to incomplete reporting
Differences of definition >>> differences of practice

Other risks and complications of ART

- Congenital anomalies
- Genetic anomalies
- Epigenetic anomalies (culture media, …)
- Cryopreservation of embryo's
- Vitrification of embryo's
- Vitrification of oocytes
- Long term fertility effects on ART-offspring
- …

Data from individual studies or meta-analyses are reassuring but more longitudinal data are needed before we can be sure about the absence of or the size of an effect

What effect do these registries have on daily practice?

- Very long-term reporting tools with long lag time (5 years)
- Big oil tanker: once a direction is taken, they move slowly but surely with strong impact on general opinion
- They give an indication of the direction we are moving in (e.g. **+ MPR**; e.g. **– IUI**)
- Sensitive to:
  - (in)completeness
  - Differences in definition, reporting units (CPR, LBR, "BESST" practice …)
  - Averaging out wide differences between countries
  - Rubbish in rubbish out

IUI-H and IUI-D 2001-2008

IUI with partner sperm							IUI with donor sperm					
<40years			>40years				<40years			>40years		
DR	2	3	DR	2	3		DR	2	3	DR	2	3
10.5	11.0	0.8	5.5	8.8	0.0	2008	13.5	9.5	0.3	6.6	3.7	0.0
10.2	11.7	0.5	6.3	9.9	0.0	2007	14.6	10.2	0.5	6.1	6.5	0.0
9.2	10.6	0.6	**4.4**	8.9	0.0	2006	**13.3**	10.5	0.6	**4.1**	6.5	0.0
12.6	11.0	1.1	**7.4**	4.9	0.7	2005	**18.9**	10.8	1.2	**9.2**	6.5	0.0
12.6	11.9	1.3	**8.2**	10.4	0.3	2004	**18.7**	11.1	0.8	**8.4**	7.1	1.4
12.2	11.4	2.2	**8.8**	6.2	0.0	2003	**16.7**	10.6	1.2	**6.3**	2.9	0.0
11.6	10.2	1.1	**6.9**	8.9	1.1	2002	**16.6**	9.6	0.6	**6.7**	5.8	1.2
12.8	10.2	1.1	**9.7**	3.8	0.0	2001	**17.1**	9.4	1.2	**8.0**	7.3	0.0

<40 years * recent decrease in delivery rate (DR)!
* twinning has remained stable, triplets down

>40 years * recent decrease in DR!
* twinning stable, triples down

Large databases
(EIM, SART, ICMART …)

- Do not tell us HOW to improve on efficacy or safety in individual practice of single centres
- For that purpose we need specific methods and tools
- Long-time: methods = clinical studies
- Short time: monitoring = dashboard of CPIs

We need a speedboat with a dashboard

- Showing easy-to-measure-and-follow-up key performance indicators (KPIs) of:
  - Clinical excellence
  - Laboratory excellence
  - Operational business excellence

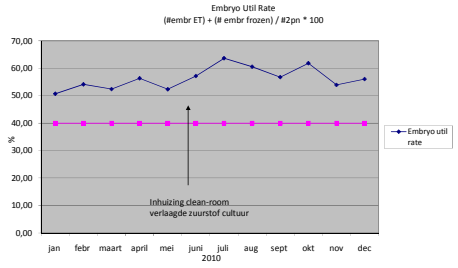
Embryo Utilization Rate (EUR)

$$EUR = \frac{\text{N of embryos transferred (A)} + \text{N of embryos cryopreserved (B)}}{\text{N of 2 PNs (C)}}$$

A = indicator of ET policy (clinical)
B = indicator of cleanroom quality (laboratory)
C = indicator of fertilization efficacy (laboratory)

man, vrouw en kind
Universitair Ziekenhuis Gent

III. Labo KPIs



Are the data available and is it affordable?

- Data available?
  - Yes for the major issues, with lag period
  - Incomplete for the less frequent issues
  - Data collection has begun in “big tanker databases”

- Affordable?
  - We do what we can
  - We need more dedicated staff in each individual centre for surveillance of quality and safety
  - This has a price: are we entitled to financial support?

Concluding remarks

Quality is more than safety (=absence of errors or complications)

- = (Cost)-efficiency, i.e. lowest cost for highest outcome
- = Accessibility (financially and geographically)
- = Safety ("do no harm" vs. "zero-tolerance")
- = Timeliness
- = Satisfaction in patients', partners' and collaborators'
- = Innovation & renovation
  - Infrastructure
  - Instruments & tools
  - Techniques and procedures
- = Structured quality control

Do you recognize any of the following symptoms?

- Belief to belong to the best performers (production) – complacency
- Focus on technical rather than management and people Issues
- Organizational Insularity and Ineffective QA programme
- Lack of Effective Corporate Oversight and centre safety oversight
- Continuous Management Directional Changes and Cost cutting
- Lack of competence in human performance evaluation
- Repeated Problems distracting attention from safety issues
- General Dissatisfaction of Regulatory Authority

They suggest shortcomings in your safety management

Prevention (of errors, risks and complications)

Not only reactive prevention = Learning from events and making improvements

Also proactive prevention = The mindset and ability to identify the nature and causes of developing problems and to develop a strong safety culture nurtured by leadership

What can ESHRE do about it?

- SIG SQART
  - Identification of potential safety hazards
  - Reflection on what level of safety for each hazard is the goal (theory vs. practice)
  - Edit guidelines on how to achieve this
  - Help devise CPI's in dashboards
    - Clinical CPI's
    - Laboratory CPI's
    - Operational (&financial) CPI's
- INTERESTED? JOIN US (jan.gerris@ugent.be and petra.desutter@ugent.be)

Have a safe journey!

IVF; patient pathways and patient satisfaction

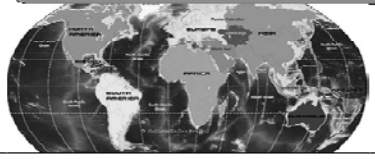
Prof.Dr. Bart CJM Fauser
University Medical Center,
Utrecht, The Netherlands

Lecture outline

- **Patient pathways**
- Patient satisfaction

Global IVF paradox

Insufficient access to treatment
- Expensive
- No health insurance coverage



Tendency Overtreatment in Western societies
- Varying indications for treatment
- Commercial environment / consumer behaviour

F&S 2012

Recruiting egg donors online: an analysis of in vitro fertilization clinic and agency websites' adherence to American Society for Reproductive Medicine guidelines

Types of donor traits and mention of these on websites (n = 50).

Desired donor trait	Not mentioned	Paid more for	"Preferred" or "in demand"
Prior donation success, no. (%)	10 (20)	32 (64)	8 (16)
Ethnicity, no. (%)	33 (66)	6 (12)	11 (22)
Test scores, no. (%)	46 (92)	1 (2)	3 (6)
Education level, no. (%)	29 (58)	9 (18)	12 (24)
Physical appearance, no. (%)	42 (84)	2 (4)	6 (12)
Creative/athletic ability, no. (%)	36 (72)	6 (12)	8 (16)

Keehn. Recruiting egg donors online. Fertil Steril 2012.

Conclusion(s): Our data, the first to systematically analyze agency and clinic websites reveal that many do not follow ASRM's guidelines. These data have critical implications for policy, practice, and research, suggesting needs for consideration of possible changes in guidelines, and/or improvements in compliance and monitoring by ASRM or others. (Fertil

FS 2005

International disparities in access to infertility services

Robert D. Nachtigall, M.D.
Institute of Health and Aging, University of California, San Francisco, San Francisco, California

TABLE 3

International utilization of IVF.

IVF cycles/million population per year	% optimal IVF utilization	Countries
<15	1%	China, India, Pakistan, Indonesia, Egypt
<150	10%	United States, Japan, Russia, Argentina, Italy
<500	33%	United Kingdom, Germany, France, Brazil, Switzerland, Iran, Saudi Arabia, Belgium, Australia, Greece
<750	50%	Netherlands, Sweden, Denmark, Iceland
>1,500	100%	Israel

Note: Adapted from Collins (11).

Nachtigall. International infertility disparities. Fertil Steril 2005.

HR 2012

The diversity of regulation and public financing of IVF in Europe and its impact on utilization

K. Berg Brigham[1], B. Cedars[1], and K. Dhenni[1]

IVF utilization in Europe, most recent data available

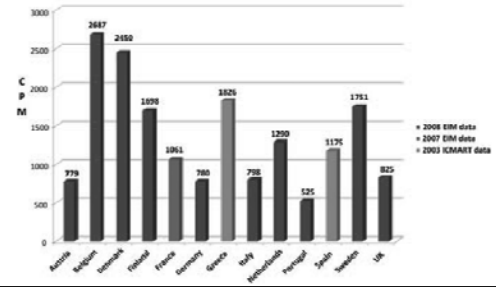


Table II Legal regulation of IVF coverage in Europe (2009).

