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D.I.R.-Annual 2015

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Preface

D.I.R Annual 2015 – The German IVF-Registry

V. Blumenauer, U. Czeromin, K. Fiedler, C. Gnoth, L. Happel, J.-S. Krüssel, M.S. Kupka, A. Tandler-Schneider

Once again it is our great pleasure to present the 2015 annual report of the data collected by the German IVF-Registry (D.I.R). The Registry looks back onto more than 30 years of diligent data collection, extraction, and evaluation.

Since 1996, the German IVF-Registry has been electronically collecting data for each initiated treatment cycle. Meanwhile, more than 1.2 million ART cycles (ART: Assisted Reproduction Technology) have been documented in the database. The prospective documentation as well as the cycle-by-cycle data collection are of particular value and make the German IVF-Registry unique world-wide.

By August 30, 2016, 130 of the 134 centers organized in the non-profit federal association D.I.R had reported their data to the German IVF-Registry. Because of technical hurdles in the centers, three could not export their data.

97,796 cycles have been documented. A total of 57,998 women were treated in 2015, resulting in a mean of 1.7 cycles per woman. We are happy to note that despite the grave changes in reimbursement regulations in 2004, the number of treatment cycles has since been increasing steadily. For IVF and ICSI, the pregnancy rate per embryo transfer was 31.9% – a slight increase from the 31.2% in 2014.

72.7% of the pregnancies led to a birth. A birth rate of 20.5% per oocyte treatment and 23.5% per embryo transfer has been achieved. For a 25 year old woman, the probability of becoming pregnant WITHOUT any medical assistance averages at 23%. For a 35 year old woman this probability decreases to 16%, according to the [Bundesgesundheitsblatt 2013; 56: 1633–41].

These data demonstrate the high quality of reproductive medicine in Germany, leading to impressive results even under the restrictive legislation: in accordance with the “Embryo Protection Act” of 1990, the elective single embryo transfer (eSET) is still unlawful in Germany. Egg donation is forbidden as well. Cryopreservation is allowed for usually 2-PN stage oocytes only. The regulation that only a maximum of three embryos may be transferred has certainly led to positive effects. Due to the increasing quality of stimulation, improved oocyte treatment, and changes in transfer technology, the average number of transferred embryos has decreased by more than 25% in fresh cycles since 1997. By transferring no more than an average of 1.86 embryos after IVF as well as ICSI, the doctors for reproductive medicine in Germany have continued to adhere to their responsible approach towards the reduction of multiples.

To improve the documentation of pregnancy outcomes, the quality offensive initiated already for the 2014-data collection, led to a remarkable additional decrease in the lost-for-follow-up rate for 2015: 94.4% pregnancy outcomes have been documented! 62% of the exporting centers have arrived at a documentation rate of more than 95% – a remarkable result. Good and diligent documentation is proof of a highly organized and efficient workflow. The prospective cycle-by-cycle data collection is another quality feature of the German IVF-Registry, a feature that sets the German IVF-Registry apart from any other registry in the world.

The results of the comprehensive data collection in the German IVF-Registry and its reports have been cited in numerous scientific publications, nationally as well as internationally, lending support and impetus to scientific research.

Furthermore, the data have contributed to the continuous improvement of quality within the German centers for reproductive medicine. Physicians, biologists, and patients alike have benefited from the tedious work necessary to collect, export, and evaluate as well as publish the data. Therefore, we express our gratitude to all those involved:

Thank you and keep up the good work!



Prof. Dr. med. Jan-Steffen Krüssel



Dr. med. Ute Czeromin
President of the Board



Dr. med. Andreas Tandler-Schneider



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D.I.R Annual 2015 – Tables

Number of Treatments in 2015

Centers for IVF-, ICSI-, and Cryo Transfer Treatments



Members of the German IVF-Registry 2015

n= 134

Registry Participants 2015*

n=130

Data Received by Deadline Aug 30 2016*

n=130

Documented Treatment Cycles

n=97,796 (100.0 %)

Plausible

n=96,124 (98.3%)

Prospective (all Cycles)

n=85,529 (89.0%)

Prospective (IVF, ICSI, IVF/ICSI)

n=55,985 (89.3%)

Number of Women Treated**

n=57,998

Mean Number of Treatment Cycles per Woman

1.7

Registry Participants 1982 – 2015

IVF-, ICSI- and Cryo Transfer Treatments



	1982	1986	1990	[...]	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015*
IVF	5	28	53	For values from 1991 to 2004 see www.deutsches-ivf- register.de	117	120	118	117	119	121	124	117	128	128	130
ICSI	0	0	0		117	120	118	120	119	124	128	120	130	128	130
Cryo	0	0	0		109	109	112	112	117	120	125	119	130	128	130
Total	5	28	53		117	121	118	120	121	124	128	120	130	128	130

*) Due to their technical prerequisites, three centers could not export their data

**) Base quantity: Total number of women, including implausible treatment cycles

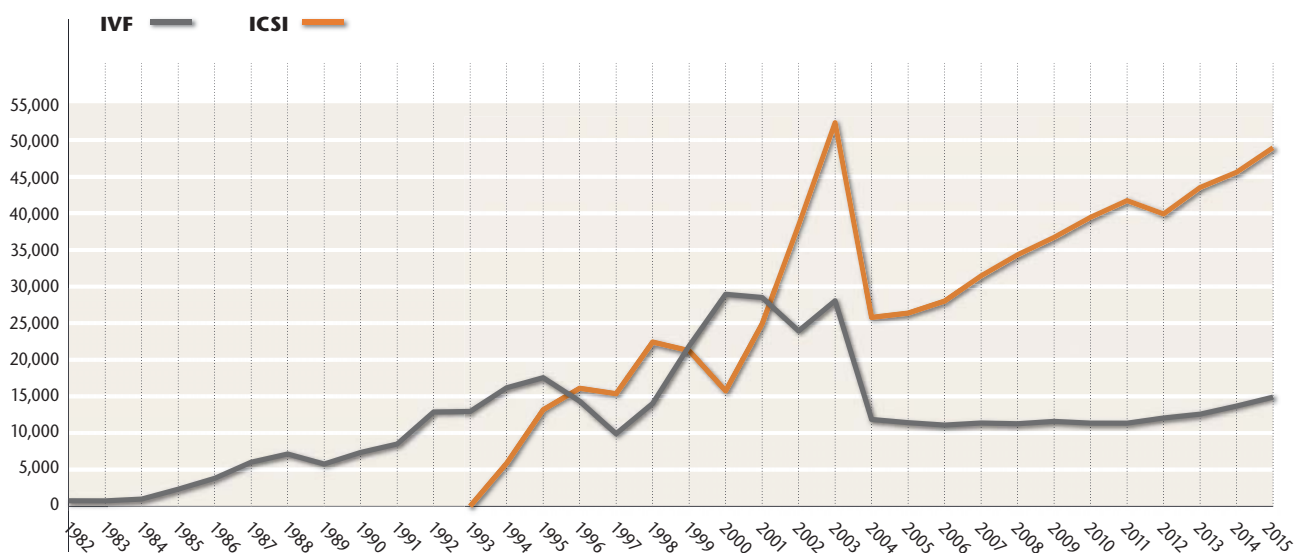
Total Number of Treatment Cycles 2015

IVF, ICSI, IVF/ICSI, Cryo Transfer – Prospective Data

	IVF	ICSI	IVF/ICSI	Cryo Transfer	No Treatment	Total
n	13,002	41,972	1,011	21,477	8,067	85,529
%	15.2	49.1	1.2	25.1	9.4	100.0

Number of Ovum Pick-up Cycles (OPU) 1982–2015

IVF, ICSI* – Prospective and Retrospective Data



	1982	1986	1990	[...]	2002	2003	2004	[...]	2011	2012	2013	2014	2015
IVF	742	3,806	7,343	For values from 1991 to 2001 see www.deutsches-ivf-register.de	23,936	28,058	11,848	For values from 2005 to 2010 see www.deutsches-ivf-register.de	11,341	12,047	12,569	13,675	14,900
ICSI					38,370	52,376	25,785		41,735	39,911	43,523	45,605	48,958
Total**	742	3,806	7,343		62,306	80,434	37,633		53,076	51,958	56,092	59,280	63,858

*) OPUs leading to an IVF- and/or ICSI oocyte treatment

Where IVF/ICSI is not explicitly mentioned, the treatments were added to ICSI.

Number of Treatments 1982–2015



IVF, ICSI, IVF/ICSI, Cryo Transfer – Prospective and Retrospective Data

	1982	1986	1990	[...]	2002	2003	2004	[...]	2011	2012	2013	2014	2015
IVF	742	3,806	7,343	For values from 1991 to 2001 see www.deutsches-ivf-register.de	23,936	28,058	11,848	For values from 2005 to 2010 see www.deutsches-ivf-register.de	11,341	12,047	12,569	13,675	14,900
ICSI					37,692	51,389	25,339		40,641	38,897	42,381	44,427	47,779
IVF/ICSI					678	987	446		1,094	1,014	1,142	1,178	1,179
Cryo					14,923	14,265	16,883		19,228	19,293	20,633	21,893	23,470
None*					9,802	11,133	4,928		6,618	6,117	6,708	7,210	8,796
Total**	742	4,201	8,653		87,044	105,854	59,448		78,922	77,368	83,433	88,383	96,124

From 1999 on each initiated cycle is documented.

