Assisted Reproductive Technology (ART) in Europe 2016 and development of a strategy of vigilance

Preliminary results generated from European registers by ESHRE

European IVF Monitoring (EIM),

a consortium of representatives from National Registers

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Conflict of interest

I declare that I have no commercial or financial interests pertaining to the subject of this presentation or its content.

European IVF-Monitoring (EIM)

- The European IVF Monitoring Consortium was established in 1999 to collect, process and publish European data on clinical results and side-effects of assisted reproductive technology (ART), follow-up of children‘s well-being but also the availability and structure of services in the various European countries.

- The EIM is a „bottom up“-type of data collection assembling the representatives of the national registries of almost all European countries.

European IVF-Monitoring (EIM)

The EIM Consortium collects ART data (on a voluntary basis) on:

Quantity – Availability – Efficacy – Safety – Quality - Trends

Techniques:

IVF – ICSI
FER (frozen embryo replacement)
FOR (frozen oocyte replacement)
ED (egg donation)
IUI
PGT
IVM
Embryo donation
Fertility preservation

51 European countries (geographically)

EIM covers approximately 84% of the European countries, active in ART
(with the results of 4 countries still pending and 4 countries incomplete)

2016

Countries	36
Centers	1 198
Cycles	803 741
Children	165 975

- Have never submitted data (n=7)
- First year of data collection
- Not able to report data

EIM, 1997 - 2016

year	countries	clinics	cycles	cycle-increase (%)	ART infants
1997	18	482	203 225		35 314 *
1998	18	521	232 225	+ 14.3	21 433 *
1999	21	537	249 624	+ 7.5	26 212 *
2000	22	569	275 187	+ 10.2	17 887 *
2001	23	579	289 690	+ 5.3	24 963 *
2002	25	631	324 238	+ 11.9	24 283
2003	28	725	365 103	+ 12.6	68 931
2004	29	785	367 056	+ 0.5	67 973
2005	30	923	419 037	+ 14.2	72 184
2006	32	998	458 759	+ 9.5	87 705
2007	33	1029	493 420	+ 7.6	96 690
2008	36	1051	532 260	+ 7.9	107 383
2009	34	1005	537 463	+ 1.0	109 239
2010	31	991	550 296	+ 2.4	120 676
2011	33	1034	609 973	+ 11.0	134 054
2012	34	1093	640 144	+ 4.9	143 844
2013	38	1169	686 261	+ 7.2	149 466
2014	39	1279	776 556	+ 13.1	170 163
2015	38	1343	849 811	+ 9.4	182 529
2016*	36	1198	803 741		165 975
total			9 658 486		1 826 956

year countries clinics cycles cycle increase (%) ART infants

* with the results of 4 countries still pending and 4 countries incomplete

IUI : 2 674 241 (2002-2016)

eshre

Characteristics of the national registers

compulsory	20 countries	
voluntary	16 countries	
based on individual cycles	13 countries	
public access to individual clinic data	7 countries	
all clinics are reporting (44.4%)	16 countries	+2

Austria, Belgium, Bulgaria, Denmark, Estonia, Finland, France, Greece, Iceland, Italy, Malta, Norway, Portugal, Slovenia, Switzerland, The Netherlands

Not all clinics reporting (56.6%) — 20 countries

Albania, Armenia, Bosnia, Czech Republic, Georgia, Germany, Hungary, Ireland, Latvia, Lithuania, Northmacedonia, Moldova, Montenegro, Poland, Romania, Russia, Serbia, Spain, Sweden, Ukraine

15 countries with >10 000 cycles in 2016

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Belgium	24 459	28 751	7 674	28 521	29 130	29 709	35 407	28 845	30 300	30 929
Bulgaria	-	-	-	-	-	-	-	-	-	11 009
Czech Republic	15 060	19 607	19 431	20 020	20 319	22 689	27 553	28 759	30 107	32 543
Denmark	14 067	13 476	14 992	15 954	14 560	15 171	15 143	16 167	17 454	17 696
France	67 572	68 446	74 475	79 427	85 253	85 487	84 214	90 434	93 918	104 773
Germany	62 322	69 902	67 349	62 571	67 354	71 251	76 422	81 177	96 512	99 226
Greece	-	-	-	-	-	-	18 278	24 120	27 149	NA
Italy	43 708	47 829	52 032	58 860	63 777	64 197	64 446	68 896	73 405	77 559
Norway	-	-	-	-	-	-	-	10 925	10 325	10 280
Poland	-	10 490	12 068	13 325	15 504	16 919	13 865	23 594	25 781	30 105
Russia	26 983	31 217	42 110	34 026	57 094	63 176	67 861	94 985	110 723	121 235
Spain	54 620	38 245	54 266	58 735	68 756	67 869	78 152	109 275	119 875	140 909
Sweden	15 061	16 107	16 714	17 628	18 562	18 077	18 266	18 213	18 603	18 989
Switzerland	-	-	-	-	-	-	-	-	10 038	10 960
The Netherlands	19 699	21 164	22 061	23 627	24 182	25 173	24 951	25 141	26 136	27 129
Ukraine	-	-	-	-	-	12 542	15 968	16 983	19 264	20 411
UK	46 688	50 555	54 314	57 856	60 377	60 621	61 728	63 504	NA	NA

