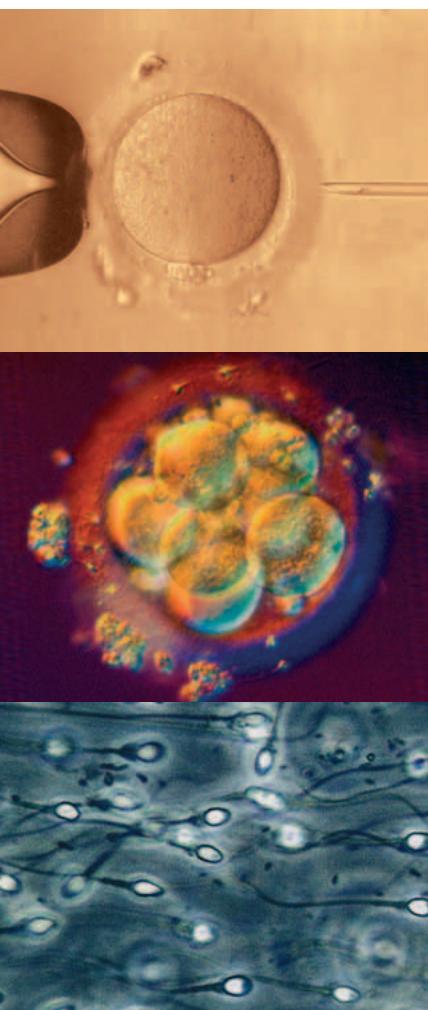


Journal für

Reproduktionsmedizin und Endokrinologie

– Journal of Reproductive Medicine and Endocrinology –

Andrologie • Embryologie & Biologie • Endokrinologie • Ethik & Recht • Genetik
Gynäkologie • Kontrazeption • Psychosomatik • Reproduktionsmedizin • Urologie



D.I.R-Annual 2016 - The German IVF-Registry

Blumenauer V, Czeromin U, Fehr D, Fiedler K, Gnoth C

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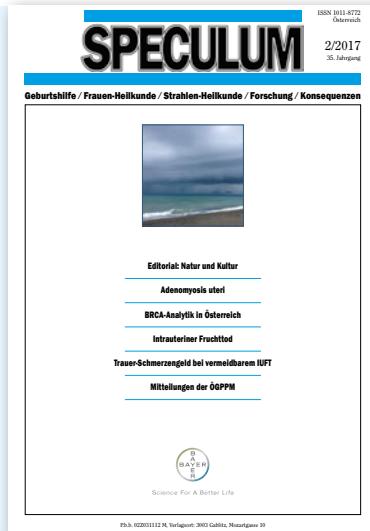
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Andrologie • Embryologie & Biologie • Endokrinologie • Ethik & Recht • Genetik
Gynäkologie • Kontrazeption • Psychosomatik • Reproduktionsmedizin • Urologie

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C. Abbing, M. Behrman, J. Bräse, C. Egger, K. König, P. Hadj, E. Merkle,
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Preface

D-I-R Annual 2016 – The German IVF-Registry

V. Blumenauer, U. Czeromin, D. Fehr, K. Fiedler, C. Gnoth, J.-S. Krüssel, M.S. Kupka, A. Ott, A. Tandler-Schneider

Once again it is our great pleasure to present the 2016 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 1.5 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.

This Yearbook 2016 is more than in previous years a yearbook of change and of organizational efforts undertaken by all authors and contributors. After years of data control and reconciliation, administrative work and programming, the implementation of a new data system was carried out in the centers. The new D-I-R data record was rolled out, which meanwhile has been mapped in the established recording software. To this end, the new ARTbox® interface was activated and the new D-I-R own data acquisition software DIRproNOVA® was installed by a first group of centers. This was a major change and required huge modifications within the existing, heterogeneous IT environments of those pioneering centers. We want to express our thanks to everyone contributing to this process: the software companies, the D-I-R data management group, the D-I-R office, and particularly the associates within those centers.

In the meantime, 111 of the 134 D-I-R member centers migrated to the new system. They are already maintaining the new D-I-R data set by exporting their data to the D-I-R database using the new

ARTbox®. Another 19 centers are currently in the process of conversion.

Two new records have been achieved by German reproductive medicine as documented in this yearbook: for the first time after the year 2003 which had special influences, more than 100,000 cycles were registered for 2016, and in 2015 more than 20,000 children were born.

The 2016 yearbook is based on exploitable exports from 128 centers, for which a number of 100,844 plausible cycles was documented. A total of 62,797 women were treated in 2016, resulting in a mean of 1.7 cycles per woman. We are happy to note that the pregnancy rate per transfer in fresh cycles was at 32.3%, whereas the pregnancy rate per transfer in cryo cycles was 27.0%. In the previous year, 2015, the documented birth rate per embryo transfer was 23.6% in fresh cycles and 17.2% in cryo cycles, with a still very good general pregnancy outcome documentation of 94.7%.

Remarkably, 73.2% of the pregnancies led to a birth. A birth rate of 23.6% per embryo transfer was achieved. For comparison, the probability for a 25 year old woman to become 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].

This year, again, particular attention was placed on the known problems of multiple pregnancies within ART cycles. In 2015, the rate of twin births was 21.5% in fresh cycles and 15.3% in cryo cycles. As this rate is still too high, we dedicated the editorial 2017 to the motto „LESS is MORE“.

The data presented in this yearbook 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 1.80 embryos after IVF and 1.83 for ICSI, the doctors for reproductive medicine in Germany have continued to adhere to their responsible approach towards the reduction of multiples.

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 2016 – Tables



Number of Treatments in 2016

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

Members of the German IVF-Registry 2016 n=134

Registry Participants 2016*	n=128
Data Received by Deadline Sep 21st 2017*	n=128
Documented Treatment Cycles	n=103,981 (100.0%)
Plausible	n=100,844 (97.0%)
Prospective (all Cycles)	n=91,710 (90.9%)
Prospective (IVF, ICSI, IVF/ICSI)	n=58,988 (90.1%)
Number of Women Treated**	n=62,797

Mean Number of Treatment Cycles per Woman 1.7

Number of Treatments 1982–2016

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



	1982	1986	1990	[...]	2002	2003	2004	[...]	2012	2013	2014	2015	2016	Prospectivity 2016 in %
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 2011 see www.deutsches-ivf-register.de	12,047	12,569	13,675	15,105	15,476	89.5
ICSI					37,692	51,389	25,339		38,897	42,381	44,427	48,532	48,897	90.3
IVF/ICSI					678	987	446		1,014	1,142	1,178	1,194	1,214	89.2
Cryo					14,923	14,265	16,883		19,293	20,633	21,893	23,226	24,842	93.0
None ¹					9,802	11,133	4,928		6,117	6,708	7,210	11,671	13,552	70.5
Total²	742	4,201	8,653		87,044	105,854	59,448		77,368	83,433	88,383	99,728	103,981	90.9

^{*}) Due to their technical prerequisites, five centers could not export their data

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

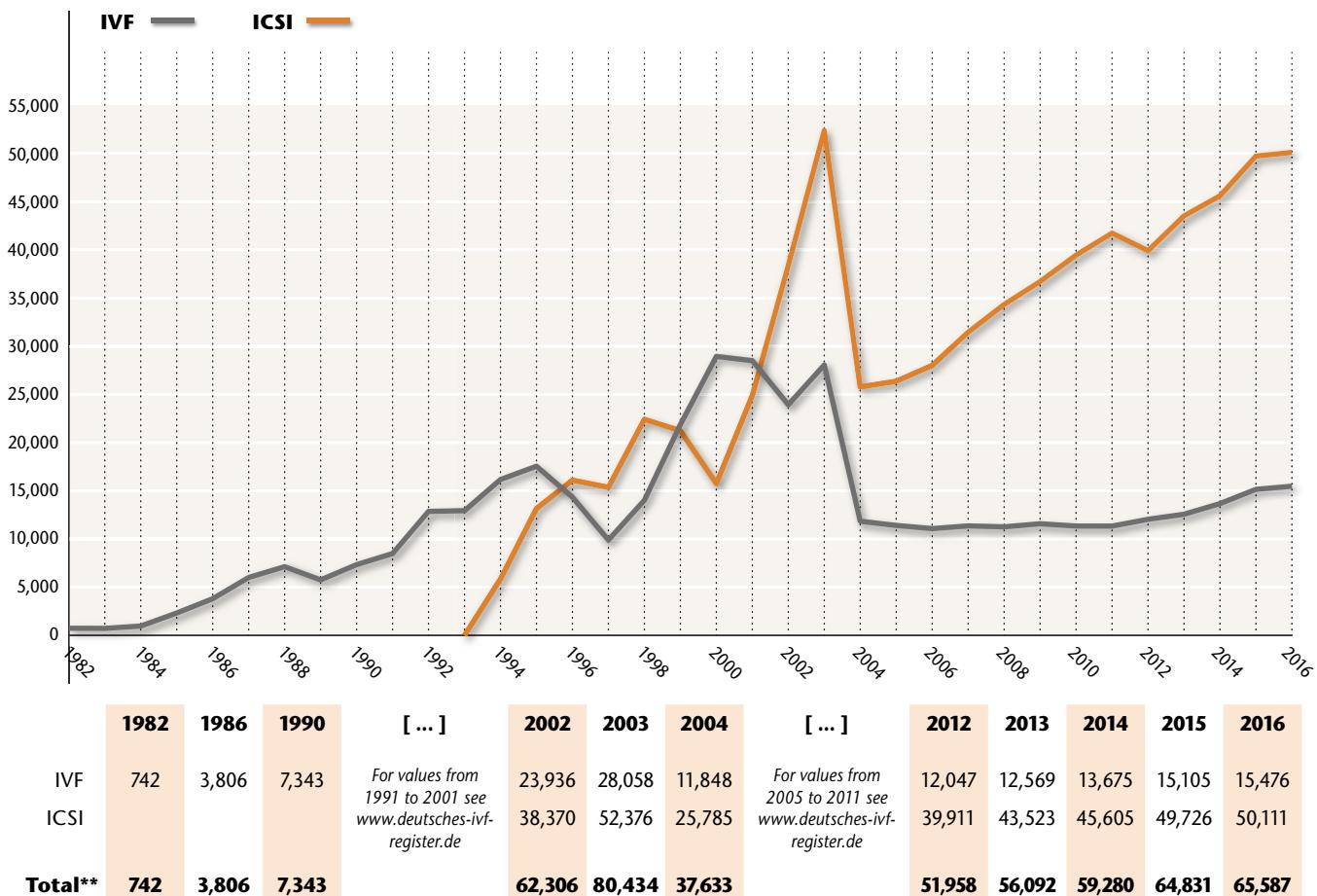
From 1999 on each initiated cycle is documented.