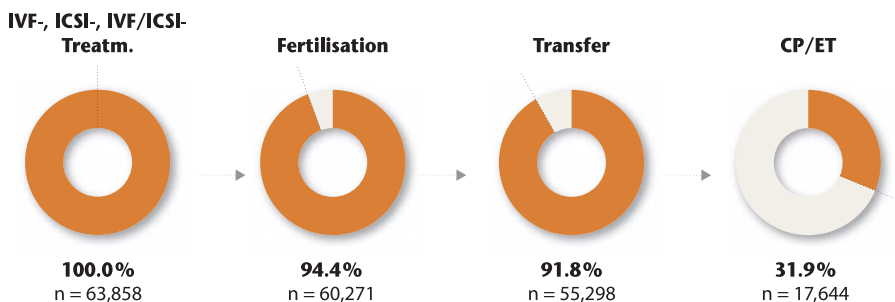
*) No treatment: treatments aborted prior to oocyte culture

**) "Total" may contain GIFT cases. Documentation has been neglected since 2005 due to lack of statistical relevance

Summary of Statistics in Brief 2015 – CoD Aug 30 2016



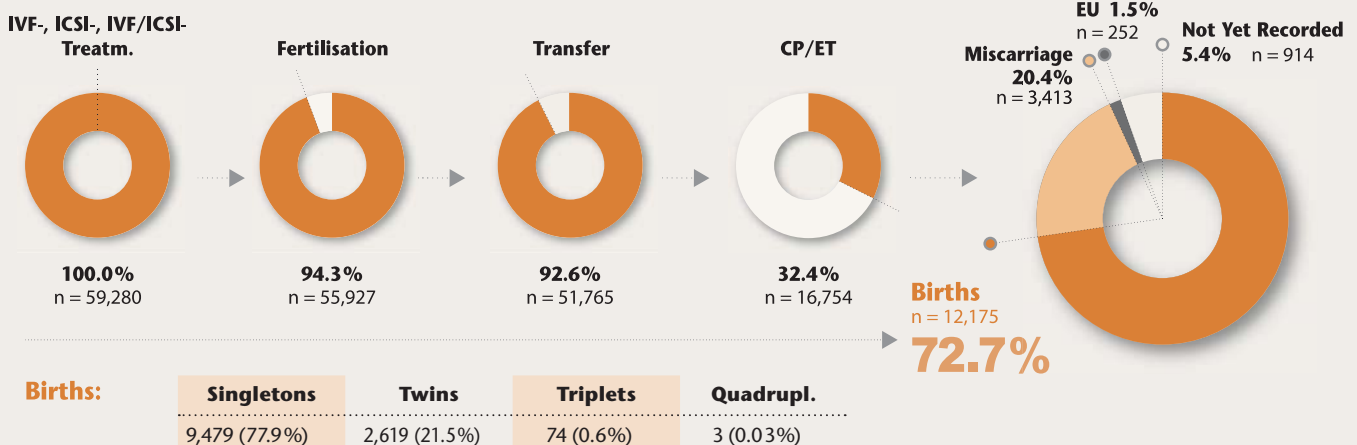
IVF, ICSI and IVF/ICSI – Prospective and Retrospective Data



Summary of Statistics in Brief 2014 – CoD Aug 30 2016

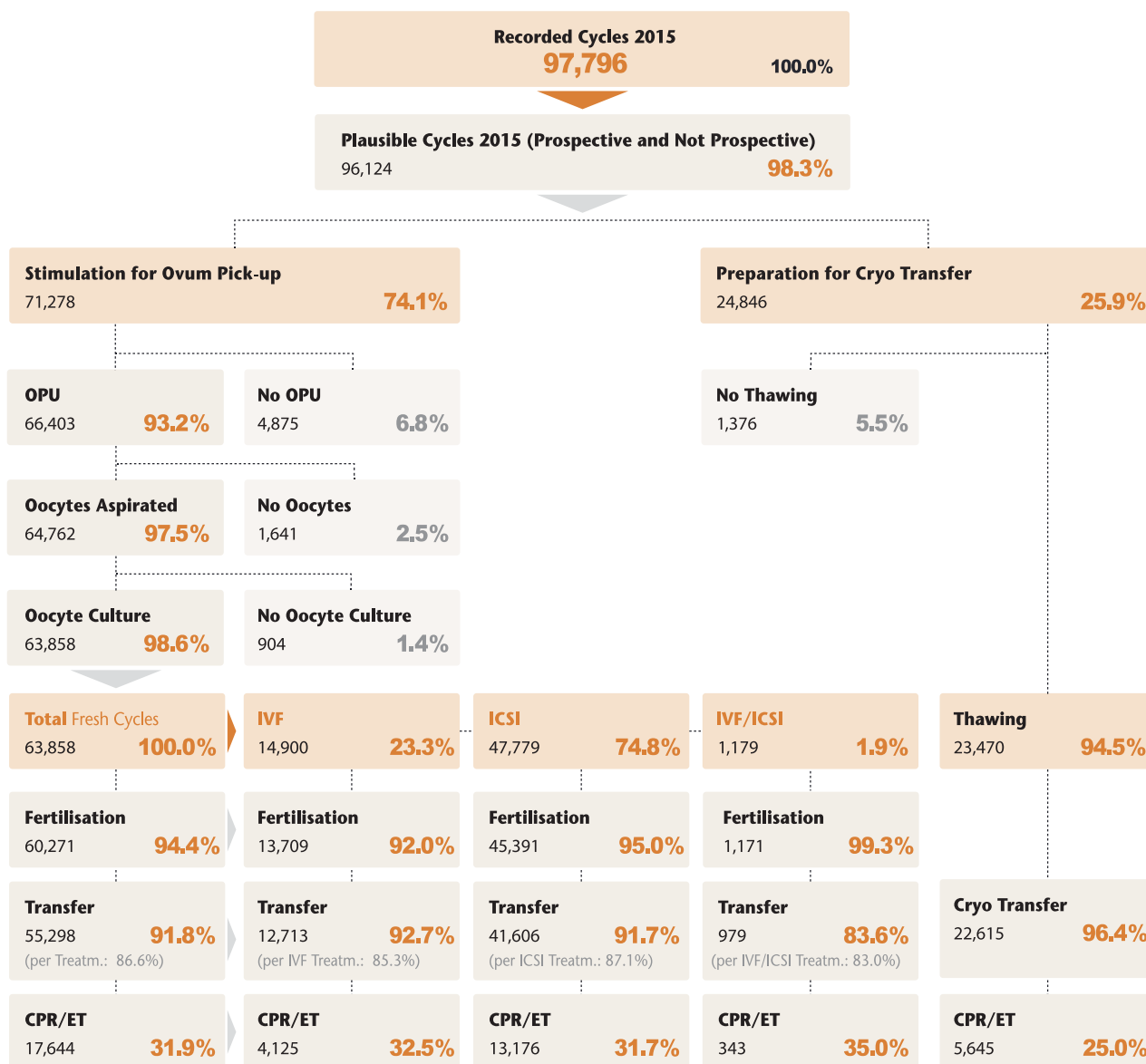


IVF, ICSI and IVF/ICSI – Prospective and Retrospective Data



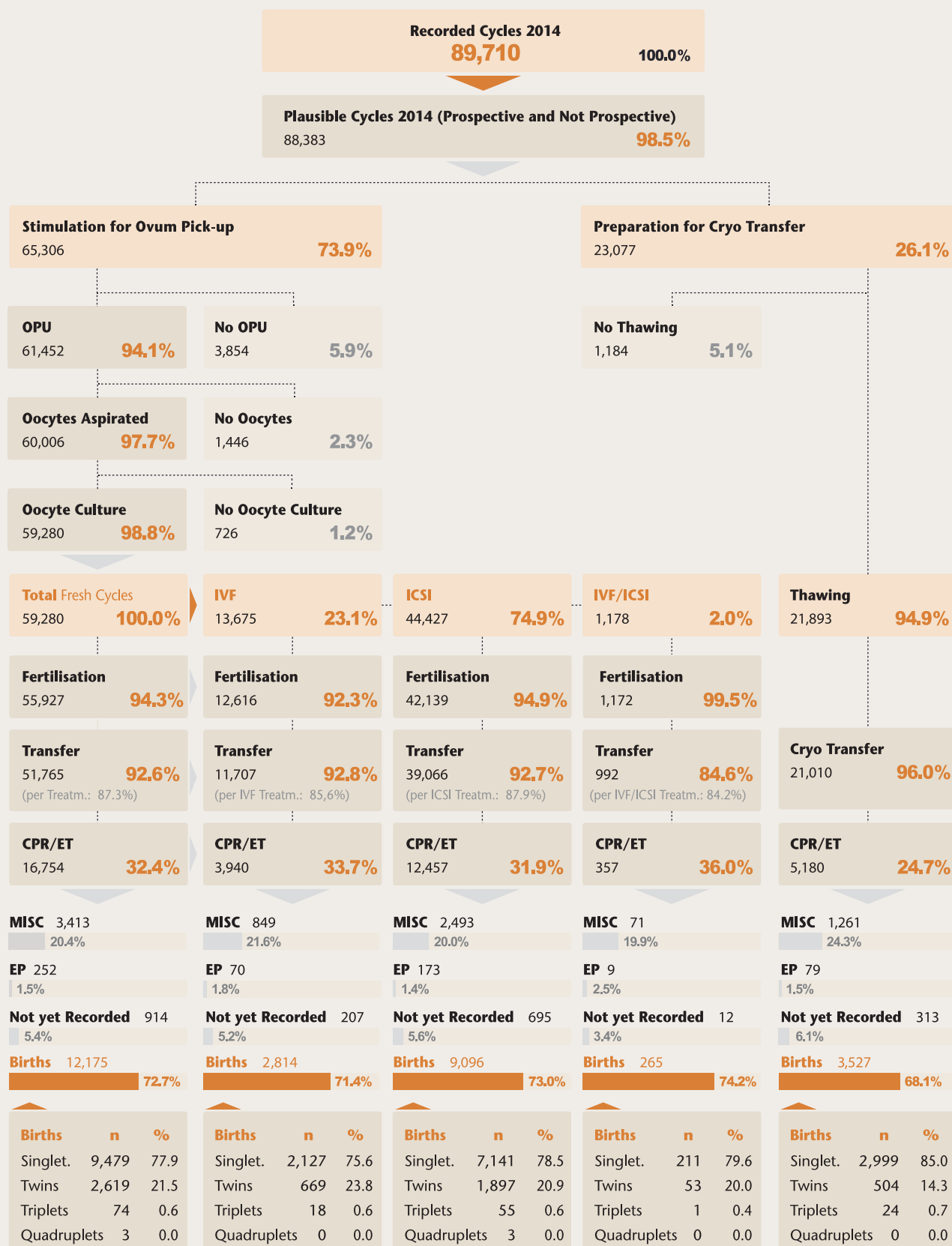
D·I·R Statistics in Brief 2015 – CoD Aug 30 2016