Treatment cycles 2016

	2016
IVF	128 626
ICSI	359 858
FER	222 189
ED	64 892
PGD	23 421
IUI-H	151 020
IUI-D	44 300

488 484 ↓

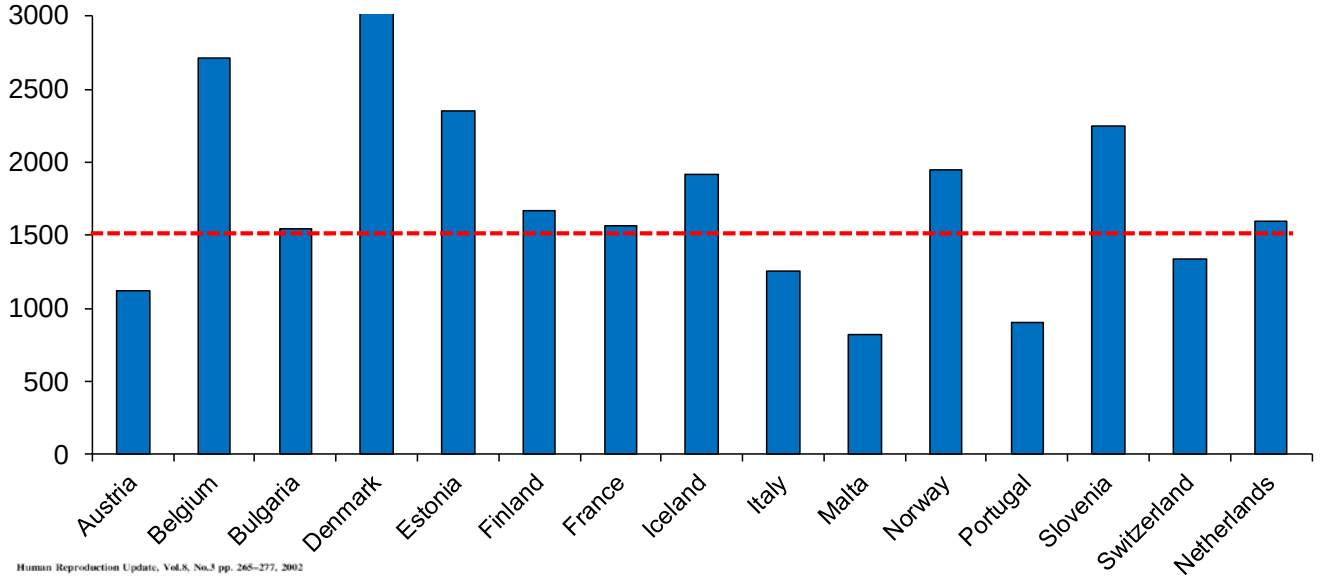
↑ ↑ ↑ ↓ ↓

Availability

Number of cycles per 1 million inhabitants

(countries with 100% participation)

10 out of 15 countries



Human Reproduction Update, Vol.8, No.3 pp. 265–277, 2002

An international survey of the health economics of IVF and ICSI

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The global need for ART is estimated to be at least 1.500 cycles/million population per year.

HRU 2002;8:1-9

Efficacy

Pregnancy rate (%) per aspiration 2016

	2016	2016 vs 2015
IVF	27.1	-1.4
ICSI	24.3	-1.9
FER	30.5	+1.3
ED	48.5	-1.1

FER: PR/thawing
ED : PR/fresh ET

Pregnancy rates (%) per aspiration IVF - 2016

Montenegro	57.1	Netherlands	31.0	Serbia	25.9
Lithuania	52.9	Russia	29.9	Iceland	25.6
Ireland *	40.4	Portugal	29.4	Estonia	25.2
Latvia	36.9	Sweden	29.3	Switzerland	24.3
Ukraine	36.8	Poland	29.3	Finland	23.8
Austria	33.9	Germany	28.8	Bulgaria	21.7
Northmacedonia	33.8	Norway	28.8	Italy	21.6
Slovenia	33.0	Belgium	27.8	France	21.1
Romania	31.6	Spain	26.3	Denmark	20.9

* Incomplete data for Ireland, no data ready for Armenia, Georgia, Greece and Hungary

Pregnancy rates (%) per aspiration ICSI - 2016

Lithuania	42.6	Austria	28.5	Switzerland	24.5
Moldova	41.9	Romania	28.3	Belgium	24.2
Serbia	41.4	Estonia	28.0	Finland	23.8
Albania	41.0	Latvia	27.5	Portugal	23.0
Ireland*	38.8	Sweden	27.4	Czech Republic	22.5
Northmacedonia	35.5	Germany	27.0	Denmark	22.5
Bosnia	33.8	Montenegro	27.0	Spain	22.4
Netherlands	32.9	Bulgaria	26.3	France	21.4
Iceland	30.2	Poland	26.0	Italy	18.7
Ukraine	30.1	Russia	25.9		
Norway	29.6	Slovenia	25.8		

* Incomplete data from Ireland, yet no data from Armenia, Georgia, Greece and Hungary

Pregnancy rate (%) per transfer 2016

	Total	Cleavage stage embryos*	Blastocyst embryos*
IVF	38.0	31.0	41.6
ICSI	38.2		
FER	31.4	28.2	40.3
ED	48.5	42.9	53.6

*Reported in 23 countries for IVF+ICSI, 19 countries for FER and 13 countries for ED

