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
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
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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)

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.

Service Realization

Service Realization

Purchasing and production processes

Planning Customer Communication Design and development Service Provision Patient’s feedback

Control Control Control Control
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

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
- Continuous quality improvement
  - ISO 9001

Environment
- Compliance with Laws and continuous improvement
  - ISO 14001

Safety
- Compliance with Laws and continuous improvement
  - OHSAS 18001

Other activities
- Gains, market shares, personnel, processes, communication, ETHICS

TOTAL QUALITY MANAGEMENT
- Total control of all corporate activities
- High corporate performance
- Customer and personnel satisfaction
Performance management includes activities that ensure 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.

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
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.

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.

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 all damages occurring between the prejudicial event and its solution

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

Mainly pecuniary losses

Visible

Direct Damages

Visible Insurable

Estimable

Indirect Damages

Not visible

Not insurable

Consequential Damages

Difficult to assess

Their effects continue also when pre-existing conditions are re-established

Total Quality Management - Tools

Personnel Involvement

Suggestion Programme

Employees Satisfaction Survey

Evidence-based Decision making

Cost – Benefit Analysis

Planning

Business continuity planning

Take home message

TQM = management philosophy and corporate practice that aims to involve all members of an organization in the continual improvement of all aspects of an organization in order to achieve the objectives of the organization and to provide customer satisfaction

TQM in Healthcare = rigorous set of processes and technologies to measure, improve, and control the quality of care based on what is important to the patient and the patient's outcomes

QUALITY OF ORGANIZATION

QUALITY OF CARE

(Patient satisfaction + better outcome)
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 (IQ)
- 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 & backup), 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


- 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”).

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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

Goal-Orientated Training – Example
The revised course (first held in Stockholm, June 2011) is not WHO-compliant, but it will educate participants on where there are differences, and why they exist.

Text book for the course: Björndahl et al., 2010.

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 (ariight) / sperm bind to wall?
- 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.

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**Sperm Concentration Training**

% difference in concentration

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**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
- 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 1:187-204, 1962)

Training To Assess Grade “a” Motility

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

Motility Assessment Training

- % Rapid Progressive Training
- % within 5% of reference value
- Series 1, 2, 3, 4
- Agreement: reference value ± 5%, Series 1-4
- Columns: % mature, % progression, % rapid
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)

<table>
<thead>
<tr>
<th></th>
<th>Concentration</th>
<th>Total motility</th>
<th>Prog motility</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>-2.3 ± 7.4</td>
<td>+0.3 ± 3.0</td>
<td>+0.4 ± 2.6</td>
</tr>
<tr>
<td>B</td>
<td>-1.7 ± 4.9</td>
<td>-0.8 ± 3.1</td>
<td>-0.8 ± 2.9</td>
</tr>
<tr>
<td>C</td>
<td>+4.5 ± 7.3</td>
<td>-1.0 ± 3.3</td>
<td>-0.6 ± 3.3</td>
</tr>
<tr>
<td>D</td>
<td>-0.5 ± 7.0</td>
<td>+1.6 ± 2.9</td>
<td>+1.0 ± 2.8</td>
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</table>

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

Quality of Semen Analysis Results

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

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

Barratt CL et al., ESHRE special interest group for andrology basic semen analysis course: a continued focus on accuracy, quality, efficiency and clinical relevance. Hum Reprod 26:3207-3212, 2011.


Mortimer D, Practical Laboratory Andrology, Oxford University Press, 1994.

Mortimer D & Mortimer ST, Quality and Risk Management in the IVF Laboratory, Cambridge University Press, 2005.

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 requirements
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, CO₂/O₂
  - 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

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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 clinic's 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

<table>
<thead>
<tr>
<th>Month</th>
<th>OPU</th>
<th>ER</th>
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<tbody>
<tr>
<td>September</td>
<td>70</td>
<td>60</td>
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<td>October</td>
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<td>May</td>
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<tr>
<td>June</td>
<td>115</td>
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2011  2012
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

Crisis Meetings
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 picked up by the MEA during manufacture QC
  - Clinics reported problems
    - Blastocyst rate down
    - Indicators of within-batch variations

- **TQM in an oil-crisis**
  - Monitoring
    - Implantation rate below action level
  - Action
    - Internal audit
  - Finding
    - Substandard incoming 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

![Graph showing monthly pregnancy rates and implantation rates for 2011 and 2012.]

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

![Graph showing frozen embryo replacements by month for 2011 and 2012.]

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.

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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...
  - Definitely
  - 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..?
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...
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

Study in Belgium – May 18th, 2013

- Dominance of the apprentice-tutor model
- Self-management philosophy of educational portfolio
- European or National Government 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 Council 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 Pillars 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

LAST®: 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
A practical test on fine psychomotor skills related to stitching and knotting operations.

HYST®: Hysteroscopic Skills Training and Testing Method
A 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.

<table>
<thead>
<tr>
<th>Gynaecological Endoscopic Surgeon</th>
</tr>
</thead>
</table>

Endoscopic Psychomotor Skills (EPS)
- Laparoscopic Instrument handling including the fine psychomotor skills to perform suturing and fine surgical acts.

Endoscopic Surgical Skills (ESS)
- Surgical skills with knowledge of anatomy, pathology, treatment options, etc.
A Gynaecological endoscopic surgeon needs 2 specific practical skills.

