Epidemiology of infertility

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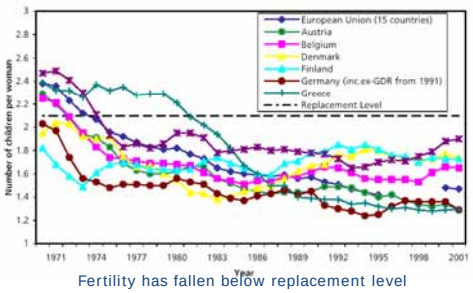
Which questions must be answered by non-infectious epidemilogy?

- **Epidemiology** is the study of factors affecting the health and illness of populations, and serves as the foundation and logic of interventions made in the interest of public health and preventive medicine
- Assess the health states and health needs of a target population;
- Implement and evaluate interventions that are designed to improve the health of that population;
- Efficiently and effectively provide care for members of that population in a way that is consistent with the community's cultural, policy and health resource values.

Epidemiology of infertility

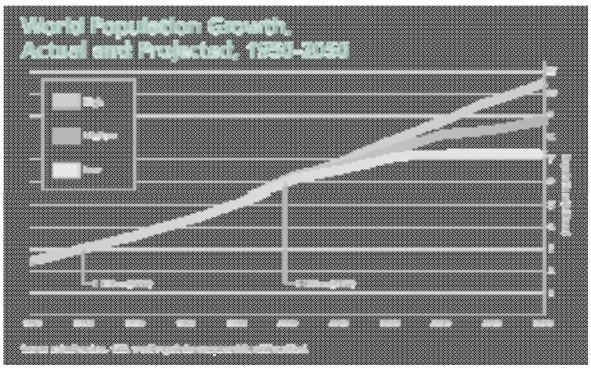
- Prevalence of infertility
- Outcome of Pregnancy
- Access for infertility treatment
- Using of different methods of inferility treatment
- Demand of patients for ART
- Geographical distribution of infertility in Ukraine

Across Europe, the number of births has been steadily declining over the years



Fertility has fallen below replacement level

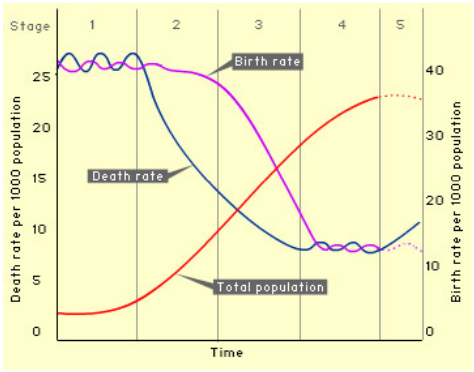
Source: RAND Corporation, 2004



Fertility Rate World Map

From: wikipedia.com

Demographic Transition



From: Wikipedia.com

Human Reproduction , 2007
International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care
Jacky Boivin, Laura Bunting, John A.Collins and Karl G.Nygren

Scales of infertility

- All population 100%
- Voluntary childless ? (3-5%)
- Non-voluntary childless 12-18%
- Couples who wish to treat (from all) – 7,2-10,8%
- Couples who accepted ART -3,6-5,4%

Aim of our study

- Investigate prevalence of infertility in Ukraine
- Investigate ratio of infertility patients who asked medical treatment
- Investigate access for ART infertile patients
- Predict potential demand for ART in Ukraine

General study design

- Data State Committee of Statistics Ukraine (http://ukrstat.gov.ua/)
- Personal interview of 1658 respodents

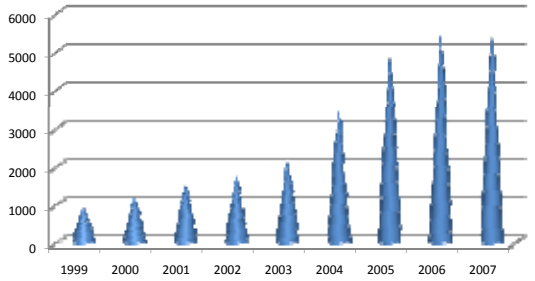
Main figures

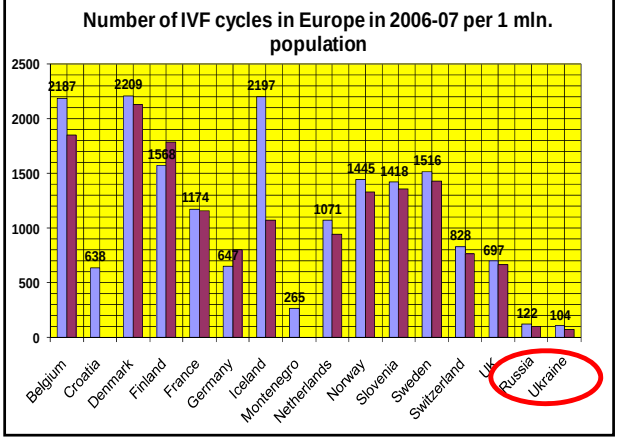
(data Consulting Company Medexpert, 2010)