Country	Coverage level	Maximum cycles covered	Age limit (years)	Only medical indications
Austria	Partial	4	Strict female <40, Male <50	Yes
Belgium	Full	6	Strict <40	Yes
Denmark	Partial	3	Strict <40	No
Finland	Partial	Varies	None	No
France	Full	4	Strict <43	Yes
Germany	Partial	3	Strict female <40, male <50	Yes
Greece	Partial	Varies	Strict <50	Yes
Italy	Partial	Varies	Soft (child-bearing age)	Yes
Netherlands	Full	3	Strict <45	Yes
Portugal	Partial	Varies	None	Yes
Spain	Partial	3	Soft	Yes
Sweden	Full	Varies	Soft (child-bearing age)	
UK	Partial	Varies	Strict <40	

Berg Brigham, HR 2012

Cross border reproductive care in six European countries

2010

F. Shenfield[1,*], J. de Mouzon[2], C. Pennings[3], A.P. Ferraretti[4], A. Nyboe Andersen[5], G. de Wert[6], and V. Goossens[7] the ESHRE Taskforce on Cross Border Reproductive Care[1]

human reproduction

Table VIII Treatment sought according to the recipient country.

Recipient country	Forms (n)	Infertility treatment*		PGD/PGS	Donation*		
		ART	IUI		Semen	Oocyte	Embryo
Belgium	359	71.9	33.4	5.2	20.5	6.8	0.3
Czech Republic	251	98.4	1.6	5.6	9.5	52.4	11.9
Denmark	154	46.8	55.5	0.6	40.9	1.3	0.6
Slovenia	64	100	0.0	0.0	0.0	0.0	0.0
Spain	190	98.4	5.8	2.1	4.1	62.2	4.7
Switzerland	196	59.7	54.1	0.5	27.4	1.0	0.5
Total	1214*	73.0	22.2	3.2	18.3	22.8	3.4

standard of success in assisted reproduction

(debate series, n=16: Hum Reprod 2004)

- **'BESST**, birth emphasizing a successful singleton at term' *(Min)*
- 'Narrow to infant outcomes with optimal prognosis' *(Schieve)*
- 'Healthy lower order birth' *(Dickey)*
- 'Informed choice by couple after appropriate counselling' *(Buckett)*
- 'Elective SET rate per center' *(Land)*
- 'BESST with other denominator' *(Davies)*
- 'Three parameters; oocyte #, implantation or deliveries/embryo' *(Pinborg)*
- 'Consider outcomes per treatment rather than cycle' *(Heijnen)*
- 'Singleton live births also including preterm births' *(Wennerholm)*
- 'Value cryopreservation on cumulative pregnancy rates' *(Tiitinen)*
- 'Cumulative singleton/twin delivery rate / oocyte pick-up' *(Germond)*
- **Discussion closed** *(Barlow)*

Pitfalls in the success per IVF cycle paradigm

- Optimal children outcomes not well defined
- A cycle can be extremely long and complex
- Treatment burden / drop outs NOT considered
- Complications NOT considered
- Cost NOT considered

→ Assess outcomes per started treatment or per given period of time

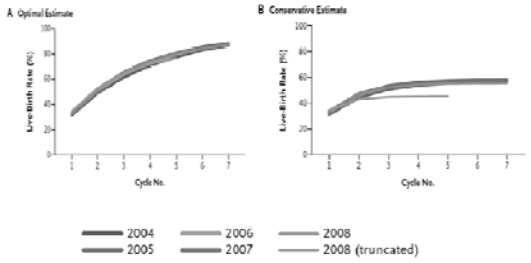
Lecture outline

- Patient pathways
- Patient satisfaction

Cumulative Birth Rates with Linked Assisted Reproductive Technology Cycles

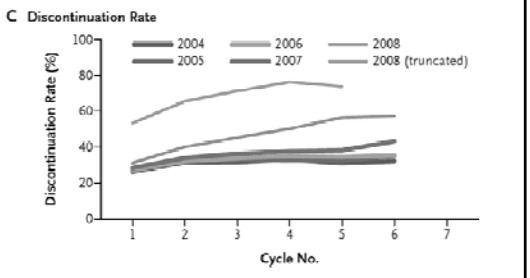
NEJM 2012

Barbara Luke, Sc.D., M.P.H., Morton B. Brown, Ph.D., Ethan Wantman, M.B.A., Avi Lederman, B.A., William Gibbons, M.D., Glenn L. Schattman, M.D., Rogerio A. Lobo, M.D., Richard E. Leach, M.D., and Judy E. Stern, Ph.D.

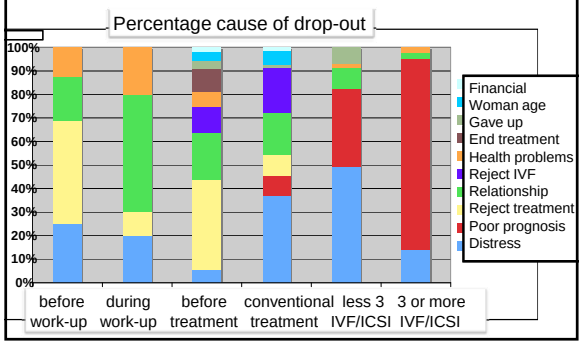


Cumulative Birth Rates with Linked Assisted Reproductive Technology Cycles

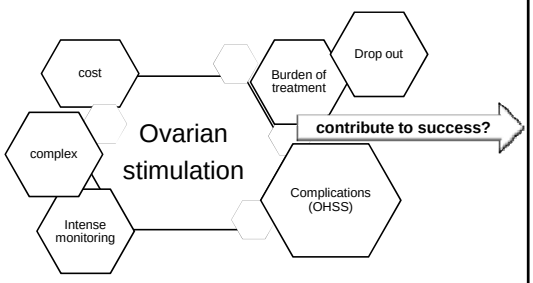
NEJM 2012



When and why do subfertile couples discontinue their fertility care? A longitudinal cohort study in a secondary care subfertility population



Ovarian hyperstimulation for IVF - the bigger picture



Maternal death related to IVF in the Netherlands 1984–2008

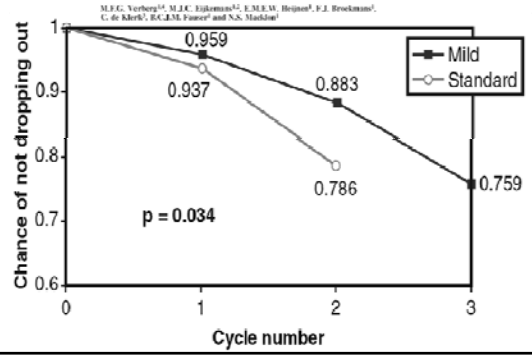
HR 2010

D.D.M. Braat[1,*], J.M. Schutte[2], R.E. Bernardus[3], T.M. Mooij[4], and F.E. van Leeuwen[4]

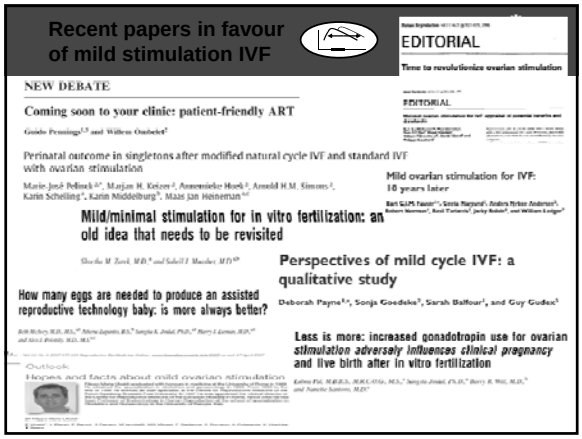
Aim	Collect information regarding death within 1 year (and related to) IVF, 1984-2008, The Netherlands
Results	• Total ~100.000 IVF treatment cycles • 6 death directly related to IVF (3 OHSS, 3 thombosis and sepsis after oocyte pick-up) • 17 death directly related to IVF pregnancy (pre-eclampsia, cerebral hemorrhage, sepsis, vascular dissection, pulmonary embolism, liver failure, portal hypertension) • 8 death unrelated to IVF
Conclusions	• Overall mortality related to IVF pregnancy higher than general population • World-wide underreporting IVF related mortality • Underling national registry and reporting

Why do couples drop-out from IVF treatment? A prospective cohort study

M.F.G. Verberg[1,4], M.J.C. Eijkemans[2,3], E.M.E.W. Heijnen[1], F.J. Broekmans[1], C. de Klerk[1], B.C.J.M. Fauser[1] and N.S. Macklon[1]