<table>
<thead>
<tr>
<th>EPS</th>
<th>ESS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endoscopic Psychomotor Skills</strong></td>
<td><strong>Endoscopic Surgical Skills</strong></td>
</tr>
<tr>
<td>Computer game skills to learn in a skill lab</td>
<td>One to one teaching</td>
</tr>
<tr>
<td>No skilled tutor necessary</td>
<td>Minimal LPS necessary to enter the training</td>
</tr>
<tr>
<td>Learning process similar to swimming or biking</td>
<td>Skilled tutor necessary</td>
</tr>
</tbody>
</table>

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 the 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.
LAparoscopic Skills Training and Testing model.

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

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

Test proficiency should grant for perfect laparoscopic instrument handling capabilities.

LASTT exercise 1: Camera navigation

LASTT exercise 2: Hand eye coordination
LAST exercise 3: Bimanual coordination

Results exercise 3
Novices versus Experts 30 repetitions

Correlation exposure to laparoscopy and E3 score

150 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

<table>
<thead>
<tr>
<th></th>
<th>LAC'T task</th>
<th>intermediate</th>
<th>essential</th>
</tr>
</thead>
<tbody>
<tr>
<td>pre-course</td>
<td>60%</td>
<td>30.5%</td>
<td>5%</td>
</tr>
<tr>
<td>post-course</td>
<td>60%</td>
<td>30.5%</td>
<td>5%</td>
</tr>
</tbody>
</table>

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 % 25 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 % 25 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 % 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 account 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 remain 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 exercises to acquire the LPS skills.
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

<table>
<thead>
<tr>
<th>ESGE Laparoscopic Procedure Classifications</th>
<th>ESGE Hysteroscopic Procedure Classifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>First level (basic)</td>
<td>First level (basic)</td>
</tr>
<tr>
<td>Diagnostic Laparoscopy</td>
<td>Diagnostic Hysteroscopy</td>
</tr>
<tr>
<td>Tubal Sterilization</td>
<td>Simple procedures (excluding the use of laser or electro-surgery):</td>
</tr>
<tr>
<td>Cyst Aspiration</td>
<td>o Target biopsies</td>
</tr>
<tr>
<td>Biopsies</td>
<td>o Removal of IUCD</td>
</tr>
<tr>
<td>Second level (intermediate)</td>
<td>o Minor intrauterine adhesions</td>
</tr>
<tr>
<td>Salpingotomy / salpingectomy</td>
<td></td>
</tr>
<tr>
<td>Cystectomy</td>
<td></td>
</tr>
<tr>
<td>Moderated Adhesiolysis</td>
<td></td>
</tr>
<tr>
<td>Minimal/mild Endometriosis</td>
<td></td>
</tr>
<tr>
<td>Third level (advanced)</td>
<td></td>
</tr>
<tr>
<td>Hysterectomy</td>
<td></td>
</tr>
<tr>
<td>Myomectomy</td>
<td></td>
</tr>
<tr>
<td>Urinary Incontinence</td>
<td></td>
</tr>
<tr>
<td>Extensive Adhesiolysis</td>
<td></td>
</tr>
<tr>
<td>Severe Endometriosis</td>
<td></td>
</tr>
<tr>
<td>Bowel or bladder lesions reparation</td>
<td></td>
</tr>
<tr>
<td>Pelvic floor disorders</td>
<td></td>
</tr>
<tr>
<td>Oncology (Lymphadenectomy, radical hysterectomy, axiloscopy)</td>
<td></td>
</tr>
<tr>
<td>Pelvic floor disorders</td>
<td></td>
</tr>
<tr>
<td>Recto-vaginal endometriosis</td>
<td></td>
</tr>
<tr>
<td>Polyp resection</td>
<td></td>
</tr>
<tr>
<td>Resection of type 0 myoma</td>
<td></td>
</tr>
<tr>
<td>Endometrial ablation</td>
<td></td>
</tr>
<tr>
<td>Treatment of uterine septum</td>
<td></td>
</tr>
<tr>
<td>Tubal canulation</td>
<td></td>
</tr>
</tbody>
</table>
4. Surgical Examination

For level 1: theoretical exam only

TEST:
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

<table>
<thead>
<tr>
<th>MODE</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal Models</td>
<td>Visual problems, costs, animal model for endoscopic surgery</td>
<td>Allows immediate assessment of surgical skills, reproductive surgery</td>
</tr>
<tr>
<td>Video</td>
<td>Objectivation, time consuming, possibility of cheating</td>
<td>Assessment of surgical skills, costs</td>
</tr>
<tr>
<td>Simulator</td>
<td>Only skills assessment, initial investment</td>
<td>Hardware lasts for a long time, easily updatable</td>
</tr>
<tr>
<td>Electronic assessment</td>
<td>Software preparation, objective, cheap, comparable, fast</td>
<td>Assessment and validation of surgical skills, extremely realistic, cost (anti-cheating system)</td>
</tr>
<tr>
<td>Live surgery</td>
<td>Time consuming, costs, unrealistic in case of a high number of applicants</td>
<td>Assessment and validation of surgical skills, extremely realistic, cost (anti-cheating system)</td>
</tr>
</tbody>
</table>

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 distinguished 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

<table>
<thead>
<tr>
<th>Level</th>
<th>Accessible Learning</th>
<th>Specific Endoscopic Skills</th>
<th>Surgical Practice Curriculum</th>
<th>Surgical Examination</th>
<th>Continuing Medical Education</th>
<th>Diploma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Winners Bachelor</td>
<td>First Surgeon ESSE Class A</td>
<td>Under Validation ESGE</td>
<td>EBCOG Project Definition</td>
<td>Bachelor in Endoscopy</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Winners GLS</td>
<td>First Surgeon ESSE Class A</td>
<td>Under Validation ESGE</td>
<td>EBCOG Project Definition</td>
<td>Gynaecological Laparoscopic Hysteroscopic Reproductive Surgeon</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Winners EPS</td>
<td>First Surgeon ESSE Class A</td>
<td>Under Validation ESGE</td>
<td>EBCOG Project Definition</td>
<td>Laparoscopic Pelvic Surgeon</td>
<td></td>
</tr>
</tbody>
</table>

### Testimonium Management

1. The Certification of the Specific Endoscopic Skills (LASTT / HYSTT / SUIT / 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.
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.