1) No treatment: treatments aborted prior to oocyte culture

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

Number of Ovum Pick-Up Cycles (OPU) 1982–2016

IVF, ICSI* – Prospective and Retrospective Data

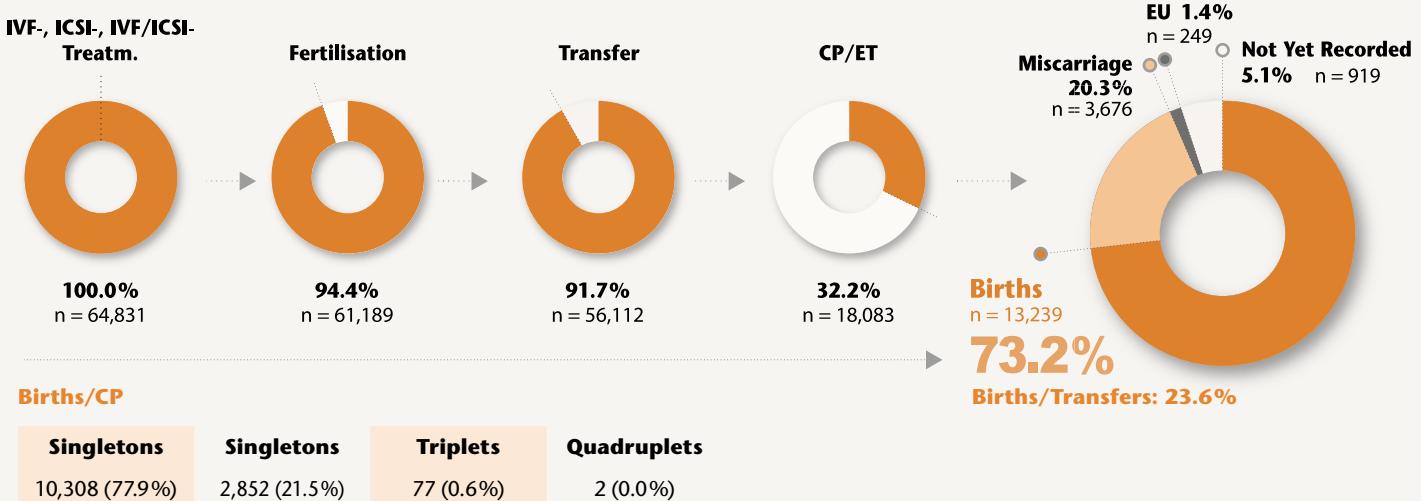


*) OPUs leading to an IVF- and/or ICSI oocyte treatment

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

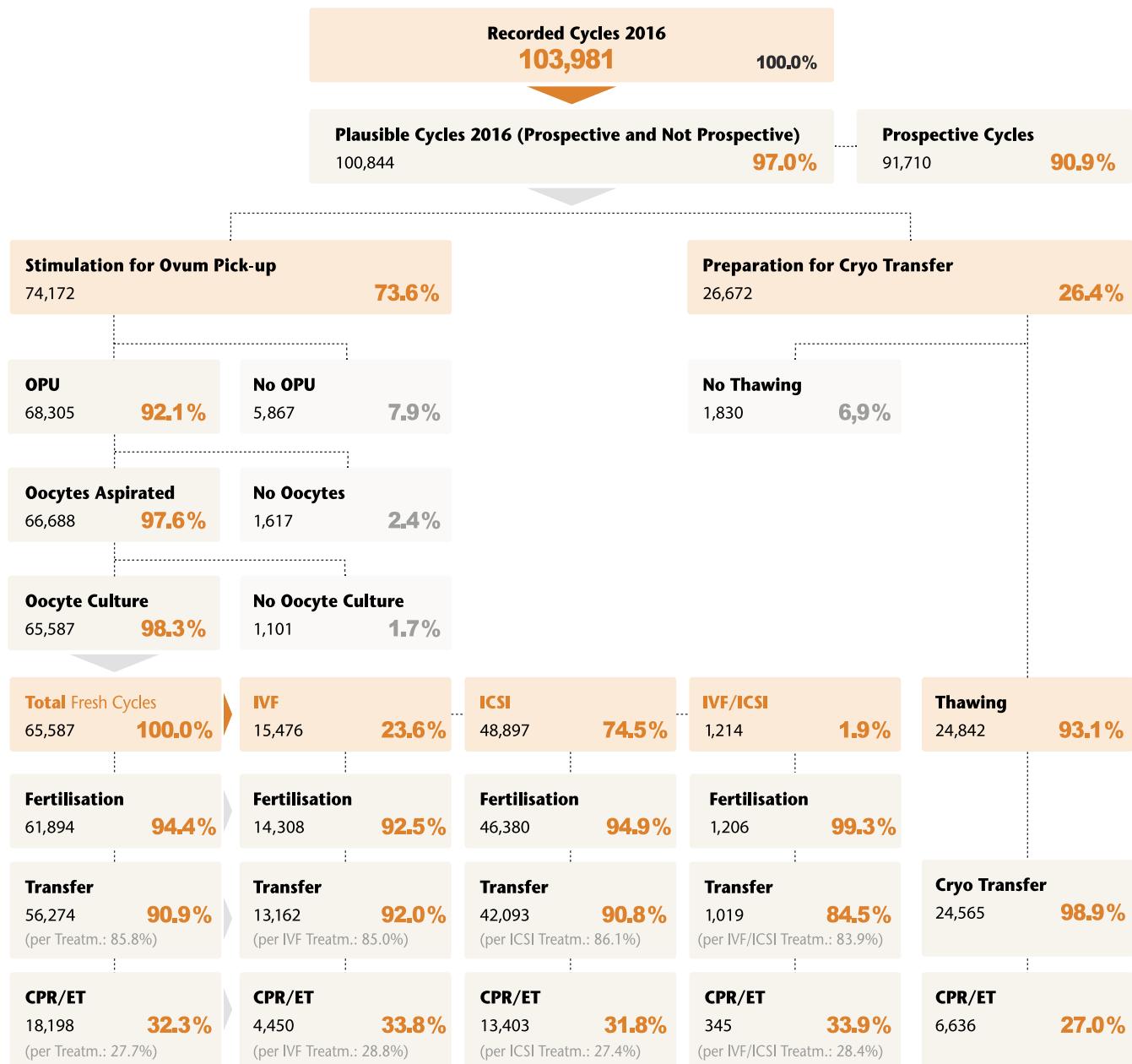
Summary of Statistics in Brief 2015 – CoD Sep 21st 2017