Egg donation, 2016

22 countries reported

	Fresh	FER	FOR
Transfers	24 194	29 502	11 196
Clinical pregnancies	11 744 (48.5%)	11 869 (40.2%)	4 902 (43.7%)
Deliveries	7 988 (33.0%)	7 993 (27.1%)	3 349 (29.9%)

Fresh: fresh embryo replacement
FER: frozen embryo replacement
FOR: frozen oocyte replacement

Embryo donation, 2016

12 countries reported

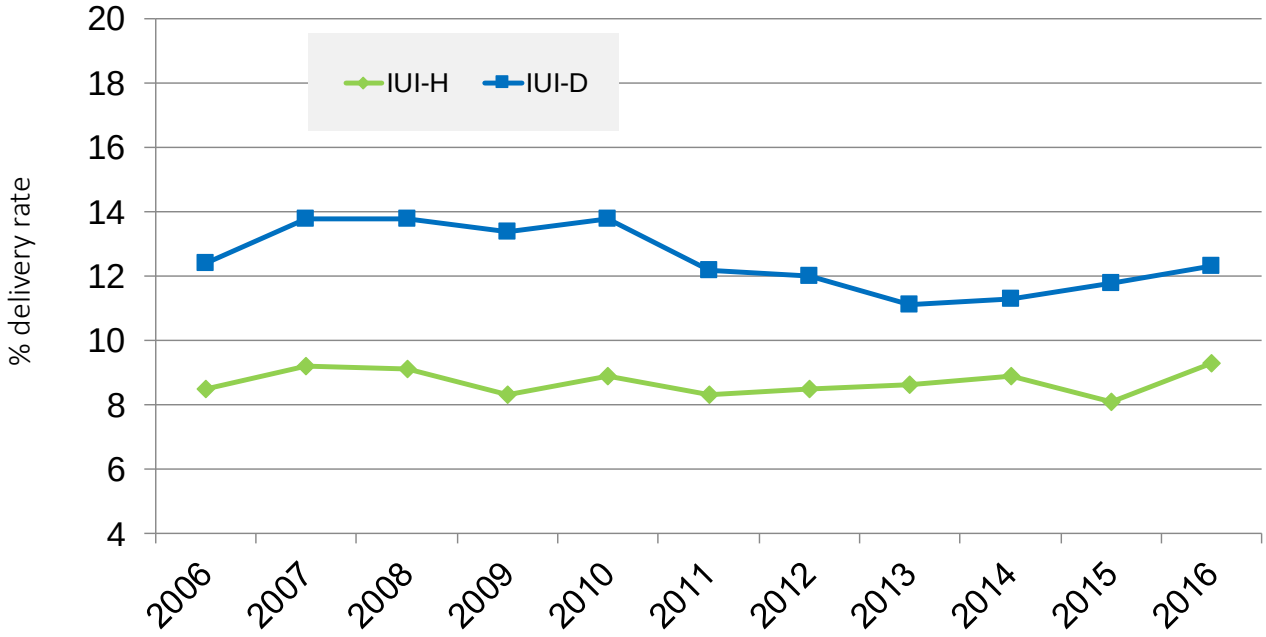
	n
Transfers	6 050
Clinical pregnancies	2 406 (39.8%)
Deliveries	1 623 (26.8%)

IUI-H and IUI-D, 2016

	Cycles	Deliveries	%
IUI-H ≤ 34 y.	56 919	5 572	9.8
IUI-H 35-39 y.	35 231	2 847	8.1
IUI-H ≥ 40 y.	9 372	343	3.7
Total*	151 020	14 016	9.3
IUI-D ≤ 34 y.	18 814	2 857	14.8
IUI-D 35-39 y.	16 608	1 834	10.9
IUI-D ≥ 40 y.	5 294	218	4.0
Total*	44 300	5 453	12.3

* Totals differ from the sum of the age categories as for some countries the age stratification is missing

IUI-H and IUI-D



Safety

Complications 2016

24 countries reported

	n	%	
OHSS	1 844	0.24	0.44 %
Bleeding	942	0.10	
Infection	113	0.01	
Maternal deaths	0	0.00	2
Fetal reductions	371	0.05	

Towards true surveillance and vigilance...

Introduction of the term „serious adverse event“, such as:

In medicine

- ✓ OHSS
- ✓ Multiple pregnancy/delivery
- ✓ Infection
- ✓ Bleeding
- ✓ Maternal Death

In embryology

- Mix up or loss of traceability of gametes and embryos
- Misdiagnosis in PGT
- Accidental loss of gametes and embryos
- Contamination with microagents