Rationale reproductive surgeon

ESHRE SIG Reproductive Surgery

Ways of examination – Practical and theoretical skills
Surgical training

Bachelor Certification
Applications 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
Applications 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 free.
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 responsibility 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-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 premature
  - Ischemic 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: all locations

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Number of participants</th>
<th>95% confidence interval</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical pregnancy rate</td>
<td>9/10</td>
<td>3.54 ± 3.08</td>
<td>P &lt; .001</td>
<td></td>
</tr>
<tr>
<td>Implantation rate</td>
<td>9/10</td>
<td>3.54 ± 3.08</td>
<td>P &lt; .001</td>
<td></td>
</tr>
<tr>
<td>Miscarriage rate</td>
<td>9/10</td>
<td>1.9 ± 4.1</td>
<td>P &lt; .001</td>
<td></td>
</tr>
<tr>
<td>Preterm delivery rate</td>
<td>9/10</td>
<td>1.9 ± 4.1</td>
<td>P &lt; .001</td>
<td></td>
</tr>
<tr>
<td>Intrauterine adhesion</td>
<td>9/10</td>
<td>1.9 ± 4.1</td>
<td>P &lt; .001</td>
<td></td>
</tr>
<tr>
<td>Intrauterine infection</td>
<td>9/10</td>
<td>1.9 ± 4.1</td>
<td>P &lt; .001</td>
<td></td>
</tr>
</tbody>
</table>

**Expected:** lower pregnancy rate (PR), more miscarriages

**Evidence:**
- Significantly lower PR, IR, LBR, higher MCR
- No difference in Preterm Delivery Rate

Influence of myomas on reproductive function: intracavitary distorsion

<table>
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<tr>
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<tr>
<td>Clinical pregnancy rate</td>
<td>1/2</td>
<td>1.5 ± 1.5</td>
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</tbody>
</table>

**Expected:** clear influence on PR, ...

**Evidence:**
- Significantly lower PR, IR, LBR, higher MCR
- No studies on PDR

Influence of myomas on reproductive function: no intracavitary distorsion (IM and SS)

<table>
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<tr>
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</tr>
</tbody>
</table>

**Expected:** no/little influence on PR, ...

**Evidence:**
- No difference in PR
- Significantly lower IR, LBR and higher MCR
- No difference in PDR (2 studies)
Influence of myomas on reproductive function: SS

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


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

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


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

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

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

- 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

Guidelines concerning myomas in women with subfertility (1)

- Subserosal myomas: remove only if symptomatic

- Submucous (=intracavitary) myomas (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
Before and after treatment with GnRH agonists

Volume reduction 40%

Before and after treatment by retrograde embolization

Other concomittant diseases

- Anemia
  - Iron deficiency
  - Sickle cell
  - Hemoglobinopathies
- 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

Model of ovarian non-growing follicle (NGF) decay
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.
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

<table>
<thead>
<tr>
<th></th>
<th>Baber</th>
<th>Bergh</th>
<th>Roest</th>
<th>Serour</th>
<th>Govaerts</th>
</tr>
</thead>
<tbody>
<tr>
<td>N cycles</td>
<td>600</td>
<td>10,125</td>
<td>2,495</td>
<td>3,500</td>
<td>1,500</td>
</tr>
<tr>
<td>OHSS + hoop</td>
<td>-</td>
<td>0.7%</td>
<td>0.7%</td>
<td>1.7%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1.3%</td>
<td>0.7%</td>
<td>0.1%</td>
<td>0.2%</td>
<td></td>
</tr>
<tr>
<td>Adnex torsion</td>
<td>-</td>
<td>-</td>
<td>0.1%</td>
<td>-</td>
<td>0.1%</td>
</tr>
<tr>
<td>Infection</td>
<td>0.5%</td>
<td>0.3%</td>
<td>0.3%</td>
<td>0.3%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Total</td>
<td>1.8%</td>
<td>1.7%</td>
<td>1.1%</td>
<td>2.1%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

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)tortion**

- 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
- SGA: X 4
- Infant mortality: X 5
- Cerebral Palsy: X 5 to 10

Maternal Morbidity

<table>
<thead>
<tr>
<th>Condition</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eclampsia</td>
<td>2.8 (2.7-2.9)</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>1.1 (1.0-1.2)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3.7 (2.3-5.8)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>12.9 (2.7-62.3)</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>2.7 (2.0-3.5)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>7.1 (4.5-11.3)</td>
</tr>
<tr>
<td>Post partum haemorrhage</td>
<td>1.9 (1.8-1.9)</td>
</tr>
<tr>
<td>Caesarean delivery</td>
<td>2.2 (2.1-2.2)</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>2.3 (1.7-3.2)</td>
</tr>
</tbody>
</table>
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 lifetime
- 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 trial: 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 pregnancies 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)

<table>
<thead>
<tr>
<th>PREC</th>
<th>AVERAGE</th>
<th>CLEAVE GROWTH</th>
<th>DM STAGE (N)</th>
<th>PREC</th>
<th>AVERAGE</th>
<th>CLEAVE GROWTH</th>
<th>DM STAGE (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM5</td>
<td>10.58</td>
<td>6.64 (1.49, 5.64)</td>
<td>28/120</td>
<td>DM5</td>
<td>11.18</td>
<td>9.72 (7.18, 11.72)</td>
<td>19/174</td>
</tr>
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</table>

