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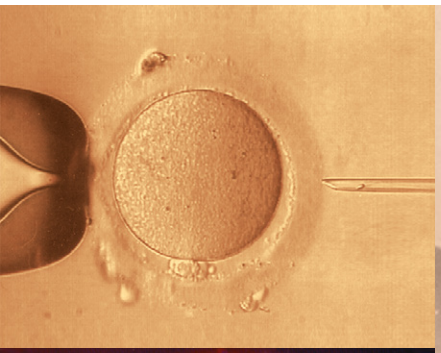

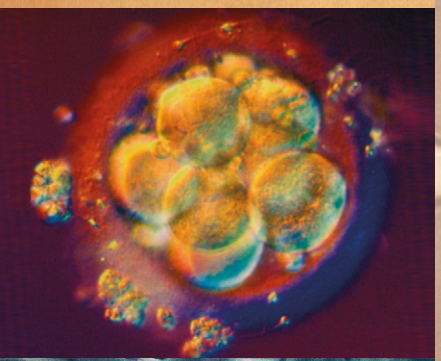

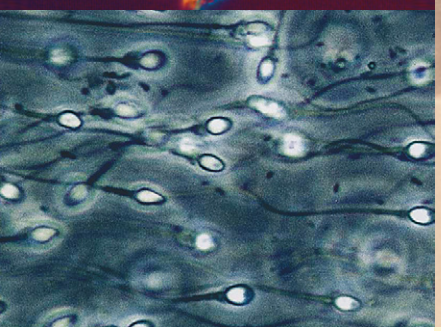

D.I.R-Annual 2023

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Preface
D·I·R Annual 2023 – The German IVF-Registry

S. Bartnitzky, V. Blumenauer, U. Czeromin, D. Fehr, C. Grewe, J.-S. Krüssel, M. S. Kupka, A. Tandler-Schneider, S. Tauchert

Dear Ladies and Gentlemen, dear Colleagues, dear D·I·R people,

We are pleased to present to you the 2023 Annual!

Background of this Annual

The D·I·R currently has 141 member centers. This Annual contains information on the treatment cycles from 2022 (cycle outcomes and births) and the treatment cycles from 2023 (cycle outcomes) of all 141 centers. The evaluations were conducted based on the database status as of May 15, 2024.

In preparing this Annual, we once again became aware of the complexity of registry work for both professional and volunteer staff, and how the quality of the registry depends not only on the careful data collection within the centers but also on the IT structures of the data collection software, the ARTbox® interface, and the data evaluation tool. Milestones have been achieved here, allowing again all center exports, regardless of the data collection software used, to be integrated into the evaluation.

This Annual

As usual, we have updated the standard evaluations for 2022 and 2023 based on the data available as of May 15, 2024.

For the 2023 Annual, we have benefited from all the work invested in the IT structure through the evaluation software QLIK®.

Special evaluations in this Annual focus on:
- The cryopreservation of oocytes and their use
- Dependency of birth weight and weeks of pregnancy in fresh and thawed cycles in relation to the number of culture days

One result of these evaluations to anticipate: All our born children (1997–2022) have reached the next "magical" number of our data treasure, with 412,230 children documented in the D·I·R. These children represent exactly the combined population of the cities of Mülheim an der Ruhr and Magdeburg.

*Ferti*PROTEKT and D·I·R

In this Annual, the cooperation with the *Ferti*PROTEKT Network e.V. is once again highlighted. We are pleased that these evaluations have become part of our Annual! This cooperation is a delightful example of the synergetic effects of respectful collaboration among colleagues working in solidarity. Since the statutory health insurance obligation for fertility preservation measures for fertility-threatening diseases came into effect in July 2021, there has been only a slight increase in the number of treatment cycles with FertiPROTEKT indication, from 580 in 2020 to 967 cycles in 2023.

DERI and D·I·R

At the beginning of 2023, the IT structures for the registration of heterologous and homologous inseminations of the German Insemination Registry (DERI), hosted by the Working Group for Donor Insemination e.V., were created for DERI member centers. Utilizing synergies, this register, independent of the D·I·R, was linked to the existing structures of the data collection software, interfaces to and from the ARTbox® and the registry database. Here again, there was no need to reinvent the wheel – from our perspective, this is also a successful example of collegial cooperation.

GDPR

The implementation of the GDPR in May 2018 caused a significant additional workload for the centers. At the request of the D·I·R, staff at the centers obtained consent from patient couples for the transmission of pseudonymized treatment datasets. For the year 2023, the register contains 92% pseudonymized, 7.5% anonymized, and 0.5% subsequently revoked datasets.

Importantly, in this context, is the unfortunately not yet final ruling of the European Court of First Instance (EUG T-557/20) of April 26, 2023. Following an appeal on July 5, 2023, the case is pending before the CJEU under case number C413/23P. The EUG ruled that after pseudonymization by the data transmitter (for us, the center) to the recipient (for us, the register), the personal reference can be considered removed if the recipient has no legal means of re-establishing the personal reference. As a result, the register's activities would not be subject to the GDPR due to the lack of personal reference. It would be desirable for this to be reflected in future jurisprudence to reduce the GDPR-based bureaucratic burden on the centers.

Since the D·I·R operates nationwide, the health data protection laws of the states (13 of 16 federal states have their own legal regulations) cannot be uniformly implemented by us.

The following still applies

For the transmission of anonymized datasets, only informing the patients is sufficient; for the transmission of pseudonymized datasets, the consent of both partners is required, unless doctors are obliged to report under a state-specific medical profession law.

This leads to another plea for the transmission of pseudonymized datasets

As being physicians active in reproductive medicine ourselves, we are aware of the effort that obtaining patient consent involves, including the necessary engagement and information that this requires. It must be repeatedly emphasized that only a large number of pseudonymized datasets will allow patient-specific evaluations of cumulative pregnancy rates, FertiPROTEKT, and in the future, also for PGT, even though cross-center evaluations are no longer possible due to the elimination of the National Patient ID.

At this point: Thank you for your effort, your dedication in conversations with patients, your organizational and documentation efforts in the legally compliant implementation of the GDPR for the benefit of our register's quality!

Small Politics – Cost Coverage for ART

The cost coverage for assisted reproductive technology (ART) continues to suffer and imposes a significant financial burden on affected couples. Federal funds have been reduced, and state funds are no longer or still not available in many states. Most recently, the state of North Rhine-Westphalia announced the discontinuation of funding as of January 1, 2025, after applications were no longer processed in 2024 due to unclear financing.

From a medical perspective, it is an incomprehensible fact that in cases of tubal sterility, microsurgical fertilization is routinely financed, yet another therapy for the same condition can only be billed as a benefit by statutory health insurance at 50%.

A 100% benefit within the framework of § 27a of the German Social Code (SGB V) would be a fair social legislative decision that honors the financial, emotional, and time investment of couples who take on the responsibility of wanting to become parents with the respect that it deserves.

Politics at large

The changes in reproductive medicine announced in the 2021–2025 coalition agreement have been discussed but nothing has been decided! The report of the Commission on Reproductive Self-Determination and Reproductive Medicine has been available to the Federal Government since April 24, 2024. On the subject of egg donation, it states: "The reasoning on which the legislator based the ban on egg donation in 1990, particularly the goal of avoiding split motherhood, must today be regarded as outdated and no longer convincing." The commission did not address the legalization of elective single embryo transfers or the legalization of pronuclear stage donation. A representative of medical ethics in the commission, Prof. Claudia Wiesemann from Göttingen, is quoted in the German Medical Journal of April 16, 2024, as saying: "The selection of the best developing embryo is not only legitimate but ethically imperative."

Thanks

We sincerely thank all those who contributed to making this Annual a reality:

We thank the D·I·R Data Management, and with it, Markus Kimmel.

He took on the challenge of using the QLIK® evaluation software. He critically examined and identified pitfalls in the data collection programs MedITEX and DIRproNOVA with the service providers CRITEX GmbH, and with the company QuinniSoft for their data collection software and pushed for improvements.

And last but not least

With the help of Transact GmbH, he developed, controlled, and applied the evaluation algorithms for the evaluations using QLIK® software so that we could reap the benefits of this work for this Annual. Not only for the Annual but also for the individual centers in the form of KPIs and the individual center profiles in the national comparison, data evaluation through the program QLIK® applied by Markus Kimmel has become more stringent, efficient, and flexible.

The efforts have paid off

He provided us with valid evaluation results for this Annual through good organization and stringent data processing and tirelessly motivated everyone involved to work. He developed the tools for creating the individual center KPIs and center profiles – thereby developing a tool that allows the individual D·I·R member centers to receive their individual data on a quarterly basis.

We thank our designer Soo-Hee Kim for the beautiful layout, and especially for her patience and dedication. Even this year, it was unavoidable that she had to incorporate our numerous change requests right up to the last minute before printing.

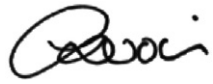
We also thank the Annual partners, who generously supported us financially, enabling us to hold this Annual in our hands once again.

Our thanks go to the Curatorium and especially to the Curatorium member of AGRBM, Ms. Dipl. Biol. Verona Blumenauer.

And most importantly, our special thanks go to the centers for their conscientious data collection and transmission. We also thank the centers for their generous financial contributions, without which the further development and improvement of the database and data evaluation would not have been possible.

In creating this Annual and the necessary preparatory work, we have witnessed great acceptance of the German IVF-Register:

Your D·I·R Board



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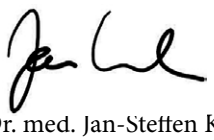

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In a Nutshell – 2022's and 2023's Findings of the German IVF-Registry

- All 141 member centers of the German IVF-Registry exported their data from the years 2022 and 2023 as of the reporting date. The number of plausible treatment cycles amounted to 127,973 cycles in 2023, representing a slight increase of 1 % compared to 2022.
- In 64.1 % of the cycles, a treatment to retrieve eggs was initiated, while 35.9 % of the cycles involved previously frozen eggs. The proportion of cryo cycles has continued to increase.
- The pregnancy rates per embryo transfer in fresh cycles were 31 % in 2023, and the pregnancy rates in cryo cycles per embryo transfer were 30.7 % in 2023, making them nearly equal.
- Despite the increasing prevalence of single embryo transfer (SET) to avoid higher-grade multiple pregnancies, the improvement in pregnancy rates in cryo cycles is particularly noteworthy. In 2017, the pregnancy rate per embryo transfer had been 26.2 %; by 2023, it had risen to 30.7 %.
- The birth rates per embryo transfer in 2022 were 22.5 % for fresh cycles and 22.1 % for cryo cycles.
- The dependence of pregnancy and birth rates on age is significant. Women aged 30-34 have a pregnancy rate per embryo transfer of 39.3 % and a birth rate of 31.2 %. In contrast, for women aged 41-44, the pregnancy rate per embryo transfer drops to 17.0 %, and the birth rate to 8.4 %. *See the IVF example from 2018-2022.*
- The continuous decline in multiple births is encouraging. Between 2017 and 2022, they were reduced by a full 10 percentage points in fresh cycles and by more than 7 percentage points in thawing cycles! The multiple birth rate in 2022 was 12.0 % in fresh cycles and 8.2 % in cryo cycles; in 2017, these rates were 22.0 % and 15.4 %, respectively. *See D·I·R Annual 2018.*
- In all treatment cycles where the prognosis for a successful outcome is good, single embryo transfer is increasingly being used. Although the pregnancy rates are slightly lower with the transfer of a single embryo, the multiple pregnancy rates rise dramatically when two embryos are transferred in this patient group, leading to higher rates of pregnancy complications and preterm births.
- The cumulative birth rate after multiple transfers following just one egg retrieval is significant when the option for cryopreservation is available and utilized. After one fresh transfer and two cryo transfers, half of the couples can already celebrate the birth of a child, even though only one fresh treatment cycle was performed.
- To date, 412,230 children have been born following in-vitro fertilization cycles. This is equivalent to the combined population of the cities of Mülheim an der Ruhr and Magdeburg. The proportion of preterm births (births before the end of the 37th week of pregnancy) in 2022 was 18 % for singletons, 86.2 % for twins, and 100% for triplets.
- Reproductive medical techniques are safe – the risk of overstimulation as a result of hormone therapy was 0.2 %, and complications from egg retrieval, such as bleeding, were 0.8 %.