In treatment with donor gametes

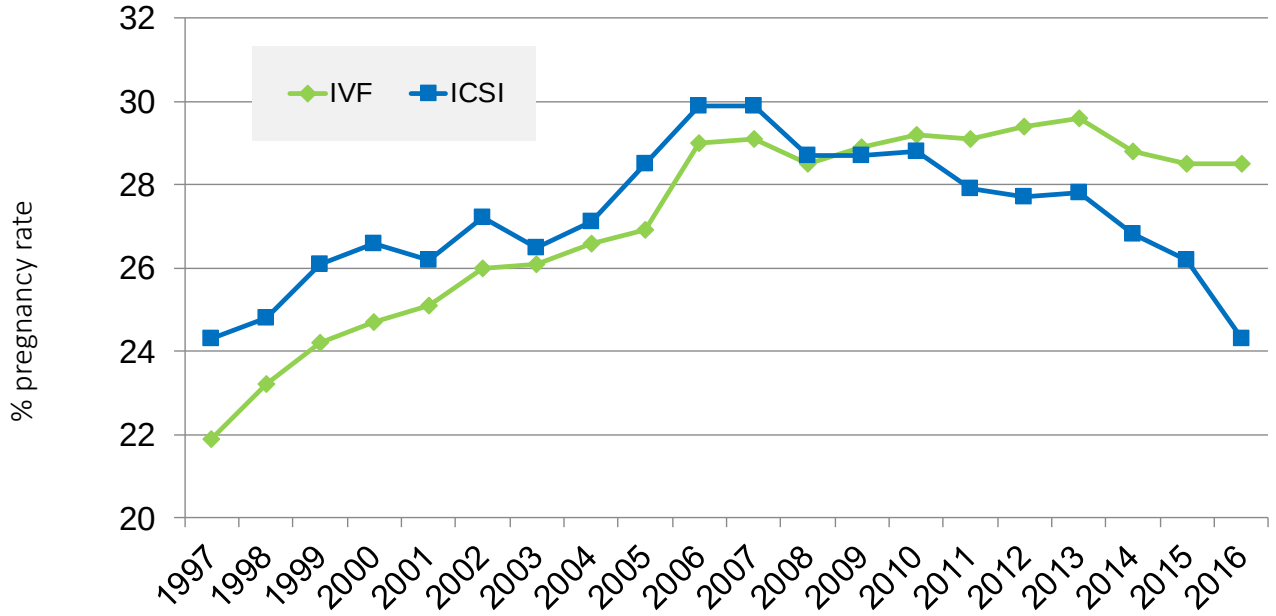
- Hereditary disease in the offspring

Guide to the quality and safety of tissues and cells for human application
EDQM, European Council

Quality and trends

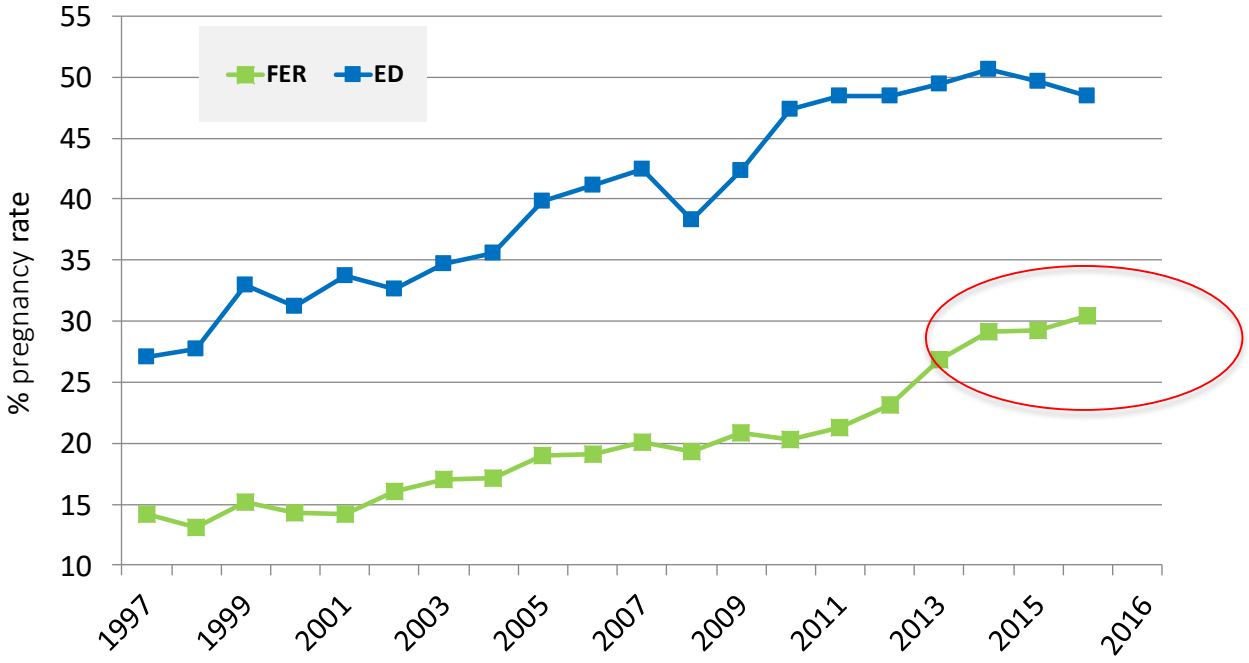
IVF / ICSI 1997-2016

Pregnancy rates per aspiration



FER: Pregnancy rate per thawing

ED : Pregnancy rate per transfer (fresh)