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



D·I·R Statistics in Brief 2016 – CoD Sep 21st 2017

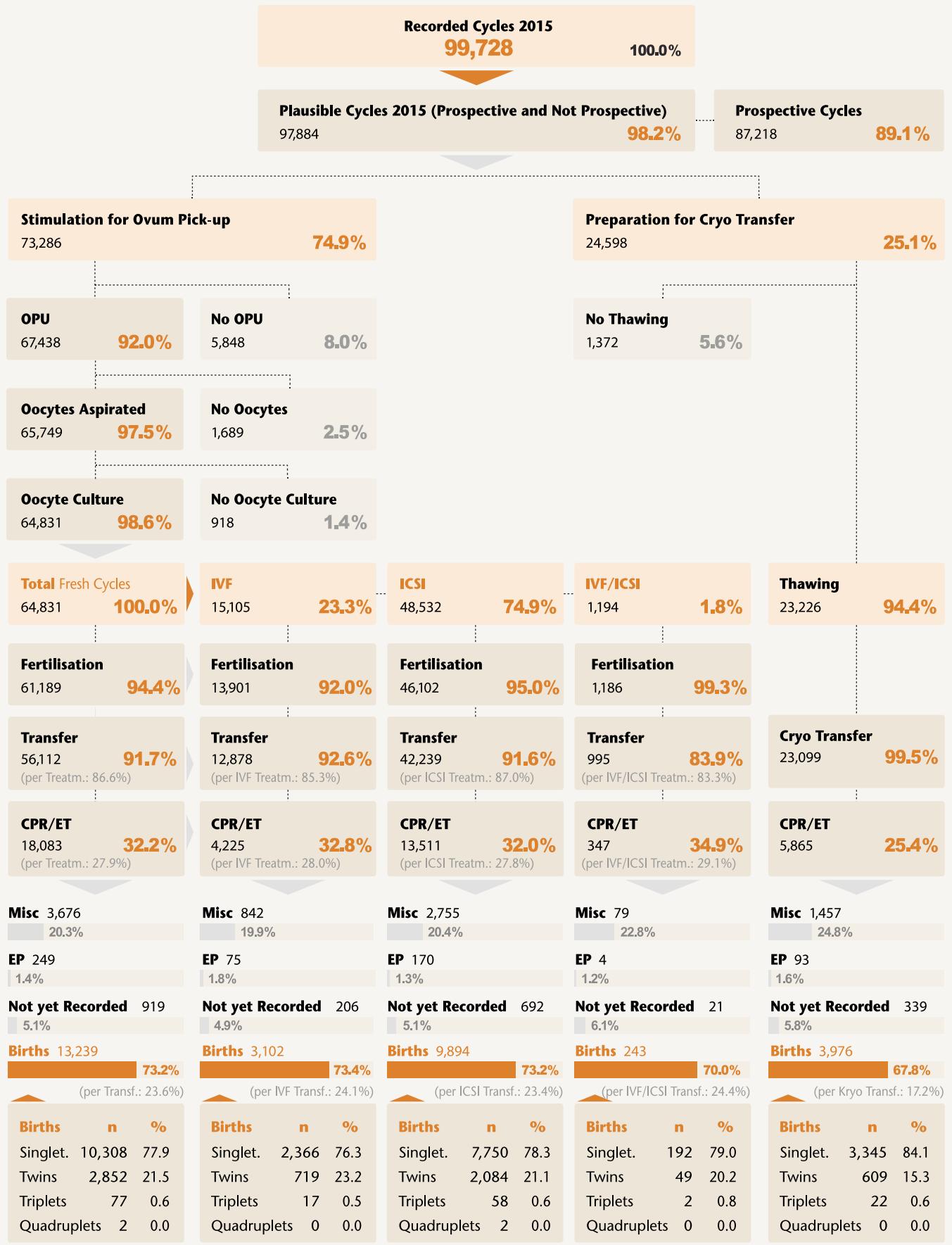
German IVF Registry – Prospective and Retrospective Data



D.I.R Statistics in Brief 2015 – CoD Sep 21st 2017



German IVF Registry – Prospective and Retrospective Data



Clinical Pregnancies (CP), Miscarriages (MISC), Ectopic Pregnancies (EP), Birth Rate and Children 2015

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 26.0%, ICSI 25.5%, IVF/ICSI 27.3%

	IVF		ICSI		IVF/ICSI		Cryo Transfers	
	n	%	n	%	n	%	n	%
Treatment Cycles	15,105		48,532		1,194		23,226	
Treatments with documented pregnancy outcome	14,899		47,840		1,173		22,887	
Transfers	12,878		42,239		995		23,099	
Clinical Pregnancies	4,225	100.0	13,511	100.0	347	100.0	5,865	100.0
No Information	206	4.9	692	5.1	21	6.1	339	5.8
Live Births	3,102	73.4	9,894	73.2	243	70.0	3,976	67.8
Miscarriages	842	19.9	2,755	20.4	79	22.8	1,457	24.8
included above: induced abortions and fetal reduction*	40 (59)		129 (179)		5 (5)		53 (60)	
Ectopic Pregnancies	75	1.8	170	1.3	4	1.2	93	1.6
Children	3,855		12,100		296		4,629	
Still Births**	31	0.8	138	1.1	4	1.4	37	0.8
Malformations	43	1.1	158	1.3	6	2.0	64	1.4
Baby-Take-Home-Rate per Transfer		24.1		23.4		24.4		17.2
Baby-Take-Home-Rate per Treatm.***		20.5		20.4		20.4		17.1
		20.8 ¹		20.7 ¹		20.7 ¹		17.4 ¹
		21.8 ²		21.7 ²		22.0 ²		18.4 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

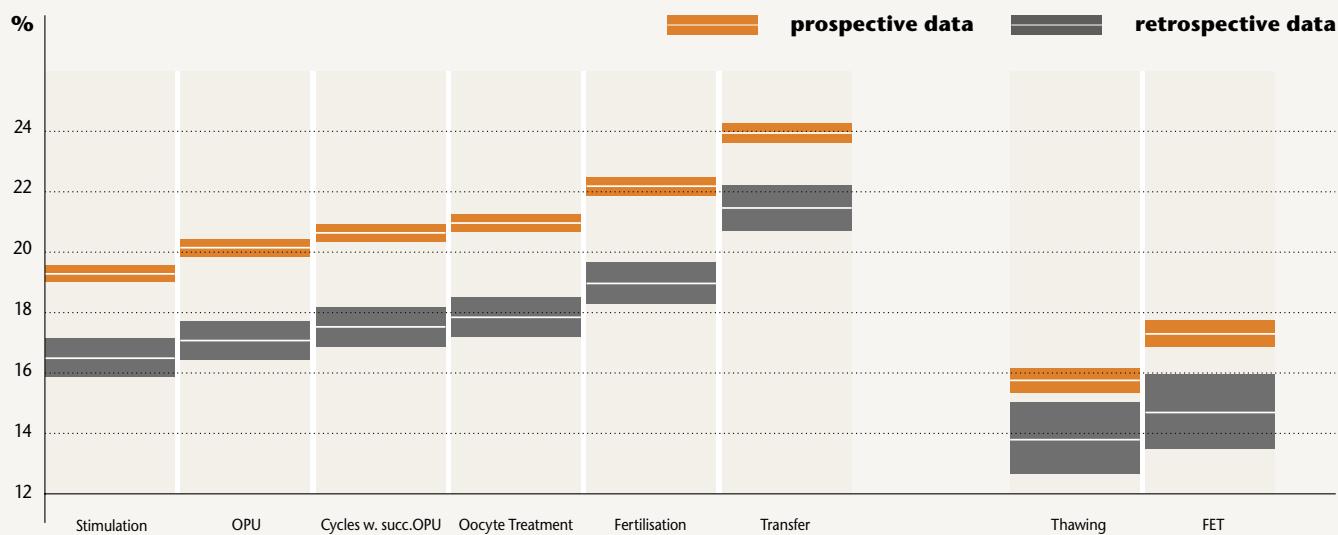
***) Percentage of births per number of treatments

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

Birth Rate per Treatment Level in Fresh and Cryo Treatment Cycles 2014 and 2015

Prospective and Retrospective Data



	Stimulation	OPU**	Cycles with successful OPU:	Oocyte Treatment	Fertilisation	Transfer	Thawing	FET**
Prospective Numbers	113,078	109,343	106,725	105,080	99,300	92,013	43,747	39,856
Birth	21,805	22,032	22,028	22,030	22,030	22,033	6,893	6,893
Upper Confid. Limit*	19.6	20.4	20.9	21.3	22.5	24.3	16.2	17.7
Birth/Treatm. %	19.3	20.2	20.6	21.0	22.2	24.0	15.8	17.3
Lower Confid. Limit*	19.0	19.9	20.4	20.7	21.9	23.6	15.4	16.9
<hr/>								
Retrospective Numbers	16,937	16,709	16,277	15,988	15,043	13,297	4,263	4,002
Birth	2,793	2,853	2,853	2,853	2,853	2,854	588	588
Upper Confid. Limit*	17.1	17.7	18.2	18.5	19.7	22.2	15.0	16.0
Birth/Treatm. %	16.5	17.1	17.5	17.8	19.0	21.5	13.8	14.7
Lower Confid. Limit*	15.9	16.4	16.9	17.2	18.3	20.7	12.7	13.5

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

** OPU = Oocyte Pick-Up FET = Frozen Embryo Transfer

Births as a Function of Number of Embryos Transferred and Age Groups 2000–2015

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

Woman's Age in Years	Singletons		Twins		Triplets		Quadruplets		Total	
	n	%	n	%	n	%	n	%		
<= 24	1 Embryo	189	97.9	4	2.1	0	0.0	0	0.0	193
	2 Embryos	1,755	76.1	540	23.5	10	0.4	0	0.0	2,305
	3 Embryos	278	67.6	111	27.0	20	4.9	2	0.5	411
	Total	2,222	76.4	655	22.5	30	1.0	2	0.1	2,909
25 – 29	1 Embryo	2,296	95.7	94	3.9	9	0.4	0	0.0	2,399
	2 Embryos	19,443	75.2	6,292	24.3	127	0.5	4	0.0	25,866
	3 Embryos	2,819	68.8	1,050	25.6	226	5.5	3	0.1	4,098
	Total	24,558	75.9	7,436	23.0	362	1.1	7	0.0	32,363
30 – 34	1 Embryo	6,256	96.9	191	3.0	7	0.1	0	0.0	6,454
	2 Embryos	43,643	76.0	13,549	23.6	250	0.4	3	0.0	57,445
	3 Embryos	8,206	70.8	2,899	25.0	473	4.1	7	0.1	11,585
	Total	58,105	77.0	16,639	22.0	730	1.0	10	0.0	75,484
35 – 39	1 Embryo	6,567	97.1	188	2.8	6	0.1	0	0.0	6,761
	2 Embryos	34,418	81.8	7,497	17.8	146	0.4	2	0.0	42,063
	3 Embryos	11,474	76.8	3,125	20.9	344	2.3	2	0.0	14,945
	Total	52,459	82.2	10,810	17.0	496	0.8	4	0.0	63,769
>= 40	1 Embryo	1,600	96.0	64	3.9	2	0.1	0	0.0	1,666
	2 Embryos	5,526	89.4	642	10.4	11	0.2	1	0.0	6,180
	3 Embryos	3,342	87.0	471	12.3	27	0.7	0	0.0	3,840
	Total	10,468	89.6	1,177	10.1	40	0.3	1	0.0	11,686