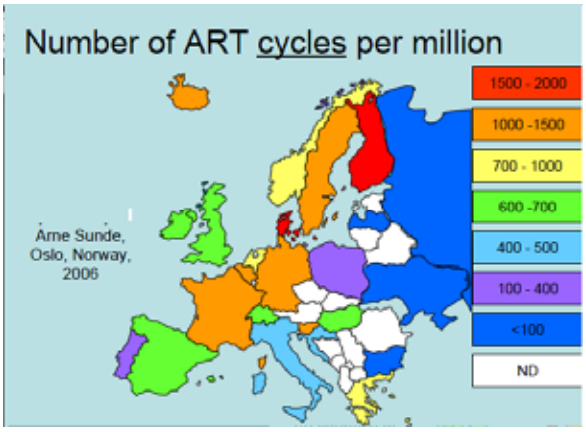
Indicator	Value
% of infertile couples, duration infertility more than 10 years	16%
% of unfertile couples, duration of infertility more than 1 year	14%
% of infertile couple referred for medical care	52%
% of infertile couple for ART	2%

Characteristics	Type of infertility treatment								
	Hormones	Antiinflammation	Hydrotubation of tubes	Physiotherapy	Laser treatment	Laparosocopy	SPA	ART	ANOTHER
Всего	24,2	48	15,5	18,9	4,7	4,7	14,9	**2,2**	**18,8**
15-24	21,4	62,3	12,5	14,1	5,2	1,8	7,2	**0**	**17,7**
25-34	26,8	46,8	16,2	19,1	6,1	5,3	15,3	**3,1**	**16,3**
35-44	20	32,6	17,5	25	0	7,4	24,9	**2,4**	**29,9**

Number of IVF cycles in Ukraine 1999-2007







What is the demand of IVF cycles for 1 million population?

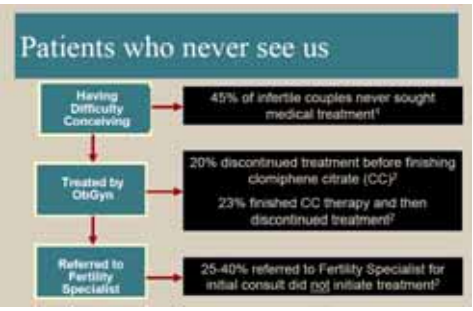
- 1500 cycles /year are needed/million population as a minimum to address infertility

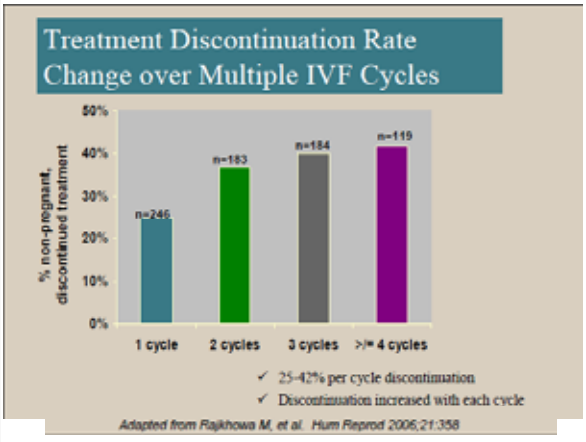
Collins, J Sem Reprod Med **19**: 279-89, 2001

Demand for Ukraine

- Population – 46. 000.000 (2009)
- Demand - 69.000 cycles ART per year
- Real provided 2009 (assessment) - 8000 cycles

Michael Alper, 2007





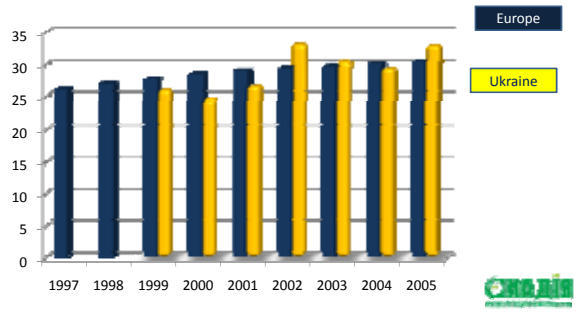
Scales for success

- Infertile couples – 100%
- Required ART – 55-60%
- Come to doctors – 30%
- Go to ART – 2-15%
- Achieved success – 0,8- 5%

What could we do as a medical professional?