Total: 216.00 (21.20, 17.60)

(From the analysis, Figner's chi-square: Figner's chi-square)

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

Live birth

<table>
<thead>
<tr>
<th></th>
<th>eSET</th>
<th>DET</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth</td>
<td>27%</td>
<td>42%</td>
<td>0.50 (0.40, 0.63)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Multiple live birth</td>
<td>2%</td>
<td>29%</td>
<td>0.04 (0.01, 0.13)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* 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

Multiple Live birth

<table>
<thead>
<tr>
<th></th>
<th>eSET</th>
<th>DET</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth</td>
<td>6</td>
<td>5</td>
<td>1.20 [0.23, 6.19]</td>
<td>0.54 [0.10, 2.93]</td>
</tr>
<tr>
<td>Multiple live birth</td>
<td>1</td>
<td>1</td>
<td>0.22 [0.07, 0.71]</td>
<td>0.64 [0.28, 1.47]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 4.09, df = 7 (P = 0.77); I² = 0%
Test for overall effect: Z = 5.92 (P < 0.00001)

Heterogeneity: Chi² = 5.39, df = 7 (P = 0.61); I² = 0%
Test for overall effect: Z = 5.82 (P < 0.00001)
### Fresh & Frozen eSET vs Fresh DET: Livebirth

<table>
<thead>
<tr>
<th></th>
<th>eSET N = 350</th>
<th>DET N = 353</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth</td>
<td>38%</td>
<td>42%</td>
<td>0.83 (0.61, 1.12)</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.85 (0.62, 1.16)*</td>
<td>0.26*</td>
</tr>
<tr>
<td>Multiple live birth</td>
<td>1%</td>
<td>32%</td>
<td>0.02 (0.00, 0.13)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* 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

<table>
<thead>
<tr>
<th></th>
<th>eSET N = 54</th>
<th>DET N = 54</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth</td>
<td>41%</td>
<td>35%</td>
<td>1.27 (0.58, 2.76)</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.43 (0.13, 1.42)*</td>
<td>0.17*</td>
</tr>
<tr>
<td>Multiple live birth</td>
<td>2%</td>
<td>32%</td>
<td>-</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

* 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 subgroups (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
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)
Cornual pregnancy after IVF

Cervical pregnancy

Uterus 15 x 8 x 4 cm
Cervix 8.5 x 8 cm wide
Cervical tissue invaded by placental tissue = placenta increta
Endometrium with pseudo-decidualisation

Low-cervical amniotic sac

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!
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 …
<table>
<thead>
<tr>
<th><strong>AIR TRAFFIC</strong></th>
<th><strong>ART</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>“Absolute” safety comes with a price…</td>
<td>In ART too safety has a price…</td>
</tr>
<tr>
<td>When the price rises too high, safety concerns laxen…</td>
<td>When the price rises too high, risks are taken (multiples)…</td>
</tr>
<tr>
<td>People WANT to fly…</td>
<td>People WANT children…</td>
</tr>
<tr>
<td>There appears to be a balance</td>
<td>There is a trade-off between desired outcome and risks</td>
</tr>
<tr>
<td>Zero – tolerance is impossible: nobody says stop flying!</td>
<td>Zero-tolerance is theoretical: nobody says stop ART!</td>
</tr>
</tbody>
</table>

---

**The Columbia Accident Investigation Board**

“In our view, the NASA organizational culture 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"

<table>
<thead>
<tr>
<th>Safety issue</th>
<th>Zero tolerance level (ZTL)</th>
<th>Realistic lowest tolerance level (RLTL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple pregnancies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monozygotic MPs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OHSS (severe)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding at OPU</td>
<td></td>
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</tr>
<tr>
<td>Cytogenetic abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effects of freezing &amp; vitrification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epigenetic effects (media)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncological effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal deaths</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal reduction</td>
<td></td>
<td></td>
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<tr>
<td>Psychosocial effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Future fertility of ART-children</td>
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Practice
Individual Fertility centre

Regional

National

Supranational

Global

Determinants of practice conduction

- (personal) ethics & economics
- peers with shared values/agreements
- culture & societal norms
- data from professional bodies
- data from registries & politics (laws)
- data from professional bodies
- data with a world perspective (e.g. ICMART)

Monitoring outcome (efficacy and safety)

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

Main CPI’s for fresh IVF + ICSI 1997-2006

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<td>21.7</td>
<td>1.0</td>
<td>26.6</td>
<td>27.1</td>
<td>30.1</td>
<td>29.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>236480</td>
<td>20.0</td>
<td>56.1</td>
<td>21.5</td>
<td>2.3</td>
<td>47966</td>
<td>21.0</td>
<td>0.8</td>
<td>26.9</td>
<td>28.5</td>
<td>30.3</td>
</tr>
<tr>
<td>2004</td>
<td>225480</td>
<td>19.2</td>
<td>55.3</td>
<td>22.1</td>
<td>3.3</td>
<td>45128</td>
<td>21.7</td>
<td>1.0</td>
<td>26.6</td>
<td>27.2</td>
<td>29.5</td>
</tr>
<tr>
<td>2003</td>
<td>234142</td>
<td>15.7</td>
<td>55.9</td>
<td>24.9</td>
<td>3.5</td>
<td>47212</td>
<td>21.0</td>
<td>1.1</td>
<td>26.1</td>
<td>26.5</td>
<td>29.6</td>
</tr>
</tbody>
</table>
### Main CPI’s for fresh IVF + ICSI 1997-2015

