Journal für

Reproduktionsmedizin und Endokrinologie

– Journal of Reproductive Medicine and Endocrinology –

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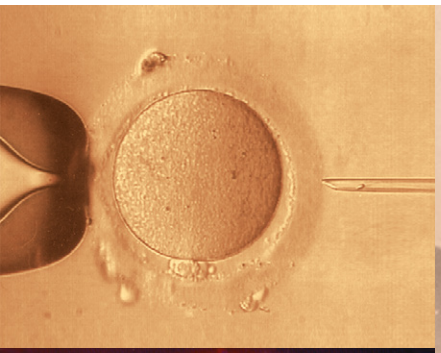

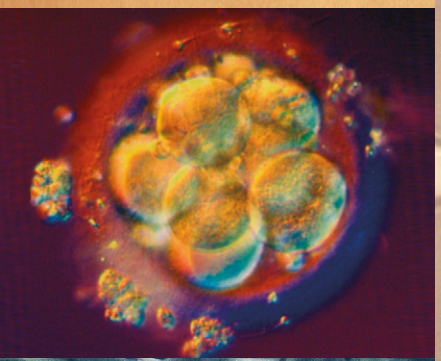

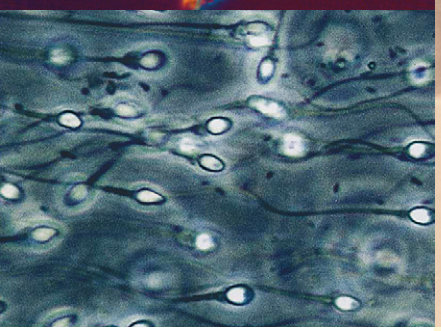

D.I.R-Annual 2019

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

Krüssel JS, Kupka MS, Ott A, Tandler-Schneider A

J. Reproduktionsmed. Endokrinol 2020; 17 (5), 196-239

www.kup.at/repromedizin

Online-Datenbank mit Autoren- und Stichwortsuche

Offizielles Organ: AGRBM, BRZ, DVR, DGA, DGGEF, DGRM, D·I·R, EFA, OEGRM, SRBM/DGE

Indexed in EMBASE/Excerpta Medica/Scopus

Krause & Pachernegg GmbH, Verlag für Medizin und Wirtschaft, A-3003 Gablitz

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Preface
D·I·R Annual 2019 – 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 annual report of the data collected by the German IVF-Registry (D·I·R). The 2019 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, nearly 2.0 million ART cycles (ART: Assisted Reproduction Technology) since 1982 and nearly 320,000 children born since 1997 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 2019 is like the Yearbook 2018 a yearbook of change and of organizational efforts undertaken by all authors and contributors. After years of data control and reconciliation, administrational work and programming, the implementation of a new data system has been rolled out to the IVF-clinics. This is still 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.

The 2019 yearbook is based on exploitable exports from 131 centers, for which a number of 110,786 plausible cycles was documented. A total of 62,990 women were treated in 2019, resulting in an average of 1.8 cycles per woman. We are happy to note that the pregnancy rate per transfer in fresh cycles was 31.6%, whereas the pregnancy rate per transfer in cryo cycles was 29.6%. In the previous year, 2018, the documented birth rate per embryo transfer was 23.5% in fresh cycles and 20.0% in cryo cycles, with a very good general pregnancy outcome documentation of 95.0%.

Remarkably, 71.8% of the pregnancies led to a birth. A birth rate of 22.3% 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 [BGBl 2013; 56: 1633–41].

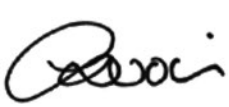
In the last years particular attention was placed on the known problems of multiple pregnancies within ART cycles. In 2018, the rate of twin births was 19.2% in fresh cycles and 12.7% in cryo cycles. This rate is still too high, but we can see a small decrease in multiple birth for the first time!

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, improvements in oocyte and embryo treatment, and changes in transfer technology, the average number of transferred embryos has decreased by more than 25% in fresh cycles since 1997. Nevertheless, on average 1.7 embryos after IVF and ICSI were transfered.

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!



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Prof. Dr. med. Jan-Steffen Krüssel

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D·I·R Annual 2019 – Tables

Number of Treatments in 2019

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

Members of the German IVF-Registry 2019	n = 137
Registry Participants 2019*	n=131
Data Received by Deadline Jun 2nd 2020*	n=131
Documented Treatment Cycles	n=110,786
Number of Women Treated**	n=62,990
Mean Number of Treatment Cycles per Woman	**1.8**

Type of plausible treatment 2015 – 2019

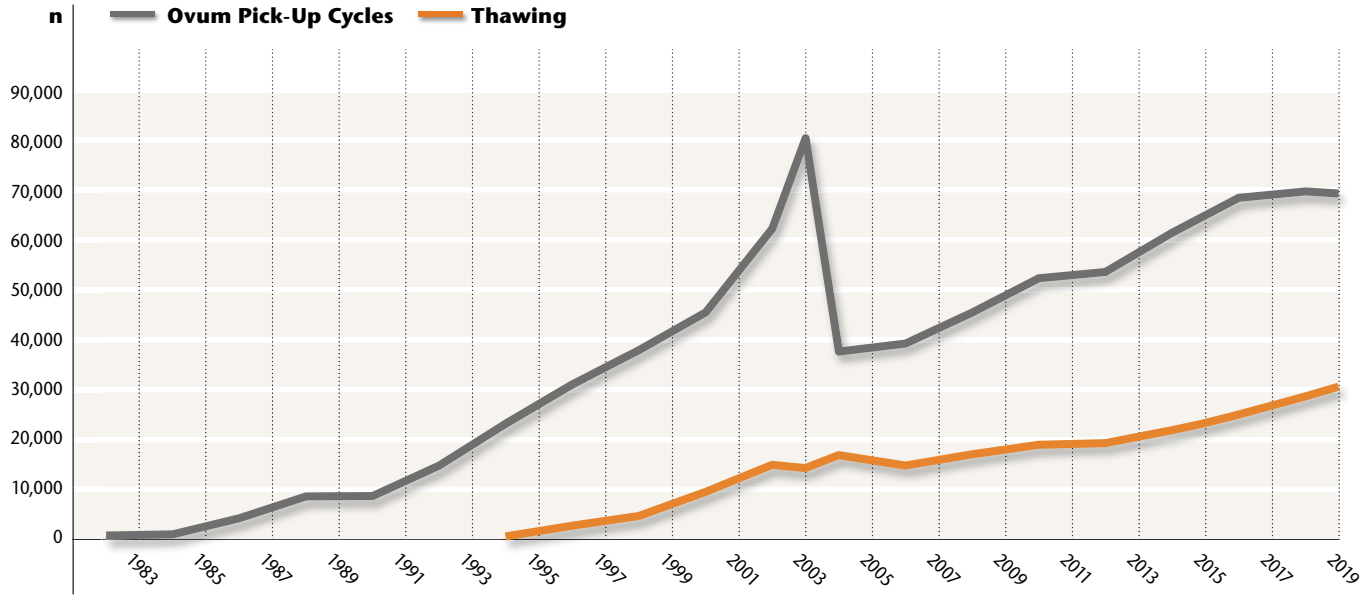
IVF, ICSI, IVF/ICSI, Cryo Transfer – Prospective and Retrospective Data

	2015		2016		2017		2018		2019	
	n	%	n	%	n	%	n	%	n	%
IVF	15,164	15.8	15,879	15.8	15,606	15.2	17,285	16.4	17,690	16.5
ICSI	48,674	50.6	48,690	48.3	47,471	46.3	46,604	44.3	45,381	42.3
IVF/ICSI	1,223	1.3	1,203	1.2	1,170	1.1	1,439	1.4	1,330	1.2
Freeze all - MII					1,347	1.3	1,307	1.2	1,856	1.7
Freeze All - PNs and Embryos					517	0.5	436	0.4	933	0.9
Cryo	23,571	24.5	25,008	24.8	27,234	26.6	28,698	27.3	30,666	28.6
Mixed Fresh and Cryo Cycles					235	0.2	286	0.3	254	0.2
None (= Break-off before oocyte treatment or thawing)	7,492	7.8	9,974	9.9	8,907	8.7	9,047	8.6	9,263	8.6
Total Plausible Cycles	**96,124**		**100,754**		**102,487**		**105,102**		**107,373**	

*) Six centers could not be part of the nationale analyses.
All centers used the interface ARTbox®.
**) Base quantity: Total number of women, including implausible treatment cycles

Number of Oocyte Retrievals (Freshcycles) 1982 – 2019
Number of Thawing Cycles 1994 – 2019
Registry Participants 1982 – 2019

IVF, ICSI* – Prospective and Retrospective Data



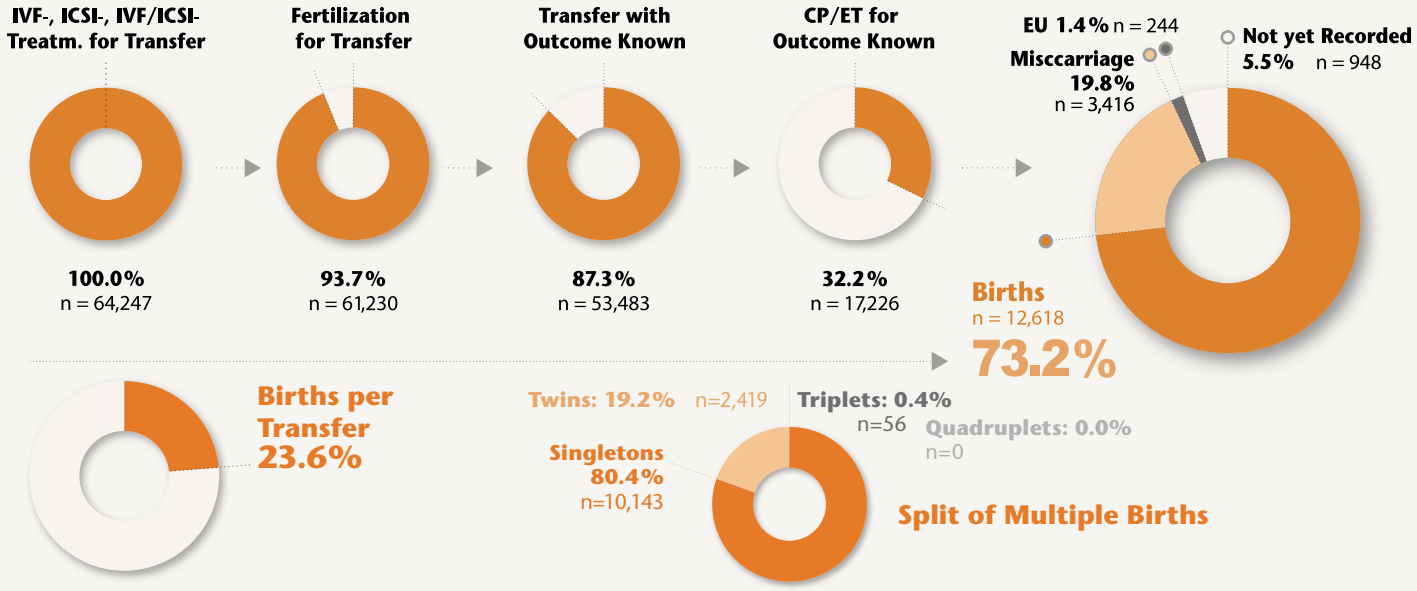
	1982	1986	1990	[...]	2002	2003	2004	[...]	2015	2016	2017	2018	2019
.	742	4,201	8,653		62,306	80,434	37,633		67,438	68,469	68,634	69,757	69,337
IVF	742	3,806	7,343	*For values from 1991 to 2001 see www.deutsches-ivf-register.de*	23,936	28,058	11,848	*For values from 2005 to 2014 see www.deutsches-ivf-register.de*	15,164	15,879	15,606	17,285	17,690
ICSI*					37,692	51,389	25,339		49,897	49,893	48,641	48,043	46,711
Thawing					14,923	14,265	16,883		23,226	25,045	27,234	28,698	30,666
Registry Participants	**5**	**28**	**53**		**112**	**116**	**120**		**130**	**128**	**127**	**131**	**131**

Data for 1982 to 2014 are published and available. Separate presentation of GIFT, ZIFT, IVF/ICSI was abstained from.

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

Summary of Statistics in Brief 2018 – CoD Jun 2nd 2020

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



Quality of Documentation 2018/2019

Plausible and Prospectively Documented Cycles, Cycle- and Pregnancy-Outcomes

Analyses results can only be as good as the underlying data.
The D·I·R-team is grateful to all participating centers and their meticulous work!

Plausible Cycles 2019

107,373 plausible cycles out of **110,786** documented cycles. **96.9%** of documented cycles are plausible. This does unfortunately not imply completeness of data required, thus impeding detaileed analyses.

Prospectively Documented Cycles 2019

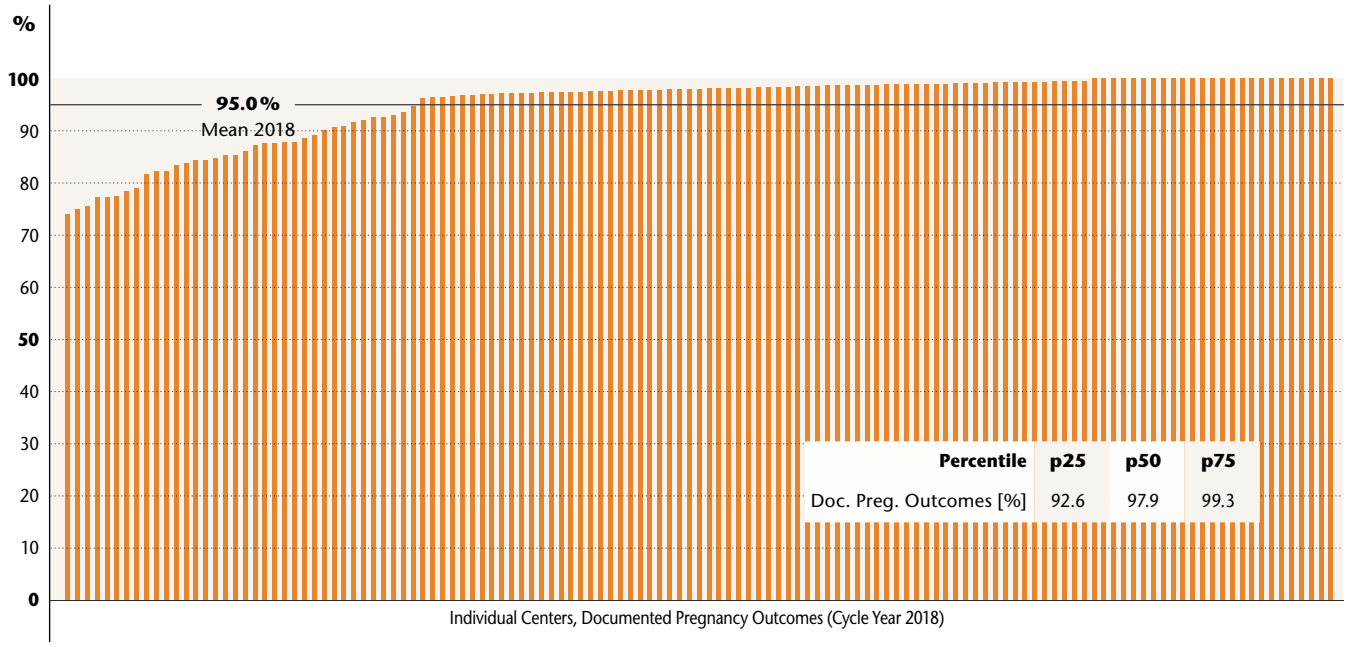
97,147 prspecticely documented cycles out of **107,373** plausible cycles. **90.5%** of documented cycles were prospectively documented. Worldwide, only the German IVF Registry separatly shows the prospective cycles. This in inself is an indicator for quality!

Documented Cycle-Outcomes 2019

In **81,700** out of **82,242** embrytransfers, the cycle outcome was documented (**99.3%**).

Documented Pregnancy Outcomes 2018

In **23,966** out of **25,230** clinical pregnancies, the pregnancy outcome was documented (**95.0%**).



We are well aware that the meticulous documentation of these relevant data is troublesome, laborious and recource-binding.