German IVF Registry – Prospective and Retrospective Data



D·I·R Statistics in Brief 2014 – CoD Aug 30 2016

German IVF Registry



Clinical Pregnancies (CP), Miscarriages (MISC), Ectopic Pregnancies (EP), and Still Births (SB) 2014

Prospective and Retrospective Data

Birth Rate/Transfer for patients with two embryos transferred and a surplus of at least two 2-PN-stage embryos:
IVF 22.7%, ICSI 22.0%, IVF/ICSI 26.0%

	IVF		ICSI		IVF/ICSI		Cryo Transfer	
	n	%	n	%	n	%	n	%
Treatment Cycles	13,675		44,427		1,178		21,893	
Treatm. with Doc. Preg. Outcome	13,468		43,731		1,166		21,580	
Clinical Pregnancies	3,940	100.0	12,457	100.0	357	100.0	5,180	100.0
No Information	207	5.2	695	5.6	12	3.4	313	6.1
Live Births	2,814	71.4	9,096	73.0	265	74.2	3,527	68.1
Miscarriages	849	21.6	2,493	20.0	71	19.9	1,261	24.3
included above: induced abortions and fetal reduction*	50 (60)		162 (226)		5 (8)		75 (100)	
Ectopic Pregnancies	70	1.8	173	1.4	9	2.5	79	1.5
Children	3,519		11,112		320		4,079	
Still Births**	32	0.8	93	0.7	3	0.8	15	0.3
Malformations	49	1.2	132	1.1	1	0.3	58	1.1
Baby-Take-Home-Rate***		20.6		20.5		22.5		16.1
		20.9 ¹		20.8 ¹		22.7 ¹		16.3 ¹
		21.7 ²		21.6 ²		23.3 ²		17.0 ²

*) Number of cycles in which an induced abortion was documented. A more detailed differentiation cannot be supplied at this time.
The brackets contain the number of embryos

**) Number of still births in relation to the number of children born

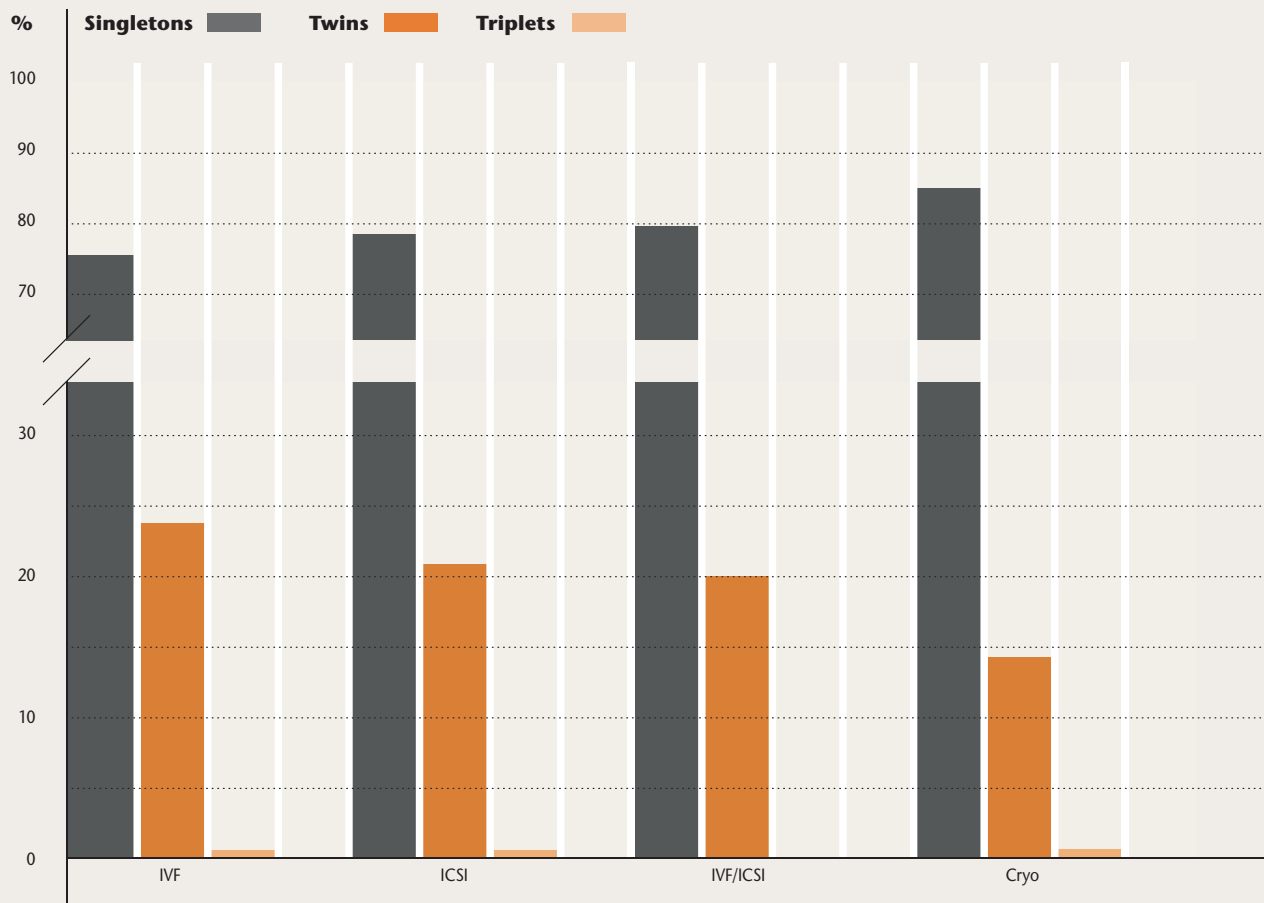
***) Percentage of births per number of treatments

¹⁾ Cycles with unknown pregnancy outcome were subtracted from the base quantity (see „Treatments with documented pregnancy outcome“)

²⁾ For cycles with unknown pregnancy outcome, the probable birth rate (births/pregnancy) was calculated and added to the number of known births

Multiple Births 2014

Prospective and Retrospective Data



	IVF			ICSI			IVF/ICSI			Cryo Transfer		
	n	%	%	n	%	%	n	%	%	n	%	%
CP/ET	3,940	100.0		12,457	100.0		357	100.0		5,180	100.0	
Births	2,814	71.4	100.0	9,096	73.0	100.0	265	74.2	100.0	3,527	68.1	100.0
Singletons	2,127	54.0	75.6	7,141	57.3	78.5	211	59.1	79.6	2,999	57.9	85.0
Twins	669	17.0	23.8	1,897	15.2	20.9	53	14.8	20.0	504	9.7	14.3
Triplets	18	0.5	0.6	55	0.4	0.6	1	0.3	0.4	24	0.5	0.7
Quadruplets	0	0.0	0.0	3	0.0	0.0	0	0.0	0.0	0	0.0	0.0
No Information	207	5.2		695	5.6		12	3.4		313	6.1	
Miscarriages	849	21.6		2,493	20.0		71	19.9		1,261	24.3	
EPs	70	1.8		173	1.4		9	2.5		79	1.5	

Births as a Function of Number of Embryos Transferred and Age Groups 2000 – 2014

IVF, ICSI, IVF/ICSI, Cryo Transfer – Prospective and Retrospective Data

Woman's Age in Years		Singletons		Twins		Triplets		Quadruplets		Total
		n	%	n	%	n	%	n	%	n
<= 24	1 Embryo	171	97.7	4	2.3	0	0.0	0	0.0	175
	2 Embryos	1,719	76.4	521	23.2	10	0.4	0	0.0	2,250
	3 Embryos	278	67.6	111	27.0	20	4.9	2	0.5	411
	Total	2,168	76.4	636	22.4	30	1.1	2	0.1	2,836
25 – 29	1 Embryo	2,072	96.0	81	3.8	6	0.3	0	0.0	2,159
	2 Embryos	18,046	75.4	5,788	24.2	111	0.5	2	0.0	23,947
	3 Embryos	2,782	68.7	1,039	25.7	224	5.5	3	0.1	4,048
	Total	22,900	75.9	6,908	22.9	341	1.1	5	0.0	30,154
30 – 34	1 Embryo	5,321	96.7	177	3.2	7	0.1	0	0.0	5,505
	2 Embryos	39,735	76.3	12,117	23.3	223	0.4	3	0.0	52,078
	3 Embryos	8,060	70.8	2,848	25.0	469	4.1	7	0.1	11,384
	Total	53,116	77.0	15,142	22.0	699	1.0	10	0.0	68,967
35 – 39	1 Embryo	5,591	97.1	160	2.8	6	0.1	0	0.0	5,757
	2 Embryos	30,272	82.3	6,399	17.4	111	0.3	2	0.0	36,784
	3 Embryos	11,191	76.8	3,047	20.9	338	2.3	2	0.0	14,578
	Total	47,054	82.4	9,606	16.8	455	0.8	4	0.0	57,119
>= 40	1 Embryo	1,320	95.7	57	4.1	2	0.1	0	0.0	1,379
	2 Embryos	4,454	90.4	462	9.4	9	0.2	1	0.0	4,926
	3 Embryos	3,147	87.1	445	12.3	23	0.6	0	0.0	3,615
	Total	8,921	89.9	964	9.7	34	0.3	1	0.0	9,920

Total number of births 2000 – 2014: 168,996

Births as a Function of Number of Embryos Transferred and Treatment Method 2000 – 2014



Prospective and Retrospective Data

IVF

	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	
1 Embryo	2,753	98.4	41	1.5	4	0.1	0	0.0	2,798
2 Embryos	21,930	77.0	6,438	22.6	112	0.4	1	0.0	28,481
3 Embryos	6,222	68.5	2,467	27.2	382	4.2	6	0.1	9,077
Total	30,905	76.6	8,946	22.2	498	1.2	7	0.0	40,356