<table>
<thead>
<tr>
<th>Year</th>
<th>Total cycles</th>
<th>OHSS</th>
<th>All compl.</th>
<th>OHSS</th>
<th>All compl.</th>
<th>OHSS</th>
<th>All compl.</th>
<th>OHSS</th>
<th>All compl.</th>
<th>OHSS</th>
<th>All compl.</th>
<th>OHSS</th>
<th>All compl.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>525640</td>
<td>2947 (0.6%)</td>
<td>976 (0.19%)</td>
<td>652 (0.12%)</td>
<td>49 (0.09%)</td>
<td>1</td>
<td>394</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>492442</td>
<td>2470 (0.5%)</td>
<td>991</td>
<td>574</td>
<td>64</td>
<td>3</td>
<td>364</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>459170</td>
<td>2753 (0.8%)</td>
<td>938</td>
<td>544</td>
<td>42</td>
<td>0</td>
<td>466</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>418111</td>
<td>3347 (1.2%)</td>
<td>1048</td>
<td>523</td>
<td>362</td>
<td>4</td>
<td>526</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2004</td>
<td>367066</td>
<td>2858 (0.8%)</td>
<td>1125</td>
<td>520</td>
<td>362</td>
<td>102</td>
<td>528</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>365103</td>
<td>2646 (0.7%)</td>
<td>NA</td>
<td>799</td>
<td>135</td>
<td>0</td>
<td>680</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2002</td>
<td>324238</td>
<td>2148 (0.7%)</td>
<td>1156</td>
<td>322</td>
<td>227</td>
<td>0</td>
<td>661</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>289690</td>
<td>1851 (0.6%)</td>
<td>569</td>
<td>395</td>
<td>0</td>
<td>256</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>279267</td>
<td>1586 (0.6%)</td>
<td>652 (0.23%)</td>
<td>388 (0.14%)</td>
<td>36 (0.13%)</td>
<td>0</td>
<td>256</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 embryos
- Vitrification of embryos
- 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, "BESS" practice...)
  - Averaging out wide differences between countries
  - Rubbish in rubbish out

<table>
<thead>
<tr>
<th>IUI-H and IUI-D 2001-2008</th>
<th>IUI with partner sperm</th>
<th>IUI with donor sperm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;40years</td>
<td>&gt;40years</td>
</tr>
<tr>
<td></td>
<td>DR 1</td>
<td>2</td>
</tr>
<tr>
<td>2008</td>
<td>3.3</td>
<td>0.5</td>
</tr>
<tr>
<td>2007</td>
<td>4.0</td>
<td>0.7</td>
</tr>
<tr>
<td>2006</td>
<td>3.3</td>
<td>0.5</td>
</tr>
<tr>
<td>2005</td>
<td>3.3</td>
<td>0.5</td>
</tr>
<tr>
<td>2004</td>
<td>3.3</td>
<td>0.5</td>
</tr>
<tr>
<td>2003</td>
<td>3.3</td>
<td>0.5</td>
</tr>
</tbody>
</table>

- Recent decrease in delivery rate (DR)!
- Twinning has remained stable, triplets down!
- Recent decrease in DR!
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)

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

A = indicator of ET policy (clinical)
B = indicator of cleanroom quality (laboratory)
C = indicator of fertilization efficacy (laboratory)
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 SOART
  - 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
Types of donor traits and mention of these on websites (n = 50).  

<table>
<thead>
<tr>
<th>Desired donor trait</th>
<th>Not maintained</th>
<th>Paid more for</th>
<th>Preferred or “in demand”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity, %</td>
<td>33 (66)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex preference, %</td>
<td>47 (94)</td>
<td>2 (4)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Education level, %</td>
<td>29 (58)</td>
<td>9 (19)</td>
<td>12 (24)</td>
</tr>
<tr>
<td>Physical appearance, %</td>
<td>47 (94)</td>
<td>2 (4)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>Caucasian/European, %</td>
<td>58 (126)</td>
<td>6 (12)</td>
<td>9 (18)</td>
</tr>
</tbody>
</table>

Note: Percentages do not total 100 due to missing or not applicable data.

International disparities in access to infertility services  

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

Table 2

<table>
<thead>
<tr>
<th>International utilization of IVF*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population per year</td>
</tr>
<tr>
<td>----------------------------------</td>
</tr>
<tr>
<td>1990</td>
</tr>
<tr>
<td>1995</td>
</tr>
<tr>
<td>2000</td>
</tr>
<tr>
<td>2005</td>
</tr>
<tr>
<td>2010</td>
</tr>
<tr>
<td>2015</td>
</tr>
</tbody>
</table>