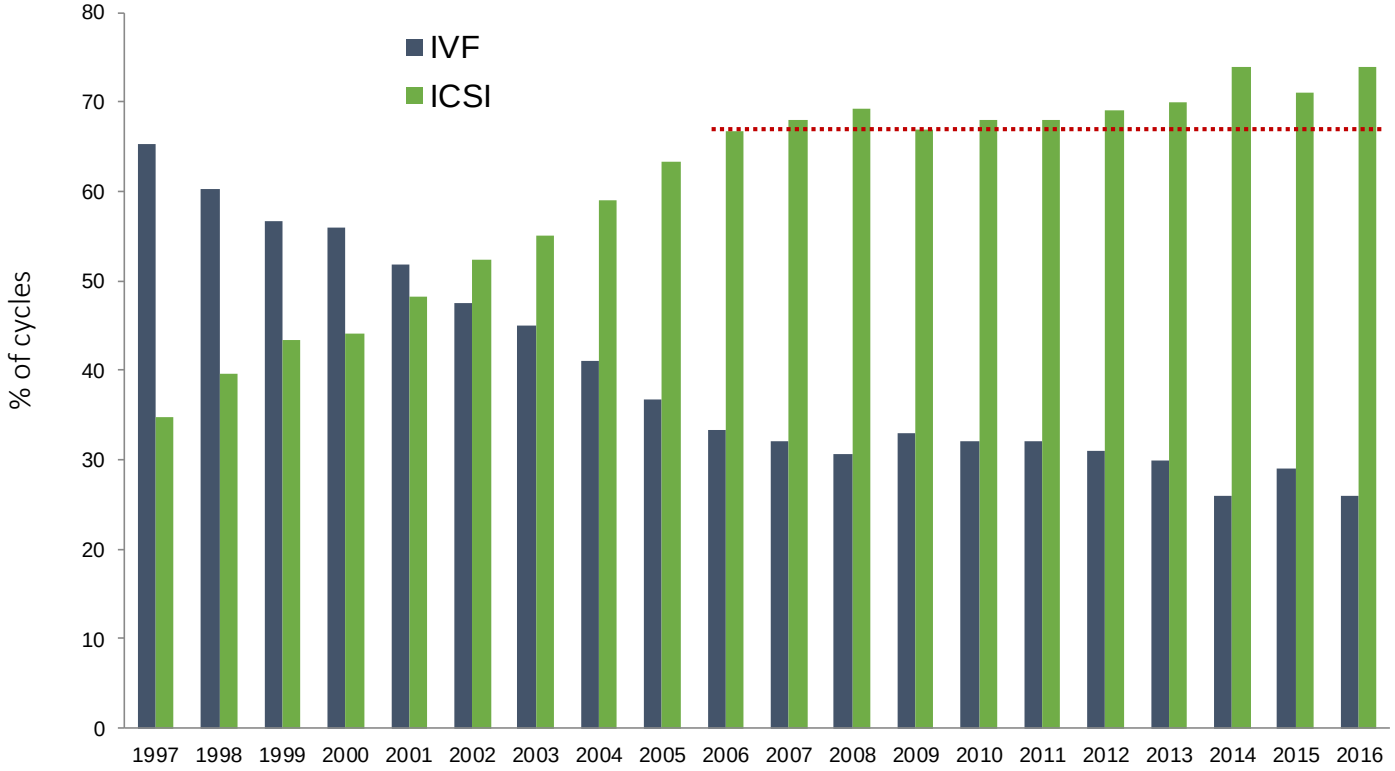


“Cumulative delivery rates” after fresh and FER

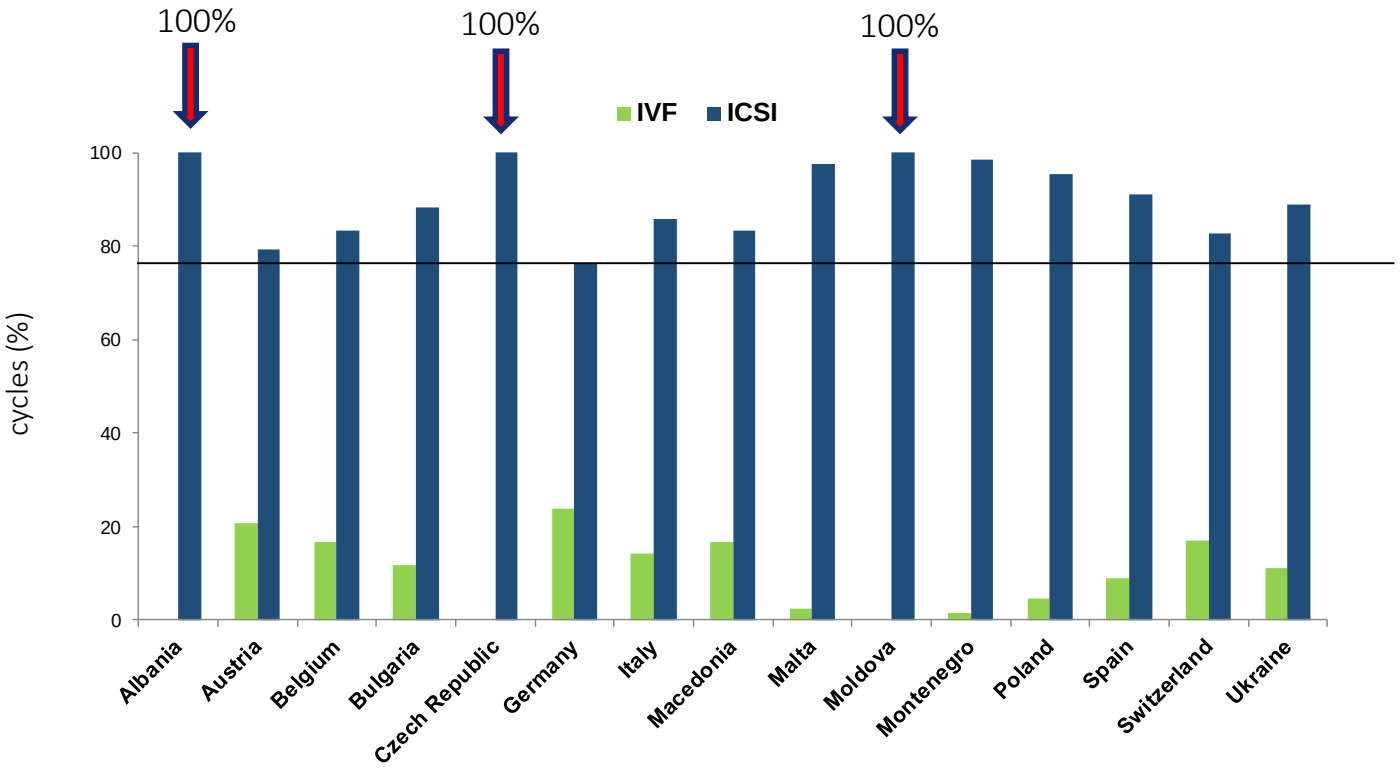
(treatments observed within 1 y.)