Our recommendations if pregnancy does not occur:

1. Don't be afraid! Seek advice from a fertility center and then make your decision. Choose a center that is a member of D·I·R, which makes these annuals possible.

2. Don't wait too long: The chances of successful treatment depend on age.

3. Take advantage of the single embryo transfer, blastocyst culture, and cryopreservation: Not a single fertilized egg is lost, and you have another chance with minimal effort after thawing, even for a second child!

Brief overview of the most important results for the public

This year, we again present the most important results on the following pages in a brief overview.

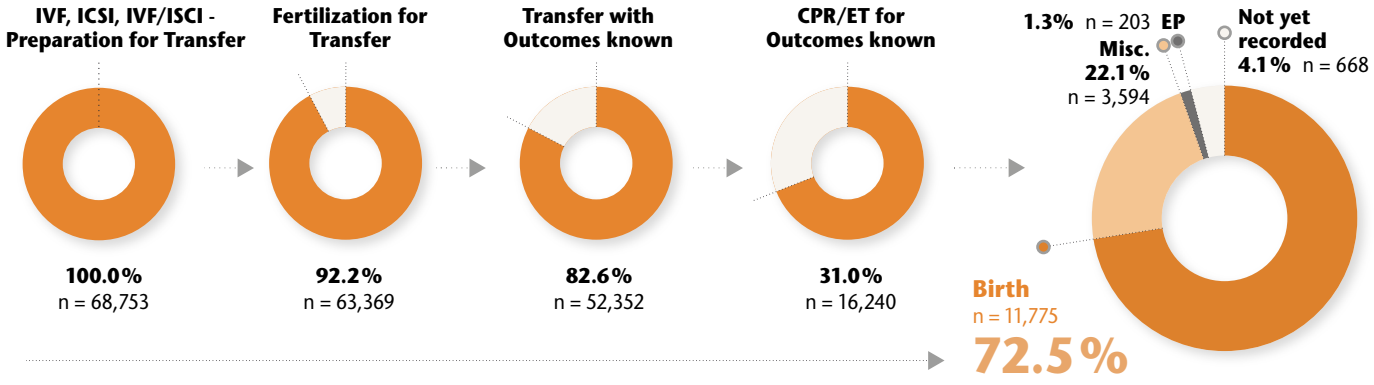
The first analysis shows the results of the treatments conducted in 2022 up to the birth.

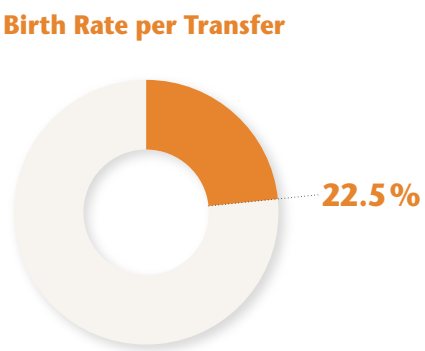
The second analysis on the next page shows the age-dependent development of both the pregnancy rate per embryo transfer and the births and miscarriages.

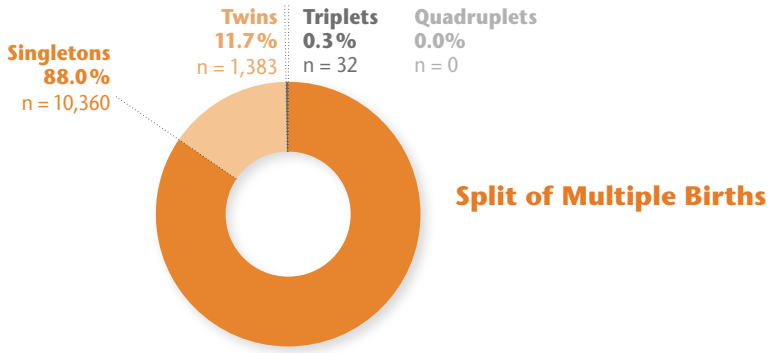
The third analysis, on the page after the next, is dedicated to the cumulative pregnancy rate per embryo transfer, regardless of whether it is a fresh embryo transfer or a thaw cycle. The cumulative pregnancy rate after four transfers is over two-thirds (67.4%).

Summary D·I·R Statistic in Brief 2022 – CoD May 15th, 2024

IVF, ICSI, IVF/ISCI - Prospective and Retrospective Data







In 2022, 68,753 fresh cycles for egg retrieval and treatment were conducted in Germany. This is 3,526 cycles fewer than in the previous year. This decrease is offset by the increase in the freezing of untreated oocytes.

In 82.6% of the cases, an embryo transfer was performed with a known cycle outcome. This is also slightly less than in 2021, and is due to the freezing of fertilized oocytes or embryos without transfer (Freeze All).

The birth rate per transfer in 2022 was 22.5%, similar to 2021 (23.4%), with a significantly decreased rate of multiple births. This is seen as a success of the Single Embryo Transfer strategy.

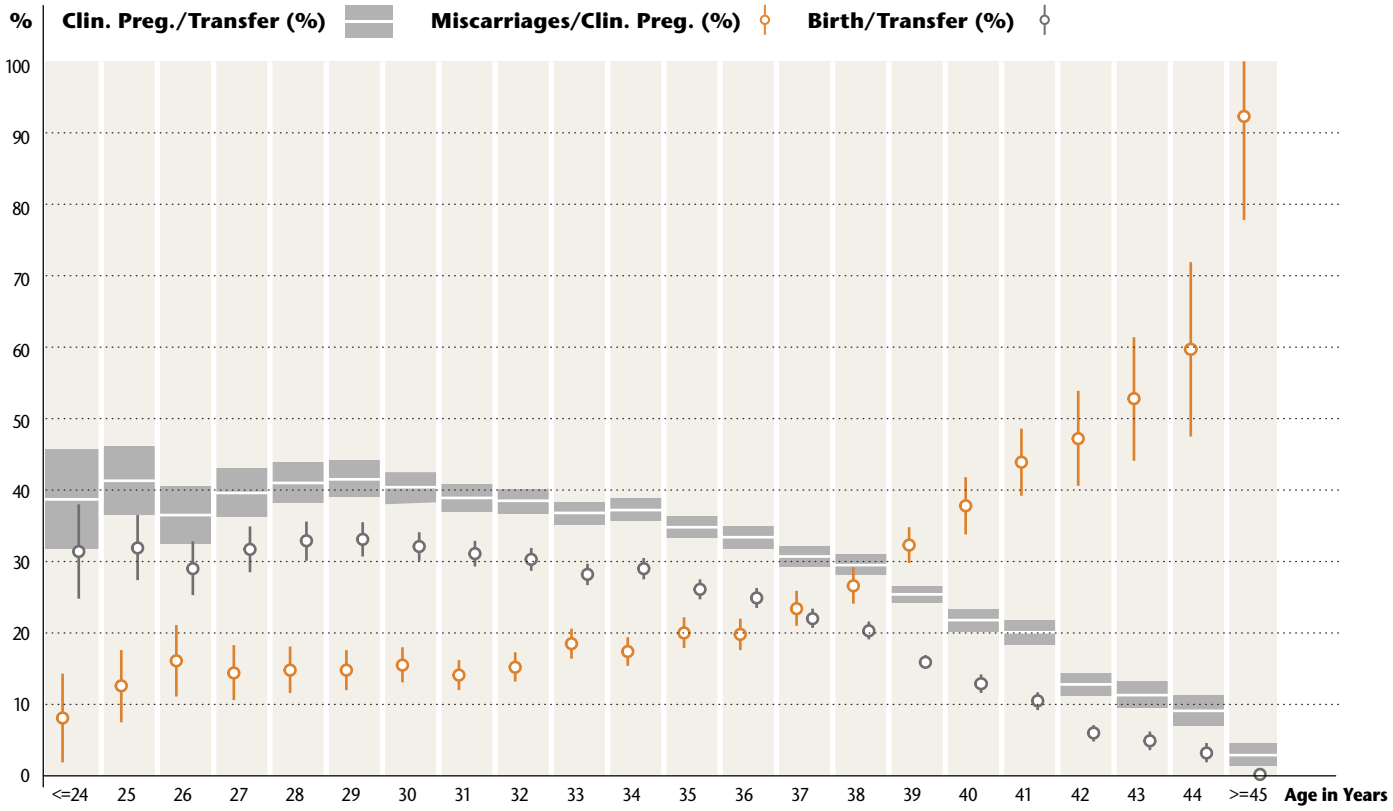
While there were still 2,013 twin births in 2021 (15.2%), this number dropped to 1,383 twin births in 2022 (11.7% of all births)!

Meanwhile, 88% of births are singleton births. Even though the multiple birth rate has significantly decreased to a total of 12%, it still remains on the higher side compared to Europe. Countries like those in Scandinavia or the Netherlands have multiple birth rates in the natural range of less than 5%. Nonetheless, we are pleased in Germany about the sharply declining trend in multiple births, which carry a higher risk of preterm birth at over 80%.

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2022

Prospective Data

IVF, ICSI, IVF/ICSI 2022



	<=24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	>=45	
n	193	404	565	807	1,118	1,466	2,094	2,642	3,113	3,592	3,690	3,843	3,749	3,726	3,807	5,358	2,567	2,166	1,702	1,127	685	445	**ET**
%	38.7	41.3	36.5	39.6	41.0	41.5	40.4	38.9	38.5	36.8	37.2	34.8	33.4	30.7	29.5	25.4	21.8	20.1	12.8	11.3	9.1	2.9	**CP/ET**
n	60	129	163	255	367	485	670	821	942	1,012	1,067	1,001	932	819	773	850	330	226	101	55	22	1	**Birth**

Pregnancy, abortion and birth rates are presented here as a 95% confidence interval. So with a 95%-probability, the true mean lies within the defined confidence interval.

In this graphic, we present the development of pregnancy rates, miscarriage rates, and birth rates depending on age. The statistics refer exclusively to fresh cycles and combine IVF and ICSI. Pregnancy and birth rates are calculated per embryo transfer.