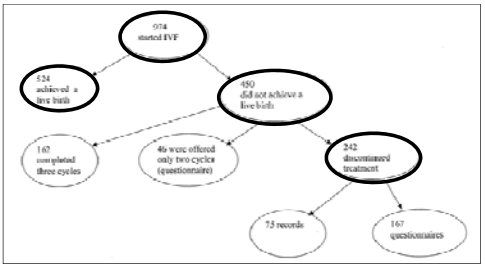


Recent papers in favour of mild stimulation IVF



CONTROVERSY: WHY COUPLES DISCONTINUE IVF TREATMENT

Why do couples discontinue in vitro fertilization treatment? A cohort study



A prospective investigation into the reasons why insured United States patients drop out of in vitro fertilization treatment F&S 2010

Objective	Why insured patients drop out of IVF in the USA ?
Design	Women < 40 yrs, private clinic, insured, not pregnant, who did not return
Results	**39% of termination due to stress** - toll on couples relationship - too anxious or depressed **Suggestion for patient support** - written information on how to deal with psychological stress - easy access to psychologist or social worker
Conclusions	US patients similar reasons for terminating IVF compared to Europe and Australia

Organizational determinants of patient-centered fertility care: a multilevel analysis F&S 2011

Accessibility
Information and communication
Respect and autonomy
Continuity of care
Emotional support
Partner involvement

2012

Why do patients discontinue fertility treatment? A systematic review of reasons and predictors of discontinuation in fertility treatment

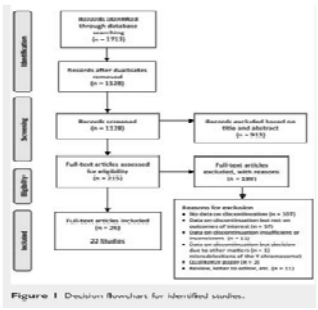
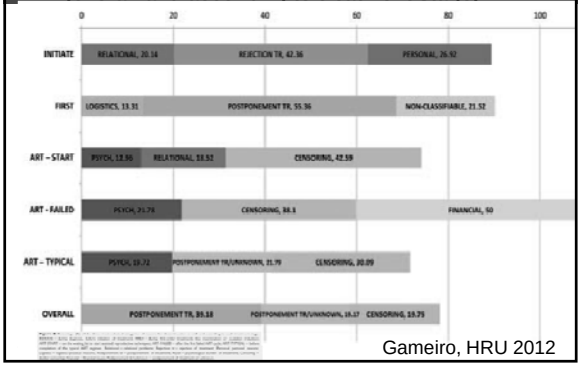


Figure 1 Decision flowchart for identified studies.

Percentage of the three most selected categories of reasons for discontinuation (overall and accoridng to treatment stage)



Gameiro, HRU 2012

2013

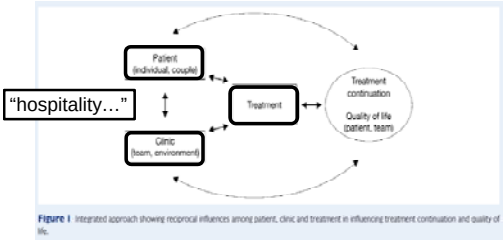
Why we should talk about compliance with assisted reproductive technologies (ART): a systematic review and meta-analysis of ART compliance rates

S. Gameiro[1,2], C.M. Verhaak[3], J.A.M. Kremer[4], and J. Boivin[1]

Tackling burden in ART: an integrated approach for medical staff

HR 2012

Jacky Boivin[1,*], Alice D. Domar[2], Daniel B. Shapiro[3], Tewes H. Wischmann[4], Bart C.J.M. Fauser[5], and Christianne Verhaak[6]



"hospitality…"

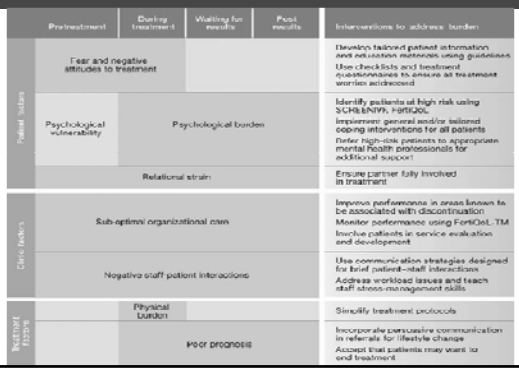
Figure 1 Integrated approach showing reciprocal influences among patient, clinic and treatment in influencing treatment continuation and quality of life.

Table 1 Factors cited by patients as contributing to their decision to end treatment

Patient (individual, couple)	Clinic (team, environment)	Treatment
Fear and negative treatment attitudes	Sub-optimal organizational care	Physical burden
• Unfavourable attitudes to treatment (e.g. fear about health of baby, perceiving treatment to be unnatural, perceived costs) • Values (ethical, moral) and preferences incompatible with treatment • Idiosyncratic barriers	• Stressful care (disorganized, assembly-line treatment, different staff on clinic visits) • Insufficient information on alternatives, inadequate co-ordination • Depersonalization (poor coordinated follow-up, results at work and without partner present) • Lack of continuity of care and negative doctor attitudes • Overly bureaucratic procedures	• Worry about physical burden, physical symptoms and discomfort • Injection protocols and adherence to treatment • Cycle monitoring • Disruption of work and daily activities • Worry about cost
Psychological and emotional factors	Negative staff-patient interactions	Handling of poor prognosis
• Pre-ART psychological profile • Difficulty in tolerating negative emotions for extended time periods • Uncertainty • Strain of repeated ART cycles	• Lack of empathy, poor listening skills, insufficient care of the man, insufficient time for questions	• Loss of hope for success (cycle number dependent)
Relational strain		
• Fear that ART will negatively impact relationship • Perceived and actual asymmetry in treatment focus between partners (particularly prevalent in early phases of medical involvement)		

Boivin, HR 2012

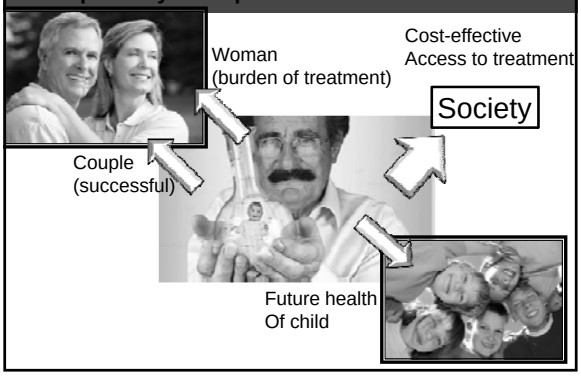
Causes of burden and associated interventions (Boivin, HR 2012)



Considerations concerning drop outs

- Frequency of discontinuation of treatment in other areas in medicine?
- Balance IVF outcomes per cycle versus per treatment strategy paradigm
- Balance burden of treatment versus efficacy
- Introduce support by social worker / psychologist
- Implement concept of hostmanship in team

CONCLUSION: IVF patient pathways and patient satisfaction



How to implement TQM

Ass.Prof. T.Mardesic PhD.
Institute Pronatal, Prague, Czech Republic

SANATORIUM PRONATAL

Presenting author has no commercial and/or financial relationships with manufacturers of pharmaceuticals, laboratory supplies and/or medical devices

Implementing TQM

- learning objectives -

- Presentation should offer an overwiew about current position of TQM in healthcare systems, its basic principles and introduction into practical implementing of TQM

Implementing TQM

- Introduction
- What is TQM
- Why to implement TQM
- Principles of TQM
- How to implement TQM
- Advantages and disadvantages of TQM
- Conclusions

Implementing TQM

- Interest in healthcare systems
- Increasing allocation of national and international resources for both private and public sector in management systems
- Healthcare providers across the globe are progressively implementing TQM

Why to implement TQM

- In the past, errors were the integral part of definition of quality (reporting non-conformities followed by corrective measures, risk management)
- Over time, the definition of quality has transformed to „zero-defect“ status by the process known as Continuous Improvement Process (CIP)
- What is excellent today may be inferior tomorrow
  ⟹ there is always room for improvement

Why to implement TQM

- Improve efficiency
- Provide high quality patient care
- Reduce costs
- TQM as a part of hospital´s „competitive strategy“ (TQM placing an emphasis on improved customer satisfaction offers the prospect of great market share and profitability)

What is TQM

- TQM is a comprehensive and structured approach to organizational management that seeks to improve the quality of products and services through ongoing refinements in response to continuous feedback.
- TQM is a holistic approach to long term success that views continuous improvement in all aspects of an organization as a **process** and **not as a short term goal.**
- TQM is a structured system for meeting and exceeding customer (patient´s) needs and expectations by creating organization-wide participation in the planning and implementation of improvement processes.