- Simplify the way to the ART of patients in the youngest age
- Increase the pregnancy rate
- Increase access for infertility treatment for patients

Pregnancy rate ART treatment in Europe and in Ukraine, 1997-2005 (EIM)



Pregnancy rate after IVF cycles in Europe,2006 (EIM)

Serbia	50.0	Poland	35.0	Switzerland	28.5
Turkey	46.8	Hungary	34.8	France	27.5
Iceland	42.4	Sweden	34.1	Belgium	26.7
Macedonia	39.4	Slovenia	34.1	Italy	26.4
Czech Republik	37.9	Ukraine	32.9	Croatia	24.8
Greece	37.1	Norway	32.4	Albania	24.6
Spain	35.8	Denmark	32.1	Netherlands	24.5
Russia	35.4	Ireland	31.8	Bulgaria	22.0
Portugal	35.4	UK	30.4	Finland	21.2
Montenegro	35.3	Germany	30.4	Lithuania	20.0

COULD WE USE ONLY PREGNANCY RATE AS INDICATOR OF OUR EFFICIENCY?

Main goal of IVF treatment is achieving singleton delivery by healthy baby.

Characteristics deliveries after IVF in Europe in 1997-2005

	2005	2003	2001	1999	1997
Singleton	**78.2**	76.7	74.5	73.7	70.4
Twin	**19.7**	22.0	24.0	24.0	25.8
Triplet	**0.8**	1.1	1.5	2.2	3.6
Quadruplet	**0.01**	0.08	0.02	0.1	0.15

Characteristics deliveries after IVF in Ukraine in 2000-2006

	2000	2001	2002	2003	2004	2005	2006
Singleton	61,00%	66,50%	61,30%	59,60%	63,50%	65,80%	73,80%
Twins	36,00%	30,00%	36,00%	38,30%	34,90%	33,20%	24,78%
Triplets	3,00%	3,50%	2,70%	2,10%	1,60%	1,00%	1,34%
Quadriplet							0,08%

How the number of delivered babies depends on number transfrerred embryos?

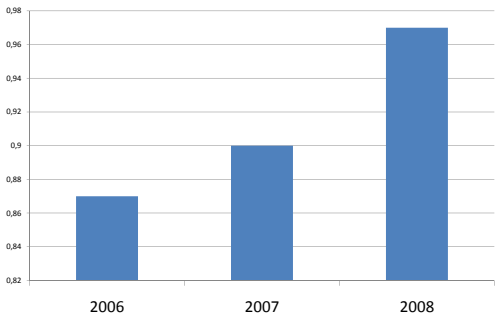
(EIM, Ukraine, 2006 ,Veselovskyy V.)

Number of embryos	Deliveries	Del/ET, %	1 fetus	%	Twins	%	Trip-lets	%
1	53	13,5%	52	98,1%	1	1,9%		
2	302	25,7%	237	78,5%	65	21,5%		
3	388	25,8%	291	75,0%	92	23,7%	5	1,3%
4	203	36,1%	123	60,6%	74	36,5%	6	3,0%
5 and more	102	32,8%	58	56,9%	40	39,2%	4	3,9%
Total	1048	26,6%	761	**72,6%**	272	**26,0%**	15	**1,4%**

Some figures

All deliveries in Ukraine 2006	454 813
Multifetal preganacies	3 957
% multifetal pregnancies from all deliveries	0,87%
Deliveries after IVF	1 048
Multifetal pregnancies after IVF	287
% multifetal pregnancies from all IVF deliveries	27,39%
Proportion of multifetal IVF deliveries from all multifetal	7,25%

Proportion of multifetal deliveries from all deliveries in Ukraine 2006-2008



Estimated yearly cost attributable to preterm infants born from multiple pregnancies associated with IVF in the United States

Year	Number of cycles with LB	Average number of embryos transferred	% Twin LB	% Triplet or higher order LB	Number of infants born preterm	Estimated health care cost ($)
2001	31,545	3.1	30.6	3.3	16,915	904,206,498
2002	35,614	2.9	29.2	3.2	15,857	993,354,434
2003	38,601	2.8	28.5	2.8	16,706	990,825,961
2004	39,106	2.7	27.5	2.2	16,247	917,217,386
2005	42,732	2.6	27.0	2.1	15,005	980,658,639

[Bromer and Seli, ASRM 2008]

Main problem – embryo selection!