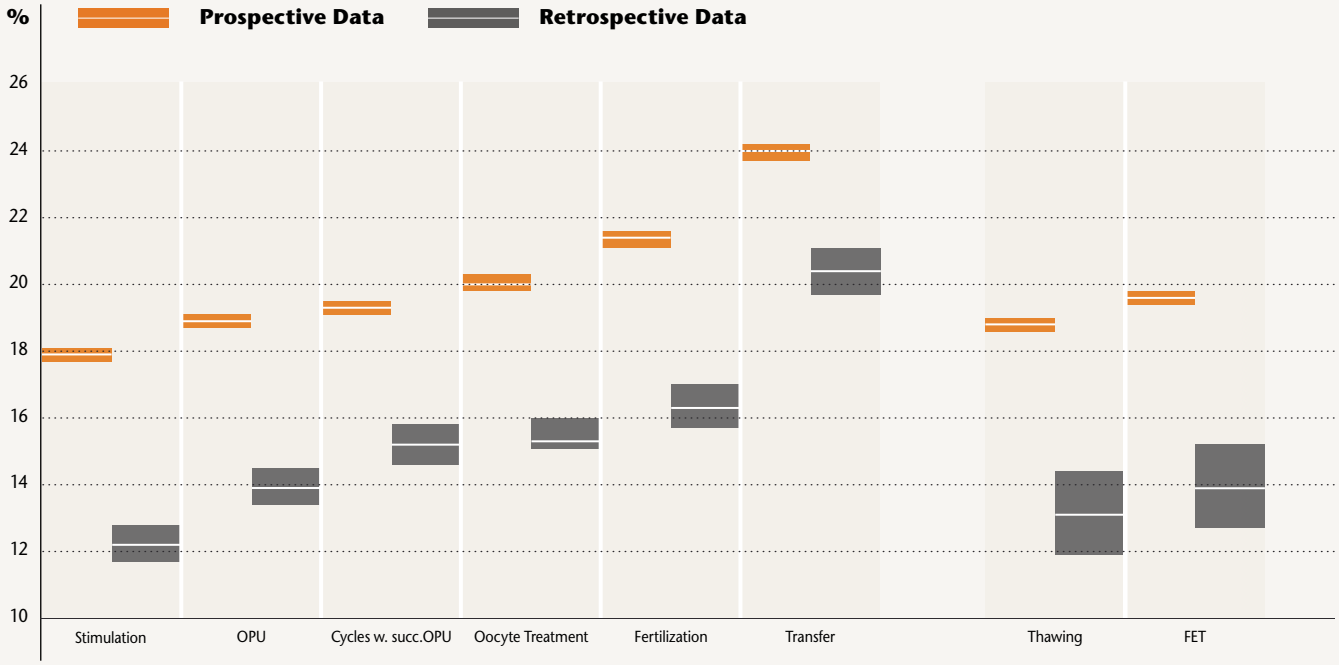
The D·I·R data analyses team is therefore very happy to stat that for the second year the percentage of prospectively documented cycles is **above 90%**.

Furthermore we are especially happy that the percentage of documented pregnancy outcomes has increased again. **72.1%** of individual centers have reached the goal of documenting **more than 95%** of pregnancy outcomes. **48.1%** have even reached a documentation rate on **>98%**, 25 centers even **100%**!

The dedicated goal of the D·I·R board of directors and board of trustees is to motivate the members of the D·I·R to furthermore keep their focus on nthe prospectivity and to achieve also for the next year a rate of documented pregnancy outcomes of **95 plus** percent.

Birth Rate per Treatment Level in Fresh and Cryo Treatment Cycles 2017 and 2018

Prospective and Retrospective Data

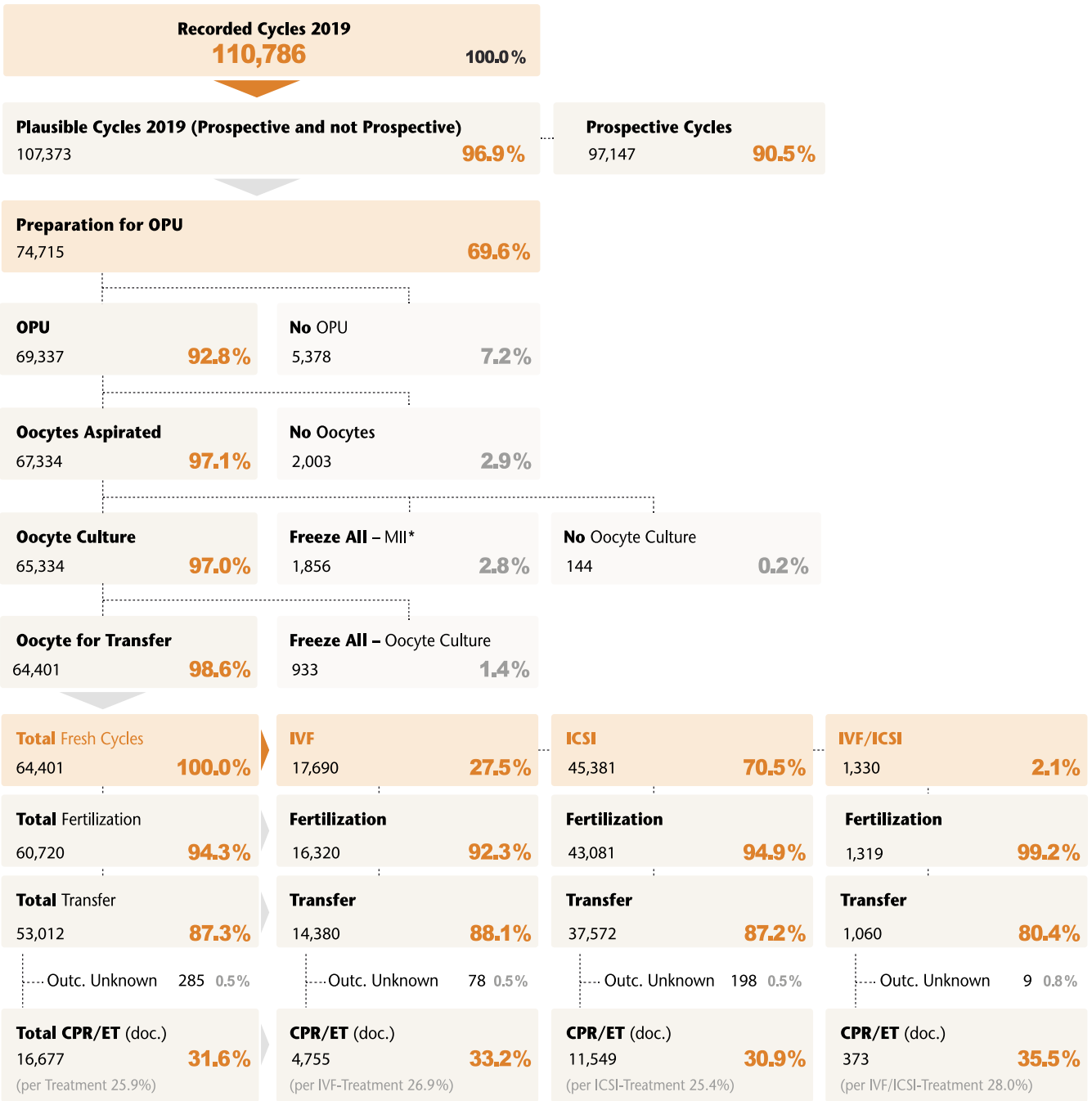


	Stimulation	OPU	Cycles with Successful OPU	Oocyte Treatment	Fertilization	Transfer	Thawing	FET
Prospective Numbers	133,909	127,038	124,120	119,789	112,303	100,119	52,051	49,844
Birth	23,983	23,983	23,983	23,983	23,983	23,983	9,776	9,776
Upper Confid. Limit*	18.1	19.1	19.5	20.3	21.6	24.2	19.0	19.8
Birth/Treatm. %	17.9	18.9	19.3	20.0	21.4	24.0	18.8	19.6
Lower Confid. Limit*	17.7	18.7	19.1	19.8	21.1	23.7	18.6	19.4
Retrospective Numbers	12,933	11,353	10,406	10,303	9,698	7,763	3,881	3,662
Birth	1,581	1,581	1,581	1,581	1,581	1,581	510	510
Upper Confid. Limit*	12.8	14.5	15.8	16.0	17.0	21.1	14.4	15.2
Birth/Treatm. %	12.2	13.9	15.2	15.3	16.3	20.4	13.1	13.9
Lower Confid. Limit*	11.7	13.4	14.6	15.1	15.7	19.7	11.9	12.7

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

D·I·R Statistics in Brief – Fresh Cycles 2019 (CoD Jun 2nd 2020)

German IVF Registry – Prospective and Retrospective Data



*) Out of 1,856 cycles with freeze-all MII oocytes, 390 cycles were performed for FertiPROTECT (=medical freezing) and 953 cycles for social freezing. 513 cycles could not be assigned to either indication.

D·I·R Statistics in Brief – Fresh Cycles 2018 (CoD Jun 2nd 2020)

German IVF Registry – Prospective and Retrospective Data

Recorded Cycles 2018
106,397 — 100.0 %

Plausible Cycles 2018 (Prospective and not Prospective)
105,102 — 98.8 %

Prospective Cycles
94,866 — 90.3 %

Preparation for OPU
74,762 — 71.1 %

OPU
69,757 — 93.3 %

No OPU
5,005 — 6.7 %

Oocytes Aspirated
67,811 — 97.2 %

No Oocytes
1,946 — 2.8 %

Oocyte Culture
65,764 — 97.0 %

Freeze All – MII*
1,307 — 1.9 %

No Oocyte Culture
740 — 1.1 %

Oocyte for Transfer
65,328 — 99.3 %

Freeze All – Oocyte Culture
436 — 0.7 %

**) Out of 1,307 cycles with freeze-all MII oocytes, 280 cycles were performed for FertiPROTECT (=medical freezing) and 791 cycles for social freezing. 236 cycles could not be assigned to either indication.*

	Total Fresh Cycles	**IVF**	**ICSI**	**IVF/ICSI**
	65,328 — 100.0 %	17,285 — 26.5 %	46,604 — 71.3 %	1,439 — 2.2 %
Total Fertilization	61,230 — 93.7 %	15,772 — 91.2 %	44,032 — 94.5 %	1,426 — 99.1 %
Total Transfer	53,627 — 87.6 %	13,926 — 88.3 %	38,572 — 89.2 %	1,129 — 79.2 %
Outc. Unknown	144 0.3 %	54 0.4 %	88 0.2 %	5 0.4 %
Total CPR/ET (doc.)	17,226 — 32.2 % (per Treatment 26.4 %)	**CPR/ET** (doc.) 4,644 — 33.5 % (per IVF-Treatment 26.9 %)	**CPR/ET** (doc.) 12,194 — 31.7 % (per ICSI-Treatment 26.2 %)	**CPR/ET** (doc.) 388 — 34.5 % (per IVF/ICSI-Treatment , 27.0 %)
Misc.	3,476 20.2 %	968 20.8 %	2,438 20.0 %	70 18.0 %
EP	247 1.4 %	96 2.1 %	147 1.2 %	4 1.0 %
Not yet Recorded	885 5.1 %	46 1.0 %	811 6.7 %	28 7.2 %
Birth (doc.)	12,618 **73.2 %** (per Transfer 23.5 %, per Treatm. 19.3 %)	**Birth** (doc.) 3,534 **76.1 %** (per Transfer 25.4 %, per Treatm. 20.4 %)	**Birth** (doc.) 8,798 **72.2 %** (per Transfer 22.8 %, per Treatm. 18.9 %)	**Birth** (doc.) 286 **73.7 %** (per Transfer 25.3 %, per Treatm. 19.9 %)

Births	n	%
Singletons	10,143	80.4
Twins	2,419	19.2
Triplets	56	0.4
Quadruplets	0	-

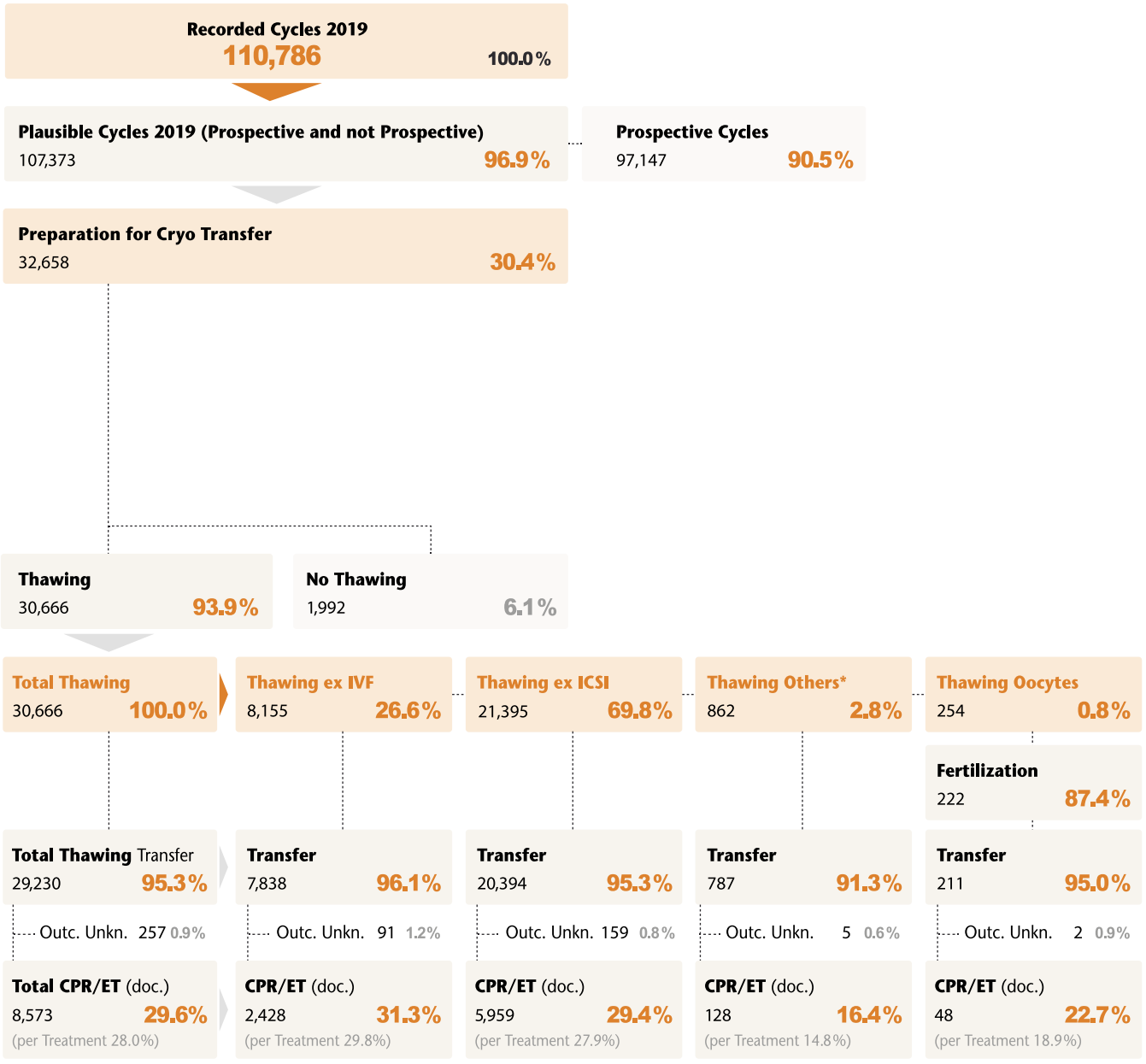
Births	n	%
Singletons	2,801	79.3
Twins	721	20.4
Triplets	12	0.3
Quadruplets	0	-

Births	n	%
Singletons	7,106	80.8
Twins	1,652	18.8
Triplets	40	0.5
Quadruplets	0	-

Births	n	%
Singletons	236	82.5
Twins	46	16.1
Triplets	4	1.4
Quadruplets	0	-

D·I·R Statistics in Brief – Cryo Cycles 2019 (CoD Jun 2nd 2020)

German IVF Registry – Prospective and Retrospective Data



*) Thawing others means cycles with unknown previous treatment, previous treatment not documented or previous treatment has partly been IVF and ICSI.