ICSI

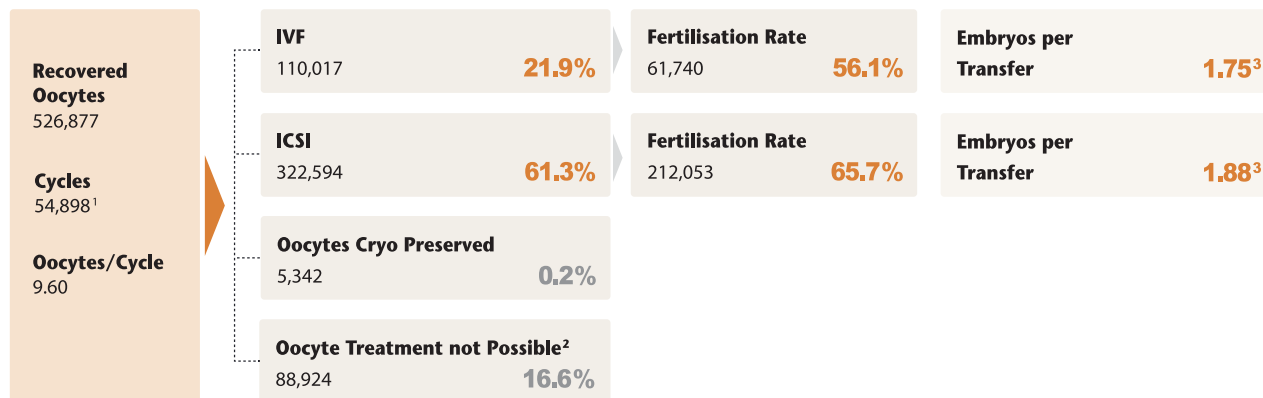
	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	
1 Embryo	7,409	98.3	119	1.6	11	0.1	0	0.0	7,539
2 Embryos	54,568	78.1	15,058	21.6	233	0.3	4	0.0	69,863
3 Embryos	14,031	75.2	4,046	21.7	568	3.0	9	0.0	18,654
Total	76,008	79.1	19,223	20.0	812	0.8	13	0.0	96,056

Cryo Transfer

	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	
1 Embryo	3,381	97.6	75	2.2	6	0.2	0	0.0	3,462
2 Embryos	16,673	85.0	2,860	14.6	76	0.4	0	0.0	19,609
3 Embryos	5,213	77.6	1,365	20.3	142	2.1	1	0.0	6,721
Total	25,267	84.8	4,300	14.4	224	0.8	1	0.0	29,792

Fertilisation Rate 2015

IVF and ICSI – Prospective Data



Embryos per Transfer³ and Children After IVF, ICSI 1997 – 2014

Prospective and Retrospective Data

		1997	[...]	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
IVF	Embryos Transf.	2.49	For values from 1998 to 2003 see www.deutsches-ivf-register.de	2.15	2.11	2.08	2.08	2.06	2.03	2.01	1.95	1.88	1.86	1.75
	Children/Transf.	0.21		0.23	0.24	0.25	0.25	0.24	0.24	0.22	0.17	0.26	0.32	0.30
	Children/Deliv.	1.31		1.25	1.23	1.23	1.24	1.24	1.22	1.24	1.26	1.22	1.08	1.25
ICSI	Embryos Transf.	2.56		2.15	2.11	2.09	2.08	2.08	2.06	2.05	1.98	1.91	1.88	1.88
	Children/Transf.	0.22		0.23	0.24	0.24	0.24	0.23	0.23	0.22	0.16	0.25	0.28	0.29
	Children/Deliv.	1.29		1.22	1.22	1.20	1.21	1.22	1.21	1.21	1.22	1.21	1.22	1.22
Cryo-Transfer	Embryos Transf.	2.34		2.14	2.10	2.10	2.07	2.07	2.05	2.04	1.96	1.79	1.65	1.67
	Children/Transf.	0.10		0.12	0.14	0.14	0.14	0.14	0.14	0.14	0.11	0.16	0.19	0.19
	Children/Deliv.	1.14		1.17	1.16	1.16	1.16	1.15	1.16	1.16	1.18	1.16	1.16	1.16

1) In 814 cases no IVF- or ICSI treatment was performed. 273 are cases in which oocytes were recovered but nevertheless a cryo transfer was performed

2) Reason: e.g. immature oocytes or no sperm available

3) Mean

Distribution of Indications 2015

IVF and ICSI – Prospective Data

IVF

Male Factor ▶	Normal		Reduced Semen Quality		Other**		Total	
Female Factor ▼	n	%	n	%	n	%	n	%
Normal	1,328	11.4	591	5.1	989	8.5	2,908	25.0
Tubal Pathology	1,698	14.6	406	3.5	644	5.5	2,748	23.6
Endometriosis	709	6.1	215	1.8	449	3.9	1,373	11.8
Hyperandrog./PCO	333	2.9	119	1.0	185	1.6	637	5.5
Ovulatory Dysf.	434	3.7	218	1.9	208	1.8	860	7.4
Psychogen. Factors	135	1.1	38	0.3	88	0.8	261	2.2
Other*	679	5.8	507	4.3	1,237	10.6	2,423	20.7
No Information	23	0.2	8	0.1	413	3.5	444	3.8
Total	5,339	45.8	2,102	18.0	4,213	36.2	11,654	100.0

ICSI

Male Factor ▶	Normal		Reduced Semen Qual.		Azoospermia		Other**		Total	
Female Factor ▼	n	%	n	%	n	%	n	%	n	%
Normal	880	2.2	10,580	27.0	1,083	2.8	3,831	9.8	16,374	41.8
Tubal Pathology	429	1.1	1,621	4.1	68	0.2	682	1.7	2,800	7.1
Endometriosis	282	0.7	1,525	3.9	62	0.2	766	2.0	2,635	6.8
Hyperandrog./PCO	148	0.4	1,070	2.7	58	0.1	542	1.4	1,818	4.6
Ovulatory Dysf.	208	0.5	1,788	4.6	118	0.3	690	1.7	2,804	7.1
Psychogen. Factors	72	0.2	479	1.2	51	0.1	216	0.6	818	2.1
Other*	553	1.4	4,535	11.6	286	0.7	4,158	10.6	9,532	24.3
No Information	34	0.1	84	0.2	11	0.0	2,320	5.9	2,449	6.2
Total	2,606	6.6	21,682	55.3	1,737	4.4	13,205	33.7	39,230	100.0

*) The indications "sperm antibodies" and "cervical factor" are included here

**) The indication "pathological function test" is included here

IVF and ICSI – Results 2014

Prospective Data

IVF 2014

	n	%	Fertilisation %	Embryo %	Transfer %	Clin. Preg. %
Performed IVF Treatm.	11,654	100.0				
Successful Fertilis.*	10,741	92.2	100.0			
Minimum 1 Embryo	10,426	89.5	97.1	100.0		
ET Performed	10,114	86.8	94.2	97.0	100.0	
Clin. Pregnancy	3,438	29.5	32.0	33.0	34.0	100.0
Birth	2,466					71.7
Miscarriage	734					21.3
Ectopic Pregnancy	65					1.9
Not Yet Recorded	173					5.0

ICSI 2014

	n	%	Fertilisation %	Embryo %	Transfer %	Clin. Preg. %
Performed ICSI Treatm.	39,230	100.0				
Successful Fertilis.*	37,274	95.0	100.0			
Minimum 1 Embryo	35,653	90.9	95.7	100.0		
ET Performed	34,730	88.5	93.2	97.4	100.0	
Clin. Pregnancy	11,240	28.7	30.2	31.5	32.4	100.0
Birth	8,226					73.2
Miscarriage	2,255					20.1
Ectopic Pregnancy	163					1.5
Not Yet Recorded	596					5.3

*) Successful fertilisation of at least one oocyte per cycle

TESE and Cryo Transfer – Results 2014

Prospective Data

ICSI/TESE 2014

	n	%	Fertilisation %	Embryo %	Transfer %	Clin. Preg. %
ICSI	2,107	100.0				
Successful Fertilis.*	1,925	91.4	100.0			
Minimum 1 Embryo	1,833	87.0	95.2	100.0		
ET Performed	1,808	85.8	93.9	98.6	100.0	
Clin. Pregnancy	531	25.2	27.6	29.0	29.4	100.0
Birth	398					75.0
Miscarriage	106					20.0
Ectopic Pregnancy	11					2.0
Not Yet Recorded	16					3.0

Cryo Transfer 2014

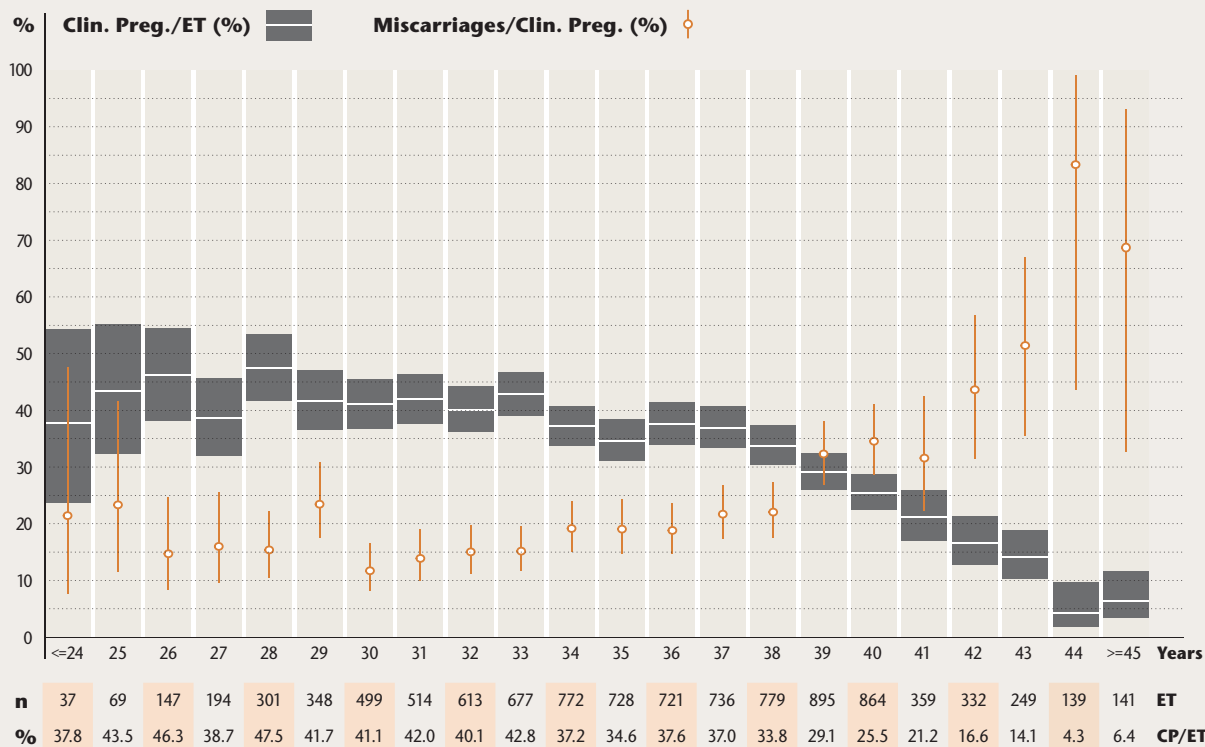
	n	%	PN %	Transfer %	Clin. Preg. %
Cryo Transfer Cycles	19,693	100.0			
Thawed PN	19,390	98.5	100.0		
ET Performed	18,907	96.0	97.5	100.0	
Clin. Pregnancy	4,661	23.7	24.0	24.7	100.0
Birth	3,225				69.2
Miscarriage	1,119				24.0
Ectopic Pregnancy	73				1.6
Not Yet Recorded	244				5.2