What is TQM

TQM is a philosophy in which core focus is meeting the customer´s (patient´s) needs and ensuring their satisfaction

What is TQM

- 1/Commitment and direct involvement of highest-level executives in setting quality goals and policies, allocation of resources and monitoring of results
- 2/realization that transforming an organization means fundamental changes (everyone´s job)
- 3/ building quality into services from the beginning
- 4/ understanding changing needs of patients and satisfying them in a cost-effective manner
- 5/ instituting leadership in place of mere supervision so that everyone performs in the best manner to improve quality and productivity thereby continually reducing total cost

What is TQM

- 6/ eliminating barriers between people and departments, so they work as teams to achieve common objectives
- 7/ instituting flexible programs for training and education

Principles of TQM

- A central principal of TQM is that mistakes may be made by people, but most of them are caused, or at least permitted, by faulty systems and processes.

ESHRE PCC London 2013

TQM –key principles

Management commitment

Employee empowerment

Fact based decision making

Continuous improvement

Customer (patient´s needs and expectations) focus

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Principles of TQM

1	**Customer focused organization**	**Understanding current and future patient´s needs Strategic decisions are „customer driven" Society is an important customer of bussiness: business ethics, safety, environment**
2	Leadership	Leaders establish the unity of purpose and direction. Responsibility for strategic planning with strong future orientation.
3	Involvement of people	People at all levels are the essence of an organization, health care institute´s success depends increasingly on the knowledge, skillls and motivation of its work force

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Principles of TQM

4	Process approach	Activities and related resources should be managed as a process
5	System approach to management	Identifying, understanding and managing a system of interrelated processes as a system contribute´s to the organization´s effectiveness and efficiency
6	Continual improvement	Permanent objective of the organization, a part of management of all processess
7	Factual approach to decision making	Effective decisions are based on the analysis of data and informations
8	Mutually beneficial supplier relationship	Organization and suppliers nare interdependent and a mutually beneficial relationship enhances the ability of both to create value

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How to implement TQM

Number of TQM models that organization can use

- ISO quality management standards
- European Foundation for Quality Management
- Malcolm Baldridge Criteria for Performance Excellence
- Deming Application Prize

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How to implement TQM
Quality Management System

VISION	
Background	Legislation EconomicaL potential Quality of services Education, research, organization
Strategy	
Evaluation	Objective evaluation (scoring)

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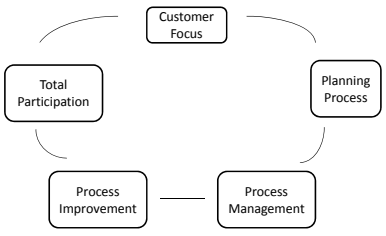
How to implement TQM
Quality Management System

Responsibility of management	Management of resources	Management of processes	Analysis and quality improvement
Strategy and QC	Human resources	QM and risk assessment	Measurabel criteria for:
Organization and structure of the clinic Standardization of procedures Atmosphere and working conditions	Space conditions, equipment	Organization Internals standards Payments Supplier´s evaluation	Management system Process evaluation Services / products Quality control Health care quality assurance
Evaluation (patients, partners, colleagues)	Software, data protection archivation	Development of new products and services	System of continual improvement Internal audits

How to implement TQM
ISO 9000 standards and TQM

- ISO 9000 does not define quality or provide any specifications of products or processes
- ISO 9000 assures that the organization has in place a well-operated QMS that conforms to the ISO 9000 standards
- Does not guarantee a quality product. No inspection of the product is involved in certification
- Consequently, an organization may be certified but still produce poor quality products (results)

A simple model of TQM



How to implement TQM

A preliminary step in TQM implementation is to assess the organization´s current reality

- Unstable funding base, weak administrative systems, lack of managerial skill, poor employee morale ⟹ TQM would not be appropriate

How to implement TQM

Companies are not very likely to adopt practices related to TQM if:

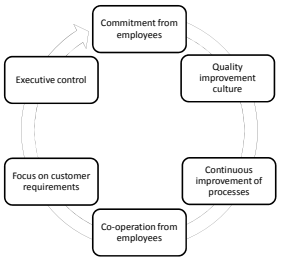
- Employes are not really disciplinned in their work
- Absence or lack of orientation towards teamwork
- Lack of cultural or demographic homogeneity
- Preference for fixed woring rules and little initiative
- Poor opinion or acceptance of training
- Staff members generally unaccustomed to relating salary and fulfillment of the company performance or results

TOXIC WORKPLACE

How to implement TQM

Steps in managing the transition

Identifying tasks to be done	**Assessing current reality** **Creating a model of the desired state (TQM)** **Securing outside consultation and training someone „in house“**
Creating necessary management structures	Management must be heavily involved
Developing strategies for building commitment	Visionary leadership needed
Designing mechanisms to communicate the change	Mechanisms beyond existing processes will need to be developed
Assigning resources	Outside consultants will always be required



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How to implement TQM

PDCA circle

Plan: define problem, collect data

Do: develop and implement a solution

Check: confirm the results through before-and-after data comparison

Act: document results, inform others about changes, recommendations for the problem to be adressed in the next PDCA cycle

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How to implement TQM

- TQM is a way of thinking, it involves cultural shift, it encompasses all aspects of an organization

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Advantages and disadvantages of TQM

- TQM is commonly understood to encompass concepts such as customer (patient´s) satisfaction, continuous improvement, management by fact or data and employee involvement
- While these concepts are easily understood, in practice many companies and clinics fail to adopt and implement TQM

Advantages and disadvantages of TQM

- According to recent figures only 20-36% of organizations that have attempted to implement a TQM program have achieved some sort of significant or even tangible improvements in quality, productivity, competitivness or financial return

Advantages and disadvantages of TQM

- It has been suggested that the implementation of TQM results in an over-emphasis on customer (patient´s) satisfaction with a relative neglect of the pursuit of profits
- The major problem with TQM is that there is a disconnection between management systems designed to measure customer satisfaction and those designed to measure business profitability, and this has often led to unwise investments in quality

Advantages and disadvantages of TQM

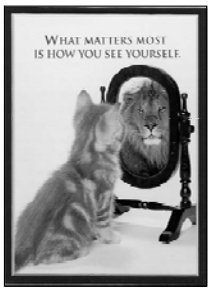
- The disadvantages of TQM is that it can lead to bureaucracy
- The money needed to implement TQM principles adds to costs
- Some managers and employee groups might be hesitant to change into a TQM based approach if the company is doing well now
- Also the benefits of TQM are not guaranteed to be successful simply based on a complete implementation. Customers (patients) themselves will decide upon the success of the company
- Also the costs of inspection of processes as well as research and development projects might be too costly

TQM - Conclusions

- Quality in today´s health care can and must be managed
- Processes, not people, are the problem
- Every employee is responsible for quality
- Quality must be measurable
- Quality improvements must be continuous
- Quality is a long term investment

TQM - Conclusions

- Quality management can only be described as „Total“ when all employees and managers become engaged in the effort and think of quality not as one-off program but as an ongoing, integral part of daily practice



THE COST OF QUALITY

Example of the IVI approach to the continuous improvement

Carlos Blanes
carlos.blanes@ivi.es

www.ivi.es

Session Objectives

- Understand **the difference between the investment in quality and the cost of non-quality.**
- To understand that **managing quality means managing processes.**
- To know the philosophy of **KAIZEN as a commonsense approach to quality management.**

2

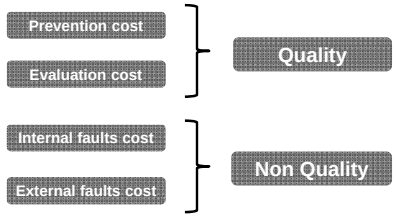
Cost and Quality

- There is a strong relation between quality and cost because:
  - It cost to produce and serve with quality
  - It cost to control and maintain quality
  - It cost to have non-quality

3

Cost and Quality

- The cost of quality should be calculated as the addiction of the following cost:



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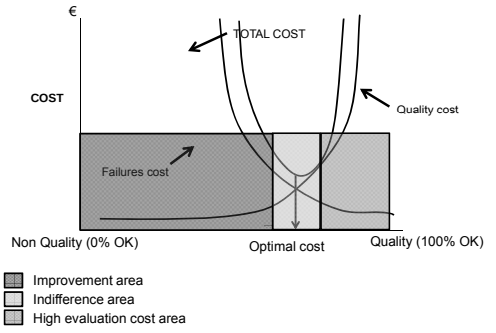
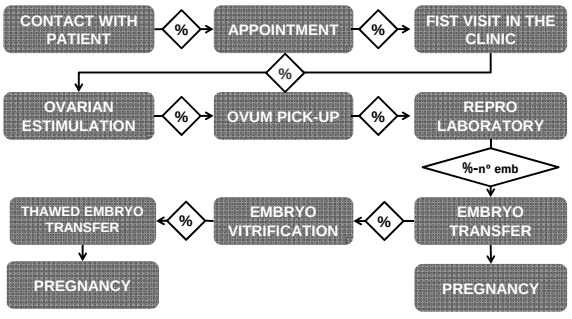
Cost and Quality



5

Identifying non-quality



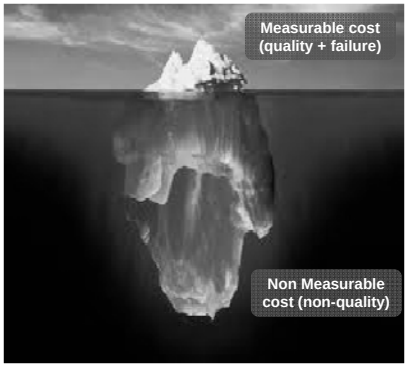
6

Identifying non-quality

- Key elements when evaluating the non-quality cost of the process:
  - Measurable cost
    - ***Material lost***
    - ***Drop out rate before the appointment***
    - ***Drop out rate before the visit***
    - ***Drop out rate before the treatment***
    - ***Drop out rate after a failure***
  - Non measurable cost (Other non-quality cost)
    - ***Clinical complications***
    - ***Image damage***
    - ***Psychological cost***
    - ***Market lost***
    - ***Low satisfaction of the Patient***
    - ***…***

7

Cost and Quality



8

Cost and Quality

"Quality is a cost" Vs. "Non-Quality is a cost"

Quality should be evaluated as an investment to eliminate the cost of non-quality

9

CONCLUSION

- Is important to evaluate the investment in quality in order to improve in the quality indicators.

Quality oriented management is worthy

10

Introduction to Quality Management

TQM	TQC	Six Sigma
Lean	KAIZEN	EFQM

Continuous Improving *to improve* ***Quality*** *and meet or exceed the* ***Customer Expectations***

11

Introduction to KAIZEN

KAIZEN

改 KAI = CHANGE

善 ZEN = GOOD

Masaaki Imai

12

Introduction to KAIZEN

KAIZEN strategy basic concepts[1]:

- *Kaizen and Management Functions*
- *Process versus Results*
- *PDCA / SDCA cycles*
- *Putting quality first*
- *Speak with data*
- *The next process is the customer*

(1) Gemba KAIZEN. Masaaki Imai 1997

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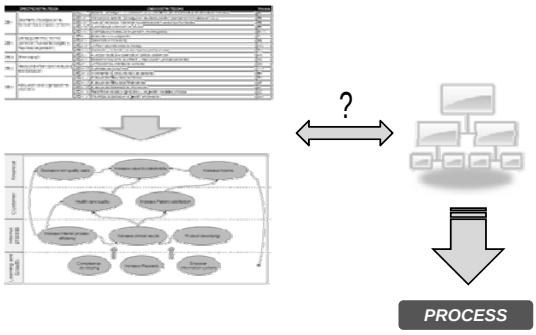
Process as a link between Strategy and Operations



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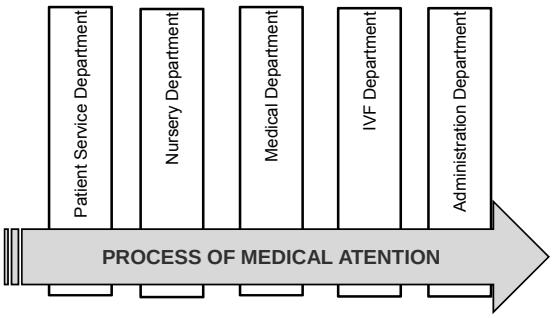
Processes in IVF Clinic



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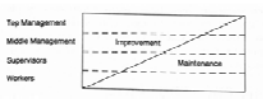
Kaizen and Management

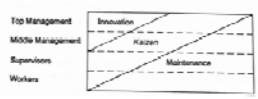


From the traditional management perspective, Management has two major functions:

- Maintenance
- Improvement

From the KAIZEN perspective, improvement can be classified as:

- Kaizen
- Innovation



Slide Source: Captures from the book, Gemba KAIZEN. Masaaki Imai 1997

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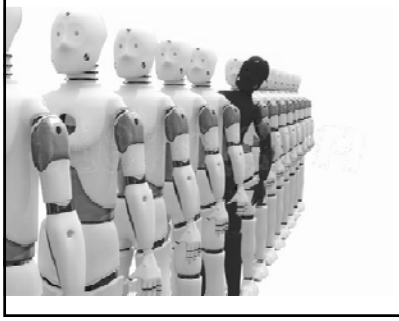
Kaizen and Management

WHY?



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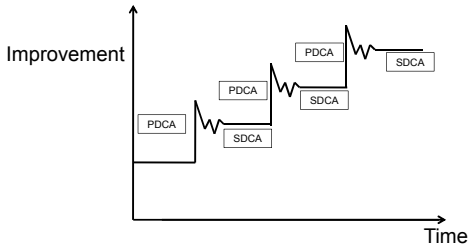
The Continuous Improvement Process: PDCA / SDCA Cycles

- **How can we deal with the Improvement Process?**
- **Steps in the process:**
  - **PDCA Cycle (Plan, Do, Check, Act)**
  - **SDCA Cycle (Standardize, Do, Check, Act)**



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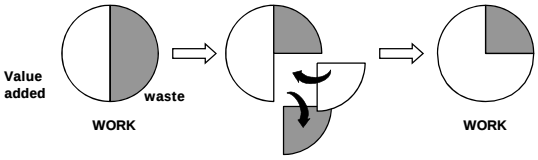
The Lean perspective

Replace waste for value-added...



... not working or consuming more resources

Same Work → Better Outcome

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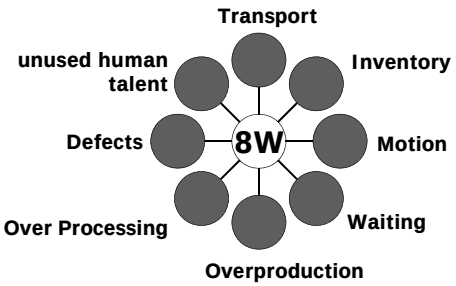
The Lean perspective



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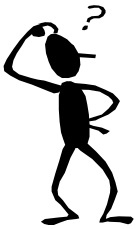
Start spinning the wheel of improvement



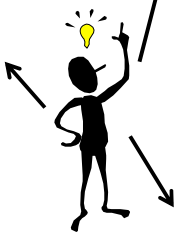
But when analyzing the processes, how can we identify the problems, wastes or the improvement issues??

21

Start spinning the wheel of improvement

Visual management:

- *5 s*
  - *Shine*
  - *Standardize*
  - *Straighten*
  - *Sort*
  - *Sustain*
- *Control Panels*
- *Kanban*



Identifying the root of the problem:

- *5 Whys*
- *Ishikawa diagrams (Fishbone) and 5 Ms*

Source: Capture from the book, Gemba KAIZEN. Masaaki Imai 1997

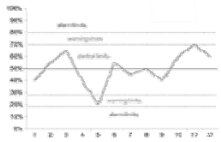
Working with process:

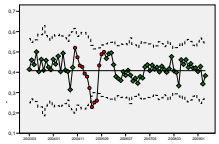
- *Quality circles*
- *Risk Management (incluir cuadro)*

22

Speaking with data

- Speaking with data is the only way not to make a feelings-driven management
- These measures are known as Key Performance Indicators (KPI)
- Shewhart Control Charts, trend analysis or variation analysis can be done to control the outcome





"What cannot be measured cannot be managed"
"Everything that is measured improves" (Peter Drucker)

23

Summary

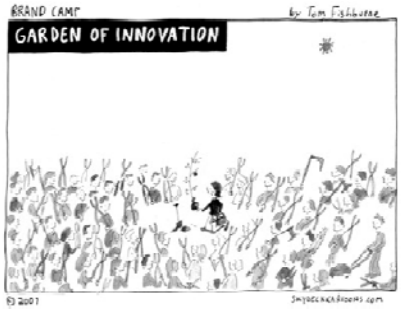
- **KAIZEN** is a business (and not only business) philosophy that chase continuous improvements to meet **customer** expectations by applying a cycle process that consist of:
  - **Planning** what to do and how to do it
  - Doing the plan
  - Checking the outcome **Measure**
  - Adjust to improve next time and **standardize**
- Kaizen will use methods and techniques for evaluating problems and improve processes
- And Remember

"Improvement is infinite"

24

Example of the IVI approach

25



THANK YOU

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Further Reading

- **Break-even Analyses: Basic Model, Variants, Extensions** (Marcell Schweitzer, Ernst Trossmann , Gerald H. Lawson**)**
- **Activity-Based Costing: Making it Work for Small and Mid-Sized Companies** (Douglas T. Hicks)
- **Activity-based Cost Management: An Executive's Guide** (Gary Cokins)
- **Costes de calidad y no calidad** (Oriol Amat i Salas)
- **Gemba KAIZEN. (**Masaaki Imai)

27

The role of the European Tissue Directive on TQM

Edgar V. Mocanu MD

RCSI and HARI, Rotunda Hospital, Dublin

Learning objectives

- Discuss if EUTC Directive and TQM have common ground.
- Understand how the EUTCD facilitates the implementation of a TQM programme in an IVF unit.