Country	Aspirations IVF-ICSI	Deliveries Fresh cycles (numbers)	Deliveries Fresh cycles per aspiration (%)	Deliveries Fresh and FER per aspiration (%)	Multiples Fresh and FER (%)
Finland	4 452	814	18.3	36.5	
Sweden	11 547	2746	23.8	40.3	2.9
Switzerland	5 579	1053	18.9	33.4	15.7
Northmacedonia	2 458	432	17.6	20.1	16.6
All	**451 129**	**83 344**	**18.5**	**28.9**	**12.7**

Distribution IVF/ICSI (1997-2016)

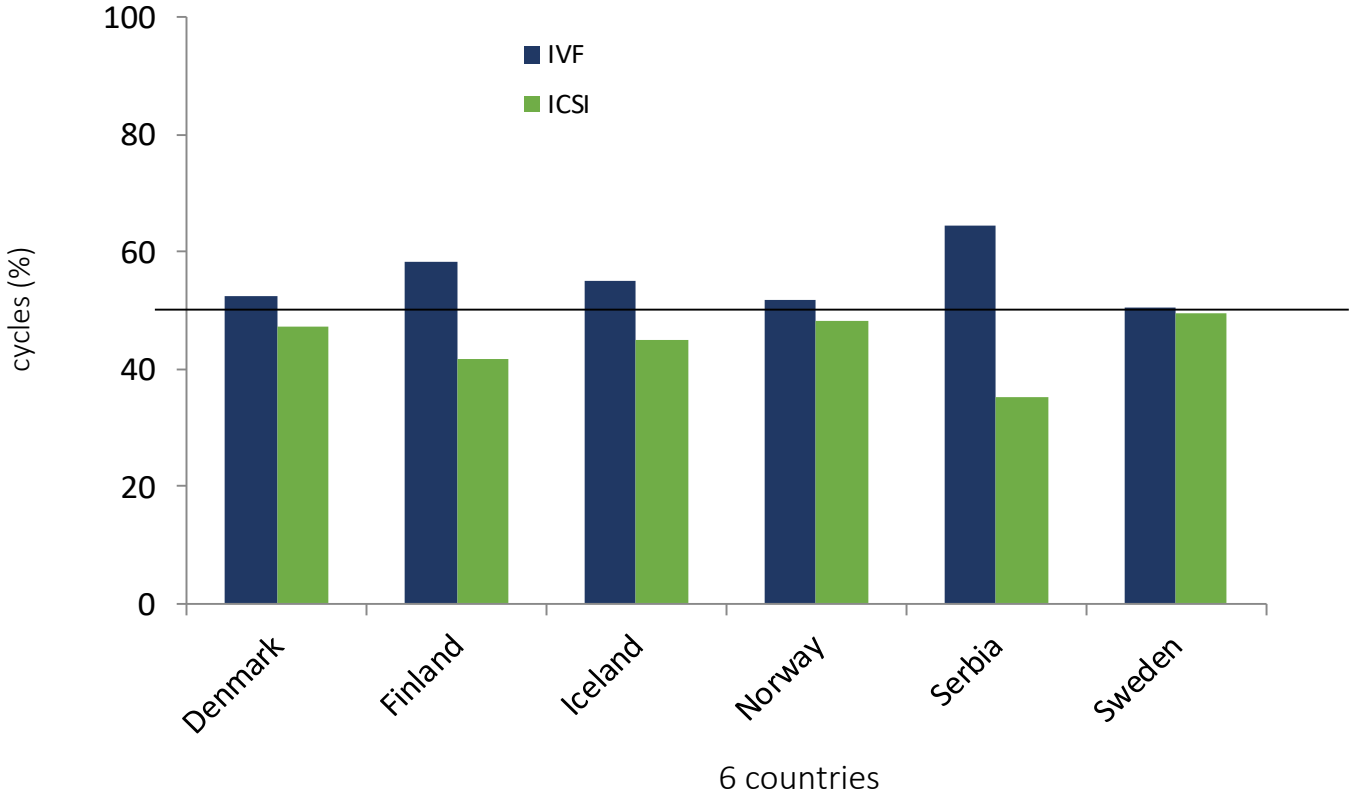


IVF versus ICSI – high use of ICSI (>75%) 2016

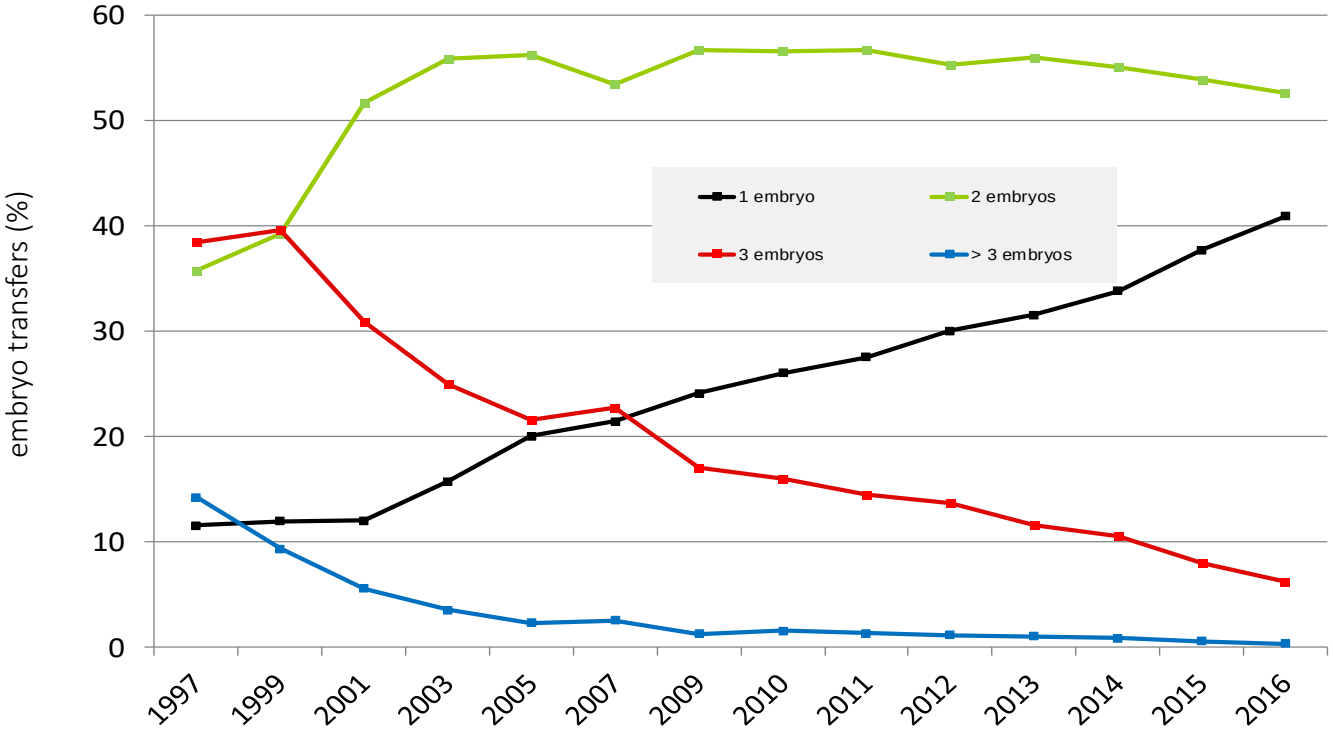


15 countries

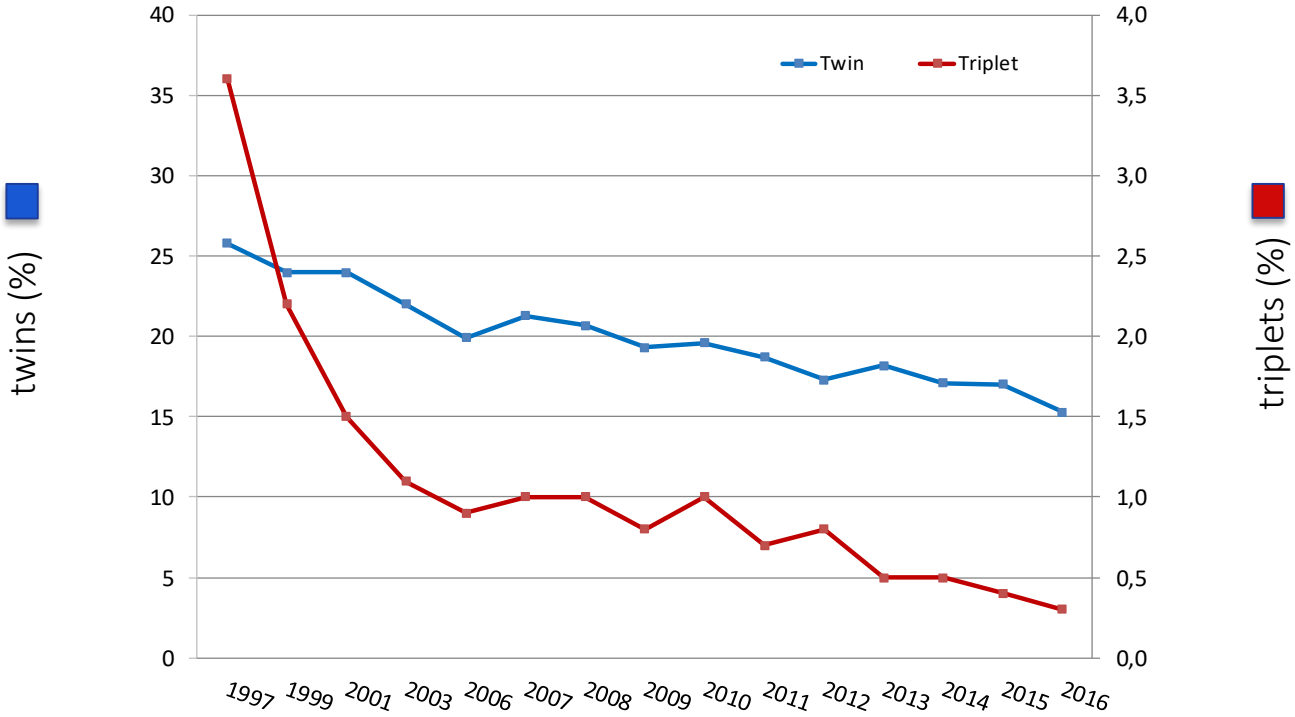
IVF versus ICSI – low use of ICSI (<50%) 2016