D·I·R Statistics in Brief – Cryo Cycles 2018 (CoD Jun 2nd 2020)

German IVF Registry – Prospective and Retrospective Data

Recorded Cycles 2018
106,397 — 100.0 %

Plausible Cycles 2018 (Prospective and not Prospective)
105,102 — 98.8 %

Prospective Cycles
94,866 — 90.3 %

Preparation for Cryo Transfer
30,340 — 29.8 %

Thawing
28,698 — 94.6 %

No Thawing
1,642 — 5.4 %

	Total Thawing	Thawing ex IVF	Thawing ex ICSI	Thawing Others*	Thawing Oocytes
	28,698 — 100.0 %	7,355 — 25.6 %	20,041 — 69.8 %	1,034 — 3.6 %	268 — 0.9 %
					Fertilization 245 — 91.4 %
	Total Thawing Transfer 27,434 — 95.6 %	**Transfer** 7,038 — 95.7 %	**Transfer** 19,220 — 95.9 %	**Transfer** 954 — 92.3 %	**Transfer** 222 — 90.6 %
	Outc. Unkn. 127 0.5 %	Outc. Unkn. 31 0.4 %	Outc. Unkn. 85 0.4 %	Outc. Unkn. 6 0.6 %	Outc. Unkn. 5 2.3 %
	Total CPR/ET (doc.) 8,004 — 29.3 % (per Treatment 27.9 %)	**CPR/ET** (doc.) 2,031 — 29.0 % (per Treatment 27.6 %)	**CPR/ET** (doc.) 5,759 — 30.1 % (per Treatment 28.7 %)	**CPR/ET** (doc.) 160 — 16.9 % (per Treatment 15.5 %)	**CPR/ET** (doc.) 54 — 24.9 % (per Treatment 20.1 %)
	Misc. 2,035 25.4 % **EP** 91 1.1 % **Not yet Rec.** 379 4.7 %	**Misc.** 578 28.5 % **EP** 34 1.7 % **Not yet Rec.** 23 1.1 %	**Misc.** 1,440 25.0 % **EP** 56 1.0 % **Not yet Rec.** 322 5.6 %	**Misc.** 15 9.4 % **EP** 1 0.6 % **Not yet Rec.** 7 4.4 %	**Misc.** 2 3.7 % **EP** 0 0.0 % **Not yet Rec.** 27 50.0 %
	Birth (doc.) 5,499 68.7 % (per Tr. 20.0 %, p. Treatm. 19.2 %)	**Birth** (doc.) 1,396 68.7 % (per Tr. 19.8 %, p. Treatm. 19.0 %)	**Birth** (doc.) 3,941 68.4 % (per Tr. 20.5 %, p. Treatm. 19.7 %)	**Birth** (doc.) 137 85.6 % (per Tr. 14.4 %, p. Treatm. 13.2 %)	**Birth** (doc.) 25 46.3 % (per Tr. 11.3 %, p. Treatm. 9.3 %)

Briths	n	%
Singletons	4,780	86.9
Twins	701	12.7
Triplets	18	0.3
Quadruplets	0	–

Briths	n	%
Singletons	1,211	86.7
Twins	182	13.0
Triplets	3	0.2
Quadruplets	0	–

Briths	n	%
Singletons	3,419	86.8
Twins	507	12.9
Triplets	15	0.4
Quadruplets	0	–

Briths	n	%
Singletons	128	93.4
Twins	9	6.6
Triplets	0	–
Quadruplets	0	–

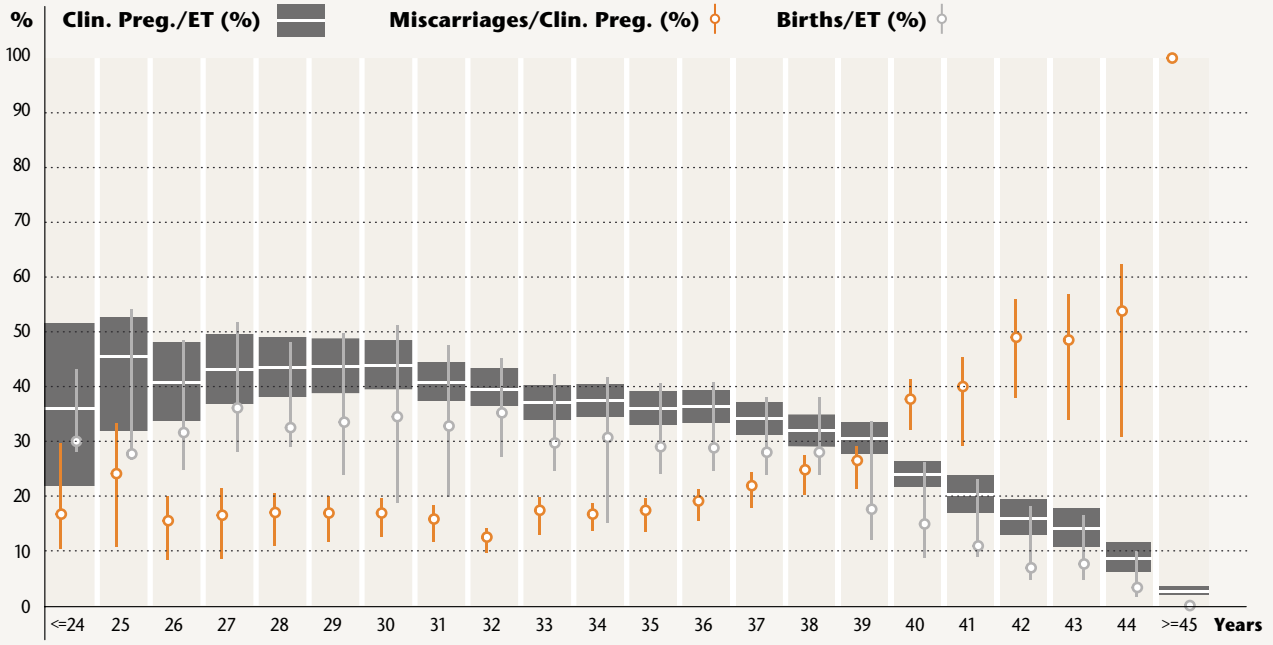
Briths	n	%
Singletons	22	88.0
Twins	3	12.0
Triplets	0	–
Quadruplets	0	–

*) *Thawing others means cycles with unknown previous treatment, previous treatment not documented or previous treatment has partly been IVF and ICSI.*

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2018

Prospective Data

IVF 2018



	<=24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	>=45	
n	50	119	174	280	366	499	656	772	819	899	911	1,046	1,058	969	1,048	1,379	545	494	320	236	152	76	ET
%	36.0	45.4	40.8	43.2	43.4	43.7	43.9	40.8	39.9	37.0	37.4	36.0	36.4	34.2	32.0	30.5	23.9	20.2	15.9	14.0	8.6	2.6	CP/ET
n	15	33	55	101	119	154	226	253	288	267	280	303	305	222	285	243	81	54	22	18	5	0	Birth

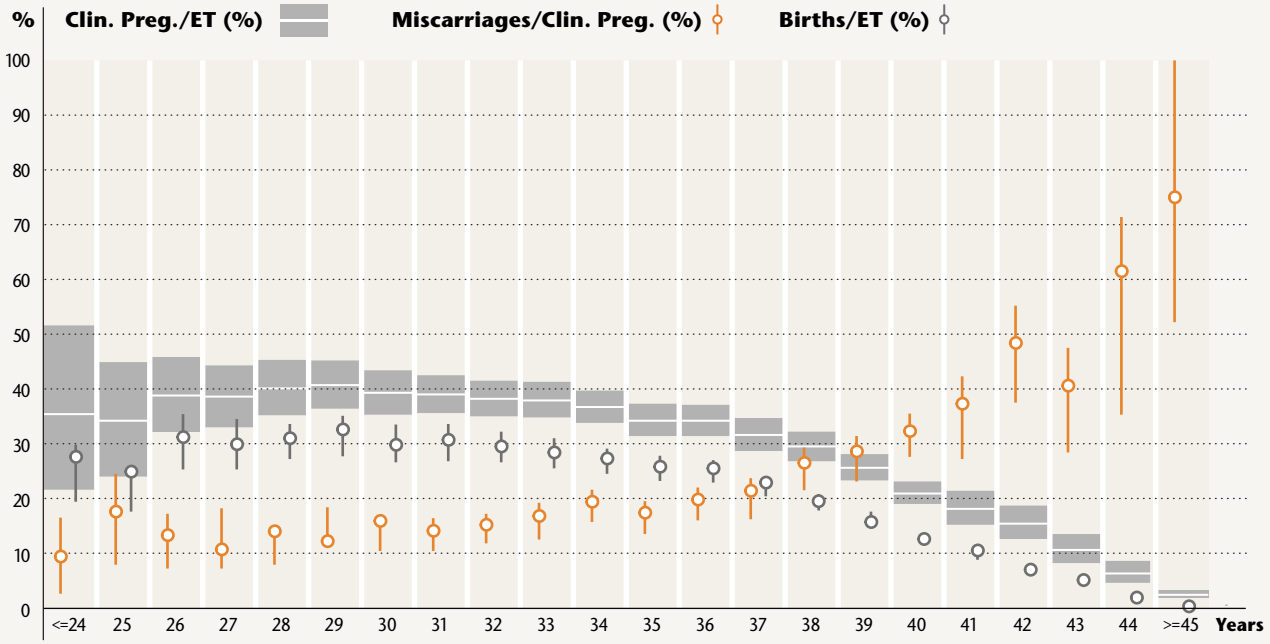
Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	1,886	4,917	6,629	678	615	417	312	196	115	**15,765**
Oocytes[1]	11.7	10.5	8.3	6.8	6.3	5.5	5.6	4.7	3.5	**9.0**
Insemination[1]	11.1	10.3	8.2	6.7	6.2	5.5	5.6	4.6	3.4	**8.9**
ET	1,488	4,057	5,500	545	494	320	236	152	76	**12,868**
ET/OPU %	78.9	82.5	83.0	80.4	80.3	76.7	75.6	77.6	66.1	**81.6**
Trans. Embr.[1]	1.8	1.7	1.8	1.7	1.8	1.8	1.8	1.7	1.7	**1.8**
CP	607	1,604	1,813	130	100	51	33	13	2	**4,353**
CP/OPU %	32.2	32.6	27.3	19.2	16.3	12.2	10.6	6.6	1.7	**27.6**
CP/ET Upper Conf. Limit* %	43.4	41.2	34.4	26.3	23.9	19.4	17.9	11.6	3.5	**34.7**
CP/ET %	**40.8**	**39.5**	**33.0**	**23.9**	**20.2**	**15.9**	**14.0**	**8.6**	**2.6**	**33.8**
CP/ET Lower Conf. Limit* %	38.2	38.1	31.8	21.6	17.0	13.0	10.8	6.2	2.0	**33.1**
CP/ET %: 2 Embr. Transf. + min. 2 2-PN Surplus	44.5	43.7	38.9	29.4	23.9	19.3	16.7	15.3	7.0	**38.1**
Misc./CP Upper Conf. Limit* %	17.6	18.9	23.1	41.4	45.4	56.0	56.8	62.4	100.0	**21.8**
Misc./CP %	**15.8**	**15.9**	**22.4**	**37.7**	**40.0**	**49.0**	**48.5**	**53.8**	**100.0**	**20.6**
Misc./CP Lower Conf. Limit* %	11.6	15.0	18.6	32.2	29.2	38.0	33.9	30.9	100.0	**19.4**
Births/ET Upper Conf. Limit* %	35.0	33.6	25.0	26.2	23.0	18.2	16.4	9.9	0.0	**31.8**
Births/ET %	32.1	32.4	24.7	14.9	10.9	6.9	7.6	3.3	0.0	25.9
Births/ET Lower Conf. Limit* %	29.8	30.6	22.5	8.7	8.9	4.7	4.7	1.5	0.0	**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 2018

Prospective Data

ICSI 2018



	<=24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	>=45	
n	181	398	541	822	1,139	1,572	1,952	2,146	2,364	2,412	2,729	2,893	2,817	2,769	2,899	4,019	1,657	1,259	991	653	412	327	ET
%	35.4	34.2	38.8	38.6	40.1	40.7	39.3	39.0	38.2	37.9	36.7	34.2	34.2	31.6	29.5	25.6	20.9	18.1	15.4	10.6	6.3	2.4	CP/ET
n	50	99	169	246	353	513	582	658	698	684	745	747	719	633	566	631	209	132	69	33	8	1	Birth

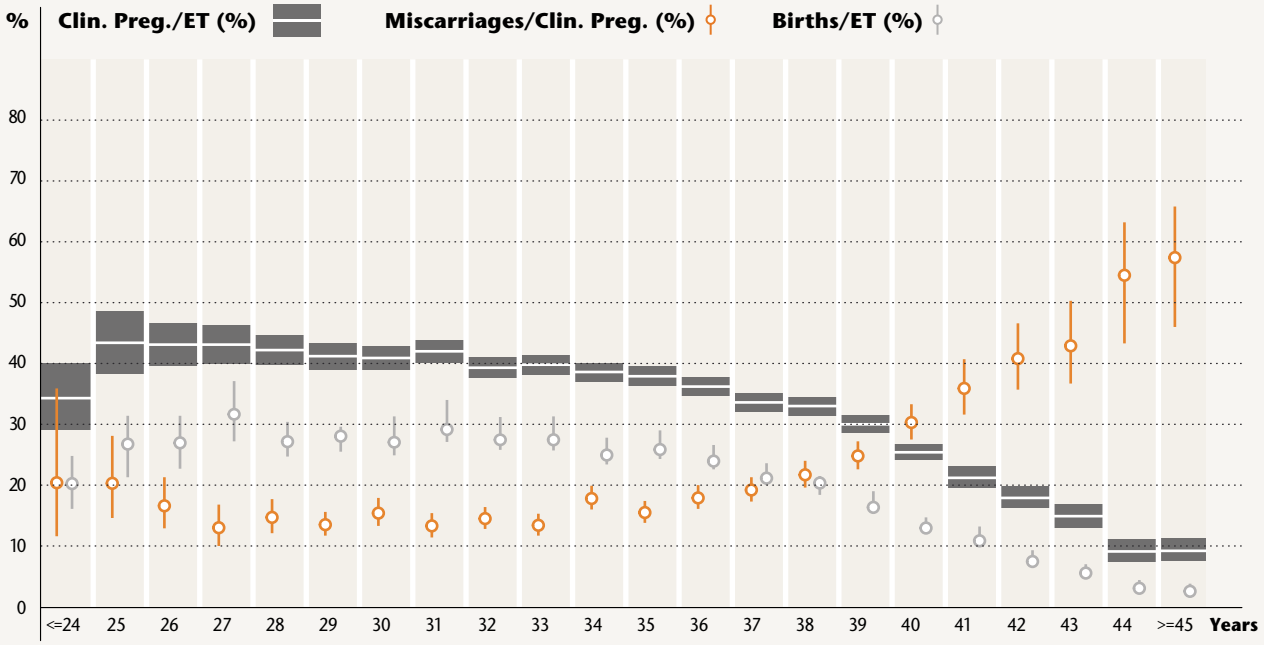
Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	5,596	13,629	18,094	2,059	1,578	1,253	875	541	491	**44,116**
Oocytes[1]	12.2	11.2	8.8	6.9	6.6	5.9	5.5	4.2	3.9	**9.6**
Injection[1]	8.9	8.6	6.8	5.4	5.2	4.6	4.1	3.9	3.2	**7.3**
ET	4,653	11,603	15,397	1,657	1,259	991	653	412	327	**36,952**
ET/OPU %	83.1	85.1	85.1	80.5	79.8	79.1	74.6	76.2	66.6	**83.8**
Trans. Embr.[1]	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	**1.7**
CP	1,824	4,423	4,712	347	228	153	69	26	8	**11,790**
CP/OPU %	32.6	32.5	26.0	16.9	14.4	12.2	7.9	4.8	1.6	**26.7**
CP/ET Upper Conf. Limit*%	40.7	39.0	31.3	23.1	21.4	18.7	13.5	8.6	3.2	**32.4**
CP/ET %	**39.2**	**38.1**	**30.6**	**20.9**	**18.1**	**15.4**	**10.6**	**6.3**	**2.4**	**31.9**
CP/ET Lower Conf. Limit*%	37.8	37.2	29.9	19.0	15.2	12.6	8.2	4.6	1.8	**31.4**
CP/ET %: 2 Embr. Transf. + min. 2 2-PN Surplus	43.7	42.3	38.1	29.0	25.0	19.5	14.2	11.9	13.8	**36.2**
Misc./CP Upper Conf. Limit*%	14.4	17.5	23.9	35.5	42.3	55.2	47.5	71.4	100.0	**20.7**
Misc./CP %	**12.8**	**16.4**	**22.7**	**32.3**	**37.3**	**48.4**	**40.6**	**61.5**	**75.0**	**19.9**
Misc./CP Lower Conf. Limit*%	11.4	16.0	21.6	27.6	27.2	37.5	28.4	35.3	52.2	**19.2**
Births/ET Upper Conf. Limit*%	30.4	28.4	21.3	13.2	10.7	7.8	5.9	2.3	0.4	**24.6**
Births/ET %	29.1	27.8	20.7	12.6	10.5	7.0	5.1	1.9	0.3	23.1
Births/ET Lower Conf. Limit*%	27.7	27.0	20.1	11.4	8.8	6.3	4.6	1.7	0.3	**21.7**

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 2014 – 2018

Prospective Data

IVF 2014 – 2018



n	271	364	743	1,124	1,663	2,140	2,768	3,190	3,594	3,962	4,319	4,587	4,635	4,272	4,510	5,138	4,484	2,232	1,724	1,281	844	661	**ET**
%	34.3	43.4	43.1	43.1	42.2	41.2	40.9	42.0	39.3	39.8	38.6	37.9	36.2	33.6	33.0	30.0	25.4	21.2	17.9	14.9	9.1	9.2	**CP/ET**
n	57	100	206	364	464	617	770	953	1.013	1.116	1.111	1.220	1.143	934	952	879	615	259	142	81	32	22	**Birth**