*) Successful fertilisation of at least one oocyte per cycle

Pregnancy Rate as a Function of Female Age 2014

Prospective Data

IVF 2014



Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	1,271	3,502	4,420	989	432	394	290	177	179	11,654
Oocytes ¹	11.4	10.6	8.6	7.2	6.3	6.4	5.0	5.1	9.6	9.0
Insemination ¹	11.2	10.4	8.4	7.1	6.2	6.3	4.9	5.0	4.6	8.9
ET	1,096	3,075	3,859	864	359	332	249	139	141	10,114
ET/OPU %	86.2	87.8	87.3	87.4	83.1	84.3	85.9	78.5	86.8	86.8
Trans. Embr. ¹	1.83	1.85	1.86	1.89	1.89	1.89	1.82	1.85	1.98	1.86
CP	475	1,244	1,318	220	76	55	35	6	9	3,438
CP/OPU %	37.4	35.5	29.8	22.2	17.6	14.0	12.1	3.4	5.0	29.5
CP/ET upper Confidence Limit* %	46.4	42.2	35.8	28.7	26.0	21.3	18.8	9.7	11.7	35.0
CP/ET %	43.3	40.5	34.2	25.5	21.2	16.6	14.1	4.3	6.4	34.0
CP/ET lower Confidence Limit* %	40.4	38.7	32.6	22.5	17.0	12.7	10.3	1.9	3.4	33.0
CP/ET %: 2 Embr.transf. + min. 2 2-PN surplus	44.6	43.2	37.1	30.2	24.5	20.1	19.1	4.4	6.4	37.3

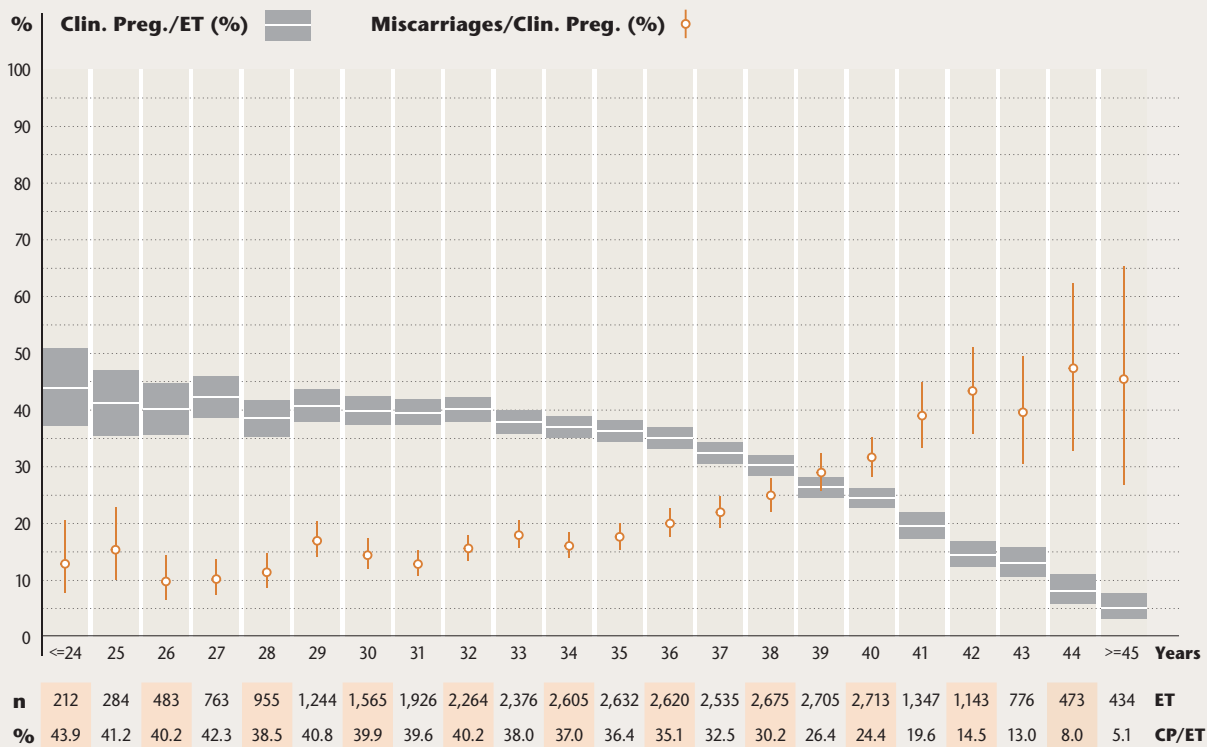
1) Mean

* With a 95%-probability, the true mean lies within the defined confidence interval.

Pregnancy Rate as a Function of Female Age 2014

Prospective Data

ICSI 2014



n	212	284	483	763	955	1,244	1,565	1,926	2,264	2,376	2,605	2,632	2,620	2,535	2,675	2,705	2,713	1,347	1,143	776	473	434	ET
%	43.9	41.2	40.2	42.3	38.5	40.8	39.9	39.6	40.2	38.0	37.0	36.4	35.1	32.5	30.2	26.4	24.4	19.6	14.5	13.0	8.0	5.1	CP/ET

Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	4,366	11,854	14,700	3,103	1,556	1,343	949	597	632	39,100
Oocytes ¹	12.1	11.1	9.1	7.6	6.9	6.5	5.2	5.6	4.2	9.5
Insemination ¹	9.2	8.6	7.1	6.0	5.3	5.1	4.3	4.4	3.5	7.4
ET	3,941	10,736	13,167	2,713	1,347	1,143	776	473	434	34,730
ET/OPU %	90.3	90.6	89.6	87.4	86.6	85.1	81.8	79.2	68.7	88.8
Trans. Embr. ¹	1.85	1.86	1.86	1.89	1.88	1.88	1.82	1.82	1.65	1.86
CP	1,602	4,162	4,222	663	264	166	101	38	22	11,240
CP/OPU %	36.7	35.1	28.7	21.4	17.0	12.4	10.6	6.4	3.5	28.8
CP/ET upper Confidence Limit* %	42.2	39.7	32.9	26.2	22.0	16.9	15.8	11.0	7.7	32.9
CP/ET %	40.6	38.8	32.1	24.4	19.6	14.5	13.0	8.0	5.1	32.4
CP/ET lower Confidence Limit* %	39.1	37.8	31.2	22.7	17.4	12.4	10.6	5.8	3.3	31.8
CP/ET %: 2 Embr.transf. + min. 2 2-PN surplus	41.8	41.2	35.1	27.4	22.7	17.6	18.4	9.2	8.1	35.6

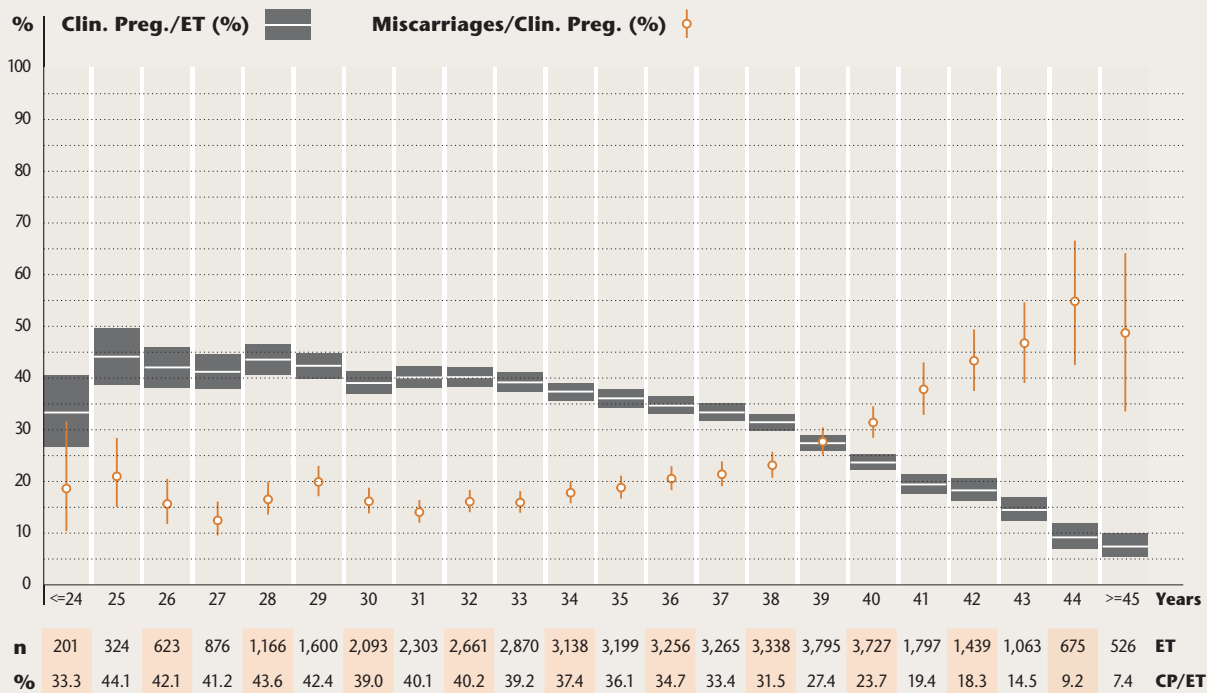
1) Mean

* With a 95%-probability, the true mean lies within the defined confidence interval.