Number of transferred embryos in IVF/ICSI



Twin and triplet deliveries after IVF and ICSI



Percentage 3+ embryo transfers. IVF and ICSI, 2016

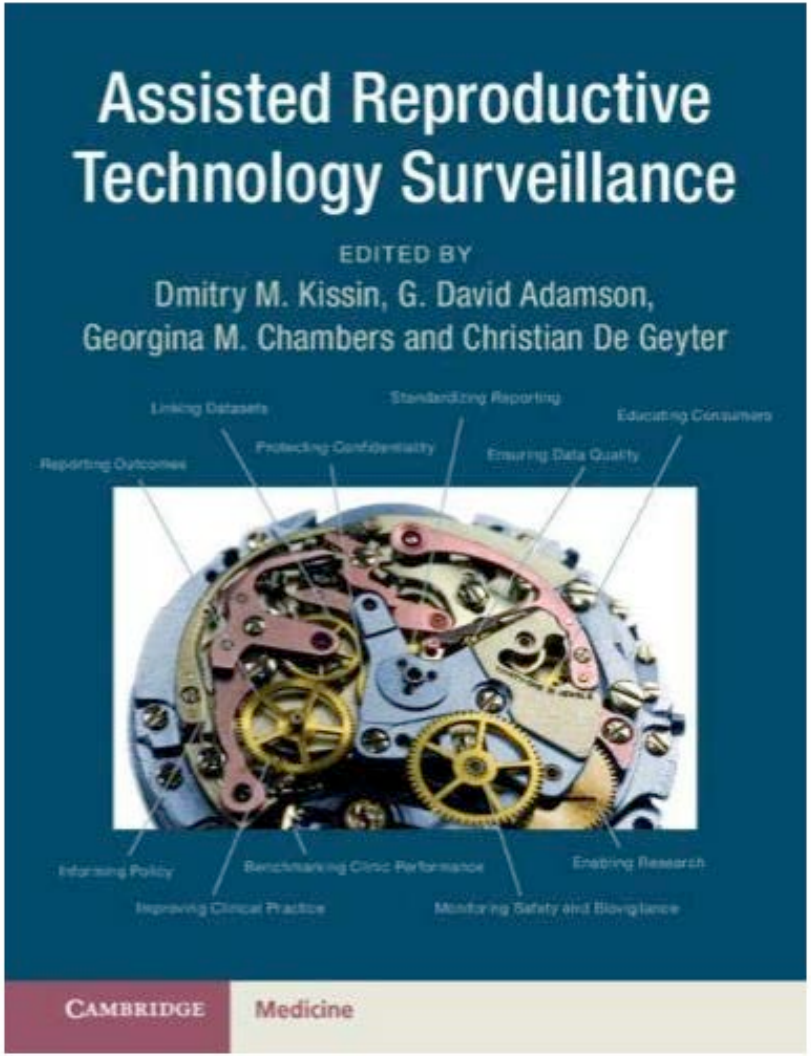
LOW < 5%	%
France	4.8
Spain	3.5
Russia	3.1
Bosnia-Herzegovina	3.0
Portugal	1.3
Czech Republic	0.6
Poland	0.6
Slovenia	0.4
Austria	0.3
Latvia	0.3
Denmark	0.2
Finland	0.0
Iceland	0.0
Albania	0.0
Sweden	0.0

HIGH > 30%	%
Lithuania	34.3
Montenegro	39.5
Serbia	60.4

Conclusions

- The EIM consortium is now active since 20 years
  and covers more than 85% of all European countries.

- The number of participating countries continues to fluctuate
  with a steady increase in the number of participating institutions.
- The use (elective) SET is on the rise, as are FER cycles.
- Pregnancy rates per aspiration after IVF and ICSI are stable,
  Whereas the efficacy of FER rises.
- Triplet+ and twin delivery rates are declining.
  No maternal deaths reported in 2016!
- Legal requirements and economic constraints have a relevant influence on the contribution of some countries to the EIM data collection. We should develop from a descriptive data registry to surveillance and vigilance in ART.



Kissin DM, Adamson GD, Chambers G, De Geyter C, Eds. Assisted Reproductive Technology Surveillance. Cambridge, United Kingdom: Cambridge University Press; 2019.

ESHRE EIM Consortium Steering Committee

Steering Committee 2017-2019

Edgar Mocanu, Tatjana Motrenko, Markus Kupka, Christine Wyns (chair-elect), Jesper Smeenk, Christian De Geyter (chair), Giulia Scaravelli, Carlos Calhaz-Jorge (past chair), Veerle Goossens (ESHRE Science Officer)