DISCLAIMER

THE SPEAKER HAS NO CONFLICT OF INTEREST.

ART practice

Offering the right expertise for the achievement of a pregnancy in the

Facilitate the conception of a healthy child with the smallest possible risk to couple

Beginning

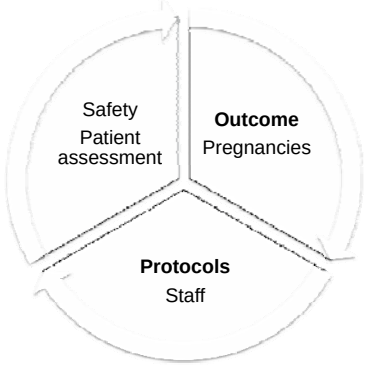
ART reality

- started without a safety record approval
- developed to more than 1 million cycles worldwide per year

- **Established techniques**
  - IVF and ICSI
  - Embryo slow freeze freeze and thaw
  - Sperm cryopreservation
  - Vitrification
  - Oocyte cryopreservation

- **Experimental**
  - ovarian tissue cryopreservation
  - in vitro maturation of oocytes
  - ovarian tissue re-implantation

ART practice maturing



Need for implementing TQM

GOOD	NOT THAT GOOD
Investigating patients Handling queries Handling complaints Treating couples = deciding upon treatment = monitoring patients = surgical procedures = laboratory care = transfer and follow-up = talking to couples Obtaining results	Saying what we do Documenting it Reviewing it regularly Proving that we do the right thing Opening communication lines with regulators Handling media Finding time to organise the above

ART – internal and external pressures

- Services need to reassure stakeholders that ART is:
  - Safe
  - Monitored
  - Audited
  - Self-improving
  - *Accessible*
  - *Recognized medical treatment*

Relevance

26th March 2013

- "total quality management, IVF" 134,000 results
- "TQM, IVF, EUTCD" 7 results

DIRECTIVES

- **2004/ 23/ EC (Mother Directive)**
  - Standards of quality and safety for human tissues and cells intended for human application (donation, procurement, testing, processing, preservation, storage, distribution)
  - Prevent the transmission of diseases
- **2006/ 17/ EC (Technical Directive 1)**
  - Donation (procurement, donation, testing) of human tissues and cells intended for human application
- **2007/ 86/ EC (Technical Directive 2)**
  - Cell and tissues (coding, processing, preservation, storage and distribution) of human tissues and cells intended for human applications

Learning objectives

- **Discuss how EUTC Directive and TQM have common ground.**
- Understand how the EUTCD facilitates the implementation of a TQM programme in an IVF unit.

Provision of the quality and safety of tissues and cells

EUTC Directive	ISO

• Quality management
• Person Responsible
• Personnel
• TC
  • Reception
  • Processing
  • Storage
  • Labelling, documentation
  • Distribution
• Relation with 3rd parties
• Coding
	• Customer focus
	• Leadership
	• Involvement of people
	• Process approach
	• System approach to management
	• Continuous improvement
	• Factual approach to decision making
	• Mutual beneficial supplier relationship

Guidance

- Was the Directive based on the principles of ISO accreditation and Quality management?

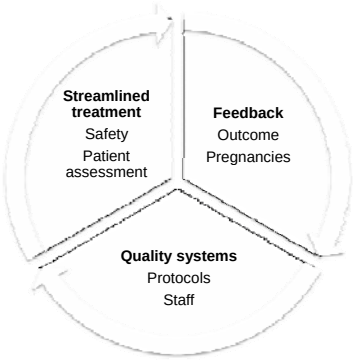
EUTC Directive	TQM in ART
• Reassure the public	• Excellent patient care
• Highest level of protection	• Highest success rates
• Safeguard public health	• Policies and protocols
• Establish standards for processes	• Continuous improvement

EUTC Directive	TQM in ART
• TE accreditation	• ISO accreditation
• Notification system	• Continuous assessment
• Inspection	• Certified training
• Inspector training	• Re-certification
• Traceability	

EUTC Directive	TQM in ART

• Quality system based on good practice
  • SOP
  • Guidelines
  • Training and reference manuals
  • Reporting forms
  • Donor records
  • Information on destination of TC
	• Quality system and CI
	  • All enumerated

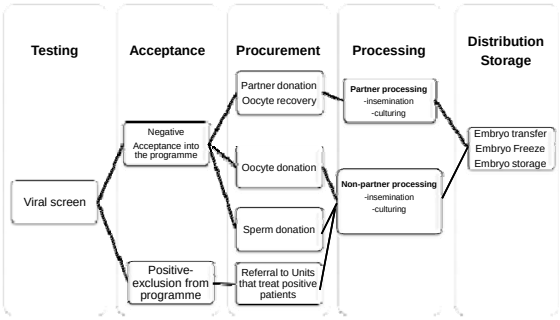
Quality/ EUTC LEAP



Learning objectives

- Discuss if EUTC Directive and TQM have common ground.
- **Understand how the EUTCD facilitates the implementation of a TQM programme in an IVF unit.**

ART steps



Quality management

- Quality assurance (QA)

  the total sum of all planned and systematic activities required in order to establish sufficient trust that a product or service meets the quality requirements as determined

- Quality control (QC)

  the operational techniques and activities which are carried out in order to meet the quality requirements

- Quality improvement (QI)

  risk management

  quality management

  SAE/SAR management

TQM

"a system of **management** based on the principle that **every member of staff** must be committed to maintaining **high standards** of work in **every aspect** of a company's operations"

TQM focus areas

- Leadership
- Processes
- Policies
- Staff development and feedback
- Partnership (customers, suppliers, etc)
- Customer feedback
- Adverse events
- KPI's

ART quality systems

- **Cover all areas of the service**
  - CLINICAL (doctors, nurses, auxiliaries)
  - ADMINISTRATION
  - LABORATORY
  - RESEARCH
  - ONCOFERTILITY SERVICES
  - TRAINING
- **Many standards**
  - ISO 9001
  - ISO 15198
  - ART TQM Certification??
- **Quality Manager**

EUTCD

- Reproductive cells = all tissues and cells intended to be used for the purpose of assisted reproduction.
- All TE (ART Units) have to fulfil safety and quality criteria:
  - Procurement, testing, donation
  - Processing, coding, preservation, storage and distribution.
- Should be:
  - Accredited
  - Designated
  - Authorized
  - Licensed by a National Competent Authority
- Have a quality system based on principles of good practice

EUTC Directive - CLINICAL

- Serological testing (HIV, HBV, HCV, Syphilis, Chlamydia)
  - Within 2 months of initial procurement and (if quality systems in place) every 24 months afterwards
- Personnel should be qualified to perform tasks and be provided with training
  - Procurement is carried out by persons with appropriate training and experience
  - Testing of donors is carried out by qualified staff
- Notification of SAR/ SAE
- Confidentiality
- Data storage

Clinical TQM in ART

- Definition of procedures (processes)
- Standard operating procedures (SOP's) = Guidelines
  - Every process
  - Simple and descriptive (flow charts best)
  - "Write what you do and do what is written!"
  - Involve the other groups as "outsiders" as they have priceless opinions
- Staff training, retraining and CPD, (recorded, signed)
  - Similar to ESHRE Embryology Diploma
- Reporting of adverse events
- Audit and change

EUTC Directive – Laboratory

- Quality management system
- Storage
- Processing materials
- Traceability
- Coding
- SAE/ SAR

EUTC Directive

Staff

- Optimum number of staff/ procedures performed
- Certified training records
- Regular re-certification/ competency assessment

