# NATURAL CYCLES in low resource countries

## Has it a place?

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ESHRE Campus From natural cycle to minimal stimulation Maribor 27-28 February 2009

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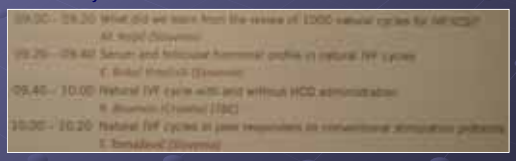
## Synthesis

27. February 2009

28. February 2009



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## objectives

- Identify unresolved issues in low resource countries
- Review and assess recent developments in NC
- Provide recommendations for practice

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## Low resources or developing countries

developing

developed

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## What is determinant ?

- National Income
- Gross Domestic Product – GDP
  *measures the value of economic activity*
- Gross National Product – GNP
  *Converted into US dollars at the official exchange rate*
  *Divided by the country population - this gives an average figure for GNP per head*

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## GDP per capita

- below average

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## Percent poverty world map

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## demography of fertility & infertility

- **regional differences**
- Africa has much higher level of fertility in than in other regions
  - it is surprising to observe that contrary to expectation
- The level of *infertility* is higher in Africa than elsewhere
  - measure of infertility is
    - proportion of women who are childless by the age of
    - 40 to 44 years
    - 45 to 49 years

    *at the end of their fecund period of life.*
- Substantial variation between countries and within regions
  - women in their forties who are childless in Africa ranges from
    - a level of a few percent in western Africa,
    - to
    - third of women in central Africa

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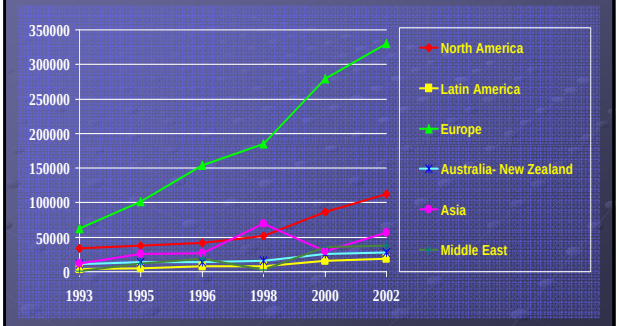
## Evolution of ART Cycles by Region

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## Availability per country

| Cycles/million | | Births/1000 | | Cycles/million | | Births/1000 | |
|---|---|---|---|---|---|---|---|
| Israel | 3263 | Netherland | 46.3 | Ireland | 466 | NewZealand | 8.7 |
| Denmark | 2040 | Denmark | 43.4 | NewZealand | 419 | Ireland | 8.0 |
| Finland | 1599 | Slovenia | 34.7 | USA | 413 | Barhain | 3.5 |
| Cyprus | 1374 | Israel | 34.2 | Lybia | 317 | Poland | 3.2 |
| Australia | 1291 | Iceland | 30.1 | Poland | 127 | Macedonia | 2.6 |
| Slovenia | 1288 | Sweden | 29.3 | Argentina | 119 | Lybia | 2.3 |
| Iceland | 1270 | Finland | 26.5 | Macedonia | 115 | Uruguay | 1.9 |
| Sweden | 1225 | Cyprus | 26.4 | Uruguay | 101 | Argentina | 1.5 |
| Germany | 1073 | Norway | 23.9 | Russia | 69 | Chile | 1.2 |
| France | 1052 | Germany | 21.9 | Brasil | 66 | Russia | 1.0 |
| Netherland | 997 | Australia | 19.2 | Chile | 65 | Brasil | 0.9 |
| Norway | 909 | Hungary | 18.7 | Venezuela | 41 | Venezuela | 0.5 |
| Switzerland | 719 | France | 15.4 | Syria | 32 | Peru | 0.2 |
| Hungary | 681 | UK | 13.7 | Peru | 23 | Syria | 0.1 |
| Bahrain | 640 | Switzerland | 13.5 | Ecuador | 9 | Ecuador | 0.1 |
| UK | 611 | Croatia | 12.3 | Dominic Rep | 2 | Guatemala | 0.02 |
| Croatia | 582 | USA | 10.0 | Guatemala | 2 | Dominic Rep | 0.01 |

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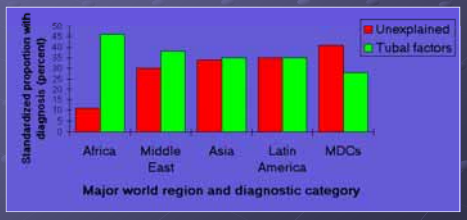
## Major cause of excess infertility