Age in Years	**<= 29**	**30 – 34**	**35 – 39**	**40**	**41**	**42**	**43**	**44**	**>=45**	**Total**
OPU	7,876	21,558	27,871	5,462	2,766	2,186	1,652	1,068	919	**71,358**
Oocytes[1]	11.5	10.4	8.4	7.1	6.3	6.1	5.5	5.0	4.7	**8.8**
ET/OPU %	80.1	82.7	83.0	82.1	80.7	78.9	77.5	79.0	71.9	**82.0**
Trans. Embr.[1]	1.8	1.9	1.8	1.9	1.9	1.9	1.9	1.8	1.8	**1.8**
CP	2,640	7,127	7,870	1,137	474	309	191	77	61	**19,886**
CP/OPU %	33.5	33.1	28.3	20.8	17.1	14.1	11.6	7.2	6.6	**27.9**
CP/ET Upper Confidence Limit* %	43.1	40.7	34.7	26.7	23.1	19.8	16.9	11.1	11.2	**34.4**
CP/ET %	**41.9**	**40.0**	**34.0**	**25.4**	**21.2**	**17.9**	**14.9**	**9.1**	**9.2**	**34.0**
CP/ET Lower Confidence Limit* %	40.6	39.2	33.4	24.1	19.5	16.2	13.1	7.4	7.5	**33.6**
CP/ET %: 2 Embr. Transf. + min. 2 2-PN Surplus	44.4	43.0	37.6	29.2	24.6	21.4	18.4	11.5	10.6	**37.4**
Misc./CP Upper Confidence Limit* %	16.1	15.9	20.6	33.3	40.7	46.6	50.3	63.2	65.8	**19.7**
Misc./CP %	**14.7**	**15.0**	**19.7**	**30.3**	**35.9**	**40.8**	**42.9**	**54.5**	**57.4**	**19.1**
Misc./CP Lower Confidence Limit* %	13.4	14.2	18.8	27.5	31.6	35.7	36.7	43.3	46.0	**18.6**
Births/ET Upper Confidence Limit* %	28.9	27.8	27.8	14.7	13.2	9.3	7.0	4.4	3.8	**23.1**
Births/ET %	27.8	27.1	27.1	13.7	11.6	8.2	6.3	3.8	3.3	22.3
Births/ET Lower Confidence Limit* %	26.7	26.5	26.5	12.7	10.8	7.5	5.5	3.3	2.8	**21.3**

1) Mean
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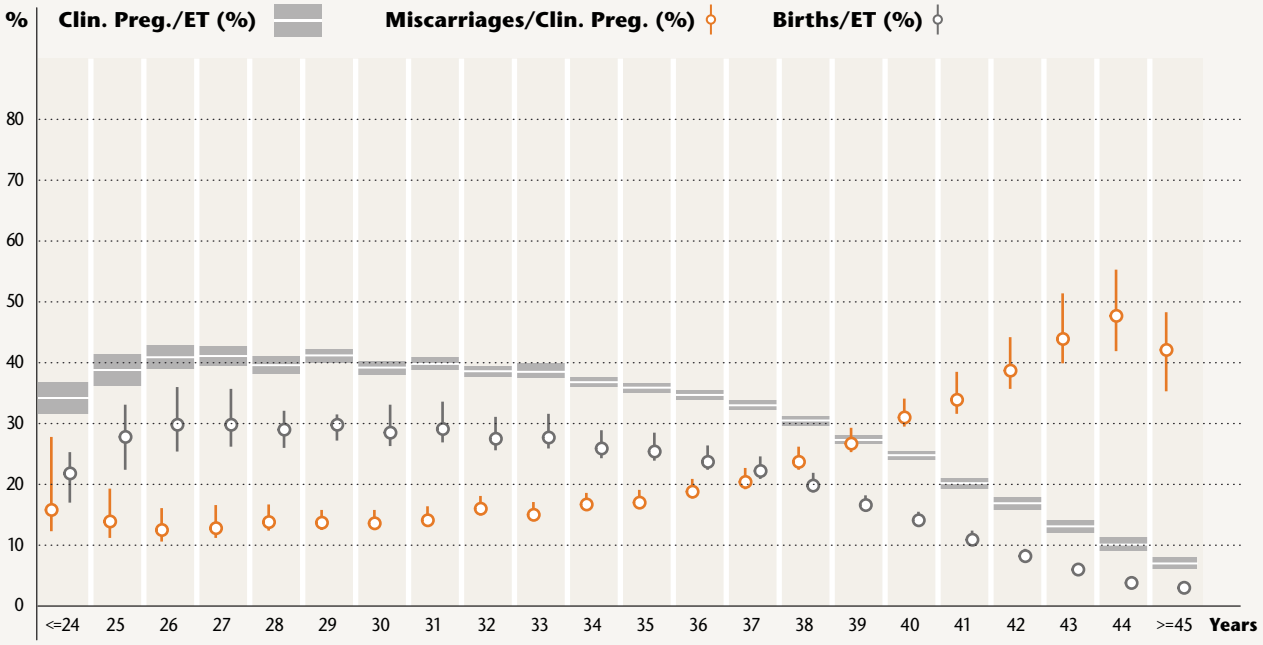
Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2014 – 2018

Prospective Data

ICSI 2014 – 2018



	<=24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	>=45	
n	1,416	1,427	2,521	3,880	5,249	7,098	8,692	10,166	11,531	12,389	13,513	14,385	14,403	14,005	14,062	16,328	14,477	7,353	5,990	3,876	2,264	2,732	**ET**
%	34.7	36.2	40.4	40.0	38.7	39.4	38.2	39.5	38.3	38.6	36.2	35.3	34.7	32.4	29.7	25.6	23.8	19.9	16.2	14.0	11.3	6.3	**CP/ET**
n	320	374	736	1,123	1,443	2,043	2,380	2,927	3,155	3,407	3,412	3,600	3,390	3,029	2,644	2,496	1,922	796	464	239	101	75	**Birth**

Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	26,477	64,870	84,843	16,119	8,640	7,009	5,185	3,235	3,587	**219,965**
Oocytes[1]	11.5	10.4	8.4	7.1	6.3	6.1	5.5	5.0	4.7	**8.8**
ET/OPU %	81.5	86.8	86.3	89.8	85.1	85.5	74.8	70.0	76.2	**85.4**
Trans. Embr.[1]	1.8	1.9	1.8	1.9	1.9	1.9	1.9	1.8	1.8	**1.8**
CP	8,407	21,429	22,976	3,447	1,465	970	541	256	173	**59,664**
CP/OPU %	31.8	33.0	27.1	21.4	17.0	13.8	10.4	7.9	4.8	**27.1**
CP/ET Upper Confidence Limit* %	39.6	38.5	31.7	24.5	20.8	17.2	15.1	12.7	7.3	**32.2**
CP/ET %	**38.9**	**38.1**	**31.4**	**23.8**	**19.9**	**16.2**	**14.0**	**11.3**	**6.3**	**31.8**
CP/ET Lower Confidence Limit* %	38.3	37.7	31.0	23.1	19.0	15.3	12.9	10.1	5.5	**31.4**
CP/ET %: 2 Embr. Transf. + min. 2 2-PN Surplus	44.4	43.0	37.6	29.2	24.6	21.4	18.4	11.5	10.6	**37.4**
Misc./CP Upper Confidence Limit* %	14.1	15.6	21.4	33.8	39.3	44.3	50.4	56.2	48.4	**19.9**
Misc./CP %	**13.3**	**15.1**	**20.9**	**30.8**	**34.6**	**38.8**	**43.1**	**48.4**	**42.2**	**19.3**
Misc./CP Lower Confidence Limit* %	12.6	14.2	18.8	29.3	32.3	35.7	39.1	42.6	35.6	**18.8**
Births/ET Upper Confidence Limit* %	28.5	27.5	21.0	14.5	12.1	8.8	7.2	5.2	3.2	**21.5**
Births/ET %	28.0	27.1	20.7	13.3	10.8	7.7	6.2	4.5	2.7	21.3
Births/ET Lower Confidence Limit* %	27.4	26.8	20.4	12.6	9.9	7.1	5.6	3.9	2.3	**20.8**

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

Results IVF, ICSI (COHS) and IVF and ICSI in Natural Cycles 2018

Prospective Data

IVF 2018

	n	%	Fertilization %	Embryo %	Transfer %	Clin. Preg. %
Performed IVF Treatm.	15,804	100.0				
Successful Fertilization*	14,384	91.0	100.0			
Minimum 1 Embryo	13,975	88.4	97.2	100.0		
ET Performed	12,868	81.4	89.5	92.1	100.0	
Clin. Pregnancy	4,353	**27.5**	30.3	31.1	**33.8**	100.0
Birth	3,329	**21.1**	**23.1**	**23.8**	**25.9**	**76.5**
Miscarriage	896					20.6
Ectopic Pregnancy	94					2.2
Not Yet Recorded	34					0.8

ICSI 2018

	n	%	Fertilization %	Embryo %	Transfer %	Clin. Preg. %
Performed ICSI Treatm.	44,478	100.0				
Successful Fertilization*	42,066	94.6	100.0			
Minimum 1 Embryo	38,821	87.3	92.3	100.0		
ET Performed	36,952	83.1	87.8	95.2	100.0	
Clin. Pregnancy	11,790	**26.5**	28.0	30.4	**31.9**	100.0
Birth	8,545	**19.2**	**20.3**	**22.0**	**23.1**	**72.5**
Miscarriage	2,350					19.9
Ectopic Pregnancy	143					1.2
Not Yet Recorded	752					6.4

IVF and ICSI in Natural Cycles 2018**

	n	%	Fertilization %	Embryo %	Transfer %	Clin. Preg. %
Treatm. Without Stim. or with Low-Dose-Stimulation**	462	100.0				
Successful Fertilization*	366	79.2	100.0			
Minimum 1 Embryo	279	60.4	76.2	100.0		
ET Performed	262	56.7	71.6	93.9	100.0	
Clin. Pregnancy	63	**13.6**	17.2	22.6	**24.0**	100.0
Birth	39	**8.4**	**10.7**	**14.0**	**14.9**	**61.9**
Miscarriage	17					27.0
Ectopic Pregnancy	0					0.0
Not Yet Recorded	7					11.1

**) Successful fertilization of at least one oocyte per cycle*
***) Natural cycle and natural cycle with low-dose-stimulation were newly defined in the data set. Only clearly allocatable cycles were included into the analyses. The total number is most likely higher.*

Results of Thawing-Cycles, TESE, IVF and ICSI with Donor Semen 2018

Prospective Data

Cryo Transfer Cycles 2018

	n	%	PN/Embryo %	Transfer %	Clin. Preg. %
Cryo Transfer Cycles	26,382	100.0			
Thawed PN/Embryo	25,676	97.3	100.0		
ET Performed	25,278	95.8	98.4	100.0	
Clin. Pregnancy	7,441	28.2	29.0	**29.4**	100.0
Birth	5,210	**19.7**	**20.3**	**20.6**	**70.0**
Miscarriage	1,871				25.1
Ectopic Pregnancy	87				1.2
Not Yet Recorded	273				3.7

TESE 2018

	n	%	Fertilization %	Embryo %	Transfer %	Clin. Preg. %
Perf. ICSI/TESE Treatm.	2,258	100.0				
Successful Fertilization*	2,134	94.5	100.0			
Minimum 1 Embryo	2,038	90.3	95.5	100.0		
ET Performed	1,954	86.5	91.6	95.9	100.0	
Clin. Pregnancy	631	27.9	29.6	31.0	**32.3**	100.0
Birth	434	**19.2**	**20.3**	**21.3**	**22.2**	**68.8**
Miscarriage	134					21.2
Ectopic Pregnancy	12					1.9
Not Yet Recorded	51					8.1

IVF and ICSI with Donor Semen 2018**

	n	%	Fertilization %	Embryo %	Transfer %	Clin. Preg. %
ART-Treatm. (donor sperm)**	1,129	100.0				
Successful Fertilization*	861	76.3	100.0			
Minimum 1 Embryo	803	71.1	93.3	100.0		
ET Performed	801	70.9	93.0	99.8	100.0	
Clin. Pregnancy	272	24.1	31.6	33.9	**34.0**	100.0
Birth	131	**11.6**	**15.2**	**16.3**	**16.4**	**48.2**
Miscarriage	64					23.5
Ectopic Pregnancy	1					0.4
Not Yet Recorded	76					27.9

**) Successful fertilization of at least one oocyte per cycle*
***) Currently, the data processing is not completely validated. Only cycles with definite data validation were included in this analysis.*

Positive Pregnancy Outcomes 2018

IVF, ICSI – Prospective and Retrospective Data

	n	%
Clinical Pregnancies	17,226	100.0
Outcome documented	16,341	94.9
Transfer	53,627	
Life-Birth-Rate per ET	12,449	23.2
Number of Transfers in Ideal Patients (<=35 Years, >=4 2PN, SET)	6,409	
Life-Birth-Rate per Transfer in Ideal Patients (<=35 Years, >=4 2PN, SET)	1,698	26.5
Number of Multiple Births After SET	39	2.3
Number of Transfers in Ideal Patients (<=35 Years, >=4 2PN, DET/TET)	23,922	
Life-Birth-Rate per Transfer in Ideal Patients (<=35 Years, >=4 2PN, DET/TET)	7,093	29.7
Number of Multiple Births after DET/TET	1,422	20.0

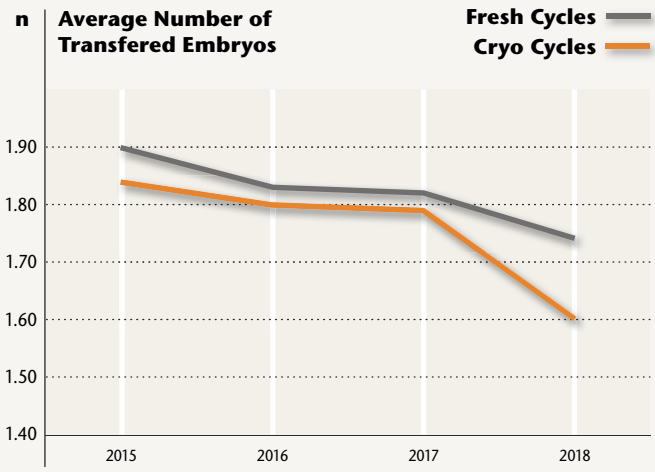
Loss of Pregnancy 2018

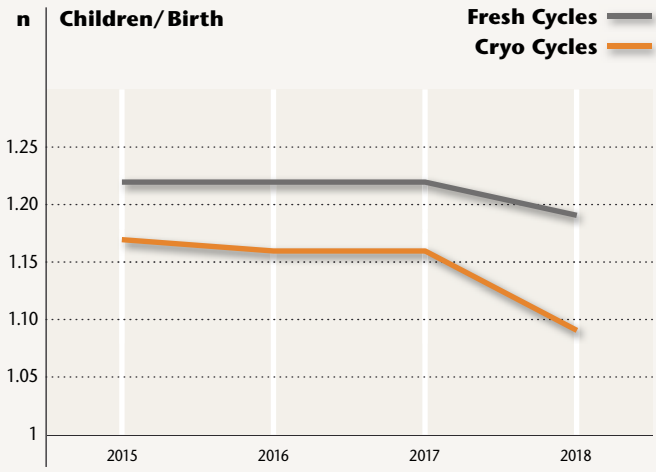
Prospective and Retrospective Data

	Treatments Fresh Cycles		Treatments Cryo Cycles	
	n	%	n	%
Clinical Pregnancies	17,226	100.0	8,004	100.0
Treatments with Known Cycle Outcome	16,341	94.9	7,625	95.3
Miscarriages	3,476	20.2	2,035	25.4
Among those: Induced Abortions	171	4.9	49	2.4
Stilborn Children	169	1.0	47	0.6

Embryos per Transfer[1] and Children per Birth 1997 – 2018

IVF, ICSI – Prospective and Retrospective Data





		1997	[...]	2015	2016	2017	2018
Fresh Cycles	Average Number of Transf. Embryos	2.56	*For values from 1998 to 2014 see www.deutsches-ivf-register.de*	1.90	1.83	1.82	1.74
	Children/Birth	1.29		1.22	1.22	1.22	1.19
Cryo Cycles	Average Number of Transf. Embryos	2.34		1.84	1.80	1.79	1.60
	Children/Birth	1.14		1.17	1.16	1.16	1.09

The number of children originating from multiple pregnancies has almost remained stable within the last decades. In 2018, we finally notice a trend to a reduction.

In summary: the number of embryos per transfer is an important factor worth looking at. It is important to allow children resulting from an ART-treatment to come into life as a singleton. Siblings are important and desirable – one at a time!