Up to the age of 31, the pregnancy rate remains over 40%. Birth rates, on the other hand, are over 30% per embryo transfer until the age of 35. From our perspective, this is very significant for advising and assessing the respective chances.

Miscarriages should also be considered in age-dependent counseling: While they are below 20% in women up to the age of 35, they rise to 37.8% at 40 years and even exceed 90% in patients over 45 years.

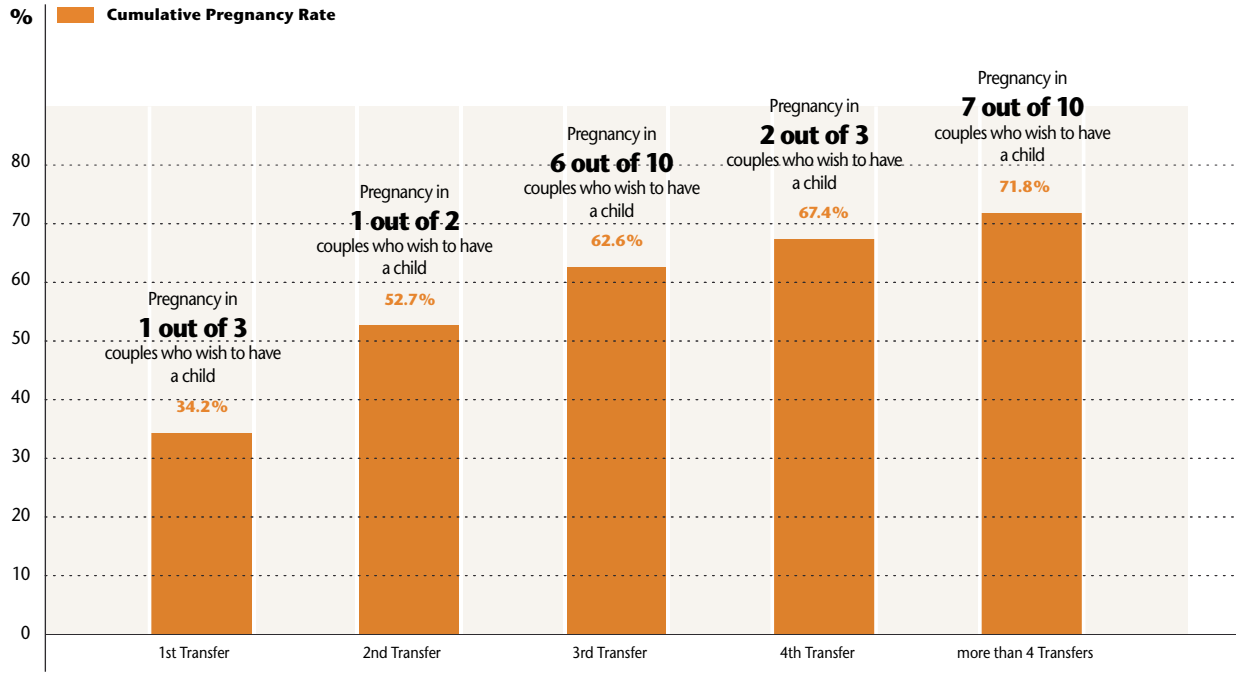
For example, a 35-year-old patient has a pregnancy rate of 34.8% and a birth rate of 26.1%.

From the age of 40, pregnancy and birth rates decrease significantly each year. Here, every year of life is crucial. Patients aged 45 or older had only 13 pregnancies (2.9%) after a total of 445 transfers, and only one birth was documented in this age group in the entire year of 2022!

Therefore, it is extremely important for counseling that fertility treatment should take place promptly, especially in the group of patients aged 35 and older, which includes most of our patients.

Pregnancies Cumulative 2020–2022

Prospective Data



2020 – 2022 total	Retrievals	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycles w. Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cum. CP	Cumulative Pregnancy Rate in %
1st Transfer	77,629	26,450	34.1	15,657	5,410	34.6	31,860	**34.2**
2nd Transfer	25,706	7,596	29.5	30,821	9,685	31.4	49,141	**52.7**
3rd Transfer	13,592	3,968	29.2	17,552	5,292	30.2	58,401	**62.6**
4th Transfer	6,403	1,767	27.6	9,402	2,698	28.7	62,866	**67.4**
>4 Transfers	5,793	1,489	25.7	10,195	2,668	26.2	67,023	**71.8**

Follow-up clinical pregnancies until Dec. 31st, 2023.

Important for counseling and assessing the chances is not only the pregnancy and birth rate per treatment or per embryo transfer but also the pregnancy rate over multiple cycles. This is particularly relevant in the era of single embryo transfer and the improved outcomes of freezing through vitrification.

For these reasons, we have calculated the pregnancy rates per transfer cumulatively, regardless of whether it is a second fresh cycle or a thawing cycle (cryotransfer).

After just two embryo transfers, 52.7 % of our patients are pregnant. After three transfers, this figure rises to six out of ten, and after four transfers, it is already over two-thirds of all fertility patients.

Also included in this consideration are cycles in which the first embryo transfer was not fresh but occurred after thawing. This may happen, for example, if a fresh embryo transfer could not be performed for medical reasons. In fact, 5,410 first embryo transfers were performed after thawing, with the pregnancy rate being even slightly higher than in fresh cycles (34.6 % versus 34.1%).

A cumulative pregnancy rate is primarily achieved through cryopreservation and subsequent transfers after thawing, without the need for further stimulation and egg retrieval.

In Germany, freezing and subsequent transfer are still not covered by public health insurance. This deters some from taking advantage of the opportunities offered by freezing and thawing. On the other hand, cryopreservation is increasingly being utilized, as the chances are at least equal and the effort is considerably lower.

Conclusion:
As disappointing as a negative pregnancy test after a transfer may be, the fact that two-thirds are pregnant after four transfers, including cryopreservation, should be encouraging and is immensely important for counseling.

Dr. med. Andreas Tandler-Schneider, Berlin (in charge)
Dr. med. Ute Czeromin, Gelsenkirchen
Prof. Dr. med. Jan-Steffen Krüssel, Düsseldorf

Main Topic: Cryopreservation of Oocytes and their Use after Thawing

In recent years, due to the establishment of new freezing methods (vitrification) and the increasing awareness of the possibility of creating a fertility reserve (FertiPROTEKT and Social Freezing), the number of cycles involving the cryopreservation of oocytes has significantly increased. The number of cycles where fertilization by ICSI was performed after oocyte thawing is also slowly rising.

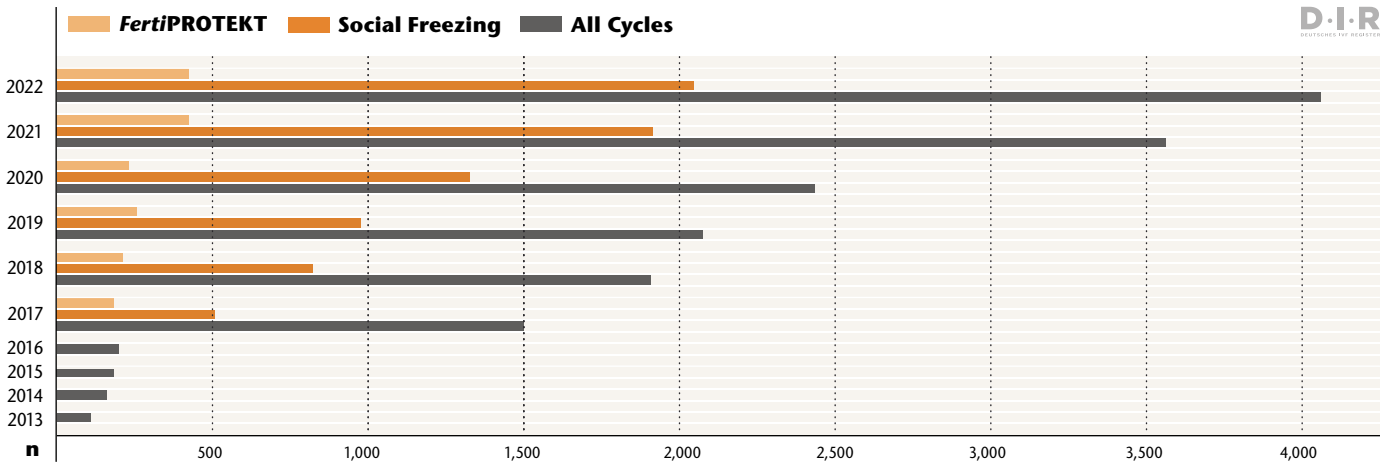
What remains unknown so far:

- How many oocytes are thawed on average?
- What is the age of the women at the time of retrieval and thawing?
- Are there differences between the groups with the FertiPROTEKT and social freezing indications?
- Are there already indications of how many women utilize a thaw cycle with fertilization?
- What is the outcome of cycles with 'fertilization after oocyte thawing'?
- Answers to many more questions…

Description of the data pool:

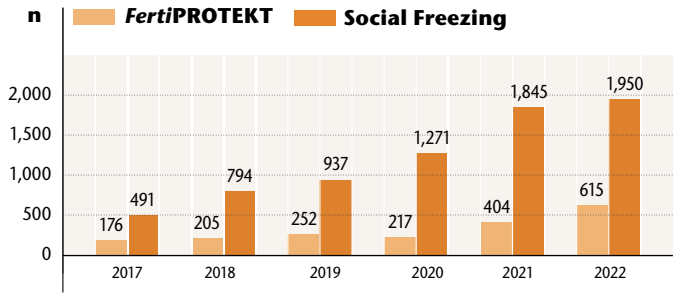
- Evaluation of cycle years 2013 to 2022 - 16,188 plausible cycles with 10,982 patients.
- Evaluation of cycles with treatments of 'only oocytes for freeze all' and 'fertilization after oocyte thawing.'
- Treatment in this context means that at least one oocyte was available for cryopreservation and at least one oocyte was available for fertilization after thawing.
- Focus was placed on the indications '*Ferti*PROTEKT' and 'social freezing.' However, in about 60% of cycles, neither of these indications is documented in the cycle datasets, and in some cycles, both indications are present.
- Important limitation: The indications '*Ferti*PROTEKT' and 'social freezing' were only added to the dataset starting in 2017. There are no cycles with indication labels from 2013 to 2016.
- Important limitation: A clear classification of 'performed treatments' has been available only since 2017. In the years 2013 to 2016, cycles with 'only oocytes for freeze all' could not be extracted because the data fields used to calculate performed treatments did not exist before 2017.
- Although we would have liked to consider the full 10-year period from 2013 to 2022, we had to limit our analysis primarily to the cycles from 2017 to 2022 due to the described limitations.
- Important limitation: Due to the lack of a 'national patient ID,' only patients and cycles treated at the same center can be analyzed.