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2010 – 2014

Prospektive Daten

IVF 2010 – 2014



Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	5,464	14,681	18,993	4,240	2,120	1,648	1,249	834	672	49,901
Oocytes ¹	11.5	10.4	8.4	7.1	6.4	6.1	5.5	5.2	4.7	8.9
ET/OPU %	87.7	89.0	100.0	87.9	84.8	87.3	85.1	80.9	78.3	92.3
Trans. Embr. ¹	1.89	1.90	1.91	1.96	1.95	1.98	1.94	1.94	1.85	1.91
CP	2,019	5,107	5,462	882	349	263	154	62	39	14,337
CP/OPU %	37.0	34.8	28.8	20.8	16.5	16.0	12.3	7.4	5.8	28.7
CP/ET upper Confidence Limit* %	43.6	40.0	33.2	25.2	21.4	20.5	16.9	12.0	10.0	33.1
CP/ET %	42.2	39.1	32.4	23.7	19.4	18.3	14.5	9.2	7.4	32.6
CP/ET lower Confidence Limit* %	40.7	38.2	31.6	22.2	17.6	16.2	12.4	7.0	5.5	32.2
CP/ET %: 2 Embr. transf. + min. 2 2-PN surplus	44.0	41.6	35.3	26.8	22.4	21.7	18.5	10.8	10.2	35.8
Misc./CP upper Confidence Limit* %	18.7	17.1	23.3	34.5	43.0	49.4	54.6	66.6	64.1	21.8
Misc./CP %	17.1	16.1	22.2	31.4	37.8	43.3	46.8	54.8	48.7	21.1
Misc./CP lower Confidence Limit* %	15.6	15.2	21.2	28.4	32.9	37.5	39.0	42.5	33.5	20.5
Births/Trans. upper Confidence Limit* %	32.0	30.2	23.1	15.7	12.5	11.2	8.5	5.2	4.4	23.3
Births/Transfer %	30.6	29.3	22.4	14.4	10.9	9.4	6.7	3.3	2.5	22.9
Births/Trans. lower Confidence Limit* %	29.2	28.5	21.7	13.2	9.4	7.8	5.2	2.0	1.4	22.4

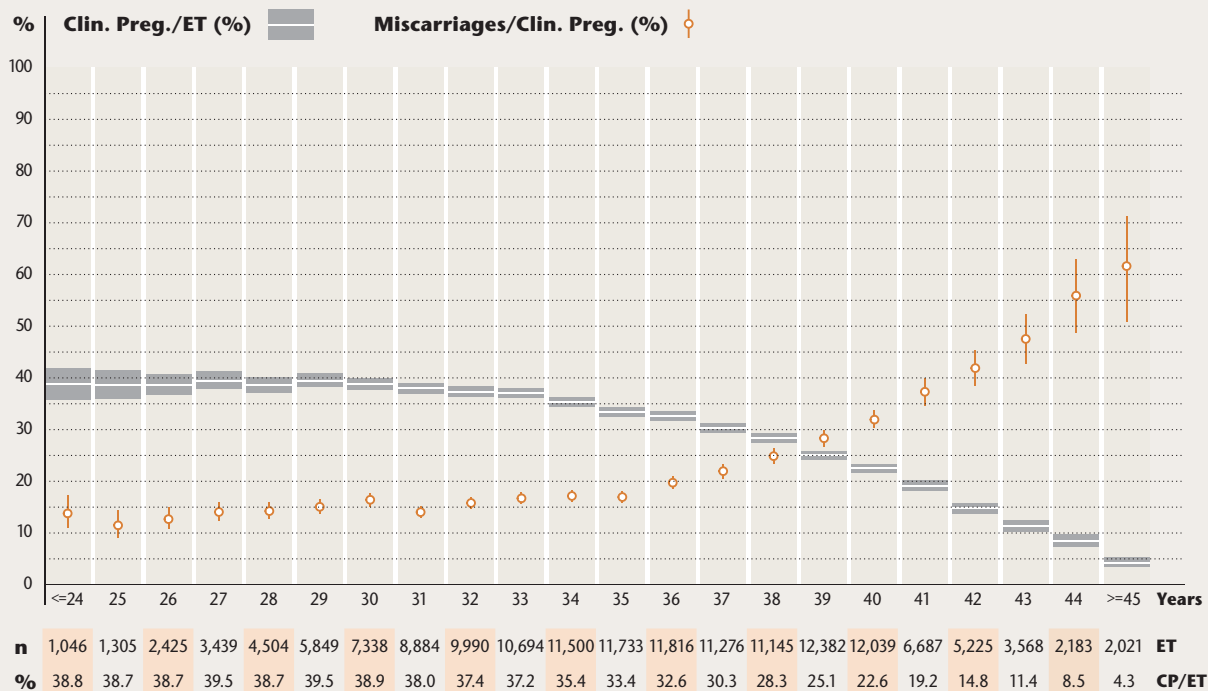
¹) Mean

* With a 95%-probability, the true mean lies within the defined confidence interval.

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2010 – 2014

Prospektive Daten

ICSI 2010 – 2014



Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	20,255	52,561	64,254	13,504	7,606	6,051	4,265	2,621	2,671	173,788
Oocytes ¹	12.3	11.1	9.1	7.6	6.9	6.4	5.8	5.3	4.3	9.5
ET/OPU %	91.7	90.8	89.2	87.9	86.3	83.7	83.3	77.6	75.7	90.4
Trans. Embr. ¹	1.90	1.91	1.92	1.96	1.96	1.94	1.93	1.87	1.80	1.92
CP	7,258	18,005	17,445	2,715	1,281	771	406	186	86	48,153
CP/OPU %	35.8	34.3	27.2	20.1	16.8	12.7	9.5	7.1	3.2	27.7
CP/ET upper Confidence Limit* %	39.8	37.7	30.3	23.4	20.2	15.8	12.6	9.8	5.3	30.9
CP/ET %	39.1	37.2	29.9	22.6	19.2	14.8	11.4	8.5	4.3	30.7
CP/ET lower Confidence Limit* %	38.3	36.7	29.5	21.8	18.1	13.7	10.3	7.4	3.4	30.4
CP/ET %: 2 Embr. transf. + min. 2 2-PN surplus	40.5	39.1	32.5	25.5	21.9	17.7	14.4	10.7	6.2	35.6
Aborte/Klin. SS upper Confidence Limit* %	14.8	16.6	22.6	33.7	40.0	45.4	52.4	62.9	71.3	20.6
Misc./CP %	14.1	16.1	22.0	31.9	37.3	41.9	47.5	55.9	61.6	20.3
Misc./CP lower Confidence Limit* %	13.3	15.6	21.4	30.2	34.7	38.5	42.7	48.7	50.9	20.0
Births/Trans. upper Confidence Limit* %	30.8	28.7	21.4	14.3	11.6	8.4	6.0	4.1	2.2	22.2
Births/Transfer %	30.0	28.3	21.0	13.5	10.7	7.6	5.1	3.1	1.3	22.0
Births/Trans. lower Confidence Limit* %	29.3	27.8	20.6	12.9	9.9	6.8	4.4	2.4	0.8	21.8

1) Mean

* With a 95%-probability, the true mean lies within the defined confidence interval.

Clinical Pregnancies (CP)/ET as a Function of the Number of Embryos Transferred and Age Groups 2015



IVF, ICSI – Prospective Data

IVF

Age in Year	1 Embryo		2 Embryos		3 Embryos		Total	
	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %
<= 24	0	0.0	27	40.7	2	0.0	29	37.9
25 – 29	198	34.3	949	42.7	29	41.4	1,176	41.2
30 – 34	588	29.1	2,707	39.9	122	41.8	3,417	38.1
35 – 39	891	19.9	3,178	37.0	274	32.5	4,343	33.2
40	216	12.5	573	27.7	138	23.9	927	23.6
41	107	12.1	247	25.5	82	20.7	436	21.3
42	100	6.0	148	18.9	37	40.5	285	17.2
43	67	3.0	148	15.5	58	19.0	273	13.2
44	57	0.0	72	8.3	35	8.6	164	5.5
45	22	0.0	35	0.0	16	12.5	73	2.7
>= 46	24	8.3	30	10.0	8	0.0	62	8.1
Total	2,270	20.5	8,114	36.4	801	29.1	11,185	32.7

ICSI

Age in Year	1 Embryo		2 Embryos		3 Embryos		Total	
	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %
<= 24	26	38.5	125	44.0	3	33.3	154	42.9
25 – 29	633	29.5	3,290	40.7	161	40.4	4,084	39.0
30 – 34	1,871	28.1	8,869	40.5	555	36.9	11,295	38.2
35 – 39	3,070	21.1	10,305	35.1	1,294	33.8	14,669	32.1
40	713	12.6	1,790	27.3	426	34.3	2,929	24.8
41	385	10.9	817	22.2	229	21.0	1,431	18.9
42	326	9.8	548	23.5	215	20.0	1,089	18.7
43	276	7.2	389	15.4	147	19.7	812	13.4
44	188	5.3	236	12.7	98	9.2	522	9.4
45	105	2.9	119	7.6	49	16.3	273	7.3
>= 46	111	2.7	89	2.2	41	7.3	241	3.3
Total	7,704	20.4	26,577	35.7	3,218	30.9	37,499	32.2

Clinical Pregnancies (CP)/ET as a Function of the Number of Embryos Transferred and Age Groups 2015