Note: *Adapted from Cochrane Library, 2006.
Berg Brigham,  
HR 2012

**Table II: Legal regulation of IVF coverage in Europe (2005)**

<table>
<thead>
<tr>
<th>Country</th>
<th>Coverage level</th>
<th>Minimum cycle covered</th>
<th>Age limit (years)</th>
<th>Egg retrieval indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>Partial</td>
<td>1</td>
<td>Stock &lt; 15; M &lt; 50</td>
<td>Yes</td>
</tr>
<tr>
<td>Belgium</td>
<td>Full</td>
<td>1</td>
<td>Stock &lt; 40</td>
<td>No</td>
</tr>
<tr>
<td>Denmark</td>
<td>Partial</td>
<td>3</td>
<td>Stock &lt; 40</td>
<td>No</td>
</tr>
<tr>
<td>Ireland</td>
<td>Partial</td>
<td>1</td>
<td>None</td>
<td>No</td>
</tr>
<tr>
<td>Russia</td>
<td>Full</td>
<td>1</td>
<td>Stock &lt; 40</td>
<td>Yes</td>
</tr>
<tr>
<td>Germany</td>
<td>Partial</td>
<td>3</td>
<td>Stock &lt; 40; M &lt; 150</td>
<td>Yes</td>
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<tr>
<td>Greece</td>
<td>Partial</td>
<td>1</td>
<td>Stock &lt; 50</td>
<td>Yes</td>
</tr>
<tr>
<td>Italy</td>
<td>Partial</td>
<td>3</td>
<td>Stock &lt; 45</td>
<td>Yes</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Partial</td>
<td>3</td>
<td>Stock &lt; 45</td>
<td>Yes</td>
</tr>
<tr>
<td>Portugal</td>
<td>Partial</td>
<td>1</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>Spain</td>
<td>Partial</td>
<td>3</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>Sweden</td>
<td>Partial</td>
<td>1</td>
<td>Stock &lt; 45</td>
<td>Yes</td>
</tr>
<tr>
<td>UK</td>
<td>Partial</td>
<td>1</td>
<td>Stock &lt; 45</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Cross border reproductive care in six European countries**

2010  
A. van den Boogaard, C. de Mouzon, O. Resche, A. R. Storer, A. J. de Weert, and Y. Godaux: the ESHRE Taskforce on Cross Border Reproductive Care

**Table VII: Treatment sought according to the recipient country.**

<table>
<thead>
<tr>
<th>Recipient country</th>
<th>Preference</th>
<th>Embryos</th>
<th>Delivery per treatment</th>
<th>Embryos</th>
<th>Delivery per treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>139</td>
<td>5.9</td>
<td>13.4</td>
<td>5.2</td>
<td>10.5</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>230</td>
<td>9.6</td>
<td>19.4</td>
<td>5.6</td>
<td>10.4</td>
</tr>
<tr>
<td>Denmark</td>
<td>69</td>
<td>10.0</td>
<td>6.6</td>
<td>4.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Norway</td>
<td>60</td>
<td>10.0</td>
<td>6.6</td>
<td>4.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Spain</td>
<td>166</td>
<td>6.4</td>
<td>3.1</td>
<td>4.1</td>
<td>1.3</td>
</tr>
<tr>
<td>Switzerland</td>
<td>78</td>
<td>3.4</td>
<td>1.4</td>
<td>2.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Total</td>
<td>714</td>
<td>7.2</td>
<td>2.2</td>
<td>19.3</td>
<td>2.2</td>
</tr>
</tbody>
</table>

**standard of success in assisted reproduction**

*debate series, n=16: Hum Reprod 2004*

1. BESST: Birth emphasizing a successful singleton at term (Min)
2. ‘Narrow to infant outcomes with optimal (prognosis’ (Schweer)
3. Healthy lower order birth’ (Schieve)
4. ‘Informed choice by couple after appropriate counselling’ (Buckett)
5. ‘Elective SET rate per center’ (Land)
6. ‘BESST with other denominator’ (Davies)
7. Three parameters: oocyte, implantation or deliveries/embryos’ (Pinborg)
8. ‘Consider outcomes per treatment rather than cycle’ (Heijnen)
9. ‘Cumulative singleton births also including preterm births’ (Wienemann)
10. ‘Value cryopreservation on cumulative pregnancy rates’ (Tiitinen)
11. ‘Cumulative singleton births / oocyte pick-up’ (Germond)
12. ‘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

- Optimal estimates
- Conservative estimates

- 2004
- 2005
- 2007
- 2008 (truncated)
Aim
Collect information regarding death within 1 year (and related to) IVF, 1994-2008, The Netherlands

Results
- Total ~100,000 IVF treatment cycles
- 6 death directly related to IVF
  - OHSS
  - Thrombosis 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
- 9 death unrelated to IVF

Conclusions
- Overall mortality related to IVF pregnancy higher than general population
- World-wide underreporting IVF related mortality
- Underlying national registry and reporting

Maternal death related to IVF in the Netherlands 1984-2008 - HR 2010
B.E. van Echten, M.C. Schachter, R.J. van Drie, S.M. Evers, and F.H. van Loon

Recent papers in favour of mild stimulation IVF
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

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

<table>
<thead>
<tr>
<th>Woman (burden of treatment)</th>
<th>Cost-effective Access to treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Future health Of child</td>
<td>Society</td>
</tr>
<tr>
<td>Couple (successful)</td>
<td></td>
</tr>
</tbody>
</table>
How to implement TQM

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

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 overview 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

• 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.
TQM –key principles

Management commitment
Employee empowerment
Fact based decision-making
Continuous improvement
Customer (patient’s needs and expectations) focus

Principles of TQM

1 Customer focused organisation

Understanding current and future patient’s needs
Strategic decisions are ”customer driven”
Society is an important customer

2 Leadership

Leaders establish the unit’s purpose and direction
Responsible for strategic planning with strong future orientation

3 Involvement of people

People at all levels are the essence of an organisation
Health care institution’s success depends increasingly on the knowledge, skills and motivation of its work force
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 contributes to the organization’s effectiveness.

6 Continual improvement
Reassessment objective of the organization is part of management of all processes.

7 Factual approach to decision making
Effective decisions are based on the analysis of data and information.

8 Mutually beneficial supplier relationship
Organizations and suppliers are interdependent and a mutually beneficial relationship enhances the ability of both to create value.