Number of Cycles Concerning 'Freeze all Oocytes' and 'Fertilization after Oocyte-Thawing' per Year and Indication

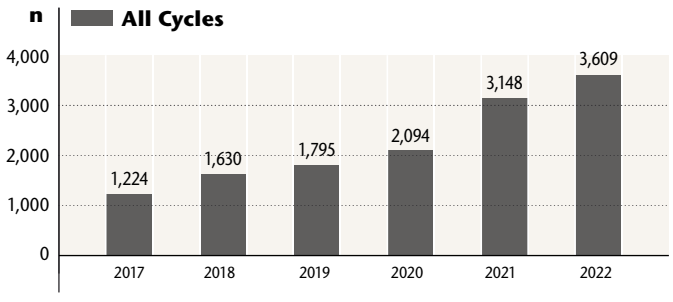


Freeze all Oocytes – Number und Outcome

Number and Development of cycles 'Freeze all Oocytes' by Indication '*Ferti*PROTEKT' and 'Social Freezing'



Number and development of all cycles 'Freeze all Oocytes'



Between 2017 and 2022

*Ferti*PROTEKT: Between 2017 and 2022, 1,869 cycles with 'oocytes for freeze all' were performed on 1,681 patients. This corresponds to an average of 1.1 cycles per patient, with the average age being 29.7 years. An average of 10.8 oocytes per cycle could be cryopreserved.

Social Freezing: Between 2017 and 2022, 7,288 cycles with 'oocytes for freeze all' were performed on 5,095 patients. This corresponds to an average of 1.4 cycles per patient, with the average age being 35.1 years. An average of 8.8 oocytes per cycle could be cryopreserved.

The age difference in oocyte retrieval cycles between patients with the *Ferti*PROTEKT indication and social freezing is significant, with a difference of 5.4 years.

	***Ferti*PROTEKT**	**Social Freezing**	**All Cyles**
Cycles	1,869	7,288	13,500
Patients	1,681	5,095	10,982
Cycles/Patient	1.1	1.4	1.5
Oocytes Cryopreserved	20,274	64,101	114,556
Cryopreserved Eggs/Cycle	10.8	8.8	7.1
Ø Age at Freezing (Years)	29.7	35.1	35.2

Fertilization after Thawing – Number and Outcome

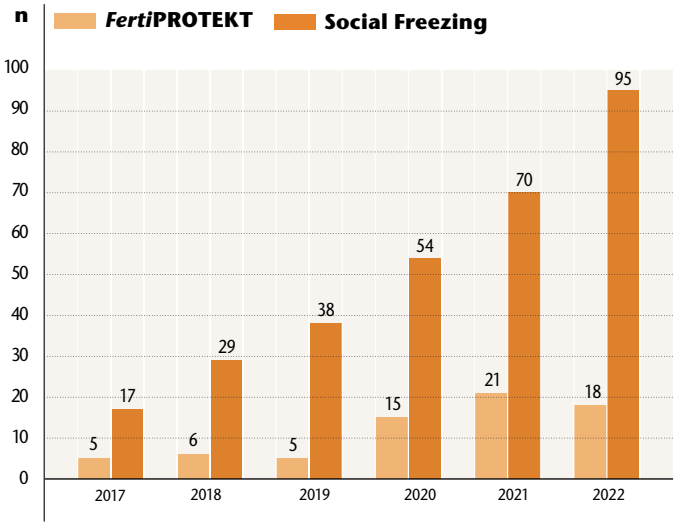
The indication-based analysis of treatment cycles with fertilization after oocyte thawing quickly reaches its limits due to the frequent absence of the corresponding marking in the fields 'Indication Woman' or 'Planned Therapy Indication.' We limited the analysis to the years 2017–2022, as the indications '*Ferti*PROTEKT' and 'Social Freezing' were only added to the dataset starting from that time. However, in 1,664 out of 2,037 cycles, the corresponding marking is still missing.

We were able to identify 62 *Ferti*PROTEKT patients with 70 treatment cycles. The pregnancy rate per embryo transfer was 25.0 %, and the birth rate per embryo transfer was 21.9 %. A notable observation is the difference between the age in the oocyte retrieval cycle (an average of 29.7 years) and the age in the treatment cycle for fertilization after oocyte thawing (an average of 36.6 years) for these *Ferti*PROTEKT patients. The miscarriage rate is low at 12.5 %, which can be attributed to the low age during the retrieval cycle.

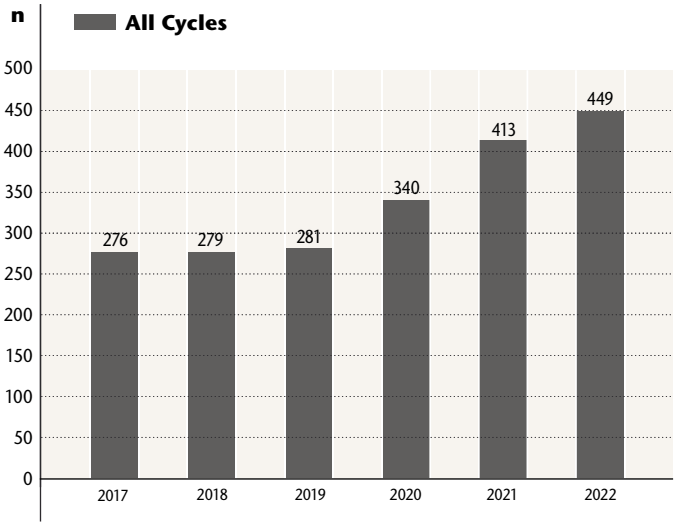
A total of 253 Social Freezing patients underwent 303 treatment cycles with fertilization after oocyte thawing. The pregnancy rate per embryo transfer was 21.3 %, and the birth rate per embryo transfer was 12.6 %, which is due to the high miscarriage rate of 40.7 %. In this group, the difference between the age in the retrieval cycle (an average of 35.1 years) and the age in the treatment cycle for fertilization after oocyte thawing (an average of 40.3 years) is also significant.

When considering all cycles with fertilization after oocyte thawing, the results are very similar to those of the Social Freezing group. However, in this case, the difference between the age in the retrieval cycle (an average of 35.2 years) and the age in the treatment cycle for fertilization after oocyte thawing (an average of 37.5 years) is only a little over two years, and the miscarriage rate is lower at 33.2 %.

Number and Development of cycles 'Fertilization after Oocyte Thawing' by Indication '*Ferti*PROTEKT' and 'Social Freezing'



Number and Development of all Cycles 'Fertilization after Oocyte Thawing'



Between 2017 and 2022

	*Ferti*PROTEKT	Social Freezing	All Cycles
Number of Patients	62	253	1.790
Average Age at Fertilization (Years)	36.6	40.3	37.5
Average Injected Eggs after Thawing	5.5	6.7	5.9
Number of Injected Eggs	385	2,205	12,062
Number of Embryos Transferred	91	370	2,514
Number of Embryos/Transfer	1.4	1.5	1.6
Number of Embryo Transfers	64	254	1,608
Embryo Transfer Rate/Egg Treatment (%)	91.4	83.8	78.9
Number of Pregnancies	16	54	368
Number of Abortions/Ectopic Pregnancy	2	22	122
Number of Births	14	32	246
Pregnancy Rate/egg Treatment (%)	22.9	17.8	18.1
Pregnancy Rate/Embryo Transfer (%)	25.0	21.3	22.9
Abortion Rate/Pregnancy	12.5	40.7	33.2
Birth Rate/Egg Treatment	20.0	10.6	12.1
Birth Rate/Embryo Transfer	21.9	12.6	15.3
Utilization per Patient of a Treatment Cycle with 'Fertilization after Egg Thawing' (%)	3.7	5.0	16.3

Outcome Quality of Treatment Cycles with 'Fertilization after Oocyte Thawing' Depending on the Number of Injected Oocytes

Questions we asked ourselves about this topic were:

- What is the thawing strategy of the centers? Is thawing performed on all frozen oocytes, or is thawing done fractionally before treating with ICSI?
- Are the possibilities of re-cryopreservation utilized?
- Is there an optimal number of oocytes injected per cycle?

Description of the Data Pool

- 2,037 plausible treatment cycles with the performed procedure 'Fertilization after oocyte thawing' in 1,790 patients from the years 2017–2022.
- 'Performed procedure' here means that at least one oocyte was available for fertilization after thawing.
- No distinction between the indications *Ferti*PROTEKT or Social Freezing.
- Patient-related evaluation of women for whom both oocyte retrieval cycles and cycles with fertilization after thawing were available in the pool.

Thawing Strategy

We identified 1,089 data sets that contained information from both 'oocytes for freeze-all' cycles and cycles with 'fertilization after oocyte thawing.' From these data sets, the number of cryopreserved oocytes available in the respective center for each patient was calculated. Please note that Information on existing oocyte storage is not part of the registry.

Results:

In 871 out of 1,089 (= 80%) cycles with 'fertilization after oocyte thawing,' all available oocytes were thawed. In another 155 out of 1,089 cycles (= 14.2%), residual stores of 3–11 oocytes were preserved. It is possible that the strategy of thawing all available oocytes, treating with ICSI, and potentially utilizing re-cryopreservation is the most effective option.

Below is a table summarizing the results of the analysis:

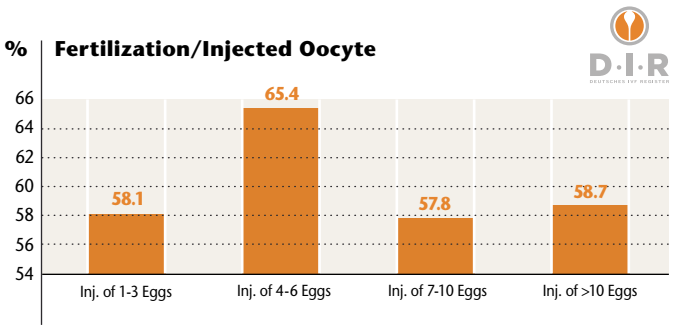
	Injection of 1-3 Eggs	Injection of 4-6 Eggs	Injection of 7-10 Eggs	Injection of >10 Eggs
Number of Cycles	560	791	467	219
Number of Patients	512	730	447	213
Average Age (Years) in the Fertilization Cycle	38.3	37.4	37.3	36.3
Number of Injected Eggs	1,226	3,391	3,817	3,088
Number 2PN	712	2,219	2,206	1,813
Fertilization Rate (%)	58.1	65.4	57.8	58.7
Average Number of Eggs Injected	2.2	5.0	8.2	14.1
Number of Embryos for Transfer	509	1.079	651	275
Number of Embryo Transfers	369	662	399	178
Number of Embryos/Transfer	1.4	1.6	1.6	1.5
Embryo Transfer Rate/Egg Treatment (%)	65.9	83.7	85.4	81.3
Cryopreservation PN (Cycles)	15	43	46	62
Cryopreservation EMB (Cycles)	8	77	114	71
Additional Cryopreservation/Transfer (Cycles) (%)	6.2	17.7*	37.8**	65.7***
Number of Pregnancies	49	154	102	63
Number of Abortions/Ectopic Pregnancy	16	47	33	14
Abortion Rate/Pregnancy (%)	32.7	30.5	32.4	22.2
Number of Births	33	107	69	49
Singletons (%)	93.9	82.2	87.0	79.6
Gemini (%)	6.0	17.8	11.6	20.4
Triplets (%)	0.0	0.0	1.4	0.0
Pregnancy Rate/Egg Treatment (%)	8.8	19.5	21.8	28.8
Pregnancy Rate/Embryo Transfer (%)	13.3	23.3	25.6	35.4
Birth Rate/Egg Treatment (%)	5.9	13.5	14.8	22.4
Birth Rate/Embryo Transfer (%)	8.9	16.2	17.3	27.5

**) Cryopreservation of 2PN and embryos was carried out in three cycles*
***) Cryopreservation of 2PN and embryos was carried out in nine cycles*
****) Cryopreservation of 2PN and embryos took place in 16 cycles*

As expected, the results of treatment cycles in which only 1–3 oocytes were treated by ICSI are significantly worse than when more oocytes were available. In these cases, the average age of the patients in the fertilization cycle is also the highest. Nevertheless, a birth rate per embryo transfer of 8.9 % was achieved, resulting in 39 children born who otherwise would not have existed without this therapy. Additionally, in 6.2 % of the cases, re-cryopreservation of surplus fertilized oocytes at the 2PN stage or embryos was performed, giving the patients a second chance for an embryo transfer and therefore to achieve a pregnancy despite this small amount of injected oocytes.