1) Mean

Culture According to the "German Middle Way" and Impact on Therapy Outcome – Fresh Cycles 2018

Prospective and Retrospective Data

Number of centers choosing >=3 x 2PN for extended culture: n=128

Oocyte Treatment (All) - Culture >= 3 x 2PN
37,935

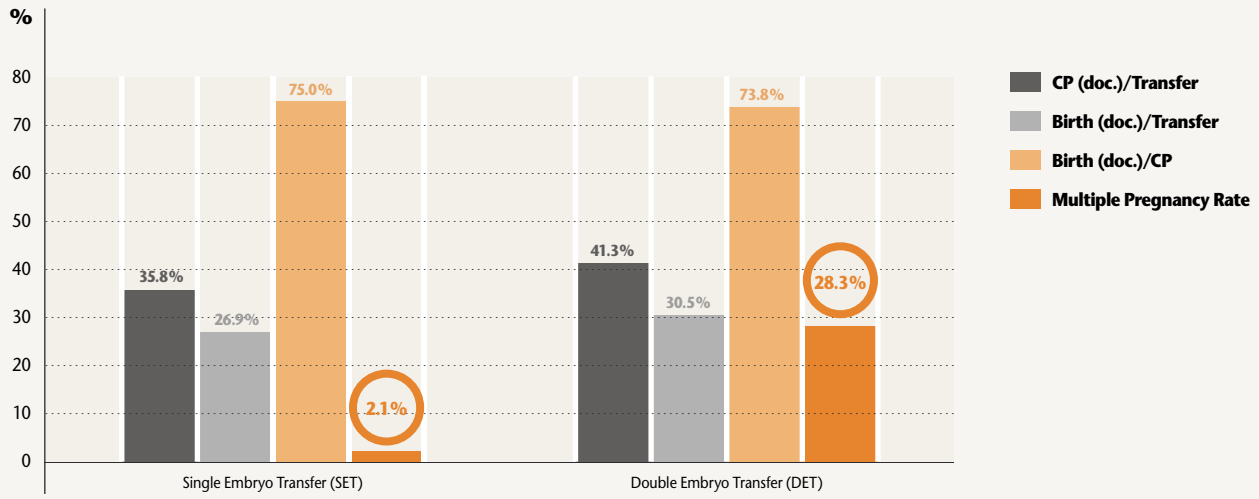
Oocyte Treatment - Culture >= 3 x 2PN for Transfer on Day 4-6
22,871

	Number of Transfer Cycles with SET Day 4-6 6,424		Number of Transfer Cycles with DET Day 4-6 15,771	
	CP/ET (doc.)* 2,299	**35.8%**	**CP/ET (doc.)*** 6,517	**41.3%**
	Outcome unknown 5	**0.1%**	**Outcome unknown** 63	**0.4%**
Miscarriage	365	15.9%	1,140	17.5%
EP	46	2.0%	88	1.4%
Not yet Recorded	163	7.1%	481	7.4%
Birth (doc.)	**1,725** per Transfer	**75.0%** 26.9%	**4,808** per Transfer	**73.8%** 30.5%

Births	**n**	**%**	**Births**	**n**	**%**
Singletons	1,688	97.9	Singletons	3,444	71.6
Twins	37	2.1	Twins	1,334	27.7
Triplets	0	0.0	Triplets	30	0.6
Quadruplets	0	0.0	Quadruplets	0	0.0

**) please note: documented clinical pregnancies per transfer on day <4: 8,410 / 31,432 = 26.8%*

Comparison SET and DET "German Middle Way" Fresh Cycles 2018



Culture According to the "German Middle Way" and Impact on Therapy Outcome – Thawing Cycles PNs 2018

Prospective and Retrospective Data

Number of centers thawing >=3 x 2PN for extended culture: n=75

Culture >=3 Vital 2PNs After Thawing (All Cycles)
7,898

Number of Transfers on Day 2-3
2,621

Culture >=3 Vital 2PNs After Thawing
5,130

Number of Transfer Cycles with SET Day 4-6
1,981

CP/ET (doc.)
666 **33.6%**

Outcome unknown
5 **0.3%**

Miscarriage	184	27.6%
EP	6	0.9%
Not yet Recorded	16	2.4%
Birth (doc.)	**460**	**69.1%**
	per Transfer	23.2%

Births	**n**	**%**
Singletons	442	96.1
Twins	15	3.3
Triplets	3	0.7
Quadruplets	0	0.0

Number of Transfer Cycles with DET Day 4-6
2,961

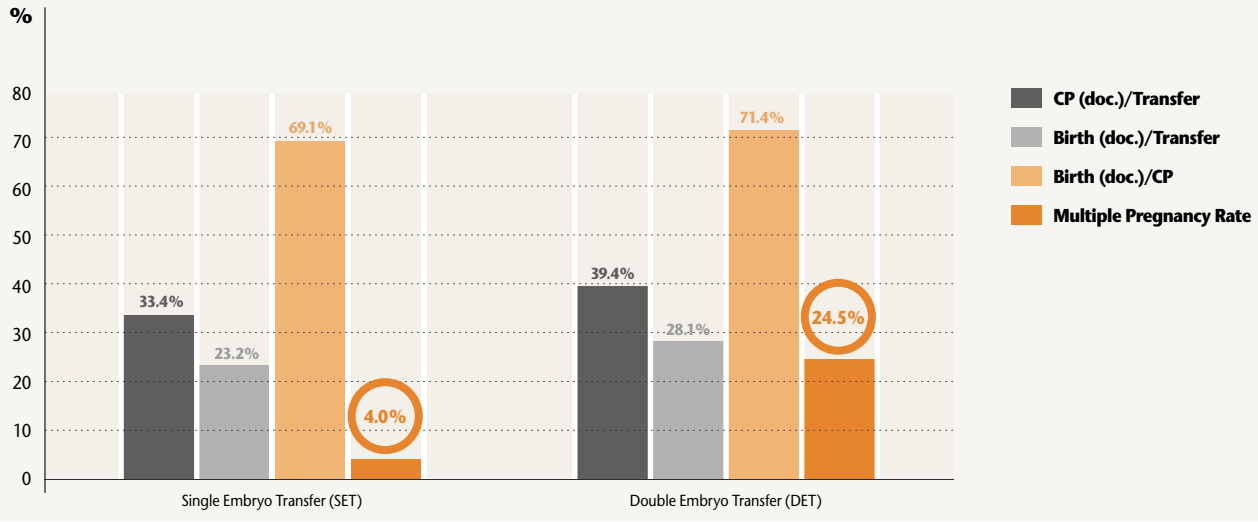
CP/ET (doc.)
1,166 **39.4%**

Outcome unknown
21 **0.7%**

Miscarriage	279	23.9%
EP	9	0.8%
Not yet Recorded	45	3.9%
Birth (doc.)	**833**	**71.4%**
	per Transfer	28.1%

Births	**n**	**%**
Singletons	629	75.5
Twins	198	23.8
Triplets	6	0.7
Quadruplets	0	0.0

Comparison SET and DET "German Middle Way" Thawing Cycles PNs



Culture According to the "German Middle Way" and Impact on Therapy Outcome – Thawing Cycles Embryos 2018

Prospective and Retrospective Data

Number of centers transfering previously cryopreserved embyos: n=144

Transfer Single ET
5,356

CP/ET (doc.)		Outcome unknown	
1,800	33.6 %	25	0.5 %

Miscarriage	416	23.1 %
EP	34	1.9 %
Not yet Recorded	107	5.9 %
Birth (doc.)	**1,243**	**69.1 %**
	per Transfer	23.2 %

Births	n	%
Singletons	1,219	98.1
Twins	24	1.9
Triplets	0	0.0
Quadruplets	0	0.0

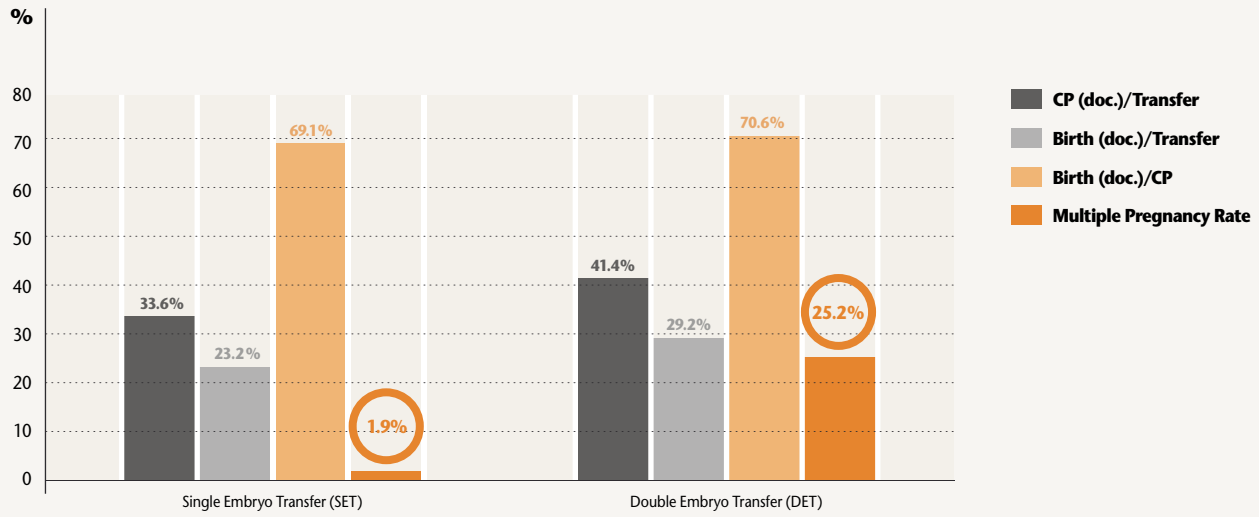
Transfer Double ET
2,319

CP/ET (doc.)		Outcome unknown	
960	41.4 %	11	0.5 %

Miscarriage	247	25.7 %
EP	11	1.1 %
Not yet Recorded	24	2.5 %
Birth (doc.)	**678**	**70.6 %**
	per Transfer	29.2 %

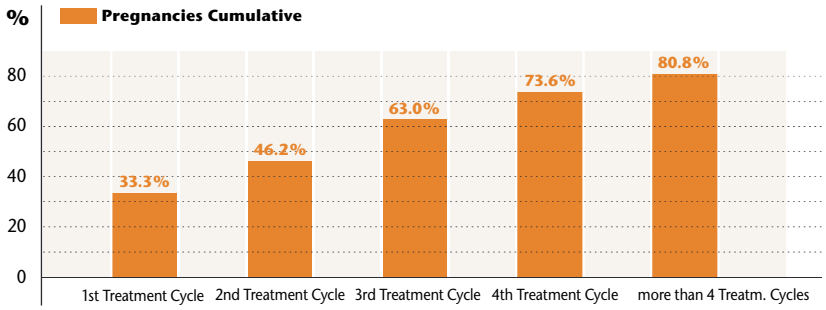
Births	n	%
Singletons	507	74.8
Twins	169	24.9
Triplets	2	0.3
Quadruplets	0	0.0

Comparison SET and DET "German Middle Way" Thawing Cycles Embryos



Pregnancies Cumulative 2016 – 2019

IVF, ICSI, Cryo Cycles – Prospective Data



2016 – 2019 (total)	Retrievals	Fresh Cycles with ET	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle w. Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cumulative Pregnancy Rate in %
1st Treatment	102,764	88,701	29,542	33.3	0	0	-	**33.3**
2nd Treatment	48,126	40,512	12,265	30.3	27,474	8,608	31.3	**46.2**
3rd Treatment	32,691	27,447	8,115	29.6	20,311	5,920	29.1	**63.0**
4th Treatment	22,115	18,449	5,534	30.0	14,259	3,958	27.8	**73.6**
>4 Treatment	50,677	40,281	11,600	28.8	38,116	10,388	27.3	**80.8**

Treatment started in 2016	Retrievals	Fresh Cycles with ET	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle w. Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cumulative Pregnancy Rate in %
1st Treatment	30,718	29,721	9,080	30.6	0	0	-	**30.6**
2nd Treatment	13,554	13,028	3,541	27.2	7,678	2,353	30.6	**50.4**
3rd Treatment	8,700	8,330	2,156	25.9	5,377	1,496	27.8	**62.7**
4th Treatment	4,921	4,982	1,258	25.3	3,484	941	27.0	**70.1**
>4 Treatment	8,194	8,189	1,822	22.2	6,539	1,696	25.9	**81.9**

Treatment started in 2017	Retrievals	Fresh Cycles with ET	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle w. Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cumulative Pregnancy Rate in %
1st Treatment	24,812	21,422	7,494	35.0	0	0	-	**35.0**
2nd Treatment	11,784	9,182	3,050	33.2	6,273	1,925	30.7	**44.0**
3rd Treatment	8,191	6,344	2,100	33.1	4,691	1,325	28.2	**64.4**
4th Treatment	5,917	4,580	1,519	33.2	3,277	915	27.9	**70.2**
>4 Treatment	14,432	10,640	3,273	30.8	10,784	2,834	26.3	**79.3**

For 244 cycles, no plausible data could be correlated to the treatment cycles. These cycles resulted in 178 additional transfers with 66 additional clinical pregnancies.

Treatment started in 2018	Retrievals	Fresh Cycles with ET	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle w. Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cumulative Pregnancy Rate in %
1st Treatment	24,038	19,144	6,714	35.1	0	0	-	**35.1**
2nd Treatment	11,628	9,345	2,901	31.0	6,606	2,132	32.3	**45.6**
3rd Treatment	7,779	6,263	1,942	31.0	4,936	1,506	30.5	**63.1**
4th Treatment	5,552	4,384	1,331	30.4	3,623	1,019	28.1	**77.1**
>4 Treatment	13,701	10,549	3,218	30.5	9,817	2,705	27.6	**81.0**

For one cycle, no plausible data could be correlated to the treatment cycle. Tis cycle did not result in a transfer.

Treatment started in 2019	Retrievals	Fresh Cycles with ET	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle w. Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cumulative Pregnancy Rate in %
1st Treatment	23,196	18,414	6,254	34.0	0	0	-	**34.0**
2nd Treatment	11,160	8,957	2,773	31.0	6,917	2,198	31.8	**44.3**
3rd Treatment	8,021	6,510	1,917	29.4	5,307	1,593	30.0	**62.1**
4th Treatment	5,725	4,503	1,426	31.7	3,875	1,083	27.9	**77.4**
>4 Treatment	14,350	10,903	3,287	30.1	10,976	3,153	28.7	**80.6**

For 3 cycles, no plausible data could be correlated to the treatment cycles. These cycles resulted in 2 additional transfers with one additional clinical pregnancy.

Oocyte Maturity Depending on Stimulation Protocol 2019

Oocyte Maturity and Development Depending on Downregulation Protocol

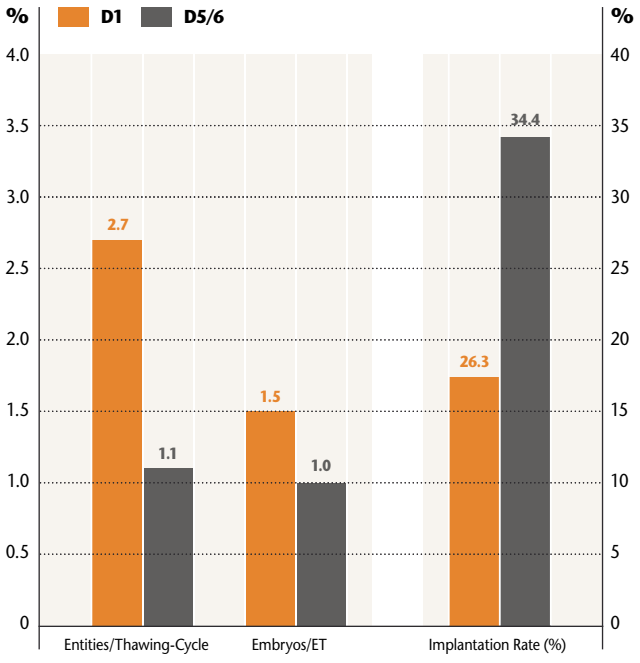
ICSI – Prospective and Retrospective Data

	Cycles	Mean Age	Oocytes Retrieved	Ooc. per Retrieval	Mature Oocytes	Mature Ooc. per Retrieval	2PN	2PN/ Oocyte Retrieval	Embryos for ET	Gestational Sacs	Implant. Rate (%)
Agonist	11,261	35.7	97,950	**8.7**	80,802	**7.2**	49,924	**4.4**	15,472	3,386	**21.9**
Antagonist	46,907	35.6	424,450	**9.0**	354,981	**7.6**	220,731	**4.7**	58,933	13,400	**22.7**

Cycles and Implantation-Rates with Transfer of Day 5/6 Embryos after Cryopreservation either on Culture Day 1 or Day 5/6

Thawing – Prospective and Retrospective Data

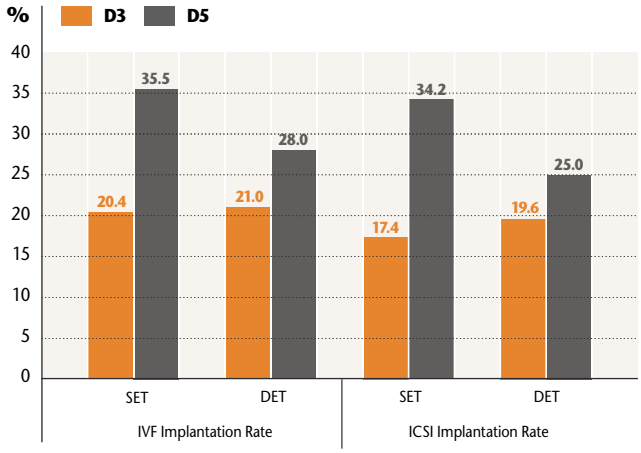
	Freezing on Culture D1	Freezing on Culture D5/6
Thawing-Cycles resulting in ET	6,682	8,829
PN/Embryos Thawed	17,864	9,984
Entities/Thawing-Cycle	**2.7**	**1.1**
Re-Cryo of Embryos	1,510	110
Embryos Available for Transfer	9,989	9,124
Re-Cryo/Cycle	0.2	0.0
Transfer	6,682	8,829
Gestational Sacs (Intrauterine)	2,627	3,139
Embryos/ET	**1.5**	**1.0**
Implantation Rate (%)	**26.3**	**34.4**