Total number of births 2000 – 2015: 186,211

Births as a Function of Number of Embryos Transferred and Treatment Method 2000–2015

Prospective and Retrospective Data

IVF

	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	
1 Embryo	3,366	10.0	49	0.5	4	0.8	0	0.0	3,419
2 Embryos	24,160	71.5	7,216	74.0	129	25.1	1	14.3	31,506
3 Embryos	6,286	18.6	2,485	25.5	380	74.1	6	85.7	9,157
Total	33,812	76.7	9,750	22.1	513	1.2	7	0.0	44,082

ICSI

	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	
1 Embryo	9,418	11.0	163	0.8	12	1.4	0	0.0	9,593
2 Embryos	61,889	72.5	17,381	80.6	289	33.2	6	40.0	79,565
3 Embryos	14,051	16.5	4,018	18.6	569	65.4	9	60.0	18,647
Total	85,359	79.2	21,561	20.0	870	0.8	15	0.0	107,805

Cryo Transfer

	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	
1 Embryo	4,347	14.9	104	2.1	10	4.0	0	0.0	4,461
2 Embryos	19,286	66.2	3,412	69.0	90	36.3	0	0.0	22,788
3 Embryos	5,494	18.9	1,432	28.9	148	59.7	1	100.0	7,075
Total	29,127	84.9	4,948	14.4	248	0.7	1	0.0	34,324

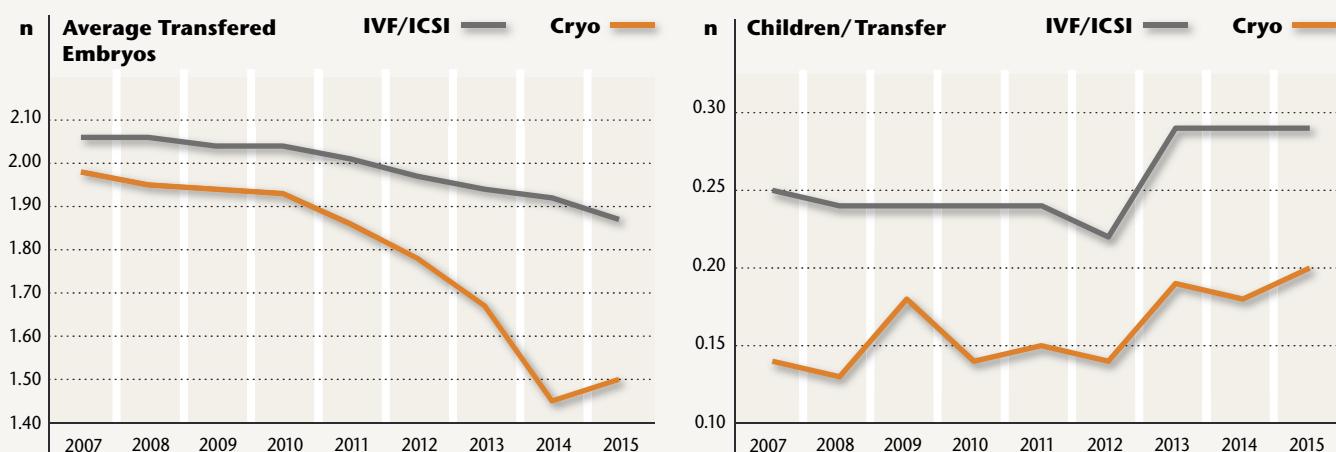
Fertilisation Rate 2016

IVF and ICSI – Prospective Data

Recovered Oocytes 540,268	IVF 118,906	22.0%	Fertilisation Rate 66.930	56.3%	Embryos per Transfer 1.80³
Cycles 56,175 ¹	ICSI 334,049	61.8%	Fertilisation Rate 220.380	66.0%	Embryos per Transfer 1.83³
Oocytes/Cycle 9.5	Oocytes Cryo Preserved 8,324	1.5%			
	Oocyte Treatment not Possible² 78,989	14.6%			

Embryos per Transfer³ and Children After IVF, ICSI 1997–2015

Prospective and Retrospective Data



	1997	[...]	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	
IVF	Embryos Transf.	2.49	For values from 1998 to 2004 see www.deutsches-ivf-register.de	2.11	2.08	2.08	2.06	2.03	2.01	1.95	1.88	1.86	1.75	1.80
	Children/Transf.	0.21		0.24	0.25	0.25	0.24	0.24	0.22	0.17	0.26	0.32	0.30	0.30
	Children/Deliv.	1.31		1.23	1.23	1.24	1.24	1.22	1.24	1.26	1.22	1.08	1.25	1.24
ICSI	Embryos Transf.	2.56		2.11	2.09	2.08	2.08	2.06	2.05	1.98	1.91	1.88	1.88	1.90
	Children/Transf.	0.22		0.24	0.24	0.24	0.23	0.23	0.22	0.16	0.25	0.28	0.29	0.29
	Children/Deliv.	1.29		1.22	1.20	1.21	1.22	1.21	1.21	1.22	1.21	1.22	1.22	1.22
Cryo Transfer	Embryos Transf.	2.34		2.10	2.10	2.07	2.07	2.05	2.04	1.96	1.79	1.65	1.45	1.50
	Children/Transf.	0.10		0.14	0.14	0.14	0.14	0.14	0.14	0.11	0.16	0.19	0.18	0.20
	Children/Deliv.	1.14		1.16	1.16	1.16	1.15	1.16	1.16	1.18	1.16	1.16	1.16	1.16

1) In 562 cases no IVF- or ICSI treatment was performed. 210 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 2016

IVF and ICSI – Prospective Data

IVF

Male Factor ▶	Normal		Reduced Semen Quality		Other**		Total	
Female Factor ▼	n	%	n	%	n	%	n	%
Normal	1,527	11.7	578	4.4	993	7.6	3,098	23.8
Tubal Pathology	1,542	11.9	476	3.7	689	5.3	2,707	20.8
Endometriosis	810	6.2	223	1.7	481	3.7	1,514	11.6
Hyperandrog./PCO	404	3.1	110	0.8	189	1.5	703	5.4
Ovulatory Dysf.	523	4.0	209	1.6	219	1.7	951	7.3
Psychogen. Factors	178	1.4	46	0.4	88	0.7	312	2.4
Other*	905	7.0	511	3.9	1,591	12.2	3,007	23.1
No Information	19	0.1	5	0.0	686	5.3	710	5.5
Total	5,908	45.4	2,158	16.6	4,936	38.0	13,002	100.0

ICSI

Male Factor ▶	Normal		Reduced Semen Qual.		Azoospermia		Other**		Total	
Female Factor ▼	n	%	n	%	n	%	n	%	n	%
Normal	1,125	2.6	11,581	26.9	1,029	2.4	3,948	9.2	17,683	41.1
Tubal Pathology	524	1.2	1,400	3.3	61	0.1	763	1.8	2,748	6.4
Endometriosis	364	0.8	1,616	3.8	53	0.1	855	2.0	2,888	6.7
Hyperandrog./PCO	138	0.3	1,027	2.4	71	0.2	540	1.3	1,776	4.1
Ovulatory Dysf.	269	0.6	1,828	4.3	126	0.3	839	2.0	3,062	7.1
Psychogen. Factors	85	0.2	458	1.1	53	0.1	248	0.6	844	2.0
Other*	757	1.8	4,710	11.0	299	0.7	5,355	12.5	11,121	25.9
No Information	9	0.0	93	0.2	9	0.0	2,750	6.4	2,861	6.7
Total	3,271	7.6	22,713	52.8	1,701	4.0	15,298	35.6	42,983	100.0

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

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

IVF and ICSI 2015

Prospective Data

IVF 2015

	n	%	Fertilisation %	Embryo %	Transfer %	Clin. Preg. %
Performed IVF Treatm.	13,002	100.0				
Successful Fertilis.*	12,163	93.5	100.0			
Minimum 1 Embryo	11,690	89.9	96.1	100.0		
ET Performed	11,344	87.2	93.3	97.0	100.0	
Clin. Pregnancy	3,746	28.8	30.8	32.0	33.0	100.0
Birth	2,752	21.2	22.6	23.5	24.3	73.5
Miscarriage	757					20.2
Ectopic Pregnancy	76					2.0
Not Yet Recorded	161					4.3

ICSI 2015

	n	%	Fertilisation %	Embryo %	Transfer %	Clin. Preg. %
Performed ICSI Treatm.	43,746	100.0				
Successful Fertilis.*	41,622	95.1	100.0			
Minimum 1 Embryo	39,132	89.5	94.0	100.0		
ET Performed	38,144	87.2	91.6	97.5	100.0	
Clin. Pregnancy	12,387	28.3	29.8	31.7	32.5	100.0
Birth	9,090	20.8	21.8	23.2	23.8	73.4
Miscarriage	2,547					20.6
Ectopic Pregnancy	166					1.3
Not Yet Recorded	584					4.7