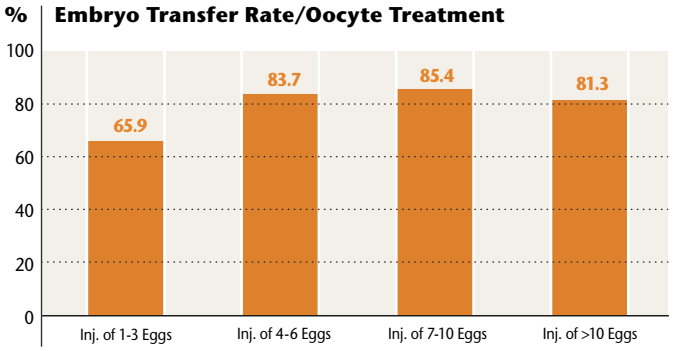
Fertilization / Injected Oocyte:

The fertilization rate fluctuates very little across all evaluated subgroups, averaging 60.3 %. For comparison: In fresh cycles, the fertilization rate in 2023 after performing ICSI was 65.6 % (Yearbook 2023, page 37). Only the fertilization rate after injecting 4–6 oocytes is identical to the fertilization rate in fresh cycles, at 65.4 %.



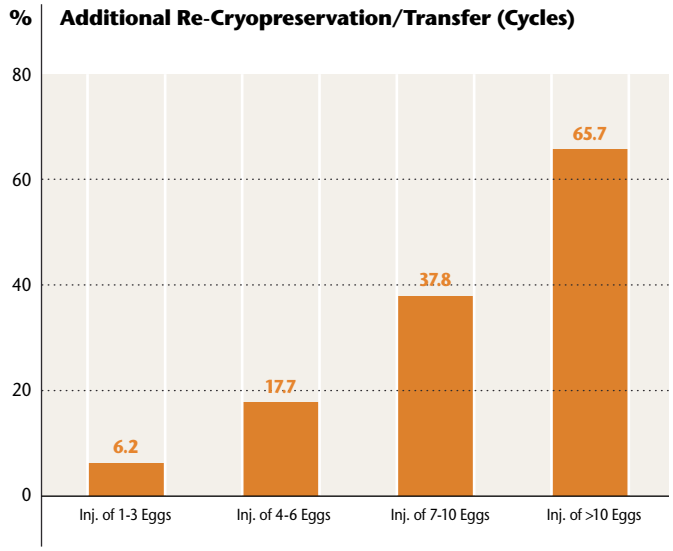
Embryo Transfer / Oocyte Treatment:

The rate fluctuates significantly across all evaluated subgroups, with a low rate of 65.9% in the group with the injection of 1–3 oocytes. Across all cycles, the average rate is 78.9 %, and in the subgroups with the injection of >= 4 oocytes, it reaches 83.9 %, approaching the rate in fresh cycles. In 2022, the rate in fresh cycles was 86 % (Yearbook 2023, page 23), if the 'freeze all' cycles are counted as potential transfers.



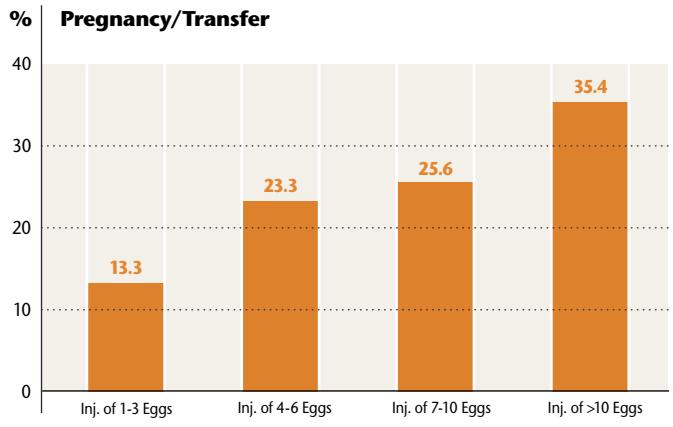
Re-Cryopreservation:

An impressive number of cycles involved additional re-cryopreservation of oocytes at the 2PN stage and/or embryos after a transfer. In fresh cycles, we find comparable figures in the center profiles that were sent to the centers. In the center profile from June 28, 2024, the nationwide share with transfer and additional cryopreservation for 2022 is reported as 38.4 % and for 2023 as 42.4 %. The table above shows re-cryopreservation rates depending on the number of injected oocytes. After injecting 1–3 oocytes, 6.2 % involved additional cryopreservation, whereas in the group with >10 oocytes injected, additional cryopreservation occurred in 65.7 %. Across all subgroups, re-cryopreservation occurred in 25.4 % of cycles after fertilization following oocyte thawing.



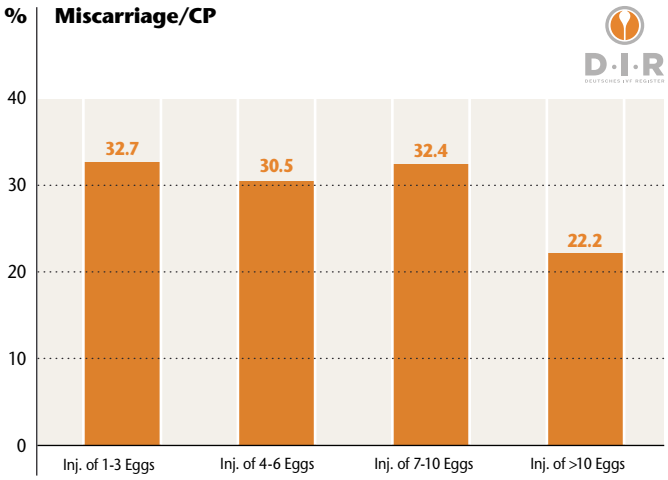
Pregnancy / Transfer:

In the subgroups with the injection of 4–6 oocytes and 7–10 oocytes, pregnancy rates of 23.3 % and 25.6 %, respectively, were seen per embryo transfer, after transferring an average of 1.6 embryos. Only in the subgroup with >10 oocytes injected was a pregnancy rate of 35.4 % observed after transferring an average of 1.5 embryos. This very high pregnancy rate came at the cost of a high rate of twin births (20.4 %). Considering that in 71 of 219 cycles in this group, additional embryos were re-cryopreserved, a decision towards single embryo transfer would be favorable in the future.



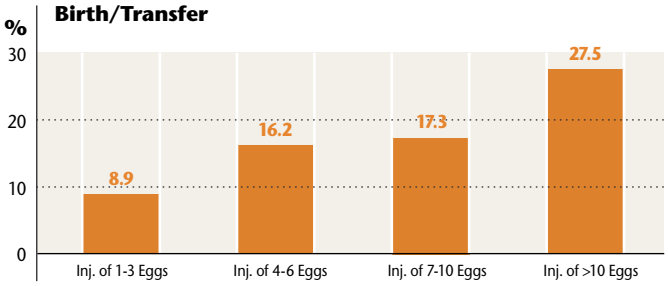
Miscarriage / Clinical Pregnancies:

In this analysis, it was not possible to indicate the patient's age at the oocyte retrieval cycle. The age references pertain to the age during the fertilization cycle. In subgroups with the injection of up to 10 oocytes, the average miscarriage rate was 31.5 %, and only in the subgroup with >10 oocytes injected was the miscarriage rate 22.2 %. Without access to the patients' ages during the retrieval cycle, a reliable interpretation of these numbers is not possible. It could be speculated that women with a larger oocyte reserve and hence higher numbers of cryopreserved oocytes were younger during the retrieval cycle, as they were also younger during the fertilization cycle, with an average age of 36.3 years, the lowest average age.



Birth / Transfer:

Across all subgroups, birth rates per oocyte treatment were 12.7 % (compared to 18.9 % in fresh ICSI cycles in 2022), and per embryo transfer, the birth rate was 16.0% (compared to 22.2 % in fresh ICSI cycles in 2022). In the groups with >=4 oocytes injected, birth rates were 15.2 % per oocyte treatment and 18.2 % per embryo transfer.



Summary:

This analysis supports the observation in recent years that the number of cycles with 'only oocytes for freeze-all' and the number of cycles with 'fertilization after oocyte thawing' have significantly increased.

However, this analysis should be seen as an approximation of the true values, as:

- Identifying the indications *Ferti*PROTEKT and social freezing was not possible in a large portion of the cycles.
- A more solid data basis has only been available since 2017.
- The observation period of six years is too short to assess how many fertilization cycles after cryopreservation will be used, given the latency observed in different groups, ranging from 2–6 years.

This analysis also shows that fertility preservation measures:

- Are meaningful and promising,
- That the centers are using this new technology comprehensively and responsibly,
- And that re-cryopreservation has established itself as part of the therapeutic regime.

This analysis provides a basis for the centers to advise on:

- The necessity of cryopreserving a large number of oocytes,
- Reevaluating the thawing strategy (thaw everything and possibly use re-cryopreservation),
- Providing an assessment of the chances of success for a planned cryopreservation.

Outlook:

The ability to identify the indications for oocyte retrieval cycles and cycles with fertilization after oocyte thawing was significantly improved with the last update of the recording software. Mandatory fields were introduced, which query the reason for this procedure for every 'freeze all' measure. In the future, the indicated reason will also be visible in thaw cycles.