Implantation Rates of D3- and D5-Embryos and Number of Embryos per Transfer

IVF, ICSI – Prospective and Retrospective Data

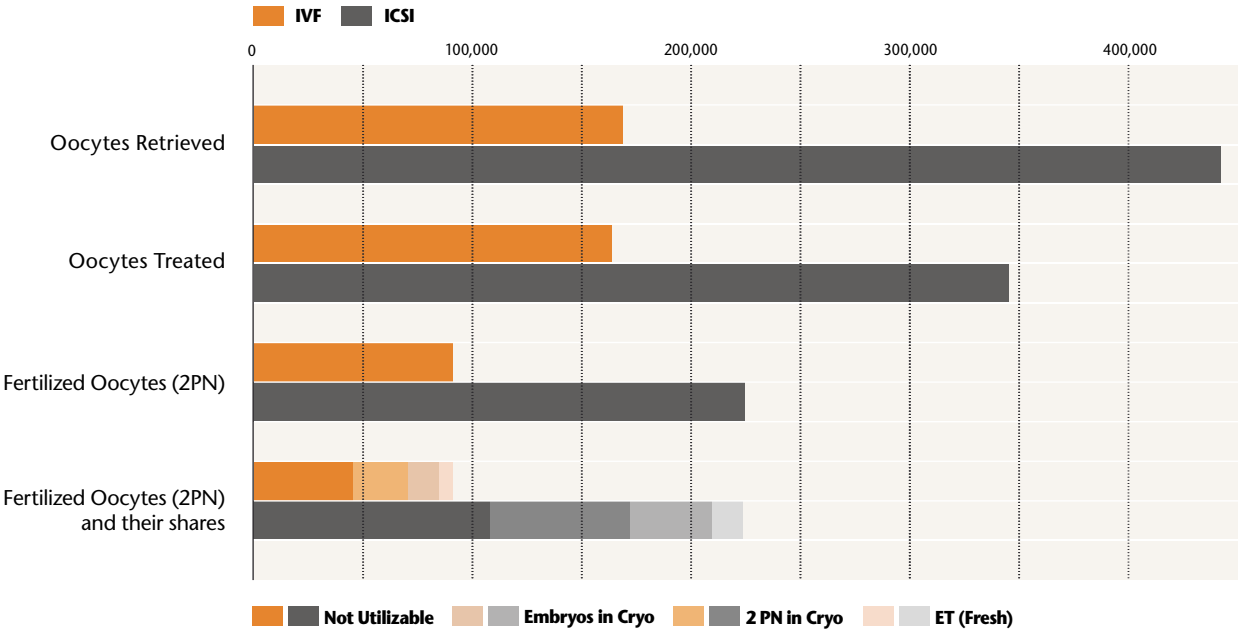
		D3 ImplRate %	D5 ImplRate %
IVF Implantation Rate	SET	20.4	35.5
	DET	21.0	28.0
ICSI Implantation Rate	SET	17.4	34.2
	DET	19.6	25.0



Evolution of Retrieved Oocytes (IVF or ICSI)

IVF, ICSI – Prospective and Retrospective Data

	IVF	%		ICSI	%	
Oocytes Retrieved	168,561	100.0		441,990	100.0	
Oocytes Treated	163,875	97.2	100.0	345,213	78.1	100.0
Fertilized Oocytes (2PN)	90,962		54.0	224,619		65.1
2PN Cryopreserved	24,896		27.4	63,958		28.5
ET (Fresh)	14,380		15.8	38,632		17.2
Embryos Cryopreserved	6,072		6.7	14,094		6.3



Clinical Pregnancies (CP)/Fresh Transfer as a Function of Embryo Quality 2019

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	256	14.5	653	15.0	1,113	11.8	471	5.5	2,493	11.7
0	2	330	22.1	788	25.4	1,273	19.2	427	9.6	2,818	19.8
0	3	5	20.0	12	8.3	42	16.7	35	14.3	94	14.9
1	0	1,593	35.7	4,554	34.3	6,236	26.0	2,358	11.4	14,741	27.3
1	1	432	32.6	1,164	34.5	1,650	27.5	611	16.4	3,857	28.4
1	2	8	25.0	25	32.0	40	20.0	51	5.9	124	16.9
2	0	3,109	44.9	7,971	44.8	9,977	37.2	2,989	22.7	24,046	38.9
2	1	11	27.3	26	23.1	77	26.0	94	12.8	208	19.7
3	0	32	25.0	150	36.7	346	30.9	380	25.0	908	29.2
Total		**5,776**	**38.6**	**15,343**	**38.4**	**20,754**	**30.4**	**7,416**	**16.6**	**49,289**	**31.8**

Clinical Pregnancies (CP)/Frozen Transfer as a Function of Embryo Quality 2019

Cryo Transfer – Prospective Data

Quality		IVF		ICSI	
ideal	Not Ideal	ET	CP/ET %	ET	CP/ET %
0	1	382	14.7	1,133	16.2
0	2	443	22.6	1,205	16.9
0	3	15	6.7	64	21.9
1	0	1,630	31.3	4,316	31.8
1	1	666	20.1	1,914	26.9
1	2	23	34.8	84	35.7
2	0	2,563	36.1	6,770	38.3
2	1	26	26.9	100	23.0
3	0	89	28.1	354	28.5
Total*		**5,837**	**30.3**	**15,940**	**31.6**

**) In 5,645 cases, resulting in an additional 1,337 pregnancies, no information has been available how many embryos had been transferred.*

Children as a Function of Week of Gestation (WoG) and Birth Weight (BW) 2018

Prospective and Retrospective Data

IVF, ICSI, IVF/ICSI

WoG	20 - 27		28 - 32		33 - 36		37 - 41		>= 42		Total
Singletons (n and %)	144	1.4	233	2.3	1,625	16.0	8,054	79.4	87	0.9	**10,143**
Average Birth Weight (g)	841		1,828		2,810		3,385		3,446		**3,221**
Twins (n and %)	268	5.5	846	17.5	2,946	60.9	768	15.9	10	0.2	**4,838**
Average Birth Weight (g)	842		1,723		2,486		2,738		2,493		**2,303**
Triplets (n and %)	24	14.3	102	60.7	42	25.0	–	–	–	–	**168**
Average Birth Weight (g)	887		1,625		1,976		–		–		**1,607**

Percentage of preterm deliveries in singleton pregnancies is 19.7%.
Percentage of preterm deliveries in twin pregnancies is 83.9%.

Cryo Transfer

WoG	20 - 27		28 - 32		33 - 36		37 - 41		>= 42		Total
Singletons (n and %)	55	1.2	99	2.1	737	15.4	3,864	80.8	25	0.5	**4,780**
Average Birth Weight (g)	941		2,005		3,124		3,551		3,594		**3,423**
Twins (n and %)	54	3.9	200	14.3	926	66.0	218	15.5	4	0.3	**1,402**
Average Birth Weight (g)	836		1,794		2,578		2,838		2,668		**2,440**
Triplets (n and %)	21	38.9	27	50.0	6	11.1	-	-	-	-	**54**
Average Birth Weight (g)	1,008		1,600		2,165		-		-		**1,433**

Percentage of preterm deliveries in singleton pregnancies is 18.7%.
Percentage of preterm deliveries in twin pregnancies is 84.2%.

Children Born 1997 – 2018

Prospective and Retrospective Data

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

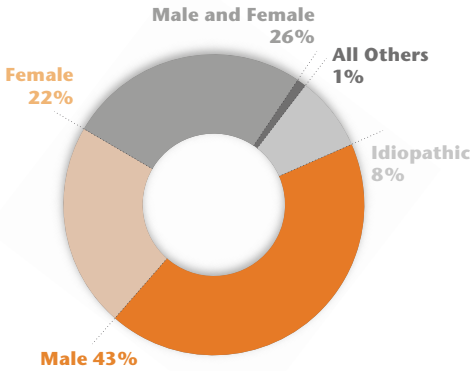
	Singletons		Twins		Triplets		Quadruplets		Total
	n	%	n	%	n	%	n	%	n
1997	4,175	58.7	1,902	32.8	492	8.4	8	0.1	6,577
1998	5,357	58.2	3,152	34.2	702	7.6	0	-	9,211
1999	6,116	60.5	3,396	33.6	600	5.9	4	0.0	10,116
2000	6,143	60.5	3,504	34.5	507	5.0	4	0.0	10,158
2001	7,726	62.2	4,252	34.3	435	3.5	0	-	12,413
2002	8,930	63.8	4,662	33.3	387	2.8	8	0.1	13,987
2003	11,922	63.1	6,334	33.6	597	3.2	24	0.1	18,877
2004	6,891	65.6	3,336	31.8	273	2.6	0	-	10,500
2005	7,038	65.8	3,440	32.1	213	2.0	12	0.1	10,703
2006	7,419	66.9	3,450	31.1	222	2.0	4	0.0	11,095
2007	8,407	66.4	4,076	32.2	183	1.4	4	0.0	12,670
2008	8,444	65.7	4,142	32.3	240	1.9	8	0.1	12,834
2009	9,016	67.3	4,152	31.0	216	1.6	8	0.1	13,392
2010	8,619	66.2	4,156	31.9	249	1.9	0	-	13,024
2011	9,388	63.3	5,131	34.7	300	2.0	0	-	14,819
2012	10,188	66.4	4,906	32.0	249	1.6	0	-	15,343
2013	11,713	64.9	6,003	33.3	327	1.8	8	0.0	18,051
2014	13,092	65.5	6,566	32.9	309	1.5	12	0.1	19,979
2015	13,702	65.4	6,942	33.2	297	1.4	8	0.0	20,949
2016	13,692	66.0	6,800	32.8	258	1.2	4	0.0	20,754
2017	14,722	66.1	7,206	32.3	342	1.5	12	0.1	22,282
2018	14,923	69.8	6,240	29.2	222	1.0	0	-	21,385
Total	**207,623**	**65.1**	**103,748**	**32.5**	**7,620**	**2.4**	**128**	**0.0**	**319,119**

Distribution of Indications 2019

IVF and ICSI – Prospective Data

	Treatments	Transfers		Clin. Preg.	
	n	n	%	n	%
No Information	100	67	67.0	21	31.3
Idiopathic	4,780	3,590	75.1	1,188	33.1
Male	25,692	22,923	89.2	7,490	32.7
Female	13,494	10,441	77.4	3,262	31.2
Male and Female	15,338	11,769	76.7	3,535	30.0
Missing Male Partner	261	212	81.2	61	28.8
Homosexuality	345	287	83.2	101	35.2
Total	**60,010**	**49,289**	**82.1**	**15,658**	**31.8**

Shares of Indications (Cycles) 2019



IVF

Male Factor ▸	Normal		Red. Semen Quality		Unknown		Other**		Total	
Female Factor ▾	n	%	n	%	n	%	n	%	n	%
Normal	1,728	10.5	615	3.7	92	0.6	1,400	8.5	3,835	23.4
Tubal Pathology	2,076	12.7	517	3.2	70	0.4	1,032	6.3	3,695	22.5
Endometriosis	1,123	6.8	283	1.7	69	0.4	798	4.9	2,273	13.9
Hyperandrog./PCO	421	2.6	124	0.8	30	0.2	220	1.3	795	4.8
Ovulatory Dysf.	486	3.0	252	1.5	65	0.4	374	2.3	1,177	7.2
Psychogen. Factors	10	0.1	4	0.0	2	0.0	31	0.2	47	0.3
Age	338	2.1	132	0.8	0	0.0	120	0.7	590	3.6
Other*	1,107	6.7	959	5.8	0	0.0	1,872	11.4	3,938	24.0
No Information	4	0.0	7	0.0	18	0.1	29	0.2	58	0.4
Total	**7,293**	**44.4**	**2,893**	**17.6**	**346**	**2.1**	**5,876**	**35.8**	**16,408**	**100.0**

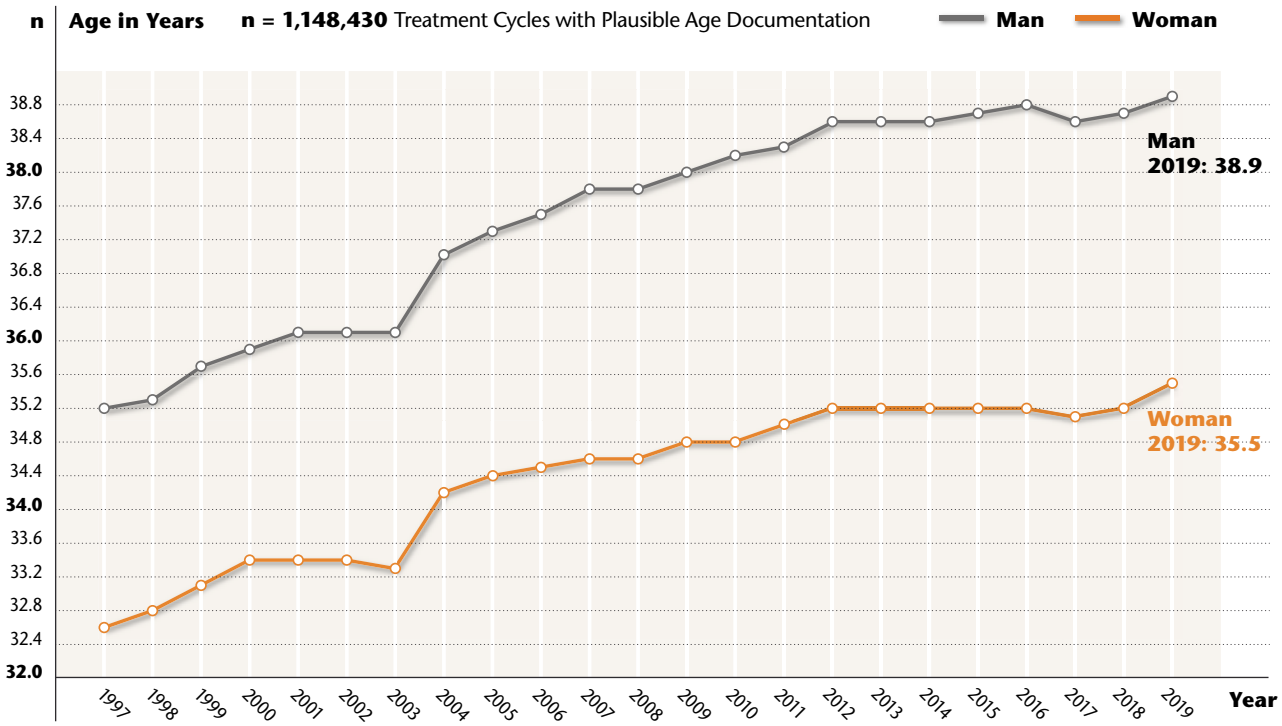
ICSI

Male Factor ▸	Normal		Red. Semen Quality		Azoospermia		Unknown		Other**		Total	
Female Factor ▾	n	%	n	%	n	%	n	%	n	%	n	%
Normal	951	2.2	9,635	22.1	1,131	2.6	185	0.4	3,675	8.4	15,577	35.7
Tubal Pathology	543	1.2	1,865	4.3	62	0.1	33	0.1	1,028	2.4	3,531	8.1
Endometriosis	419	1.0	1,767	4.1	76	0.2	59	0.1	990	2.3	3,311	7.6
Hyperandrog./PCO	139	0.3	1,051	2.4	60	0.1	29	0.1	459	1.1	1,738	4.0
Ovulatory Dysf.	237	0.5	1,721	3.9	131	0.3	111	0.3	840	1.9	3,040	7.0
Psychogen. Factors	3	0.0	27	0.1	2	0.0	1	0.0	12	0.0	45	0.1
Age	237	0.5	1,080	2.5	134	0.3	35	0.1	275	0.6	1,761	4.0
Other*	823	1.9	6,023	13.8	481	1.1	227	0.5	6,866	15.7	14,420	33.1
No Information	71	0.2	71	0.2	29	0.1	8	0.0	0	0.0	179	0.4
Total	**3,423**	**7.9**	**23,240**	**53.3**	**2,106**	**4.8**	**688**	**1.6**	**14,145**	**32.4**	**43,602**	**100.0**

**) The indications "sperm antibodies" and "cervical factor" are included here*
***) The indication "pathological function test" is included here*

Mean Age for Women and Men 1997 – 2019

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



Pregnancy-Rate per ET Subject to Preexisting Medical- and Lifestyle-Conditions

Prospective and Retrospective Data

	Hypertension	Nicotine Abuse	BMI <=25	BMI >25 + <30	BMI >=30
Number of Cycles with ET	459	4,748	54,973	10,592	9,994
CP (doc.)	131	1,491	16,970	3,371	3,167
CP (doc.) / ET	28.5	31.4	30.9	31.8	31.7

For the first time ever the data evaluation committee has attempted to evaluate anamnestic data and investigate possible relations of pre-existing medical conditions and lifestyle conditions with pregnancy rates per ET.