*) Successful fertilisation of at least one oocyte per cycle

Testicular Sperm Extraction (TESE) and Cryo Transfer 2015

Prospective Data

ICSI/TESE 2015

	n	%	Fertilisation %	Embryo %	Transfer %	Clin. Preg. %
ICSI	2,203	100.0				
Successful Fertilis.*	1,996	90.6	100.0			
Minimum 1 Embryo	1,918	87.1	96.1	100.0		
ET Performed	1,834	83.3	91.9	95.6	100.0	
Clin. Pregnancy	589	26.7	29.5	30.7	32.1	100.0
Birth	427	19.4	21.4	22.3	23.3	72.5
Miscarriage	120					20.4
Ectopic Pregnancy	13					2.2
Not Yet Recorded	29					4.9

Cryo Transfer 2015

	n	%	PN %	Transfer %	Clin. Preg. %
Cryo Transfer Cycles	21,253	100.0			
Thawed PN	21,199	99.7	100.0		
ET Performed	21,196	99.7	100.0	100.0	
Clin. Pregnancy	5,364	25.2	25.3	25.3	100.0
Birth	3,686	17.3	17.7	17.4	68.7
Miscarriage	1,327				24.7
Ectopic Pregnancy	90				1.7
Not Yet Recorded	261				4.9

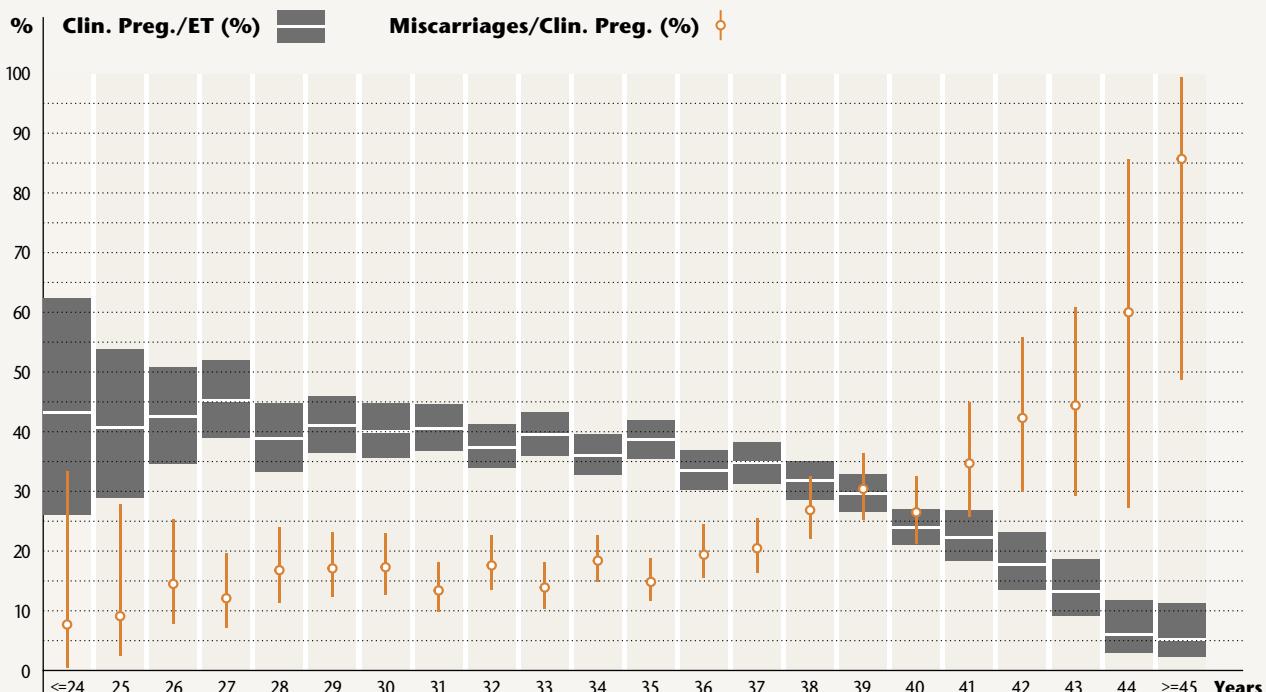
*) Successful fertilisation of at least one oocyte per cycle

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2015



Prospective Data

IVF 2015



n	30	54	146	236	321	426	491	623	697	765	874	941	892	842	842	885	930	439	292	273	165	134	ET
%	43.3	40.7	42.5	45.3	38.9	41.1	40.1	40.6	37.4	39.6	36.0	38.7	33.5	34.8	31.8	29.7	24.0	22.3	17.8	13.2	6.1	5.2	CP/ET
n	9	17	47	89	93	137	150	197	201	245	232	277	219	216	179	170	151	61	30	20	4	1	Birth

Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	1,430	3,971	5,053	1,103	515	367	343	196	171	13,149
Oocytes ¹	11.6	10.5	8.5	7.0	6.3	5.7	5.8	4.4	3.9	8.9
Insemination ¹	11.3	10.3	8.3	6.9	6.2	5.7	5.7	4.3	3.8	8.7
ET	1,213	3,450	4,448	930	439	292	273	165	134	11,344
ET/OPU %	84.8	86.9	88.0	84.3	85.2	79.6	79.6	84.2	78.4	86.3
Trans. Embr. ¹	1.84	1.84	1.83	1.88	1.92	1.77	1.90	1.82	1.95	1.84
CP	504	1,329	1,487	223	98	52	36	10	7	3,746
CP/OPU %	35.2	33.5	29.4	20.2	19.0	14.2	10.5	5.1	4.1	28.5
CP/ET upper Confidence Limit*%	44.4	40.2	35.1	27.1	26.8	23.1	18.6	11.8	11.2	34.0
CP/ET %	41.5	38.5	33.4	24.0	22.3	17.8	13.2	6.1	5.2	33.0
CP/ET lower Confidence Limit*%	38.7	36.8	32.1	21.1	18.4	13.5	9.2	3.0	2.3	32.2
CP/ET %: 2 Embr.transf. + min. 2 2-PN surplus	43.2	40.4	37.2	27.3	25.1	24.3	16.2	9.7	6.0	36.3

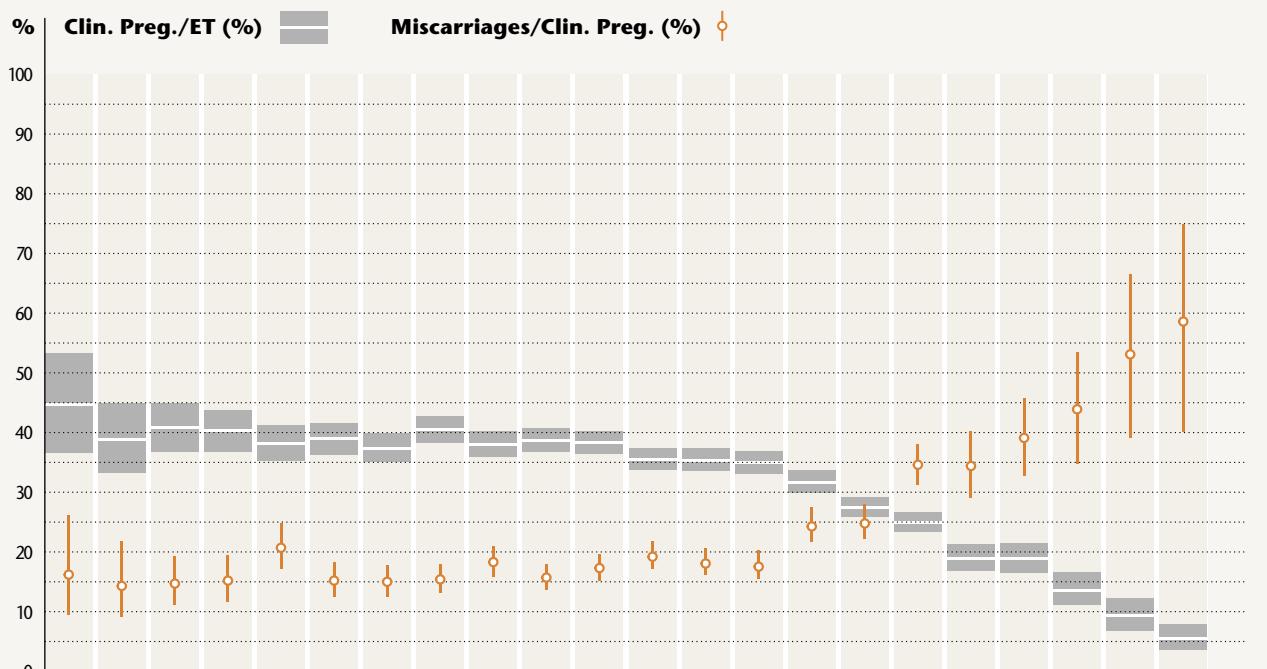
1) Mean

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

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2015

Prospective Data

ICSI 2015



n	152	288	566	785	1,062	1,431	1,697	2,066	2,255	2,575	2,783	3,033	2,975	2,803	2,837	3,215	2,966	1,459	1,096	839	529	530	ET
%	44.7	38.9	40.8	40.3	38.2	39.0	37.4	40.5	38.0	38.7	38.4	35.5	35.4	35.0	31.7	27.4	24.9	18.9	18.9	13.6	9.3	5.5	CP/ET
n	52	88	176	241	299	436	504	654	655	780	815	803	795	745	621	594	447	167	103	58	18	11	Birth

Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	4,893	12,783	16,830	3,423	1,736	1,390	1,043	662	755	43,515
Oocytes ¹	12.6	11.4	9.3	7.9	7.0	6.6	6.5	5.9	6.2	9.8
Insemination ¹	9.3	8.5	7.0	6.0	5.3	4.9	4.8	4.2	3.9	7.4
ET	4,284	11,376	14,756	2,966	1,459	1,096	839	529	839	38,144
ET/OPU %	87.6	89.0	87.7	86.6	84.0	78.8	80.4	79.9	111.1	87.7
Trans. Embr. ¹	1.83	1.83	1.83	1.85	1.82	1.85	1.77	1.77	1.72	1.83
CP	1,691	4,393	4,889	739	276	207	114	49	29	12,387
CP/OPU %	34.6	34.4	29.0	21.6	15.9	14.9	10.9	7.4	3.8	28.5
CP/ET upper Confidence Limit*%	41.0	39.6	33.4	26.6	21.3	21.5	16.5	12.3	7.9	33.0
CP/ET %	39.5	38.6	33.1	24.9	18.9	18.9	13.6	9.3	3.5	32.5
CP/ET lower Confidence Limit*%	38.0	37.7	31.8	23.3	16.8	16.5	11.1	6.9	3.7	32.0
CP/ET %: 2 Embr.transf. + min. 2 2-PN surplus	41.8	40.9	35.8	29.0	22.1	22.8	17.2	11.8	7.7	35.9

1) Mean

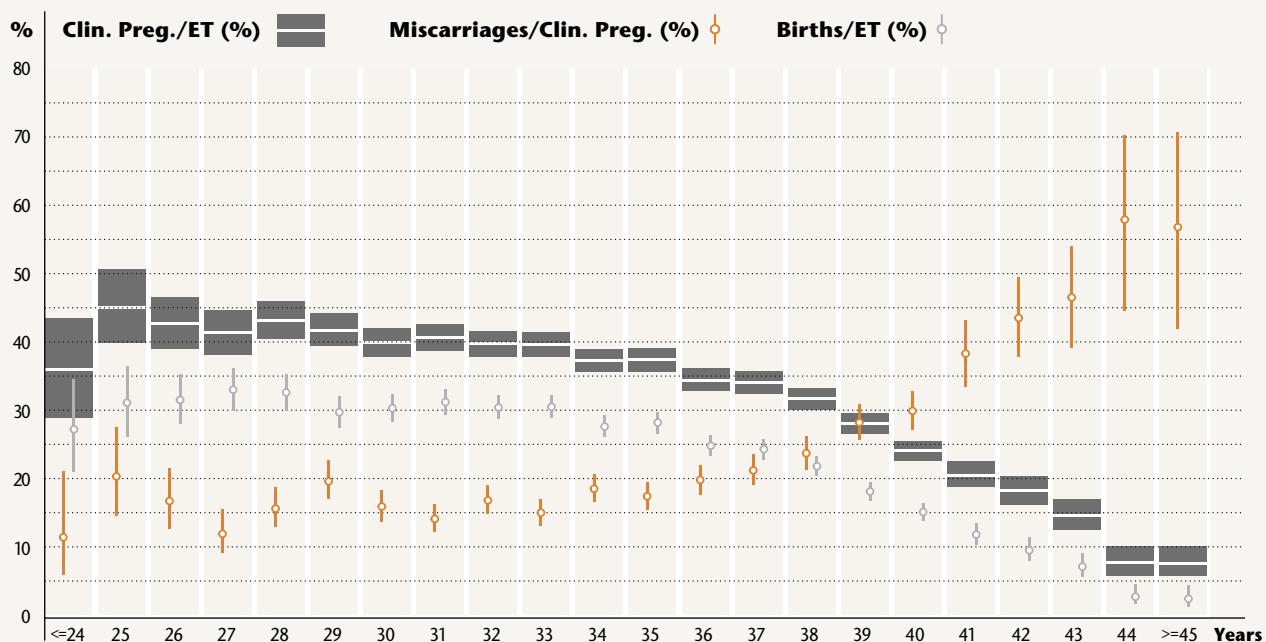
* With a 95%-probability, the true mean lies within the defined confidence interval.

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2011 – 2015



Prospektive Daten

IVF 2011 – 2015



n	195	328	660	929	1.324	1.708	2.261	2.545	2.915	3.156	3.504	3.563	3.618	3.611	3.565	3.974	4.019	1.910	1.491	1.179	745	576	ET
%	35.9	45.1	42.7	41.4	43.1	41.7	39.9	40.6	39.7	39.6	37.3	37.4	34.4	34.0	31.7	28.0	24.1	20.5	18.2	14.6	7.7	7.6	CP/ET
n	53	102	208	307	431	508	685	793	886	963	968	1.005	897	877	776	720	606	225	142	84	20	14	Birth
Age in Years																							
OPU	5,979		16,431		21,050		4,662		2,295		1,774		1,428		926		741		55,286				
Oocytes ¹	11.6		10.4		8.4		7.1		6.4		6.1		5.6		5.0		4.6		8.9				
ET/OPU %	86.0		87.5		87.1		86.2		83.2		84.0		82.6		80.5		77.7		86.4				
Trans. Embr. ¹	1.92		1.89		1.91		1.95		1.94		1.97		1.92		1.81		1.85		1.91				
CP	2,169		5,649		6,050		967		392		271		172		57		44		15,771				
CP/OPU %	36.3		34.4		28.7		20.7		17.1		15.3		12.0		6.2		5.9		28.5				
CP/ET upper Confidence Limit*%	43.6		40.1		33.7		25.5		22.5		20.4		16.9		10.1		10.1		33.5				
CP/ET %	42.2		39.3		33.0		24.1		20.5		18.2		14.6		7.7		7.6		33.0				
CP/ET lower Confidence Limit*%	40.8		38.4		32.3		22.7		18.7		16.2		12.5		5.8		5.8		32.5				
CP/ET %: 2 Embr. transf. + min. 2 2-PN surplus	44.0		41.6		36.0		27.5		23.4		22.2		18.5		9.3		10.0		35.9				
Misc./CP upper Confidence Limit*%	18.2		17.1		22.8		32.8		43.2		49.5		54.0		70.2		70.6		21.5				
Misc./CP %	16.6		16.1		21.8		29.9		38.3		43.5		46.5		57.9		56.8		20.8				
Misc./CP lower Confidence Limit*%	15.1		15.3		20.8		27.1		33.5		37.8		39.2		44.5		41.9		20.2				
Births/ET upper Confidence Limit*%	32.7		30.7		24.0		16.4		13.5		11.4		9.0		4.5		4.4		24.0				
Births/ET %	31.3		29.9		23.3		15.1		11.8		9.5		7.1		2.7		2.4		23.6				
Births/ET lower Confidence Limit*%	29.9		29.1		22.6		13.9		10.3		7.9		5.6		1.6		1.3		23.2				

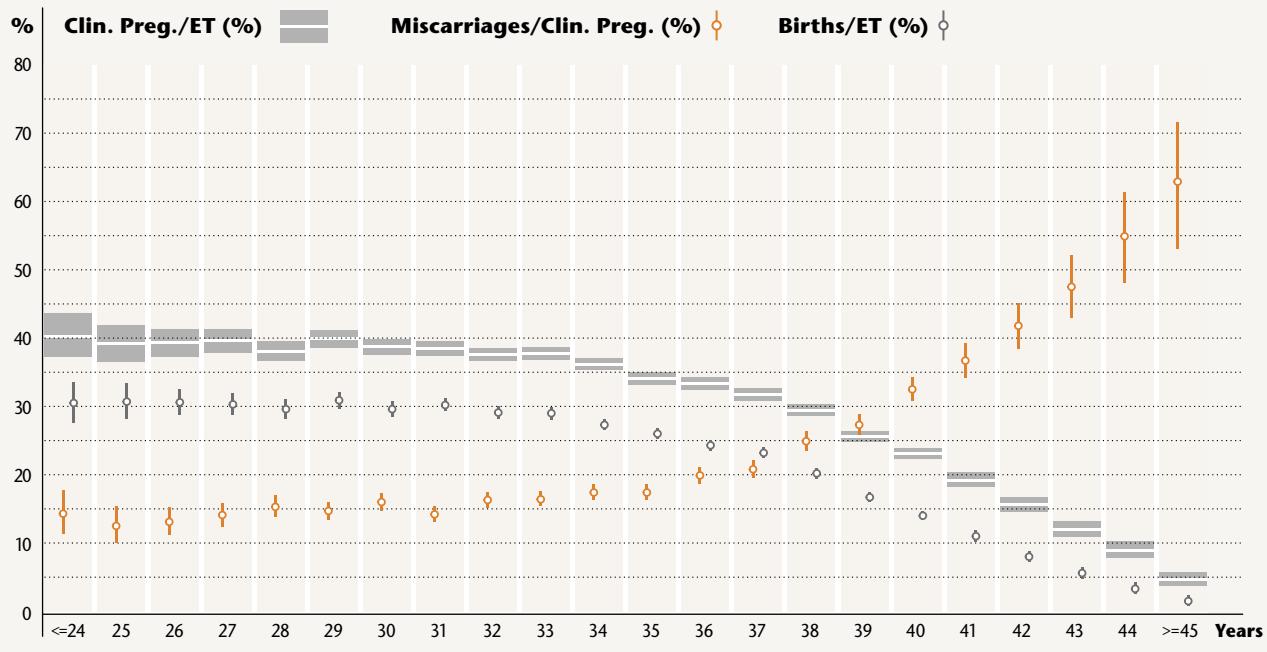
1) Mean

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

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2011 – 2015

Prospektive Daten

ICSI 2011 – 2015



n	989	1,332	2,483	3,588	4,718	6,193	7,662	9,353	10,533	11,451	12,260	12,784	12,832	12,210	11,945	13,339	12,933	6,995	5,506	3,819	2,415	2,246	ET
%	40.3	39.2	39.3	39.6	38.1	39.9	38.7	38.5	37.6	37.7	36.2	34.1	33.3	31.7	29.4	25.6	23.1	19.2	15.7	12.0	8.9	4.7	CP/ET
n	302	409	761	1,088	1,395	1,914	2,269	2,829	3,065	3,320	3,346	3,321	3,112	2,827	2,412	2,228	1,813	769	438	215	79	33	Birth

Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	21,515	56,726	70,868	14,830	8,153	6,580	4,674	2,968	2,571	188,885
Oocytes ¹⁾	12.4	11.3	9.2	7.7	7.0	6.5	5.9	5.6	5.0	9.6
ET/OPU %	89.7	90.4	89.1	87.2	85.8	83.7	81.7	81.4	87.4	87.5
Trans. Embr. ¹⁾	1.89	1.91	1.92	1.96	1.92	1.93	1.94	1.87	1.79	1.93
CP	7,586	19,282	19,431	2,989	1,345	862	459	215	105	52,274
CP/OPU %	35.3	34.0	27.4	20.2	16.5	13.1	9.8	7.2	4.1	27.7
CP/ET upper Confidence Limit*%	40.0	38.1	31.2	23.9	20.3	16.7	13.2	10.2	5.8	31.4
CP/ET %	39.3	37.6	30.8	23.1	19.2	15.7	12.0	8.9	4.7	31.2
CP/ET lower Confidence Limit*%	38.6	37.2	30.4	22.3	18.2	14.6	10.9	7.8	3.8	30.9
CP/ET %: 2 Embr. transf. + min. 2 2-PN surplus	40.8	39.5	33.6	26.3	22.2	18.9	15.1	11.2	7.8	34.2
Aborte/Klin. SS upper Confidence Limit*%	15.1	16.6	22.3	34.2	39.3	45.1	52.1	61.4	71.6	20.7
Misc./CP %	14.3	16.1	21.7	32.5	36.7	41.8	47.5	54.9	62.9	20.4
Misc./CP lower Confidence Limit*%	13.6	15.7	21.2	30.8	34.2	38.5	42.9	48.2	53.1	20.1
Births/ET upper Confidence Limit*%	31.1	29.4	22.4	14.7	11.9	8.8	6.5	4.2	2.4	22.9
Births/ET %	30.4	28.9	22.0	14.0	11.0	8.0	5.6	3.3	1.5	22.6
Births/ET lower Confidence Limit*%	29.7	28.5	21.7	13.4	10.2	7.2	4.8	2.5	0.9	22.4

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 2016

Prospective Data

IVF and ICSI

Age in Year	1 Embryo		2 Embryos		3 Embryos		Total	
	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %
<= 24	39	33.3	123	40.7	2	0.0	164	38.4
25 – 29	837	28.4	3,872	43.4	151	33.1	4,860	40.5
30 – 34	2,696	29.9	11,197	40.5	560	37.7	14,453	38.4
35 – 39	4,277	21.5	13,486	35.2	1,345	33.8	19,108	32.1
40	991	17.1	2,572	27.7	521	29.4	4,084	25.3
41	544	12.3	1,145	23.3	249	23.7	1,938	20.3
42	471	12.7	785	20.4	225	17.3	1,481	17.5
43	391	7.2	539	17.4	156	19.2	1,086	14.0
44	226	7.1	329	12.5	135	17.0	690	11.6
45	179	3.9	178	13.5	69	13.0	426	9.4
> = 46	151	5.3	186	16.7	57	5.3	394	10.7
Total	10,802	21.6	34,412	35.9	3,470	29.7	48,684	32.3

Cryo Transfer

Age in Year	1 Embryo		2 Embryos		3 Embryos		Total	
	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %	ET	CP/ET %
<= 24	9	33.3	47	21.3	3	0.0	59	22.0
25 – 29	378	23.8	1,697	30.3	103	29.1	2,178	29.1
30 – 34	1,673	21.8	5,148	28.3	413	29.3	7,234	26.8
35 – 39	2,285	20.5	5,567	25.6	664	25.2	8,516	24.2
40	267	16.9	640	22.2	140	25.7	1,047	21.3
41	159	11.9	415	19.8	120	26.7	694	19.2
42	121	12.4	244	16.8	66	19.7	431	16.0
43	63	20.6	140	16.4	49	16.3	252	17.5
44	51	13.7	83	18.1	33	9.1	167	15.0
45	17	11.8	47	12.8	13	7.7	77	11.7
> = 46	21	9.5	34	17.6	17	0.0	72	11.1
Total	5,044	20.4	14,062	26.4	1,621	25.4	20,727	24.9

Clinical Pregnancies (CP)/Fresh Transfer as a Function of Embryo Quality 2016

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	135	11.9	369	12.5	630	8.6	458	5.5	1,592	8.9
0	2	270	24.8	719	22.3	918	19.2	441	14.3	2,348	19.9
0	3	9	0.0	39	18.0	89	18.0	92	8.7	229	13.5
1	0	724	31.2	2,271	32.5	3,536	23.4	2,436	13.1	8,967	23.5
1	1	442	37.8	1,195	34.1	1,591	29.7	764	18.2	3,992	29.7
1	2	19	26.3	37	27.0	87	28.7	100	13.0	243	21.8
2	0	3,298	45.6	9,906	43.9	10,641	38.5	4,436	25.5	28,281	39.0
2	1	22	50.0	77	36.4	179	33.0	209	22.5	487	29.8
3	0	103	33.0	410	41.0	1,003	35.9	1,029	24.1	2,545	31.8
Total		5,022	40.4	15,023	39.1	18,674	32.6	9,965	20.0	48,684	32.7

Clinical Pregnancies (CP)/Frozen Transfer as a Function of Embryo Quality 2016

Cryo Transfer – Prospective Data

Quality		IVF		ICSI	
ideal	Not Ideal	ET	CP/ET %	ET	CP/ET %
0	1	199	17.6	622	9.2
0	2	305	12.7	1,152	16.1
0	3	29	13.0	127	12.8
1	0	902	21.6	3,027	23.4
1	1	557	14.1	1,821	20.9
1	2	34	25.9	172	23.2
2	0	2,586	28.6	7,718	29.5
2	1	75	28.3	219	24.0
3	0	279	28.7	903	27.1
Total*		4,966	22.6	15,761	22.6

* In 1,924 cases, resulting in an additional 814 pregnancies, no information is available on the preceding treatment.

Miscarriage (MISC) Rates as a Function of Female Age and Number of Embryos Transferred 2015

Prospective Data

IVF and ICSI

Age in Years	1 Embryo		2 Embryos		3 Embryos		Total	
	CP	MISC/CP %	CP	MISC/CP %	CP	MISC/CP %	CP	MISC/CP %
<= 24	9	11.1	73	16.4	1	0.0	83	15.7
25 – 29	267	16.9	1,785	15.4	83	22.9	2,135	15.8
30 – 34	735	17.3	4,748	15.4	269	20.8	5,752	15.9
35 – 39	877	25.5	4,870	20.3	556	24.1	6,303	21.4
40 – 44	263	44.9	1,191	33.6	370	39.5	1,824	36.4
>= 45	9	100.0	14	71.4	13	53.8	36	72.2
Total	2,160	24.3	12,681	19.1	1,292	28.0	16,133	20.5

Cryo

Age in Years	1 Embryo		2 Embryos		3 Embryos		Total	
	CP	MISC/CP %	CP	MISC/CP %	CP	MISC/CP %	CP	MISC/CP %
<= 24	8	37.5	18	27.8	1	0.0	27	29.6
25 – 29	92	25.0	490	21.2	74	25.7	656	22.3
30 – 34	278	24.1	1,519	21.1	198	19.2	1,995	21.3
35 – 39	392	23.5	1,456	24.0	235	32.8	2,083	24.9
40 – 44	103	31.1	365	37.8	122	45.1	590	38.1
>= 45	3	66.7	7	14.3	3	33.3	13	30.8
Total	876	25.0	3,855	23.8	633	30.0	5,364	24.7