Dr. med. Ute Czeromin (Lead Author)
Prof. Dr. med. Jan-Steffen Krüssel
Dr. med. Andreas Tandler-Schneider

D·I·R Annual 2023 – Tables

Number of Treatments in 2023

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

Members of the German IVF-Registry 2023	n=141
Registry Participants 2023	n=141
Data Received by Deadline May 15th 2024	n=141
Documented Treatment Cycles	n=131,000
Number of Women Treated*	n= 68,656
Mean Number of Treatment Cycles per Woman	**1.9**

Type of plausible treatment 2019 – 2023

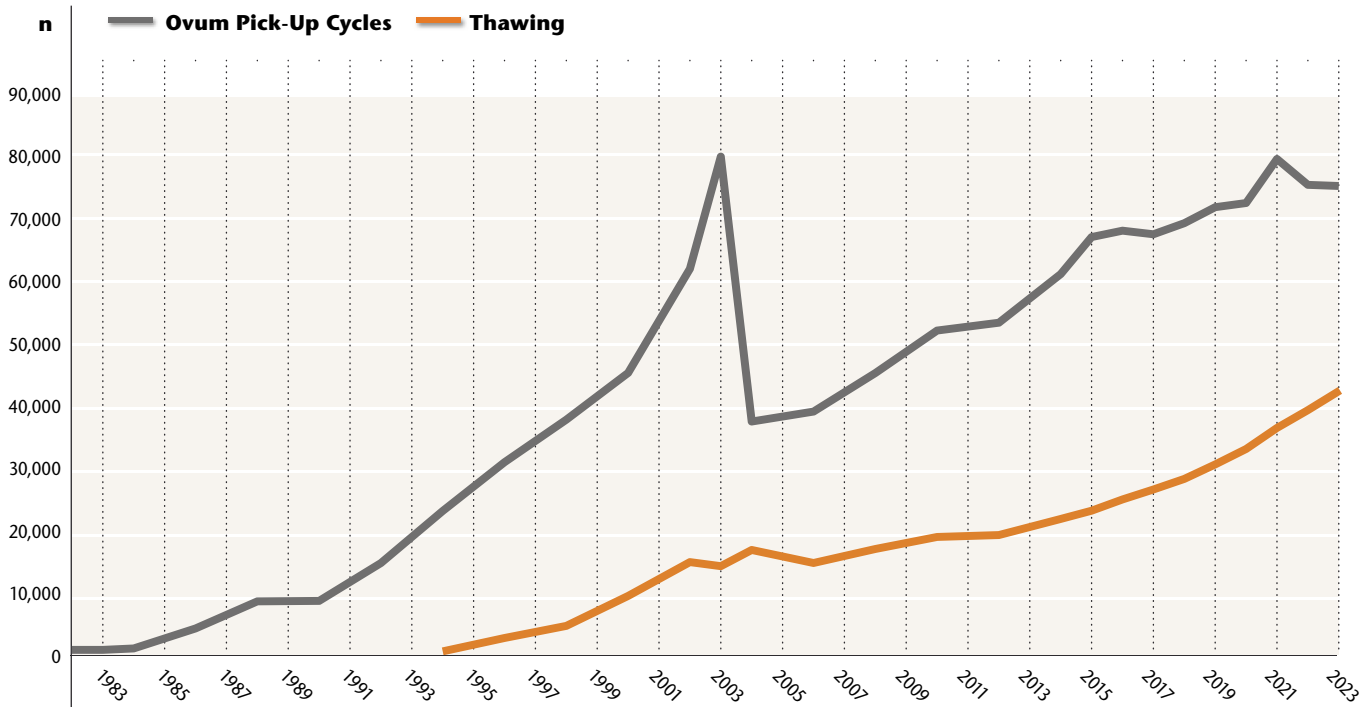
IVF, ICSI, IVF/ICSI, Cryo Transfer – Prospective and Retrospective Data

	2019		2020		2021		2022		2023	
	n	%	n	%	n	%	n	%	n	%
IVF	18,719	17.0	19,521	17.1	21,582	17.2	20,342	16.2	20,099	15.7
ICSI	47,246	42.9	46,572	40.9	50,208	40.0	47,158	37.7	45,535	35.6
IVF/ICSI	1,362	1.2	1,502	1.3	1,360	1.1	1,253	1.0	1,484	1.2
Freeze all - MII	1,858	1.7	2,213	1.9	3,260	2.6	3,768	3.0	5,218	4.1
Freeze All - PNs and Embryos	5,173	4.7	5,660	5.0	6,534	5.2	6,602	5.3	6,834	5.3
Cryo	30,700	27.9	33,195	29.1	36,599	29.1	39,474	31.5	42,658	33.3
Mixed Fresh and Cryo Cycles	268	0.2	314	0.3	402	0.3	355	0.3	416	0.3
None (= Break-off before oocyte treatment or thawing)	4,779	4.3	4,911	4.3	5,629	4.5	6,235	5.0	5,729	4.5
Total Plausible Cycles	**110,105**		**113,888**		**125,574**		**125,187**		**127,973**	

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

Number of Oocyte Retrievals (Freshcycles) 1982 – 2023
Number of Thawing Cycles 1994 – 2023
Registry Participants 1982 – 2023

IVF, ICSI* – Prospective and Retrospective Data



	1982	1986	1990	[...]	2002	2003	2004	[...]	2019	2020	2021	2022	2023
.	742	4,201	8,653		62,306	80,434	37,633		72,264	72,937	80,051	75,873	75,690
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 2018 see www.deutsches-ivf-register.de*	18,719	19,521	21,582	20,342	20,099
ICSI*					37,692	51,389	25,339		48,608	48,074	51,568	48,411	47,019
Thawing					14,923	14,265	16,883		30,700	33,195	36,599	39,474	42,658
Registry Participants	**5**	**28**	**53**		**112**	**116**	**120**		**132**	**138**	**138**	**138**	**141**

Data for 1982 to 2010 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.*

Quality of Documentation 2022/2023

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

Any evaluation is only as good as the raw data.
The yearbook team thanks the centers for their meticulous work!

Plausible cycles 2023

127,973 plausible cycles out of **131,000** documented cycles. **97.7%** of all documented cycles are plausible.

Prospectively recorded cycles 2023

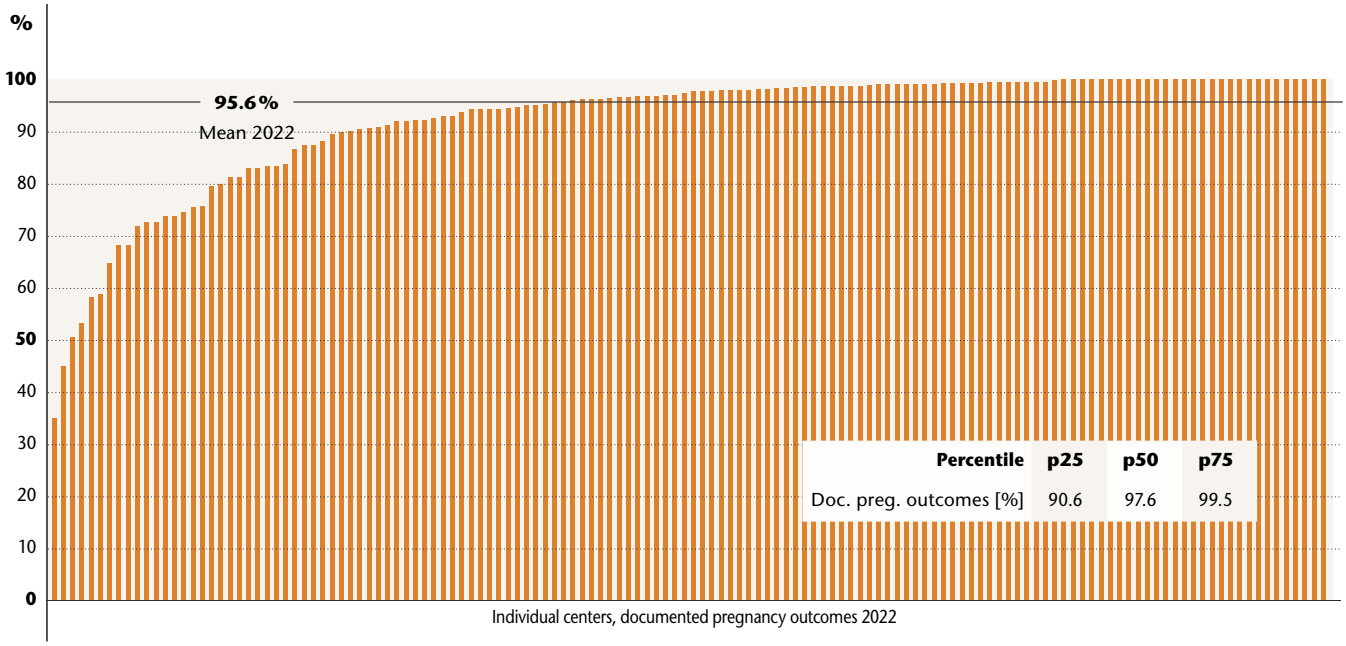
116,731 prospectively recorded cycles out of **127,973** plausible cycles. **91.2%** of all plausible cycles were recorded prospectively.
The German IVF Register is the only register worldwide that shows the number of prospectively recorded cycles.
This is a quality feature in itself!

Recorded cycle outcomes 2023

The result of the cycle was recorded in **90,309** of **90,823** embryo transfers. **99.4%** of cycle outcomes were recorded.

Recorded pregnancy outcomes 2022

The pregnancy outcome was recorded for **26,609** of **27,829** clinical pregnancies. **95.6%** of pregnancy outcomes were recorded.
The centers thus once again achieved a rate above the D·I·R target quota of **95%** and the D·I·R would like to particularly thank you for this extensive work!



We know: The work, especially on the documentation qualities mentioned here, is laborious, time-consuming and ties up resources.

With a rate of **95.6%** of documented pregnancy outcomes, the D·I·R's **95%** target for this documentation quality was exceeded for the second time!

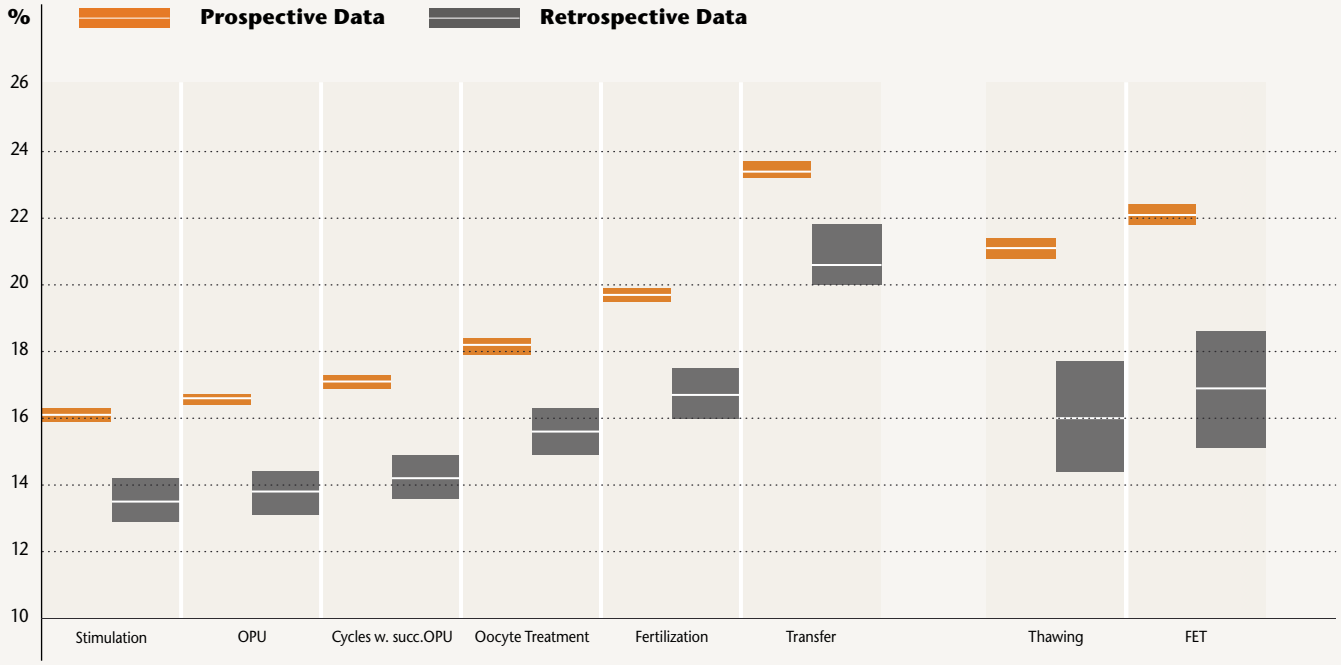
49 centers had a quota of over **99%**, **29** centers even had a quota of 100%!!