Cryo Transfer – Prospective Data

Kryo-ET

Age in Years	1 Embryo		2 Embryos		3 Embryos		Total	
	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %
<= 24	14	42.9	79	32.9	10	10.0	103	32.0
25 – 29	311	19.9	1,709	29.0	164	31.7	2,184	27.9
30 – 34	1,111	17.9	5,452	29.5	537	26.3	7,100	27.4
35 – 39	1,476	18.6	5,915	26.1	663	24.3	8,067	24.6
40	233	12.9	898	21.3	135	28.1	1,266	20.5
41	154	13.0	569	21.3	112	21.4	835	19.8
42	109	11.9	337	16.3	63	20.6	509	15.9
43	50	8.0	217	12.0	55	18.2	322	12.4
44	37	21.6	115	13.9	36	16.7	188	16.0
45	19	10.5	65	7.7	12	0.0	96	7.3
>= 46	12	0.0	48	4.2	10	20.0	70	5.7
Total	3,526	17.6	15,404	26.6	1,797	24.9	20,740	24.9

Clinical Pregnancies (CP)/Fresh Transfer as a Function of Embryo Quality 2015

IVF, ICSI, IVF/ICSI – Prospective Data

Quality		<= 29 Years		30 – 34 Years		35 – 39 Years		>= 40 Years		Total	
Ideal	Not Ideal	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %
0	1	127	14.2	365	11.5	611	7.9	429	4.4	1,532	8.3
0	2	299	26.1	816	22.8	953	19.9	411	11.7	2,479	20.3
0	3	13	23.1	58	12.1	90	13.3	80	10.0	241	12.5
1	0	723	33.2	2,077	30.8	3,480	22.9	2,269	10.0	8,549	22.3
1	1	413	33.9	1,195	34.3	1,560	30.7	705	18.7	3,873	30.0
1	2	25	36.0	70	40.0	137	25.6	105	19.1	337	27.3
2	0	3,667	43.5	9,536	42.7	10,857	37.8	4,018	24.6	28,078	38.3
2	1	20	25.0	72	40.3	199	38.7	246	22.0	537	30.7
3	0	140	43.6	491	39.9	1,202	34.9	1,225	24.3	3,058	31.9
Total		5,427	39.6	14,680	38.2	19,089	32.3	9,488	18.9	48,684	32.3

Clinical Pregnancies (CP)/Frozen Transfer as a Function of Embryo Quality 2015

Cryo Transfer – Prospective Data

Quality		IVF		ICSI	
ideal	Not Ideal	ET	CP/ET %	ET	CP/ET %
0	1	133	6.0	512	7.4
0	2	275	14.9	947	14.7
0	3	45	15.6	159	17.6
1	0	715	22.1	3,144	19.1
1	1	417	21.3	1,865	21.4
1	2	58	12.1	189	26.5
2	0	1,977	26.2	7,016	24.6
2	1	89	20.2	220	31.8
3	0	273	24.9	773	26.4
Total*		3,982	22.9	14,825	22.0

*) In 1,733 cases, resulting in an additional 1,086 pregnancies, no information is available on the preceding treatment.

Miscarriage (MISC) Rates as a Function of Female Age and Number of Embryos Transferred 2014

Prospective Data

IVF, ICSI

Age in Years	1 Embryo		2 Embryos		3 Embryos		Total	
	CP	MISC/CP %	CP	MISC/CP %	CP	MISC/CP %	CP	MISC/CP %
<= 24	15	0.0	88	10.2	1	0.0	104	10.2
25 – 29	192	9.9	1,826	16.3	81	14.8	2,099	10.5
30 – 34	465	14.6	4,712	15.9	375	18.1	5,552	12.4
35 – 39	636	18.6	4,090	21.0	596	22.7	5,322	16.7
40 – 44	197	35.5	968	33.0	401	32.9	1,566	31.2
>= 45	5	40.0	13	53.8	17	47.1	35	48.2
Total	1,510	18.3	11,697	19.1	1,471	24.1	14,678	15.9

Cryo Transfer

Age in Years	1 Embryo		2 Embryos		3 Embryos		Total	
	CP	MISC/CP %	CP	MISC/CP %	CP	MISC/CP %	CP	MISC/CP %
<= 24	6	0.0	19	21.1	4	0.0	29	13.8
25 – 29	45	17.8	425	21.2	54	22.2	524	21.0
30 – 34	218	17.4	1,402	18.4	145	19.3	1,765	18.4
35 – 39	181	21.5	1,436	26.1	196	18.9	1,813	24.9
40 – 44	72	26.4	348	27.3	91	34.1	511	28.4
>= 45	0	0.0	12	41.7	7	42.9	19	42.1
Total	522	20.8	3,642	24.9	497	23.9	4,661	22.0

Clinical Pregnancy Rate (CPR) as a Function of the Stimulation Protocol 2015

Prospective Data

IVF

	u-FSH	rec-FSH	hMG	recLH and recFSH	recFSH and hMG	Other*	No Information	Total	Perc. %
Short GnRHa	3	165	356	32	108	2	5	671	6.3
Transfer Rate (%)	0.0	94.2	92.1	94.2	94.2	50.0	100.0	94.2	
CP/ET (%)	0.0	32.6	28.4	31.5	21.8	0.0	20.0	27.3	
Long GnRHa	101	1,205	531	227	373	6	4	2,447	23.0
Transfer Rate (%)	91.0	90.1	93.6	89.9	93.2	100.0	75.0	91.0	
CP/ET (%)	30.7	39.4	33.0	36.0	32.2	66.7	33.3	36.9	
No GnRHa-Ana.	7	236	125	55	119	17	185	744	7.0
Transfer Rate (%)	33.3	91.3	90.5	97.0	84.0	88.9	82.7	88.2	
CP/ET (%)	0.0	32.4	23.9	31.1	30.2	0.0	13.9	26.9	
GnRHa-Antag.	121	3,945	1,241	698	702	49	31	6,787	63.7
Transfer Rate (%)	92.8	86.4	87.1	85.0	86.4	83.4	64.3	86.4	
CP/ET (%)	27.5	35.4	29.9	27.7	32.7	17.2	20.8	33.1	
Summe	232	5,551	2,253	1,012	1,302	74	225	10,649	100.0

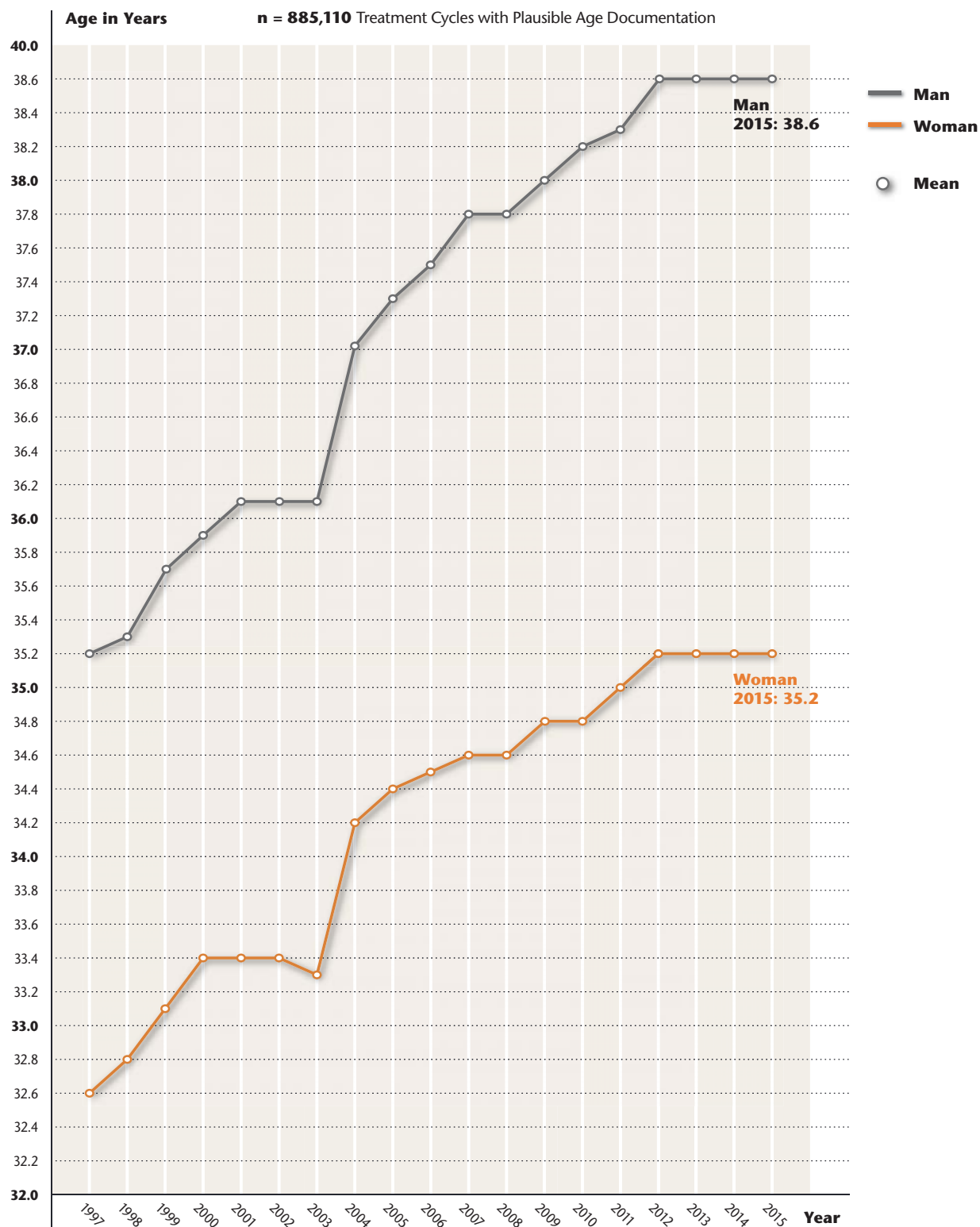
ICSI

	u-FSH	rec-FSH	hMG	recLH and recFSH	recFSH and hMG	Other*	No Information	Total	Perc. %
Short GnRHa	35	616	534	121	354	26	5	1,691	5.0
Transfer Rate (%)	82.9	92.0	92.1	91.1	98.9	55.7	100.0	91.9	
CP/ET (%)	6.7	26.0	26.0	19.9	20.1	4.6	16.7	24.0	
Long GnRHa	146	3,957	1,735	909	1,847	125	5	8,724	25.5
Transfer Rate (%)	94.0	93.7	94.6	93.3	90.2	89.8	77.8	93.2	
CP/ET (%)	36.4	36.7	31.4	35.3	30.5	26.8	14.3	33.4	
No GnRHa-Ana.	21	856	454	225	510	7	1,027	3,100	9.1
Transfer Rate (%)	90.3	90.5	88.2	88.2	82.5	58.3	84.1	86.4	
CP/ET (%)	28.6	32.6	30.2	28.9	31.2	28.6	22.9	28.7	
GnRHa-Antag.	234	11,324	3,247	2,701	2,938	41	145	20,630	60.4
Transfer Rate (%)	90.4	90.0	89.6	86.0	83.9	84.6	77.7	88.9	
CP/ET (%)	23.6	34.1	25.9	28.6	28.3	7.3	20.1	31.1	
Summe	436	16,753	5,970	3,956	5,649	199	1,182	34,145	100.0

*) e.g. u-FSH and hMG, Clomifen/rec-FSH, Clomifen/hMG etc.