Clinical Pregnancy Rate (CPR) as a Function of the Stimulation Protocol 2016

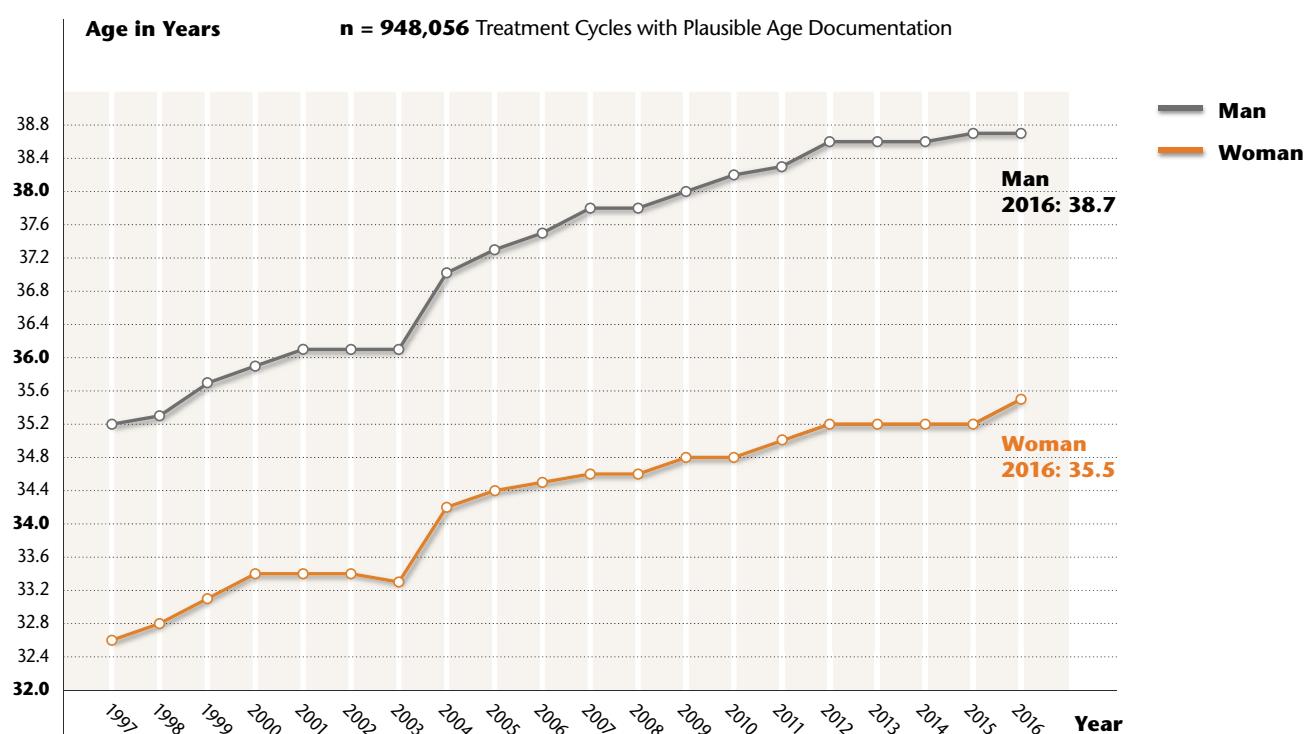
Prospective Data

IVF and ICSI

	u-FSH	rec-FSH	hMG	recLH and recFSH	recFSH and hMG	Other*	No Information	Total	Perc. %
Short GnRHa	11	717	647	198	417	0	3	1,993	4.1
Transfer Rate (%)	64.7	76.0	74.8	65.1	73.2	0.0	60.0	73.6	
CP/ET (%)	0.0	22.2	24.6	20.2	22.3	0.0	33.3	22.7	
Long GnRHa	49	4,377	2,243	1,020	2,299	4	47	10,039	20.6
Transfer Rate (%)	76.6	77.7	76.5	74.8	77.3	36.4	75.8	77.0	
CP/ET (%)	30.6	36.3	32.0	30.9	32.0	25.0	42.6	33.8	
No GnRHa-Ana.	19	1,110	800	350	509	1,330	15	4,133	8.5
Transfer Rate (%)	70.4	72.9	72.4	72.0	70.7	68.4	60.0	70.9	
CP/ET (%)	36.8	35.1	30.1	30.9	32.2	18.3	33.3	28.0	
GnRHa-Antag.	257	17,677	4,896	4,515	4,759	25	390	32,519	66.8
Transfer Rate (%)	76.0	73.2	71.3	67.2	72.0	20.0	78.0	71.8	
CP/ET (%)	31.9	35.8	27.2	32.5	29.7	24.0	23.3	32.9	
Total	336	23,881	8,586	6,083	7,984	1,359	455	48,684	100.0

Mean Age for Women and Men 1997 – 2016

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



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

Children as a Function of Week of Gestation (WoG) and Birth Weight (BW) 2015*

Singletons 2015

WoG	<25	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	>41	Total
n	46	26	15	27	38	35	55	56	99	125	202	279	583	1,215	2,335	3,145	2,861	1,805	706	13,653
BW p25	531	540	510	778	895	1,100	1,239	1,410	1,613	1,818	1,986	2,235	2,495	2,710	2,821	2,964	3,028	3,113	3,204	2,996
BW Median	608	690	695	930	1,055	1,240	1,465	1,620	1,927	2,240	2,395	2,525	2,900	3,145	3,308	3,440	3,500	3,548	3,578	3,298
BW p75	715	770	943	990	1,173	1,490	1,679	1,865	2,263	2,568	2,678	2,879	3,290	3,640	3,738	3,959	3,999	4,019	4,013	3,914

Percentiles 2015: p25 = 38th WoG, p50 = 39th WoG, p75 = 40th WoG;

Percentiles 1997–2015: p25 = 38th WoG, p50 = 39th WoG, p75 = 40th WoG

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

Twins 2015

WoG	<25	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	Total**
n	130	64	64	82	70	100	136	164	286	380	580	884	1,212	1,282	916	414	158	6,922
BW p25	489	598	745	871	970	1,127	1,255	1,398	1,475	1,648	1,855	2,050	2,183	2,244	2,325	2,466	2,613	2,173
BW Median	565	688	891	1,010	1,070	1,310	1,440	1,650	1,743	1,945	2,120	2,340	2,493	2,575	2,640	2,745	2,862	2,468
BW p75	735	828	965	1,165	1,215	1,488	1,690	1,893	1,958	2,201	2,455	2,650	2,778	2,911	2,990	2,994	3,160	2,794

Percentiles 2015: p25 = 34th WoG, p50 = 36th WoG, p75 = 37th WoG;

Percentiles 1997–2015: p25 = 34th WoG, p50 = 36th WoG, p75 = 37th WoG

Proportion of children born before the completion of the 37th WoG: 78.5%

**) The total contains 0 case with a WoG > 40

Triplets 2015

WoG	24	25	26	27	28	29	30	31	32	33	34	35	Total***
n	24	9	3	12	12	15	27	33	36	63	45	18	297
BW p25	389	696	830	873	948	1,240	1,070	1,515	1,720	1,600	1,783	1,769	1,103
BW Median	528	714	830	990	983	1,240	1,300	1,820	1,840	1,760	1,923	2,179	1,600
BW p75	653	732	830	1,008	1,033	1,240	1,510	1,930	1,910	1,950	2,050	2,210	1,948

Percentiles 2015: p25 = 30th WoG, p50 = 32nd WoG, p75 = 33rd WoG;

Percentiles 1997–2015: p25 = 30th WoG, p50 = 32nd WoG, p75 = 33rd WoG

Proportion of children born before the completion of the 37th WoG: 100.0%

***) The total contains 0 case with a WoG > 35

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

Children Born 1997 – 2015

Prospective and Retrospective Data

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

	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	
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	13,092	65.5	6,566	32.9	309	1.5	12	0.1	19,979
*	(13,040)	(65.6)	(6,508)	(32.8)	(309)	(1.6)	(12)	(0.1)	(19,869)
2015	13,702	65.4	6,942	33.1	297	1.4	8	0.0	20,949
*	(13,653)	(65.4)	(6,922)	(33.2)	(297)	(1.4)	(8)	(0.0)	(20,880)

For values from 1997 to 2001 see www.deutsches-ivf-register.de

*) The values in brackets indicate live births. Totalling 1997 – 2015:

164,286 (164,062) singletons, 83,502 (82,406) twins, 6,798 (6,614) triplets, 112 (105) quadruplets. In total: 254,698 (253,187)

MÖNCHENGLADBACH
Population of 259,996

BRAUNSCHWEIG
Population of 251,364

254,698
Children born 1997–2015

Ovarian Hyperstimulation Syndrome (OHSS) as a Function of the Stimulation Protocol 2016

IVF, ICSI, IVF/ICSI – Prospective Data

	Stimulation	%	Oocytes Retrieved	OHSS III	OHSS III/Stim %
Short GnRH	2,782	4.2	7.7	3	0.1
FSH only	1,255		8.6	2	0.2
hMG only	893		6.7	0	0.0
FSH + hMG	623		7.2	1	0.2
Other	2		21.5	0	0.0
No Information	9		3.2	0	0.0
Long GnRH	12,271	18.3	8.6	41	0.3
FSH only	6,431		8.6	12	0.2
hMG only	2,861		8.5	5	0.2
FSH + hMG	2,859		8.9	24	0.8
Other	3		5.0	0	0.0
No Information	117		5.2	0	0.0
No Analoga	8,655	12.9	9.7	8	0.1
FSH only	2,706		9.4	2	0.1
hMG only	1,534		9.8	0	0.0
FSH + hMG	832		10.3	4	0.5
Other	1		0.0	0	0.0
No Information	3,582		9.7	2	0.1
GnRH-Antagonists	43,178	64.6	8.6	94	0.2
FSH only	28,914		9.3	71	0.2
hMG only	7,072		6.4	6	0.0
FSH + hMG	6,444		8.3	16	0.2
Other	37		9.6	0	0.0
No Information	711		7.6	1	0.1
Total	66,886	100.0	8.7	146	0.2

Complications as a Function of Ovum Pick-up (OPU) 2016

Prospective Data

Total OPU's	60,195	100.0%			
			Complications	n	%
No Information	0	0.0%	Vaginal Bleeding	426	71.1
No Complications	59,596	99.0%	Intraabdom. Bleeding	57	9.5
Complications	599	1.0%	Intestinal Tract Injury	4	0.7
			Peritonitis	13	2.2
			Hospitalisation	3	0.5
			Surgery	17	2.8
			Other	79	13.2
			Total	599	100.0

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