ESHRE Embryology Certification Diploma

Processing

- Air quality, microbial colony and particle counts

EUTC Directive

Storage

- safe (monitored, locked, certified tanks)
- registration of stored material,
- separate storage for different risk patient groups

Traceability

- from the donor to the recipient
- data storage for 30 years (paper or electronic)
- Contact of reproductive material with processing devices and substances

EUTC Directive

Coding

- European code
- Identification of reproductive material

Donation identification:

- Unique ID number
- Identification of the tissue establishment

Product identification:

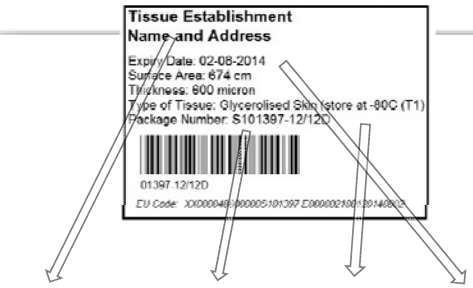
- Product code (basic nomenclature)
- Split number (if applicable)
- Expiry date

Donation identification

ISO Country Identifier	TE Code	Unique Donation Number
2 characters (alphabetic)	6 characters (alpha/numeric)	13 characters (alpha/numeric)

Product identification

Coding System Identifier	Product Code	Split Number	Expiry Date
1 character (alphabetic)	7 characters (alpha/numeric)	3 characters (alpha/numeric)	8 characters (numeric)



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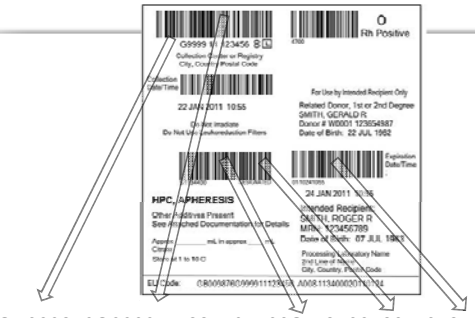

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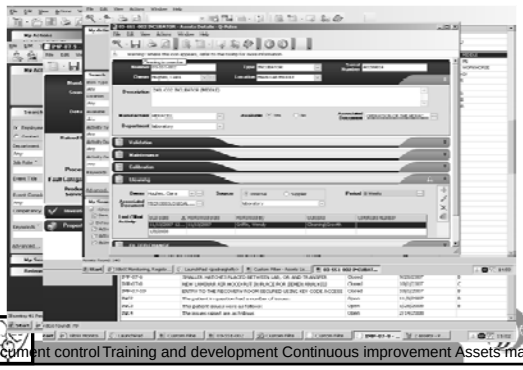
Laboratory TQM in ART

- Processes (defined and categorised)
- Standard operating procedures (SOP's) guidelines
  - Simple and descriptive (flow charts best)
  - "Write what you do and do what is written!"
- Staff training, retraining and CPD
- Stock taking
- Equipment validation
- Document control

QUALITY SYSTEM DATABASE

Kelly P et al., Fertil Steril 2008



Document control Training and development Continuous improvement Assets management

Document management

- Paper
- Computerised quality database
  - Q-Pulse
  - Windows or Mac platform
- Contains
  - All protocols
  - All contracts
  - All training records
  - All KPI's
  - All minutes of meetings

Quality systems

EUTC Directive	TQM
• Quality manager	• Quality manager
• SOP	• Regular staff meetings
• Guidelines	• Adverse events, incidents
• Training and reference manuals	• Non-conformances
• Reporting forms	• Quality masterplan + KPI's
• Donor records	• Development plan
• Information on final destination of TC	• Training and CPD
• Data stored for 30 years	• Strategic plans

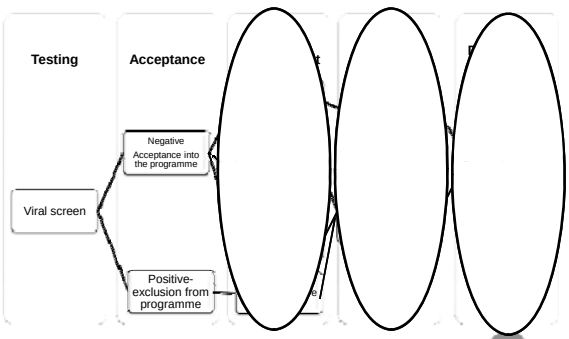
Administration TQM in ART

- Orders and purchasing
- Suppliers and supplies
  - Costs
- SOP's
  - Patient handling
  - Communication with customers
- Complaints
  - Suggestions
  - Positive feedback
- Training, retraining, CPD

EUTC Directive

- Reactions
  - Infections (bacterial, viral) transmitted through ART
  - Diseases (malignant, others)
  - Reactions to medication
- Events
  - Human error (loss of reproductive material, mix-up)
  - Equipment failure

Risk management



SAR-E

- Report <u>all</u>:
  - Adverse events
  - Adverse reactions
  - Admissions to hospital
    - OHSS
    - Bleeding
    - Infection
    - Unexpected surgery
  - Incidents
  - Non-conformances

SAR-SAE

All practice scenarios where an aspect of ART care resulted or could result in patient harm.

Processing Laboratory based infection with a proven human pathogen

Culture media event

Distribution Mix-up of gametes and embryos

Infection from non-partner donation

Storage Tank failure during cryopreservation storage, loss of gametes, embryos

Offspring Genetic condition in the offspring after non-partner donation

Infection in the offspring after non-partner donation in a previously seronegative mother

Clinical Severe reaction to a drug resulting in death

Events after cross border reproductive care

OHSS

Adverse events = positive lessons

- Analyse in depth (team)
- Address in time (with all staff)

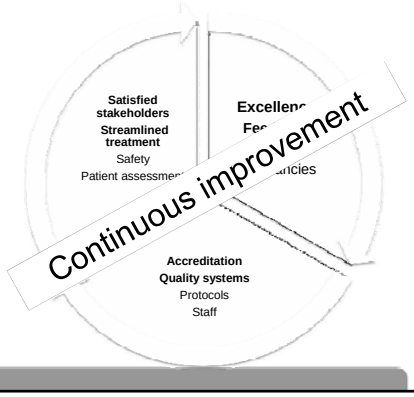
- Learn from mistakes
  - Positive corrective actions
  - Preventative action plan

- Not a matter of **WHO** but **WHAT**!

EUTC Directive serves as a platform for implementing TQM in ART

SHOULD WE STOP HERE?

ART NIRVANA (TQM)



Quality leadership

- Vision
- Goals
- Trust
- Inspiring

Leadership

- Departmental heads
  - Weekly meeting
    - Agenda
    - To do and confirmed done
  - Monthly meeting
    - Quality review
    - Data collected
    - Paper
    - 40-50 pages

Buy in from all staff

Analysis of laboratory processes

Aims:

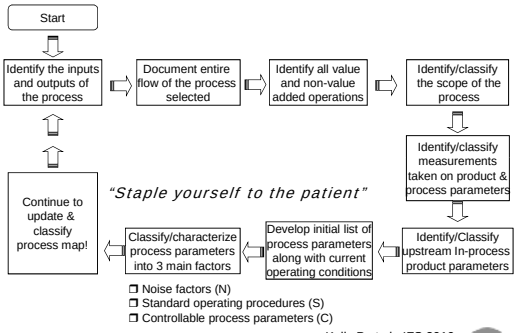
remove variation and waste in the IVF laboratory

make efficient and effective use of the available laboratory space

reduce the inventory holding costs

Kelly P et al. Hum Reprod 2009

A structured walk-through each process



- Noise factors (N)
- Standard operating procedures (S)
- Controllable process parameters (C)

Kelly P et al., IFS 2010

Results?

- 62% reduction in the value of media and consumables stored
- 40% reduction in paper records
- 36% improvement in laboratory air quality
- 8% increase in usable space within the laboratory
- the roadmap standardised processes and procedures leading to easier identification of process non-conformances with prompt actions based on newly devised visual controls.

Perfection in culture environment?