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

How to implement TQM
Quality Management System

<table>
<thead>
<tr>
<th>VISION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Background</td>
<td>Legislation</td>
</tr>
<tr>
<td></td>
<td>Economical potential</td>
</tr>
<tr>
<td></td>
<td>Quality of services</td>
</tr>
<tr>
<td></td>
<td>Education, research, organ.</td>
</tr>
<tr>
<td>Strategy</td>
<td></td>
</tr>
<tr>
<td>Evaluation</td>
<td>Objective evaluation (scoring)</td>
</tr>
</tbody>
</table>
How to implement TQM

Quality Management System

<table>
<thead>
<tr>
<th>Responsibility of management</th>
<th>Management of resources</th>
<th>Management of processes</th>
<th>Analysis and quality improvement</th>
</tr>
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<tbody>
<tr>
<td>Strategy and QC</td>
<td>Human resources</td>
<td>QM and risk assessment</td>
<td>Measurable criteria for:</td>
</tr>
<tr>
<td>Organization and structure</td>
<td>Space conditions,</td>
<td>Organization</td>
<td>Management system</td>
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<td>equipment</td>
<td>Internals standards</td>
<td>Process evaluation</td>
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<td></td>
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<td>Services / products</td>
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<td>procedures</td>
<td></td>
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<td>Quality control</td>
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<td>Software, data</td>
<td>Development of new</td>
<td>System of continual improvement</td>
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<td>(patients, partners,</td>
<td>protection archivation</td>
<td>products and services</td>
<td>Internal audits</td>
</tr>
<tr>
<td>colleagues)</td>
<td></td>
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</tr>
</tbody>
</table>

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:

- Employees are not really disciplined in their work
- Absence or lack of orientation towards teamwork
- Lack of cultural or demographic homogeneity
- Preference for fixed working 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

<table>
<thead>
<tr>
<th>Identifying tasks to be done</th>
<th>Assessing current reality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developing strategies for building commitment</td>
<td>Management must be heavily involved</td>
</tr>
<tr>
<td>Assessing current reality</td>
<td>Creating a model of the desired state (TQM)</td>
</tr>
<tr>
<td>Securing outside consultation and training someone “in house”</td>
<td>Visionary leadership needed</td>
</tr>
<tr>
<td>Designing mechanisms to communicate the change</td>
<td>Mechanisms beyond existing processes will need to be developed</td>
</tr>
<tr>
<td>Assigning resources</td>
<td>Outside consultants will always be required</td>
</tr>
</tbody>
</table>

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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 addressed in the next PDCA cycle

How to implement TQM

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

<table>
<thead>
<tr>
<th>ESHRE PCC London 2013</th>
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</table>

### 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, competitiveness or financial return.

<table>
<thead>
<tr>
<th>ESHRE PCC London 2013</th>
</tr>
</thead>
</table>

### 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.

| ESHRE PCC London 2013 |
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

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.

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
Cost and Quality

- The cost of quality should be calculated as the addiction of the following cost:
  - Prevention cost
  - Evaluation cost
  - Internal faults cost
  - External faults cost

Cost and Quality

- Quality cost
- Failures cost
- Optimal cost
- Quality (100% OK)
- Non Quality (0% OK)

Identifying non-quality

- CONTACT WITH PATIENT
- APPOINTMENT
- OVARIAN ESTIMULATION
- OVUM PICK-UP
- THAWED EMBRYO TRANSFER
- PREGNANCY
- FIST VISIT IN THE CLINIC
- REPRO LABORATORY
- EMBRYO VITRIFICATION
- EMBRYO TRANSFER
- PREGNANCY
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
  - ...

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
**CONCLUSION**

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

*Quality oriented management is worthy*

---

**Introduction to Quality Management**

- TQM
- TQC
- Six Sigma
- Lean
- KAIZEN
- EFQM

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

---

**Introduction to KAIZEN**

- KAI ZEN

KAI = CHANGE

ZEN = GOOD

Masaaki Imai
Introduction to KAIZEN

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

Process as a link between Strategy and Operations

Processes in IVF Clinic
From the traditional management perspective, Management has two major functions:
- Maintenance
- Improvement

From the KAIZEN perspective, improvement can be classified as:
- Kaizen
- Innovation

**WHY?**

**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)
The Lean perspective

Replace waste for value-added...

... not working or consuming more resources

**Same Work → Better Outcome**

The Lean perspective

8W:
- Transport
- Unused human talent
- Defects
- Over Processing
- Inventory
- Motion
- Waiting
- Overproduction

Start spinning the wheel of improvement

But when analyzing the processes, how can we identify the problems, wastes or the improvement issues??
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 Why
  - Ishikawa diagrams (Fishbone) and 5 Ms

**Working with process:**
- Quality circles
- Risk Management (cuaderno)

**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

**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
  - **Adjust** to improve next time and **standardize**
- Kaizen will use methods and techniques for evaluating problems and improve processes
- And Remember

"Improvement is infinite"
Example of the IVI approach

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)
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

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
  - Vitro fertilization
  - Oocyte cryopreservation

- Experimental
  - ovarian tissue cryopreservation
  - in vitro maturation of oocytes
  - ovarian tissue re-implantation
ART practice maturing

Safety
Patient assessment

Outcome
Pregnancies

Protocols
Staff

Need for implementing TQM

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

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 (TechnicalDirective 1)
  - Donation (procurement, donation, testing) of human tissues and cells intended for human application

  - 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

<table>
<thead>
<tr>
<th>EUTC Directive</th>
<th>ISO</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Quality management</td>
<td>• Customer focus</td>
</tr>
<tr>
<td>• Person Responsible</td>
<td>• Leadership</td>
</tr>
<tr>
<td>• Personnel</td>
<td>• Involvement of people</td>
</tr>
<tr>
<td>• TC</td>
<td>• Process approach</td>
</tr>
<tr>
<td>• Reception</td>
<td>• System approach to management</td>
</tr>
<tr>
<td>• Processing</td>
<td>• Continuous improvement</td>
</tr>
<tr>
<td>• Storage</td>
<td>• Factual approach to decision making</td>
</tr>
<tr>
<td>• Labelling, documentation</td>
<td>• Mutual beneficial supplier relationship</td>
</tr>
<tr>
<td>• Distribution</td>
<td></td>
</tr>
<tr>
<td>• Relation with 3rd parties</td>
<td></td>
</tr>
<tr>
<td>• Coding</td>
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</table>