Mean Age for Women and Men 1997 – 2015

IVF, ICSI, IVF/ICSI – Prospective and Retrospective Data



Children Born 1997–2014

Prospective and Retrospective Data

Total (IVF, ICSI, IVF/ICSI, Cryo Transfer)

	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	n
2001	7,795	62.2	4,288	34.2	450	3.6	0	-	12,533
*	(7,764)	(62.3)	(4,248)	(34.1)	(444)	(3.6)	(0)	-	(12,456)
2002	8,930	63.8	4,662	33.3	387	2.8	8	0.1	13,987
*	(8,902)	(64.0)	(4,615)	(33.2)	(382)	(2.8)	(7)	(0.1)	(13,906)
2003	11,922	63.2	6,334	33.6	597	3.2	24	0.1	18,877
*	(11,887)	(63.5)	(6,237)	(33.3)	(578)	(3.1)	(24)	(0.1)	(18,726)
2004	6,891	65.6	3,336	31.8	273	2.6	0	-	10,500
*	(6,869)	(65.8)	(3,306)	(31.7)	(262)	(2.5)	(0)	-	(10,437)
2005	7,038	65.8	3,440	32.1	213	2.0	12	0.1	10,703
*	(7,020)	(65.9)	(3,408)	(32.0)	(209)	(2.0)	(11)	(0.1)	(10,648)
2006	7,419	66.9	3,450	31.1	222	2.0	4	0.0	11,095
*	(7,402)	(67.1)	(3,417)	(31.0)	(202)	(1.8)	(4)	(0.0)	(11,025)
2007	8,407	66.4	4,976	32.2	183	1.4	4	0.0	12,670
*	(8,364)	(66.5)	(4,043)	(32.1)	(176)	(1.4)	(4)	(0.0)	(12,587)
2008	8,444	65.8	4,142	32.3	240	1.9	8	0.1	12,834
*	(8,416)	(66.1)	(4,084)	(32.1)	(230)	(1.8)	(8)	(0.1)	(12,738)
2009	9,016	67.3	4,152	31.0	216	1.6	8	0.1	13,392
*	(8,969)	(67.4)	(4,114)	(30.9)	(213)	(1.6)	(8)	(0.1)	(13,304)
2010	8,619	66.2	4,156	31.9	249	1.9	0	-	13,024
*	(8,566)	(66.4)	(4,105)	(31.8)	(239)	(1.9)	(0)	-	(12,910)
2011	9,388	63.1	5,131	34.6	301	2.0	0	-	14,820
*	(9,358)	(63.6)	(5,074)	(34.5)	(294)	(2.0)	(0)	-	(14,726)
2012	10,188	66.4	4,906	32.0	248	1.6	0	-	15,342
*	(10,158)	(66.5)	(4,880)	(31.9)	(246)	(1.6)	(0)	-	(15,284)
2013	11,713	64.9	6,003	33.3	326	1.8	6	0.0	18,048
*	(11,679)	(65.1)	(5,944)	(33.1)	(312)	(1.8)	(4)	(0.0)	(17,939)
2014	12,530	65.5	6,304	32.9	294	1.5	12	0.1	19,140
*	(12,478)	(65.6)	(6,246)	(32.8)	(294)	(1.5)	(12)	(0.1)	(19,030)

*) The values in brackets indicate live births. Totalling 1997 – 2014:

150,584 (150,409) singletons, 76,560 (75,484) twins, 6,501 (6,317) triplets, Vierlinge 104 (97) quadruplets. In total: 233,749 (232,307)

KREFELD
Population of 233,034

HALLE(SAALE)
Population of 237,858

233,749

Children born 1997–2014

Children as a Function of Week of Gestation (WoG) and Birth Weight (BW) 2014*

Total (IVF, ICSI, IFV/ICSI, Cryo Transfer)

Singletons 2014

WoG	<25	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	>41	Total
n	50	28	19	26	40	39	46	67	69	114	173	276	545	1,069	2,122	2,983	2,866	1,651	295	12,478
BW p25	553	643	707	929	1,036	1,169	1,270	1,531	1,979	2,154	2,251	2,530	2,680	2,833	2,948	3,054	3,124	3,189	3,303	3,004
BW Median	662	728	930	1,031	1,193	1,355	1,696	1,896	2,340	2,618	2,709	2,965	3,089	3,276	3,377	3,485	3,523	3,561	3,635	3,390
BW p75	895	971	1,170	1,415	1,517	1,701	2,236	2,613	2,798	3,200	3,207	3,490	3,614	3,758	3,837	4,002	4,030	4,036	4,039	3,970

Percentiles 2014: p25 = 38th WoG, p50 = 39th WoG, p75 = 40th WoG;

Percentiles 1997–2014: p25 = 38th WoG, p50 = 39th WoG, p75 = 40th WoG

Proportion of children born before the completion of the 37th WoG: 20.5%

Twins 2014

WoG	<25	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	Total**
n	106	43	44	63	65	89	148	153	230	362	551	749	1,082	1,294	892	289	72	6,246
BW p25	516	585	916	1,090	1,004	1,195	1,330	1,539	1,603	1,899	2,001	2,200	2,347	2,330	2,489	2,634	2,784	2,105
BW Median	617	849	1,026	1,188	1,233	1,491	1,582	1,921	1,923	2,103	2,295	2,487	2,596	2,649	2,720	2,871	2,982	2,510
BW p75	797	916	1,136	1,297	1,462	1,668	1,978	2,158	2,272	2,371	2,618	2,813	2,934	2,957	3,030	3,053	3,252	2,860

Percentiles 2014: p25 = 34th WoG, p50 = 36th WoG, p75 = 37th WoG;

Percentiles 1997–2014: p25 = 34th WoG, p50 = 36th WoG, p75 = 37th WoG

Proportion of children born before the completion of the 37th WoG: 79.7%

**) The total contains 14 cases with a WoG > 40

Triplets 2014

WoG	24	25	26	27	28	29	30	31	32	33	34	35	Total***
n	10	10	3	6	19	16	32	44	50	54	44	16	306
BW p25	348	812	813	775	750	1,123	1,271	1,562	1,695	1,537	1,897	1,751	1,290
BW Median	457	900	821	902	963	1,112	1,405	1,633	1,764	1,739	2,085	2,275	1,720
BW p75	598	1,006	1,010	1,038	1,206	1,112	1,557	2,017	1,891	1,908	2,282	2,492	2,005

Percentiles 2014: p25 = 30th WoG, p50 = 32nd WoG, p75 = 33rd WoG;

Percentiles 1997–2014: p25 = 30th WoG, p50 = 32nd WoG, p75 = 33rd WoG

Proportion of children born before the completion of the 37th WoG: 99.3%

***) The total contains 2 cases with a WoG > 35

*) Children with plausible birth weight and week of gestation, using prospective and retrospective data

Ovarian Hyperstimulation Syndrome (OHSS) as a Function of the Stimulation Protocol 2015

IVF, ICSI, IVF/ICSI – Prospective Data

	Stimulation	%	Oocytes Retrieved	OHSS III	OHSS III/Stim %
Short GnRH	3,412	5.4	6.3	1	0.03
FSH only	1,398		7.2	1	0.03
hMG only	1,142		6.7	0	-
FSH + hMG	629		6.5	0	-
Other	221		2.6	0	-
No Information	22		2.5	0	-
Long GnRH	12,678	20.2	9.8	65	0.50
FSH only	7,313		10.5	30	0.23
hMG only	2,559		8.1	3	0.02
FSH + hMG	2,727		9.5	28	0.21
Other	75		7.4	4	0.03
No Information	4		11.4	0	-
No Analoga	7,351	11.7	5.4	4	0.07
FSH only	2,269		6.7	0	-
hMG only	1,394		5.3	1	0.02
FSH + hMG	987		7.9	0	-
Other	2,683		3.6	3	0.05
No Information	18		2.1	0	-
GnRH-Antagonists	39,276	62.6	8.9	110	0.28
FSH only	26,635		10.5	76	0.19
hMG only	6,739		5.9	11	0.03
FSH + hMG	4,987		7.8	19	0.05
Other	657		10.7	4	0.01
No Information	258		5.1	0	-
Total	62,717	100.0	8.5	180	0.29

Complications as a Function of Ovum Pick-up (OPU) 2015

Prospective Data

Total OPU's	58,170	100.0%
No Information	0	-
No Complications	57,769	99.3%
Complications	401	0.7%

Complications	n	%
Vaginal Bleeding	259	64.6
Intraabdom. Bleeding	57	14.2
Intestinal Tract Injury	5	1.2
Peritonitis	1	0.3
Hospitalisation	10	2.5
Surgery	27	6.7
Other	42	10.5
Total	401	100.0

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