The aim of the Executive Board and the Board of Trustees is to continue to motivate the centers to draw attention to the parameter of prospectivity.

We are also aiming for a documented pregnancy outcome quota of more than *95%* again.

Birth Rate per Treatment Level in Fresh and Cryo Treatment Cycles 2021 and 2022

Prospective and Retrospective Data

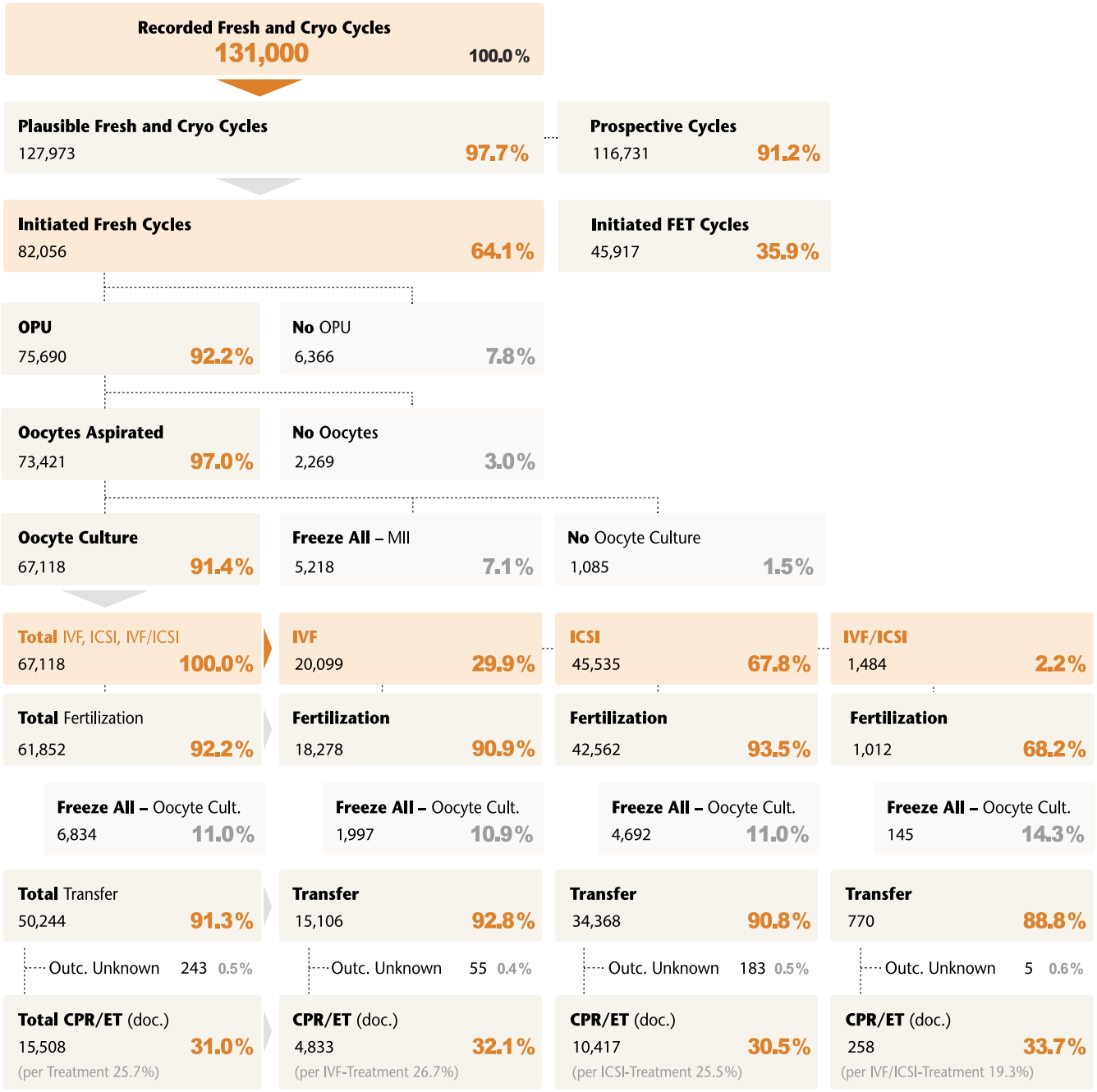


	Stimulation	OPU	Cycles with Successful OPU	Oocyte Treatment	Fertilization	Transfer	Thawing	FET
Prospective Numbers	148,558	144,495	140,113	131,784	121,572	102,283	74,200	70,995
Birth	23,924	23,924	23,924	23,924	23,924	23,924	15,680	15,680
Upper Confid. Limit*	16.3	16.7	17.3	18.4	19.9	23.7	21.4	22.4
Birth/Treatm. %	16.1	16.6	17.1	18.2	19.7	23.4	21.1	22.1
Lower Confid. Limit*	15.9	16.4	16.9	17.9	19.5	23.2	20.8	21.8
Retrospective Numbers	11,628	11,429	11,071	10,119	9,415	7,640	1,873	1,778
Birth	1,575	1,575	1,575	1,575	1,575	1,575	300	300
Upper Confid. Limit*	14.2	14.4	14.9	16.3	17.5	21.8	17.7	18.6
Birth/Treatm. %	13.5	13.8	14.2	15.6	16.7	20.6	16.0	16.9
Lower Confid. Limit*	12.9	13.1	13.6	14.9	16.0	20.0	14.4	15.1

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

D·I·R Statistics in Brief – Fresh Cycles 2023 (CoD May 15th 2024)

German IVF Registry – Prospective and Retrospective Data



For FertiPROTEKT (medical freezing), 967 cycles have been documented. Among them 840 cycles freeze all oocytes and 22 cycles freeze all oocytes cultured.
For Social Freezing, 3,700 cycles have been documented, resulting in 3,393 aspirations with an average of 10,9 oocyte retrieved. Freeze all oocytes: 3,114 cycles.
For PID, 554 cycles have been documented.

For for this and the next page:
Clinical pregnancy rates per transfer are adjusted by unknown outcomes.
Transfer rate, clinical pregnancy rates per treatment and birth rates per treatment are adjusted by freeze all oocytes cultured.

D·I·R Statistics in Brief – Fresh Cycles 2022 (CoD May 15th 2024)

German IVF Registry – Prospective and Retrospective Data

Recorded Fresh and Cryo Cycles 127,292 100.0%

Plausible Fresh and Cryo Cycles 125,187 98.3%

Prospective Cycles 113,581 90.7%

Initiated Fresh Cycles 82,542 65.9%

Initiated FET Cycles 42,645 34.1%

OPU 75,873 91.9%

No OPU 6,669 8.1%

Oocytes Aspirated 73.598 97.0%

No Oocytes 2,275 3.0%

Oocyte Culture 68,753 93.4%

Freeze All – MII 3,768 5.1%

No Oocyte Culture 1,077 1.5%

For FertiPROTEKT (medical freezing), 791 cycles have been documented. Among them 615 cycles freeze all oocytes and 37 cycles freeze all oocytes cultured.

For Social Freezing, 2,439 cycles have been documented, resulting in 2,209 aspirations with an average of 11.0 oocyte retrieved. Freeze all oocytes: 1,950 cycles.

For PID, 601 cycles have been documented.

	Total Fresh Cycles	**IVF**	**ICSI**	**IVF/ICSI**
	68,753 100.0%	20,342 29.6%	47,158 68.6%	1,253 1.8%
Total Fertilization	63,369 92.2%	**Fertilization** 18,351 90.2%	**Fertilization** 44,110 93.5%	**Fertilization** 908 72.5%
Freeze All – Oocyte Cult.	6,602 10.4%	**Freeze All** – Oocyte Cult. 1,842 10.0%	**Freeze All** – Oocyte Cult. 4,619 10.5%	**Freeze All** – Oocyte Cult. 141 15.5%
Total Transfer	52,536 92.5%	**Transfer** 15,512 94.0%	**Transfer** 36,332 92.0%	**Transfer** 692 90.2%
Outc. Unknown	184 0.4%	Outc. Unknown 36 0.2%	Outc. Unknown 143 0.4%	Outc. Unknown 5 0.7%
Total CPR/ET (doc.)	16,240 31.0% (per Treatment 26.1%)	**CPR/ET** (doc.) 4,951 32.0% (per IVF-Treatment 26.8%)	**CPR/ET** (doc.) 11,026 30.5% (per ICSI-Treatment 25.9%)	**CPR/ET** (doc.) 263 38.3% (per IVF/ICSI-Treatment 23.7%)
Misc.	3,594 22.1%	**Misc.** 1,126 22.7%	**Misc.** 2,422 22.0%	**Misc.** 46 17.5%
EP	203 1.3%	**EP** 82 1.7%	**EP** 117 1.1%	**EP** 4 1.5%
Not yet Recorded	668 4.1%	**Not yet Recorded** 202 4.1%	**Not yet Recorded** 455 4.1%	**Not yet Recorded** 11 4.2%
Birth (doc.)	11,775 72.5% (per Transfer 22.5%, per Treatm. 18.9%)	**Birth** (doc.) 3,541 71.5% (per Transfer 22.9%, per Treatm. 19.1%)	**Birth** (doc.) 8,032 72.8% (per Transfer 22.2%, per Treatm. 18.9%)	**Birth** (doc.) 202 76.8% (perTransfer 29.4%, per Treatm. 18.2%)

Births	n	%
Singletons	10,360	88.0
Twins	1,383	11.7
Triplets	32	0.3
Quadruplets	0	0.0