Closed System: 52 Hour Culturing Process

0Hr Oocyte Recovery | 6 hrs insemination | 24Hrs Fert Check

Temperature variations in IVF microenvironments
Kelly P et al., IFS 2010

49Hrs Cleavage Ass | 52Hrs Embryo Transfer

Kelly P., et al., IFS 2010

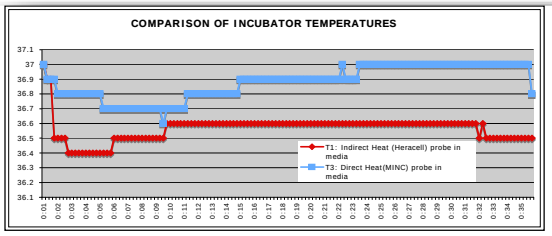
- A thermocouple linked to a datalogger was used to measure the temperature of media contained within culture dishes throughout the 52 hour culturing cycle.
- Temperature was measured every 30 seconds throughout 52 hour culturing cycle. This was repeated 6 times; 3 times using closed microenvironments for the culturing, assessment and processing of the samples and 3 times using semi-closed microenvironments.
- For safety reasons the test dish did not contain embryos but it followed a randomly selected dish containing embryos through each stage of the culturing process.
- The closed environment Cook K-MINC-1000 direct heat incubator for culturing and a Mobile IVF-1 Chamber (Humidi Crib) for assessment and processing.
- The semi-closed environment Heracell 240 indirect heat incubator for processing and a MiniTub HT50 heated stage fixed to a Nikon Inverted Microscope for assessment and processing.

Open System: 52 Hour Culturing Process

0Hr Oocyte Recovery | 6Hrs Insemination | 24Hrs Fert Check

49Hrs Clevage Ass | 52Hrs Embryo Transfer

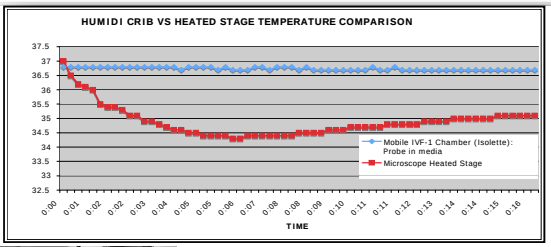
How quick does temperature recover after door opening?



Max Temperature drop after door open
Direct heat 0.3 Degrees C
Indirect Heat 0.6 Degrees C

Recovery Time after door open
Direct heat 24 Minutes
Indirect Heat 47 Minutes

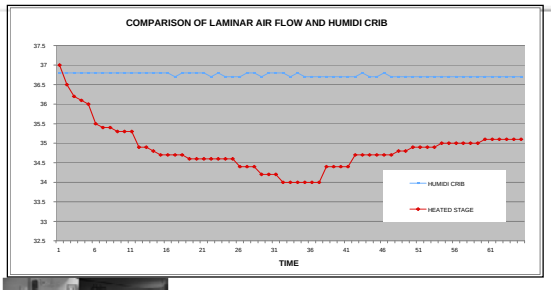
How long does it take for culture temperature to recover?



Max Temperature drop after move from incubator
Direct heat 0.2 Degrees C
Indirect Heat 2.6 Degrees C

Time for temperature to recover
Direct heat 2 Minutes
Indirect Heat >40 Minutes

TEMPERATURE CHANGES AT DISTRIBUTION



Max Temperature drop after move from incubator
Direct heat 0.3 Degrees C
Indirect Heat 3.0 Degrees C

PDCA

TQM - ART Nirvana

Reduce or eliminate

- Non-value added time
- Long processes in the laboratory
- Paper
- Unproven procedures
- Unjustified interventions
- Badly designed facilities

As such……

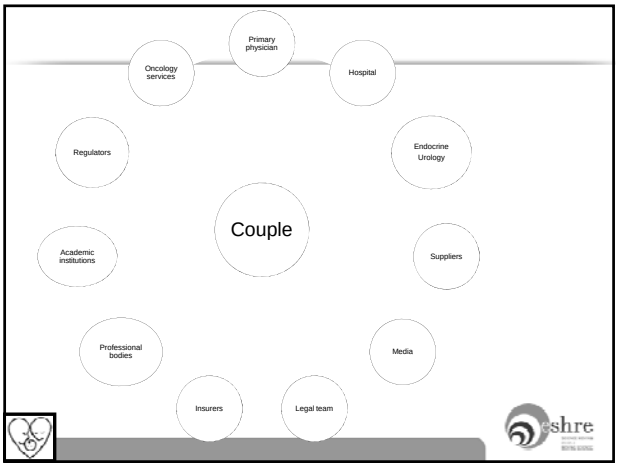
TQM is achieved, not when there is nothing more to add, but when there is nothing left to take away.

Edgar Mocanu

Toyota – “the best build cars in the world”

ART- “pregnant with healthy singleton delivery”

- Never be satisfied
- There’s got to be a better way
- Reform business when business is good
- No change is bad



Special thanks

- Padraig Kelly (Quality Manager)
- Gerri Emerson (Person Responsible)
- Ciara Hughes (Laboratory Director)

Aim at perfection in everything, though in most things it is unattainable. However, they who aim at it, and persevere, will come much nearer to it than those whose laziness and despondency make them give it up as unattainable.

Lord Chesterfield

TQM
Conclusion

Veljko Vlaisavljevic

Department of Reproductive Medicine and Gynecologic Endocrinology
University Medical Centre Maribor
Slovenia

Running of IVF Center

- 10% clinical skills
- 30% scientific skills
- 60% sheer organization

TQM= the scientific way of doing bussines

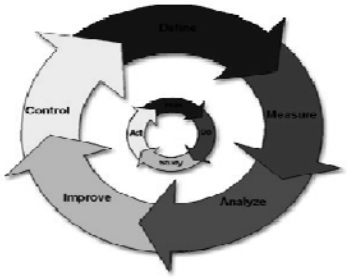
From: Mortimer D& Mortimer S.T. : Quality and risk management in the IVF laboratory. Cambrdge University Press, 2005

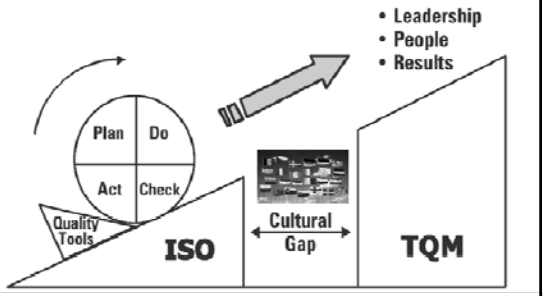
What is TQM ?

- Total → everyone is involved in
- Quality →continouously improving service to patients
- Management → with data and profound knowledge

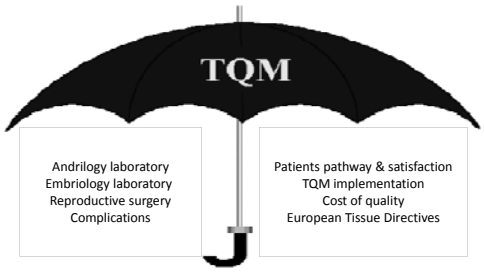
Ron Fotzgerald

The quality cycle



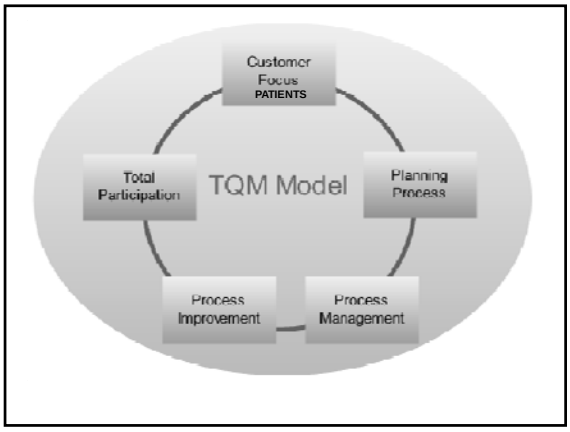


From: Frances Hill, Queen's University in Belfast,1999



Andrilogy laboratory
Embriology laboratory
Reproductive surgery
Complications

Patients pathway & satisfaction
TQM implementation
Cost of quality
European Tissue Directives


Customer Focus
PATIENTS
Planning Process
Process Management
Process Improvement
Total Participation
TQM Model

Future ?


Total Quality Management
Total Quality Management

You can now register for these upcoming ESHRE Campus events:

- Application and challenges of emerging technologies in preimplantation and prenatal diagnosis
  12-13 September 2013 - Prague, Czech Republic
- Female genital tract congenital malformations: new insights in an old problem
  27-28 September 2013 - Thessaloniki, Greece
- Introducing new techniques into the lab
  4-5 October 2013 - Barcelona, Spain
- Polycystic ovary syndrome: A new look at an old subject
  25-26 October 2013 - Rome, Italy
- Infections from conception to birth: role of ART
  7-8 November 2013 - Berlin, Germany
- Endoscopy in reproductive medicine
  20-22 November 2013 - Leuven, Belgium
- From early implantation to later in life
  28-29 November 2013 - Brussels, Belgium

Mark your calendar for:

- Premature ovarian insufficiency
  6-7 December 2013 - Utrecht, The Netherlands

www.eshre.eu
(see "Calendar")

Contact us at info@eshre.eu

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