- acquired sterility due to pathological conditions
  *especially notable in Africa*
  - tubal infertility nearly 64%
    - sexually transmitted diseases have prominent role
    - availability of medical and therapeutic interventions
  - ovarian or endocrine disturbances 24%

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## Method of choice ? IVF

- Why IVF
  - Dominance of Tubal factor:
  - STDs

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## Factors involved in infertility treatment in developing world

- Social
- Cultural
- Economic
- Demographic
- Ethnic
- Religious

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## Factors involved in infertility in developing countries

- Negative consequences of childlessness are much stronger
- Prevention and alternative methods are not always successful
- Adoption is not an option in most DC (socio-cultural, religious)
- Equity: IVF should not only be available for the rich
  - Possibility of
    - simplifying diagnostic procedures
    - simplifying clinical procedures (IVF-cycle)
    - simplifying laboratory procedures (IVF)
    - opportunity of establishing 'Reproductive Health Care Centres' with possibilities for family planning/mother-care/infertility diagnosis & treatment

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## obstacles in infertility treatment in low resource countries

- Infertility diagnostics
- Treatment feasibility and costs
- Preventive measures – how and consequences of low prevention level in low resource countries

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## Aims of IVF service in developing countries

- Cost
- Visits
- Monitoring
- Complications
- Stress

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## NC & terminologies used in the literature

| Recommended | To replace |
|---|---|
| Natural cycle IVF | Unstimulated, spontaneous cycle IVF |
| Modified natural cycle IVF | Semi-natural, controlled natural cycle IVF |
| Mild IVF | Soft, minimal stimulation, 'friendly' IVF |
| Conventional IVF | Standard, routine IVF, controlled ovarian stimulation IVF |

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## Definition simplified and revised nomenclature

| Terminology | Aim | Methodology |
|---|---|---|
| *Natural cycle IVF* | *Single oocyte* | *No medication* |
| *Modified Natural cycle IVF* | *Single oocyte* | *hCG only Antagonist & FSH/HMG add back* |
| *Mild IVF* | *2-7 oocytes* | *Low dose FSH/HMG, oral compounds & antagonist* |
| *Conventional IVF* | *≥ 8 oocytes* | *Agonist or antagonist conventional FSH/HMG dose* |

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## Advantages of NC IVF

- Systematic literature review (20 selected studies)
  *Pelnick et al Hum Rep Update 2002*
  - 1800 natural cycles
    - Embryotransfer rate 45%
    - Pregnancy rate per cycle 7.2%
    - Pregnancy rate per transfer 15.8%
  - Cancelation of CPU
    - Ovulation trigering with HCG rate of oocyte retrieval per cycle 67.3%
    - Timing of spontaneous LH surge rate of oocyte retrieval per cycle 80.6%
  - Oocite recovery rate 88.6%
  - **Fertilisation rate**
    - IVF cycles 44.2-100%
    - ICSI cycles 56.3-62.5%

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## Factors affecting pregnancy success of IVF in NC

- Patient age
- Indicatioons for IVF
- Previous IVF treatment
- Baseline value of FSH, LH, PRL
- Embryo, oocyte and semen quality
- Endometrial thicknes
- Day of ET
- Serum E2 level on day of hCG

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## NC IVF success rates

- Accurate monitoring
- Selection of patients
- Method: IVF or ICSI
- Embriootransfer: day 2 or day 5?
- Influence of patients age
- Luteal suplementation

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## AIM

- ART should be designed to be robust, repeatable and efficient
- Equipment should be basic, sturdy and strong
- Products should be solid, ready to use and with a long half-life
  - Sperm processing materials are best aseptically packaged (set or kit) and stored at room temperature
  - Embryo culture media should be robust, short-term, pre-packaged in small quantities
  - Disposables (pipette tips, screening dishes) can be pre-packaged as 'a set per patient'
- Information to the community should be discrete and applicable, taking into account sociocultural and religious differences
- A training program (with follow-up/audits) for the medical and paramedical staff should be designed.

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## But little is known about

- Real cost/benefit score in ART/IVF
- Minimal costs for IVF in:
  - Different countries worldwide
  - Low-resource countries
- Future posibilities to get:
  - Cheaper medication
  - Low-cost equipment

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## ART technology - Regional differences

- Knowledge
- Equipment
- Medical Device
- Drugs
- Procedure
- Suport system


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## NATURAL CYCLES in low resource countries

**Has it a place?**

**YES**
**as it has a place in developed countries but...**

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