- Genomic approaches (FISH or CGH?)
- Gene expression
- Morphological analysis
- Proteomic (sHLA-G)
- Metabolomic

Seli E., 2010

	FISH	Conv CGH	CGH Array	SNP Array
Invasive	+	+	+	+
Complete in 2 d	+	+	+	+
Detects single gene disorders	-	-	-	-
Number of chromosomes	9-12	23	23	23
Technically difficult	+	-	-	-
complicated stats	-	+	+	+
Whole genome amplification	-	+	+	+
Detects polyloidy	+	-	-	+

Clinical application of comprehensive chromosomal screening at the blastocyst stage

William B. Schoolcraft, M.D.,[a] Elpida Fragouli, Ph.D.,[b,c] John Stevens, M.S.,[a] Santiago Munne, Ph.D.,[d] Mandy G. Katz-Jaffe, Ph.D.,[b] and Dagan Wells, Ph.D., F.R.C.Path.[b,c]

- 45 infertile couples with at least one previous unsuccessful IVF treatment cycle (mean 2.4)
- Day 5 trophectoderm cell biopsy + CHG
- Diagnosis in 93.7%
- Aneuploidy rate 51.3%.
- Implantation rate 68.9%
- Pregnancy rate 82.2%.

[Schoolcraft et al. Fertil Steril ePub, 2009]

How could ART treatment influence for Total Fertility Rate?

Human Reproduction Vol.22, No.8 pp. 1975–2183, 2007
Advance Access publication on June 13, 2007

Can assisted reproductive technologies help to offset population ageing? An assessment of the demographic and economic impact of ART in Denmark and UK

S. Hoorens[1,3], F. Gallo[a], J.A.K. Cave[a] and J.C. Grant[a]

Table 1: Summary of key indicators

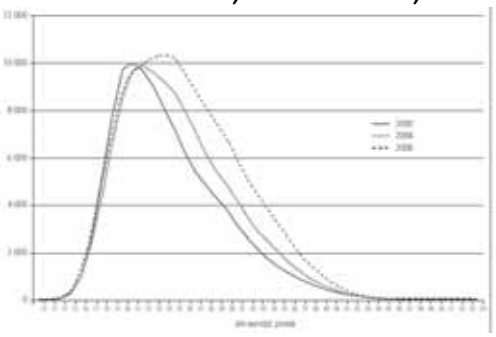
	United Kingdom (2002)	Denmark (2002)
Population	59.3×10^6	5.4×10^6
TFR	1.64	1.72
ART cycles	37 083	11 081
ART births as proportion of total births	0.014	0.042
Life expectancy	76.1 years (M) 81.1 years (F)	75.5 years (M) 80.2 years (F)
Mean age at childbirth	28.7 years (F)	29.9 years (F)
Current policy	Regional variations in reimbursement policies	Three cycles reimbursed in public clinics

Sources: Eurostat, 2006 and Nyboe Andersen *et al.*, 2006.

Table 2: Results for TFRs

	Observed TFR, 2002	TFR without ART	TFR in UK with increased access to ART	Maximum TFR with ART
UK	1.64	1.62	1.68	1.84
Denmark	1.72	1.65	na	1.89

First delivery rate by maternal age, Ukraine, 2000-2008,



Key demographic and fertility indicators, Ukraine,2006

Population	46,8 mln.
Total Fertility rate	1,31
ART cycles	5206
ART births as proportion of total births	0,0025 (1048/419268)
Life expectancy	74 years (F)
	63 years (M)
Mean age at childbirth	25,6 years (F)
Current policy	Government support 5-10 % of provided ART cycles

Modified results of Hoorens et al, 2007 with adding Ukraine

Country, year	Observed TFR	TFR w/out ART	Maximum TFR With ART	Potential,%
UK, 2002	1,64	1,62	1,84	12,1 %
Denmark, 2002	1,72	1,65	1,89	9,9 %
Ukraine, 2006	1,31	1,30	1,41	7,6 %

Main conclusions

- Average number of infertile couples are the same over the world (9-17%)
- Access for infertility and ART treatment depends from level of state reimbursement
- Demand for IVF treatment in Ukraine satisfied for 8-10%
- Access for ART treatment could influence for demography