Due to the nature of the registers data collection, these results must be interpreted with caution.

In only 0.6 % of treatment cycles resulting in an ET, hypertension was reported as a preexisting medical condition.

When BMI was automatically calculated from height and weight, nearly 10,000 cycles were performed with a BMI >30. In only 4,700 cycles however, "Adipositas per magne, BMI >30" was actively selected from the drop-down menue. In nearly 7,000 cycles, no data were reported regarding height and weight.

Clinical Pregnancy Rate as a Function of Stimulation 2019

Prospective Data

Short GnRHa	uFSH	recFSH	hMG	recFSH a. recLH	recFSH a. hMG	Long-Acting recFSH	hrFSH	Other*	No Inform.	Total	Share (%) from total
Stimulations (n)	42	2,747	245	2,877	874	218	100	315	176	7,594	12.9
Transfers (n)	25	2,157	172	2,231	697	167	77	199	91	5,816	13.1
Transfer (%)	59.5	78.5	70.2	77.5	79.7	76.6	77.0	63.2	51.7	76.6	
CP (n)	9	720	42	740	237	47	33	39	20	1,887	13.2
CP/ET (%)	36.0	33.4	24.4	33.2	34.0	28.1	42.9	19.6	22.0	32.4	
CP/Stim. (%)	21.4	26.2	17.1	25.7	27.1	21.6	33.0	12.4	11.4	24.8	

Mean age of patients with regard to this protocol: 35.4 Jahre

Long GnRHa	uFSH	recFSH	hMG	recFSH a. recLH	recFSH a. hMG	Long-Acting recFSH	hrFSH	Other*	No Inform.	Total	Share (%) from total
Stimulations (n)	96	3,009	457	2,460	1,008	62	39	28	1,372	8,531	14.5
Transfers (n)	56	2,446	371	1,952	829	50	30	12	1,110	6,856	15.4
Transfer (%)	58.3	81.3	81.2	79.3	82.2	80.6	76.9	42.9	80.9	80.4	
CP (n)	13	865	95	631	291	7	7	0	403	2,312	16.1
CP/ET (%)	23.2	35.4	25.6	32.3	35.1	14.0	23.3	0.0	36.3	33.7	
CP/Stim. (%)	13.5	28.7	20.8	25.7	28.9	11.3	17.9	0.0	29.4	27.1	

Mean age of patients with regard to this protocol: 34.9 Jahre

No GnRHa-Analoga	uFSH	recFSH	hMG	recFSH a. recLH	recFSH a. hMG	Long-Acting recFSH	hrFSH	Other*	No Inform.	Total	Share (%) from total
Stimulations (n)	20	1,277	933	1,044	358	208	28	6	57	3,931	6.7
Transfers (n)	16	1,000	729	844	282	155	20	3	33	3,082	6.9
Transfer (%)	80.0	78.3	78.1	80.8	78.8	74.5	71.4	50.0	57.9	78.4	
CP (n)	3	318	222	230	68	50	7	0	6	904	6.3
CP/ET (%)	18.8	31.8	30.5	27.3	24.1	32.3	35.0	0.0	18.2	29.3	
CP/Stim. (%)	15.0	24.9	23.8	22.0	19.0	24.0	25.0	0.0	10.5	23.0	

Mean age of patients with regard to this protocol: 35.6 Jahre

GnRHa-Antagonists	uFSH	recFSH	hMG	recFSH a. recLH	recFSH a. hMG	Long-Acting recFSH	hrFSH	Other*	No Inform.	Total	Share (%) from total
Stimulations (n)	411	18,116	1,159	9,706	3,925	1,944	440	1,563	1,392	38,656	65.8
Transfers (n)	299	14,095	795	7,093	2,977	1,460	308	920	748	28,695	64.6
Transfer (%)	72.7	77.8	68.6	73.1	75.8	75.1	70.0	58.9	53.7	74.2	
CP (n)	88	4,793	195	2,270	975	383	121	175	227	9,227	64.4
CP/ET (%)	29.4	34.0	24.5	32.0	32.8	26.2	39.3	19.0	30.3	32.2	
CP/Stim. (%)	21.4	26.5	16.8	23.4	24.8	19.7	27.5	11.2	16.3	23.9	

Mean age of patients with regard to this protocol: 35.3 Jahre

Mean age of patients with regard to all protocols:

37.9	33.9	37.5	35.6	36.3	36.7	34.6	38.7	35.9	35.2	

In 9,451 cycles, either the protocol or the type of gonadotrophin were not clearly reported. These cycles contain a high proportion of hMG, whereby the number of hMG-stimulations is falsely reported too low.
This bug is beeing analyzed, as well as the conspicuously high number of cycles with GnRH-short-protocol.

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

Ovarian Hyperstimulation Syndrome (OHSS) as a Function of Stimulation Protocol and Age Cohort 2019

IVF, ICSI, IVF/ICSI – Prospective Data

	Cycles	%	Oocytes Retrieved	OHSS III (WHO)	OHSS III/Cycles %
Short GnRHa	**7,594**	**12.9**	**8.2**	**26**	**0.3**
< = 29 Years	867		11.1	2	0.2
30 – 34 Years	2,365		9.4	9	0.4
35 – 39 Years	3,278		7.3	11	0.3
> = 40 Years	1,084		6.4	4	0.4
Long GnRHa	**8,531**	**14.5**	**9.3**	**29**	**0.3**
< = 29 Years	1,084		11.4	3	0.3
30 – 34 Years	2,811		10.6	11	0.4
35 – 39 Years	3,600		8.4	12	0.3
> = 40 Years	1,036		6.5	3	0.3
No GnRHa-Analoga	**3,931**	**6.7**	**9.3**	**13**	**0.3**
< = 29 Years	405		11.7	1	0.2
30 – 34 Years	1,144		10.3	4	0.3
35 – 39 Years	1,697		8.6	6	0.4
> = 40 Years	685		6.3	2	0.3
GnRHa-Antagonisten	**38,656**	**65.8**	**9.2**	**133**	**0.3**
< = 29 Years	4,762		11.9	11	0.2
30 – 34 Years	12,481		10.7	48	0.4
35 – 39 Years	16,265		8.3	55	0.3
> = 40 Years	5,148		5.7	19	0.4
Total*	**58,712**	**100.0**	**9.1**	**201**	**0.3**

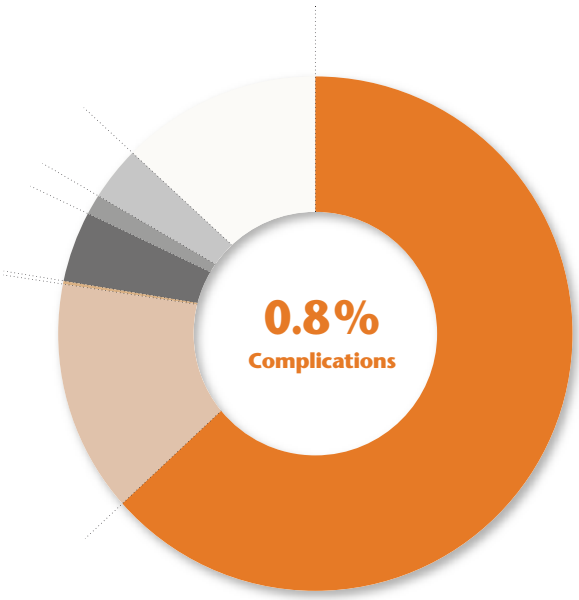
**) in 9,451 cycles, the protocol could not be reliably determinated*

Complications as a Function of Ovum Pick-up (OPU) 2019

Prospective Data

Total OPU´s	62,192	100.0%
No Information	0	0.0%
No Complications	61,671	99.2%
Complications	**521**	**0.8%**

Complications	n	%
Vaginal Bleeding	328	63.0
Intraabdom. Bleeding	75	14.4
Intestinal Tract Injury	1	0.2
Peritonitis	24	4.6
Hospitalisation	7	1.3
Surgery	18	3.5
Other	68	13.1
Total	**521**	**100.0**

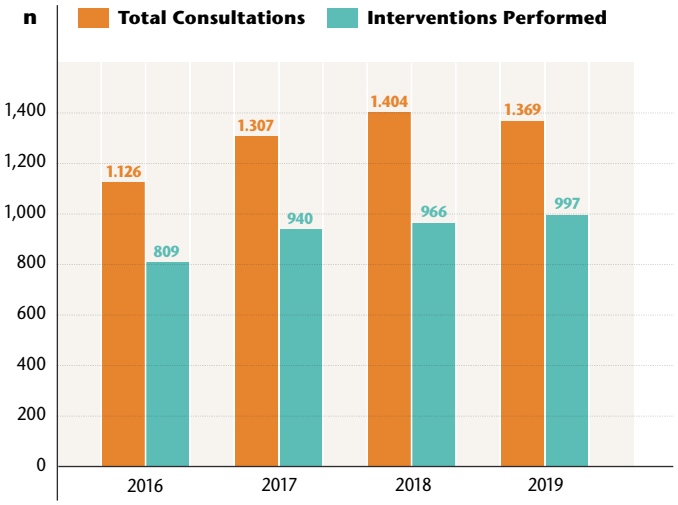


FertiPROTEKT
Netzwerk für fertilitätsprotektive Maßnahmen

For the second year in a row, the 2006 established network *Ferti*PROTEKT e.V. – a consortium of centers from Germany, Austria and Switzerland, that are engaged in fertility preservation in female patients before gonadotoxic therapies – is able to present its yearly registry data within the D·I·R yearbook.

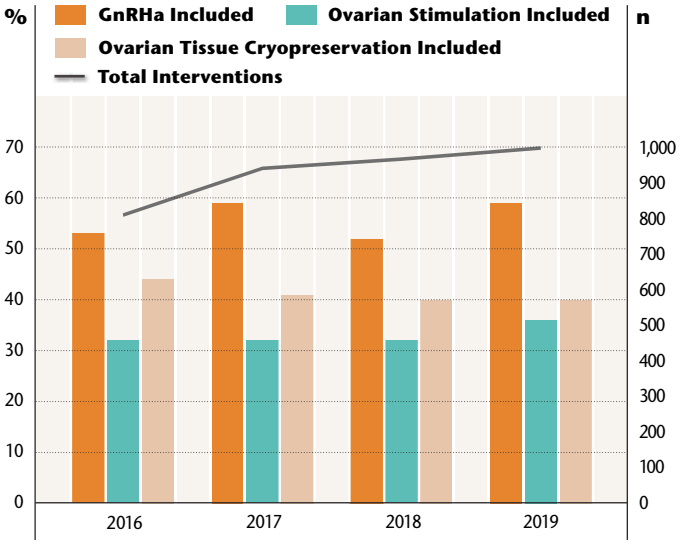
This year, however, the focus is set on the last four years, showing the data from 2016 up to 2019. Since information on ovarian tissue transplantation was scarce in the year 2019, we omit to publish about them this year, since they would not be representative.

Consultations and Interventions within the *Ferti*PROTEKT Netzwerk e.V.



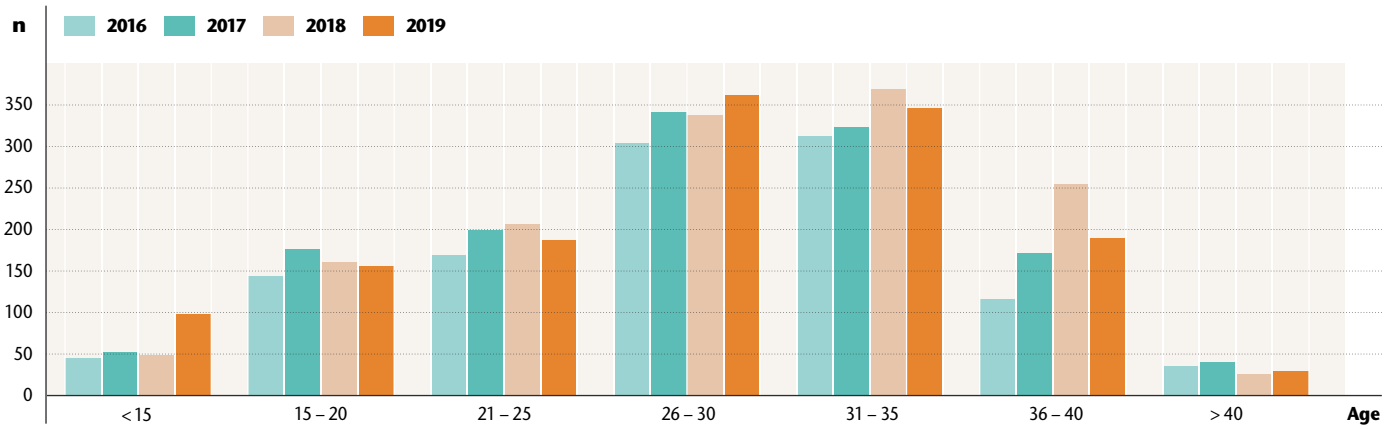
Overall, 2019 we registered less counselling visits than in 2018. However, as more interventions are registered, we assume that the number of counselling visits was still high, just not documented.

Frequency of Different Fertility Protection Methods



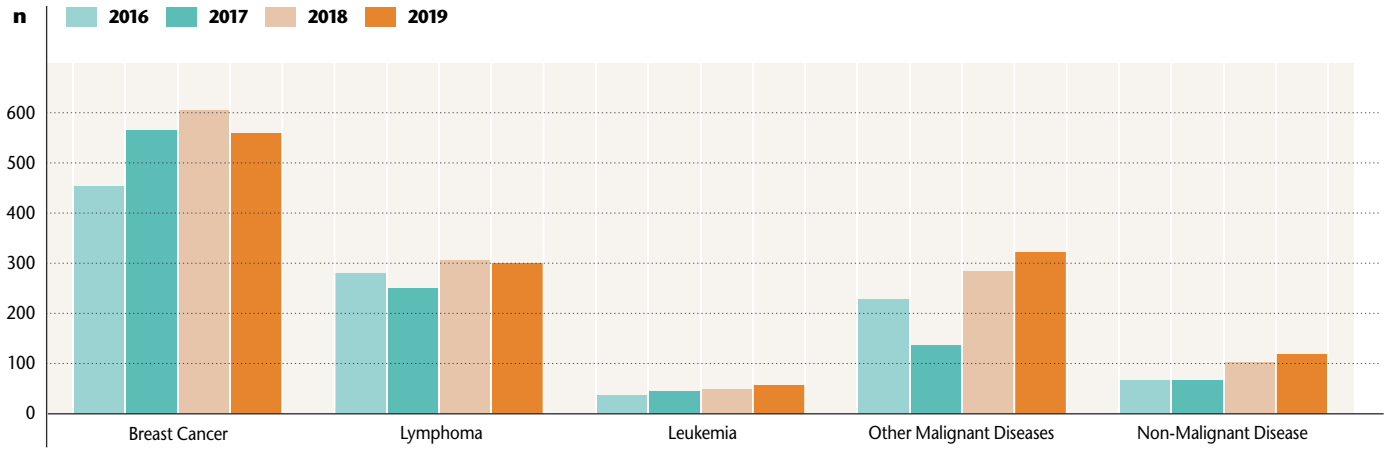
The distribution of the individual treatments remained the same within the last years.

Age Distribution of Consultations within the *Ferti*PROTEKT Netzwerk e.V.



Last year the number of children <15 years of age counselled increased dramatically. This is not due to the activity of a single center, but rather due to counselling in several university clinics. Furthermore, the reason for the reduced number of patients counselled between 36-40 years remains speculative.

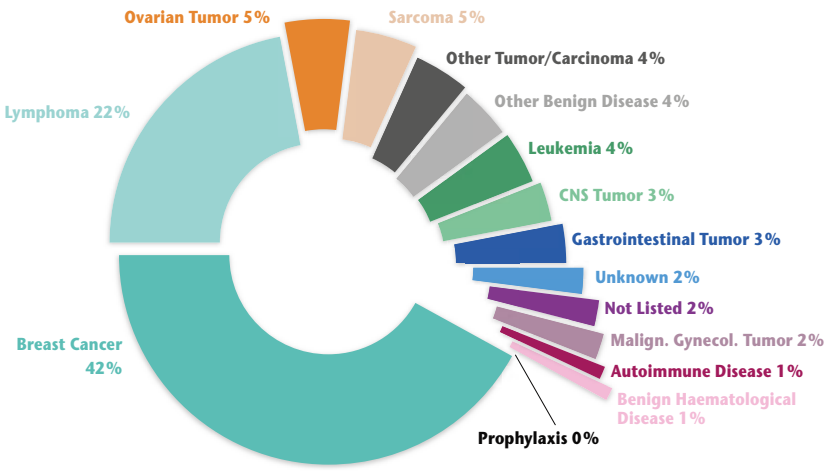
Diagnoses at Consultation



While in former days mainly patients with breast cancer and lymphoma were seen, the incidence of patients with other cancers increased in 2019. We hope that this trend will be kept up, when fertility preservation will be covered by the insurance companies in Germany and Switzerland in the near future.