Guidance

• Was the Directive based on the principles of ISO accreditation and Quality management?
<table>
<thead>
<tr>
<th>EUTC Directive</th>
<th>TQM in ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reassure the public</td>
<td>• Excellent patient care</td>
</tr>
<tr>
<td>• Highest level of protection</td>
<td>• Highest success rates</td>
</tr>
<tr>
<td>• Safeguard public health</td>
<td>• Policies and protocols</td>
</tr>
<tr>
<td>• Establish standards for processes</td>
<td>• Continuous improvement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EUTC Directive</th>
<th>TQM in ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>• TE accreditation</td>
<td>• ISO accreditation</td>
</tr>
<tr>
<td>• Notification system</td>
<td>• Continuous assessment</td>
</tr>
<tr>
<td>• Inspection</td>
<td>• Certified training</td>
</tr>
<tr>
<td>• Inspector training</td>
<td>• Re-certification</td>
</tr>
<tr>
<td>• Traceability</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>EUTC Directive</th>
<th>TQM in ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Quality system based on good practice</td>
<td>• Quality system and CI</td>
</tr>
<tr>
<td>• SOP</td>
<td>• All enumerated</td>
</tr>
<tr>
<td>• Guidelines</td>
<td></td>
</tr>
<tr>
<td>• Training and reference manuals</td>
<td></td>
</tr>
<tr>
<td>• Reporting forms</td>
<td></td>
</tr>
<tr>
<td>• Donor records</td>
<td></td>
</tr>
<tr>
<td>• Information on destination of TC</td>
<td></td>
</tr>
</tbody>
</table>
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

- Testing
- Acceptance
- Procurement
- Processing
- Distribution Storage

Negative/Donor and recipient 
screening

- Positive/Donor into programme
- Positive/Recipient into programme

- Partner donation
- Couple screening

- Sperm donation

- Embryo donor
- Embryo recipient

- Embryo frozen
- Embryo storage

- Partial in vivo donors

- Partial in vivo patients

- Referral to Units that treat positive patients
# 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
  - SA/ESAR 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

### 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

<table>
<thead>
<tr>
<th>ISO Country Identifier</th>
<th>TR Code</th>
<th>Unique Donation Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 characters</td>
<td>6 characters</td>
<td>13 characters</td>
</tr>
<tr>
<td>(alphabetic)</td>
<td>(alpha/numeric)</td>
<td>(alpha/numeric)</td>
</tr>
</tbody>
</table>

### Product identification

<table>
<thead>
<tr>
<th>Coding System identifier</th>
<th>Product Code</th>
<th>Split Number</th>
<th>Expiry Date</th>
</tr>
</thead>
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<td>7 characters</td>
<td>3 characters</td>
<td>8 characters</td>
</tr>
<tr>
<td>(alphabetic)</td>
<td>(alpha/numeric)</td>
<td>(alpha/numeric)</td>
<td>(numeric)</td>
</tr>
</tbody>
</table>
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 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

<table>
<thead>
<tr>
<th>EUTC Directive</th>
<th>TQM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality manager</td>
<td>Quality manager</td>
</tr>
<tr>
<td>SOP</td>
<td>Regular staff meetings</td>
</tr>
<tr>
<td>Guidelines</td>
<td>Adverse events, incidents</td>
</tr>
<tr>
<td>Training and reference manuals</td>
<td>Non-conformances</td>
</tr>
<tr>
<td>Reporting forms</td>
<td>Quality masterplan + KPI’s</td>
</tr>
<tr>
<td>Donor records</td>
<td>Development plan</td>
</tr>
<tr>
<td>Information on final destination of TC</td>
<td>Training and CPD</td>
</tr>
<tr>
<td>Data stored for 30 years</td>
<td>Strategic plans</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Testing</th>
<th>Acceptance</th>
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</tbody>
</table>

Viral screen

Positive exclusion: real programme

Negative exclusion: real programme
**SAR-E**

- Report all:
  - 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

Identify the inputs and outputs of the process
Document entire flow of the process
Identify all value and non-value added operations
Identify hazards and classify the scope of the process

“Staple yourself to the patient”

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
- 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
- 6 Hrs Insemination
- 24Hrs Fert Check
- 49Hrs Cleavage Ass
- 52Hrs Embryo Transfer
**COMPARISON OF INCUBATOR TEMPERATURES**

Max Temperature drop after door open
- Direct heat: 0.2 Degrees C
- Indirect Heat: 3.0 Degrees C

Recovery Time after door open
- Direct heat: 2 Minutes
- Indirect Heat: >40 Minutes

**HUMIDI CRIB VS HEATED STAGE TEMPERATURE COMPARISON**

Max Temperature drop after move from incubator
- Direct heat: 0.3 Degrees C
- Indirect Heat: 6.5 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: 0.2 Degrees C
- Indirect Heat: 3.5 Degrees C
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

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Running of IVF Center
• 10% clinical skills
• 30% scientific skills
• 60% sheer organization

TQM= the scientific way of doing business

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

What is TQM?

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

Ron Fitzgerald
The quality cycle

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

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

Andrology laboratory
Embriology laboratory
Reproductive surgery
Complications
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  
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- 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

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