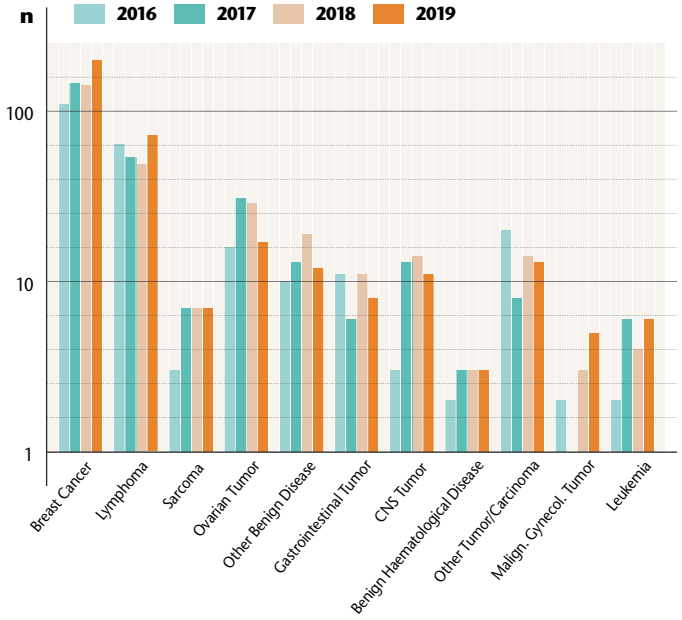
The ratio of malignant to benign diseases remains stable.

Frequent Diagnosis Groups in Register 2016 – 2019



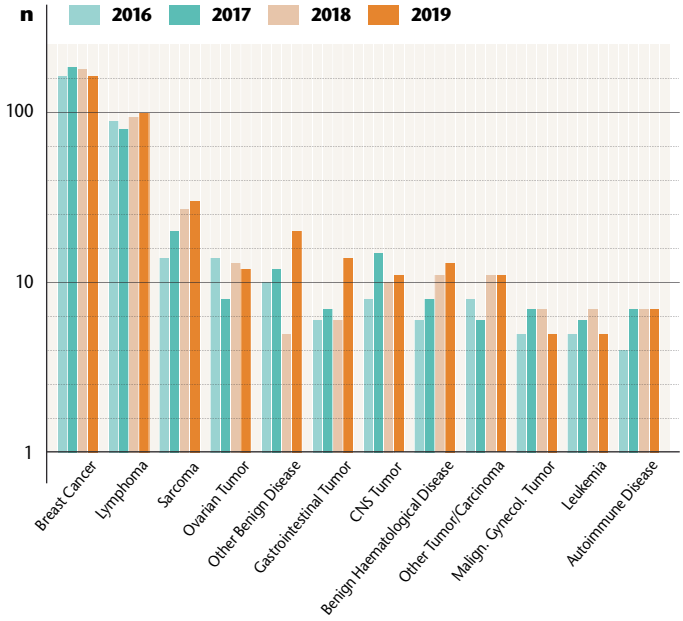
Underlying Disease when Ovarian Stimulation is Performed

Logarithmic Scale



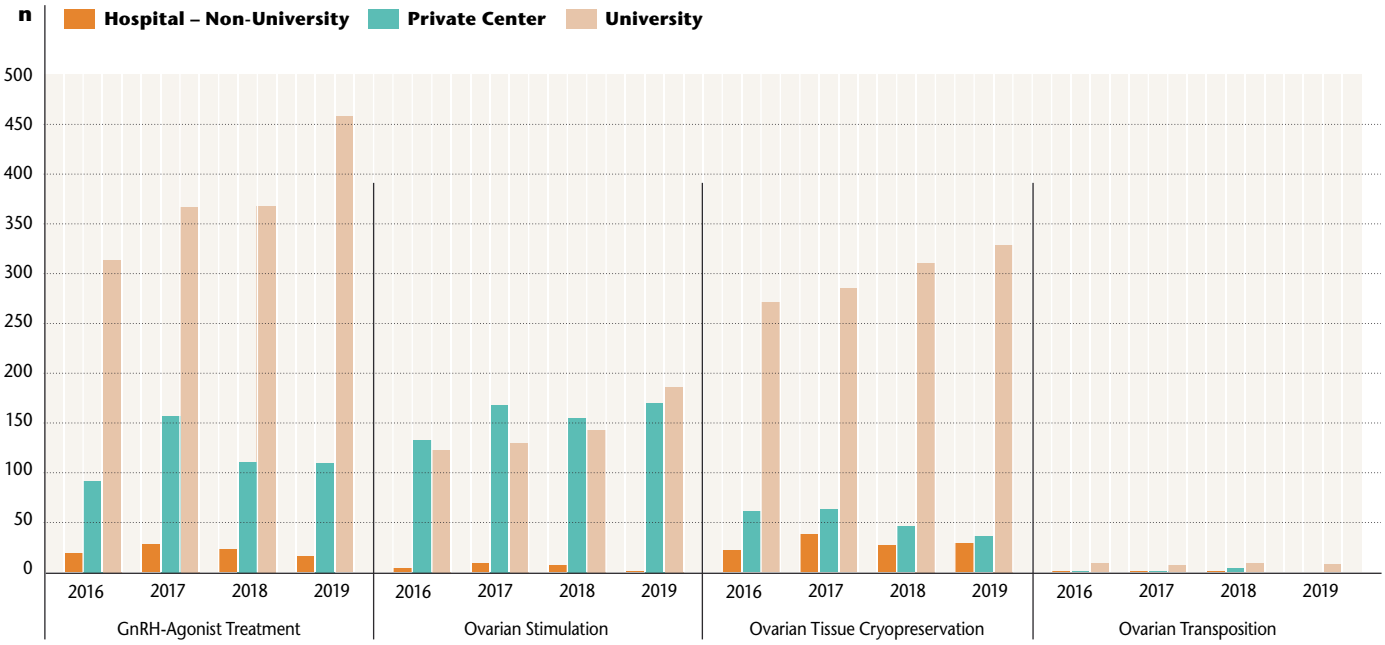
Underlying Disease when Ovarian Tissue Cryopreservation is Performed

Logarithmic Scale



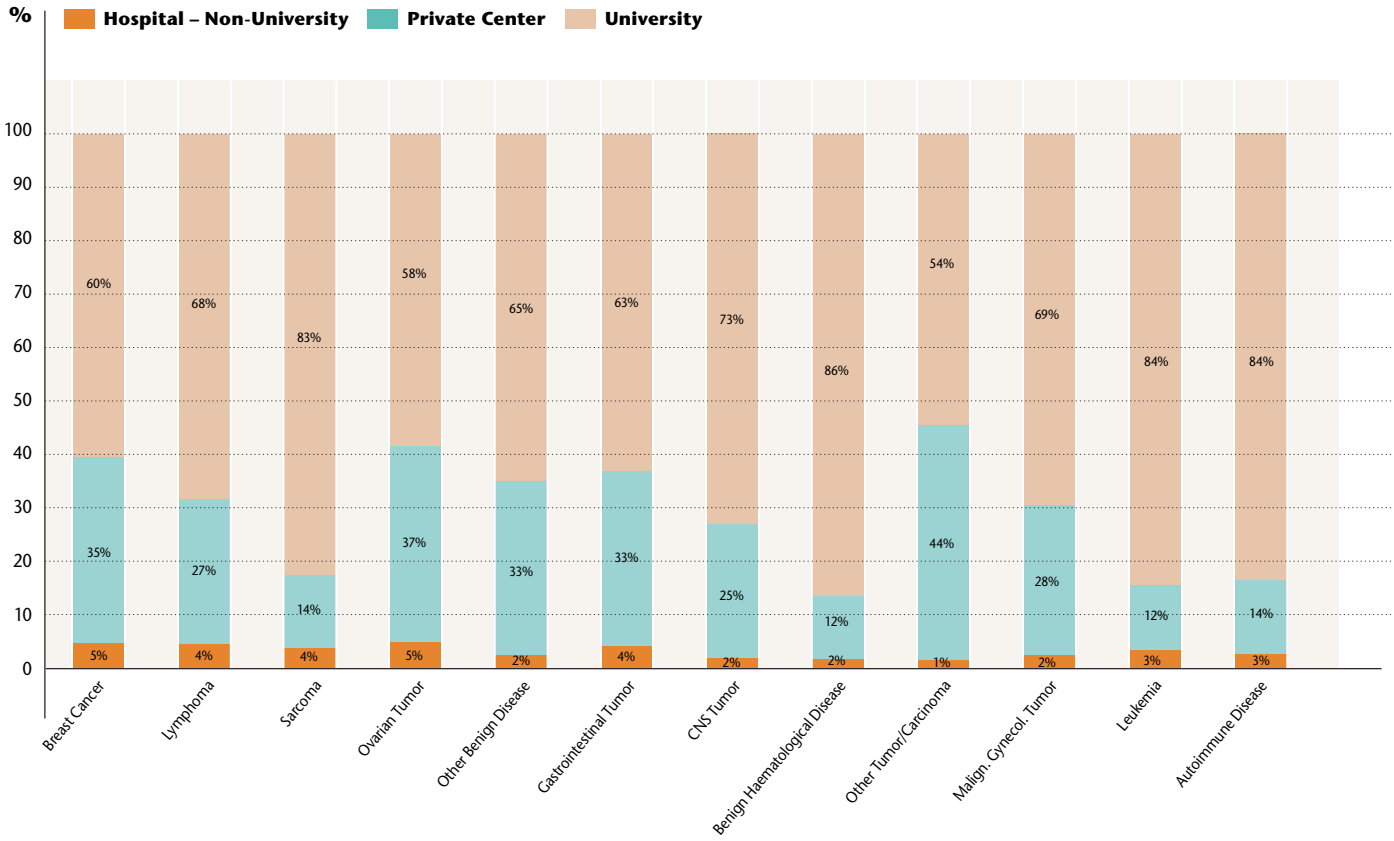
Therapies by Type of Center

FertiPROTEKT
Netzwerk für fertilitätsprotektive Maßnahmen



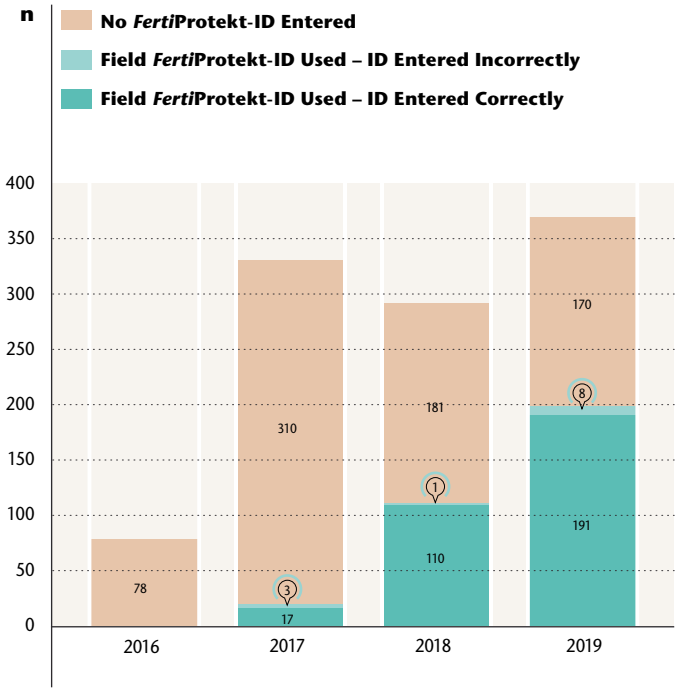
Diagnosis by Type of Center (2016 – 2019)

FertiPROTEKT
Netzwerk für fertilitätsprotektive Maßnahmen



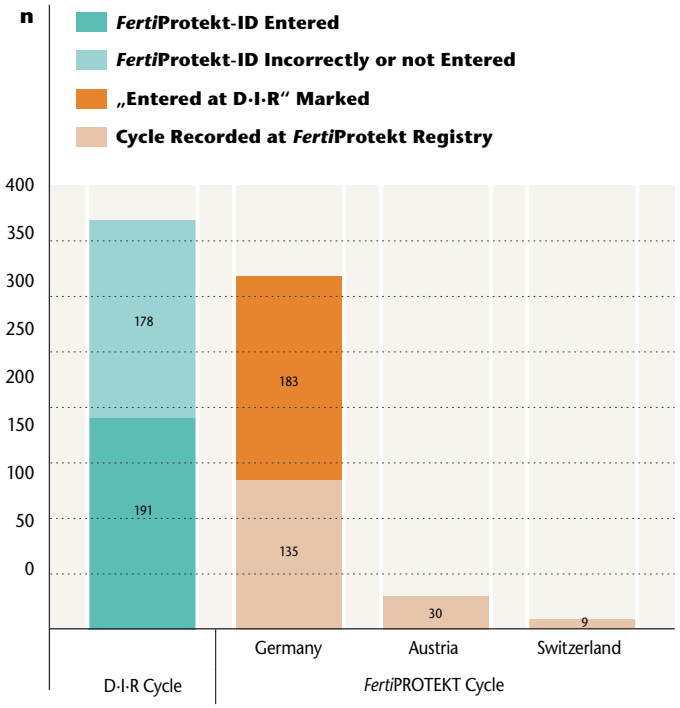
This year an increased number of GnRHa prescriptions can be noted, most likely due to the more recent articles published in favor of their use.

Entry of *Ferti*PROTEKT and *Ferti*PROTEKT-ID at D·I·R



The entry of the *Ferti*PROTEKT-ID has picked up in 2019, even before it has become a mandatory field for the documentation of ovarian stimulation cycles, and is expected to increase further in the upcoming years. This allows us to measure the quality of the treatment on one hand and to link the underlying indication of the fertility preservation on the other hand.

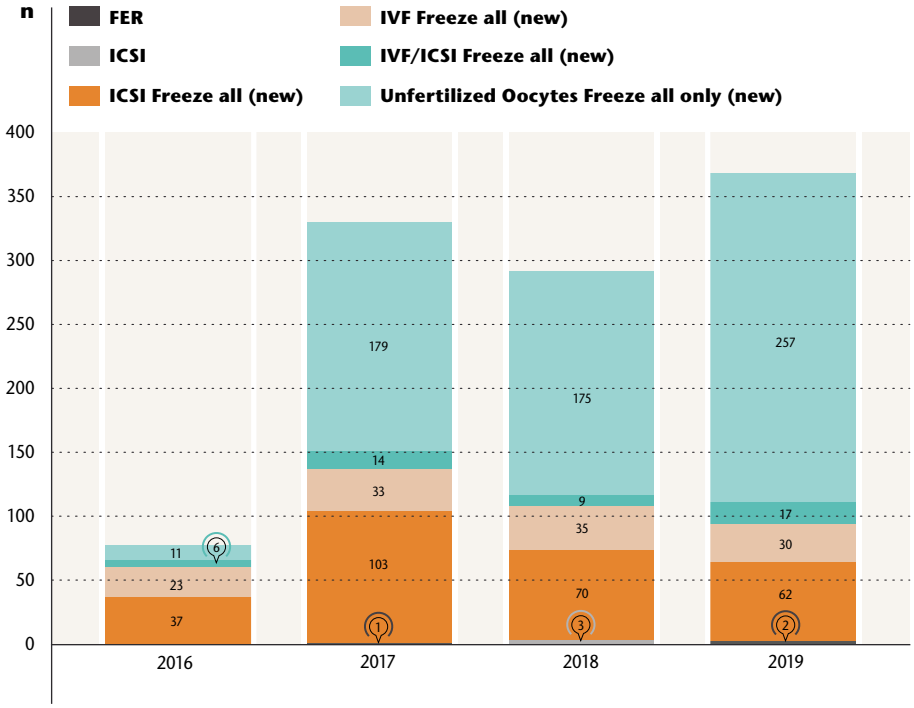
Recorded Fertility Protection Stimulation Cycles 2019



Three centers in Switzerland and six centers in Austria have recorded cycles as members of the FertiPROTEKT Netzwerk e.V.

It is currently assumed that still not all ovarian stimulations are documented within this registry, as the numbers documented differ between the two registries. Furthermore, only two cycles of cryo-embryo-transfers are noted, which is below our expectations.

Planned Treatment Cycles, Recorded at D·I·R Registry



A goal for the upcoming year will be the definition of indications for recording a cycle at the D·I·R registry as well as to simplify the submission and revision of data within the *Ferti*PROTEKT registry. In addition, an automated creation of a patient document with a *Ferti*PROTEKT-ID is planned, in order to facilitate the communication between the centers regarding one and the same patient.

Therefore, we already integrated the data from the former registries from the years before 2014 into the existing registry. All of them were updated with a *Ferti*-PROTEKT-ID, allowing to add this number in the D·I·R registry, when a cryo-embryo-transfer is performed nowadays.

Deutsches IVF-Register e.V. (D·I·R)®
List of D·I·R Members

Sorted by postal code in ascending order – as at September 2020

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