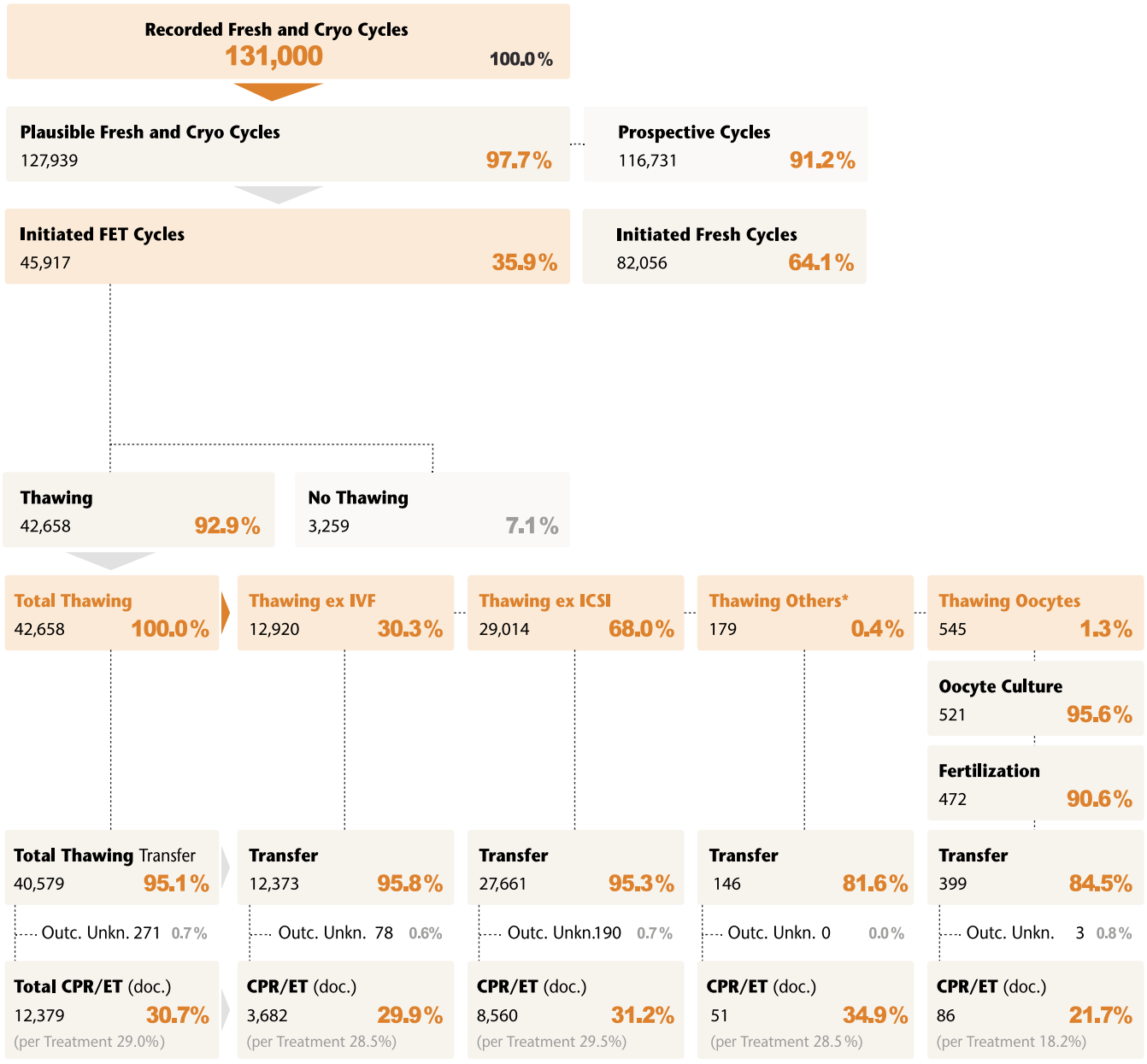
Births	n	%
Singletons	3,128	88.3
Twins	403	11.4
Triplets	10	0.3
Quadruplets	0	0.0

Births	n	%
Singletons	7,056	87.8
Twins	955	11.9
Triplets	21	0.3
Quadruplets	0	0.0

Births	n	%
Singletons	176	87.1
Twins	25	12.4
Triplets	1	0.5
Quadruplets	0	0.0

D·I·R Statistics in Brief – Cryo Cycles 2023 (CoD May 15th 2024)

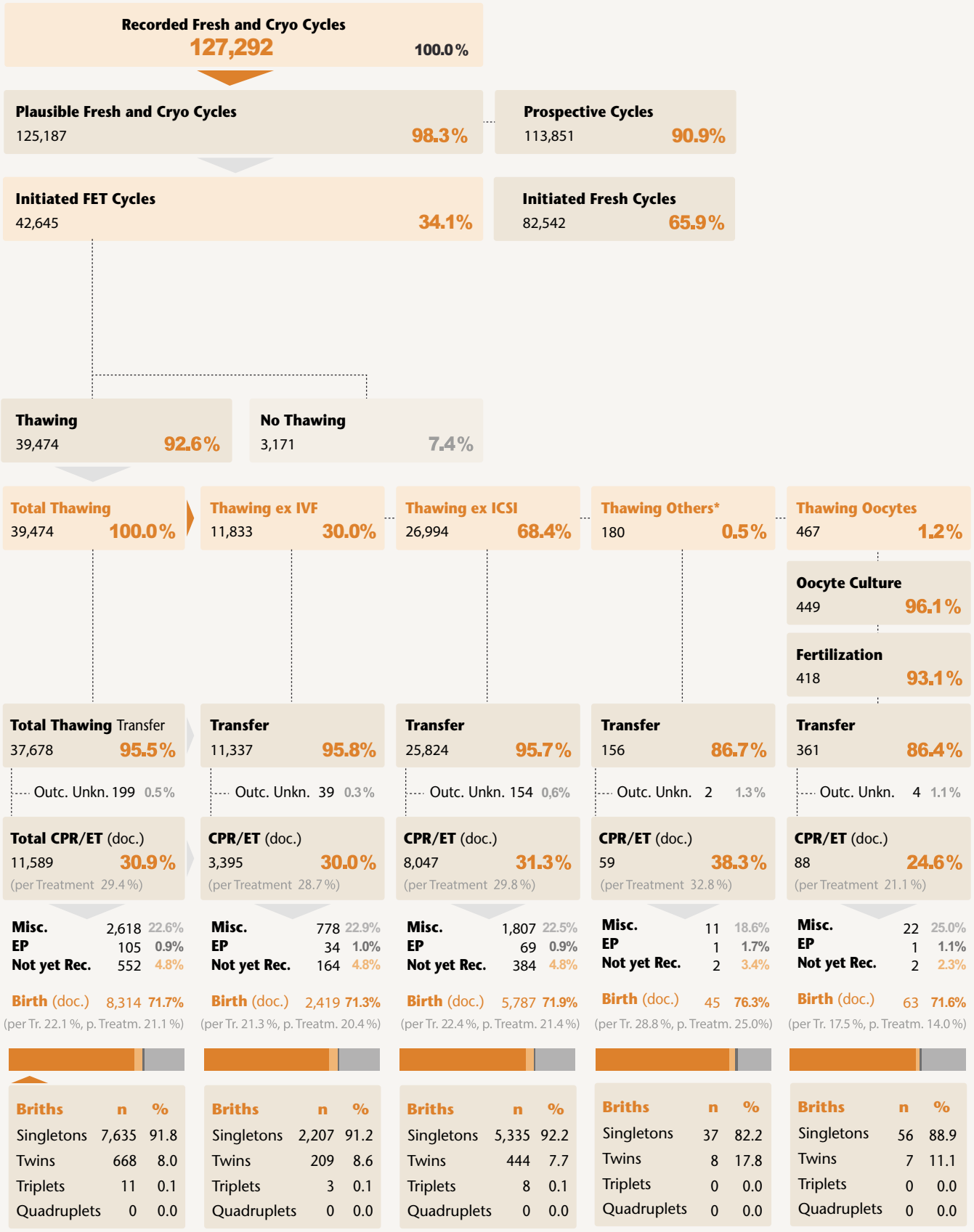
German IVF Registry – Prospective and Retrospective Data



**) 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 2022 (CoD May 15th 2024)

German IVF Registry – Prospective and Retrospective Data



Births	n	%
Singletons	7,635	91.8
Twins	668	8.0
Triplets	11	0.1
Quadruplets	0	0.0

Births	n	%
Singletons	2,207	91.2
Twins	209	8.6
Triplets	3	0.1
Quadruplets	0	0.0

Births	n	%
Singletons	5,335	92.2
Twins	444	7.7
Triplets	8	0.1
Quadruplets	0	0.0

Births	n	%
Singletons	37	82.2
Twins	8	17.8
Triplets	0	0.0
Quadruplets	0	0.0

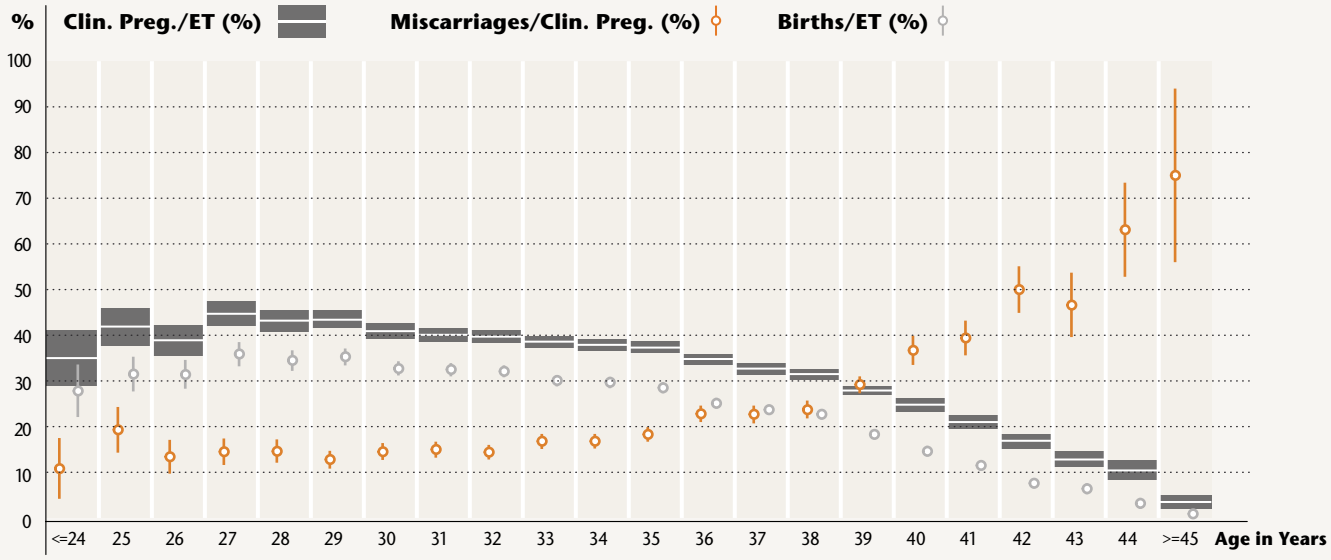
Births	n	%
Singletons	56	88.9
Twins	7	11.1
Triplets	0	0.0
Quadruplets	0	0.0

**) 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 – 2022

Prospective Data

IVF 2018 – 2022



	<=24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	>=45	
n	239	568	844	1,267	1,728	2,563	3,387	4,007	4,658	5,172	5,447	5,707	5,723	5,555	5,894	8,310	3,442	3,002	2,164	1,507	814	570	ET
%	35.0	41.9	38.9	44.7	43.2	43.4	40.9	40.1	39.7	38.6	37.9	37.3	34.8	32.7	31.5	27.9	24.8	21.0	16.9	12.8	10.4	3.5	CP/ET
n	66	179	265	454	595	902	1,107	1,299	1,493	1,553	1,613	1,623	1,435	1,312	1,335	1,520	502	343	164	96	26	5	Birth

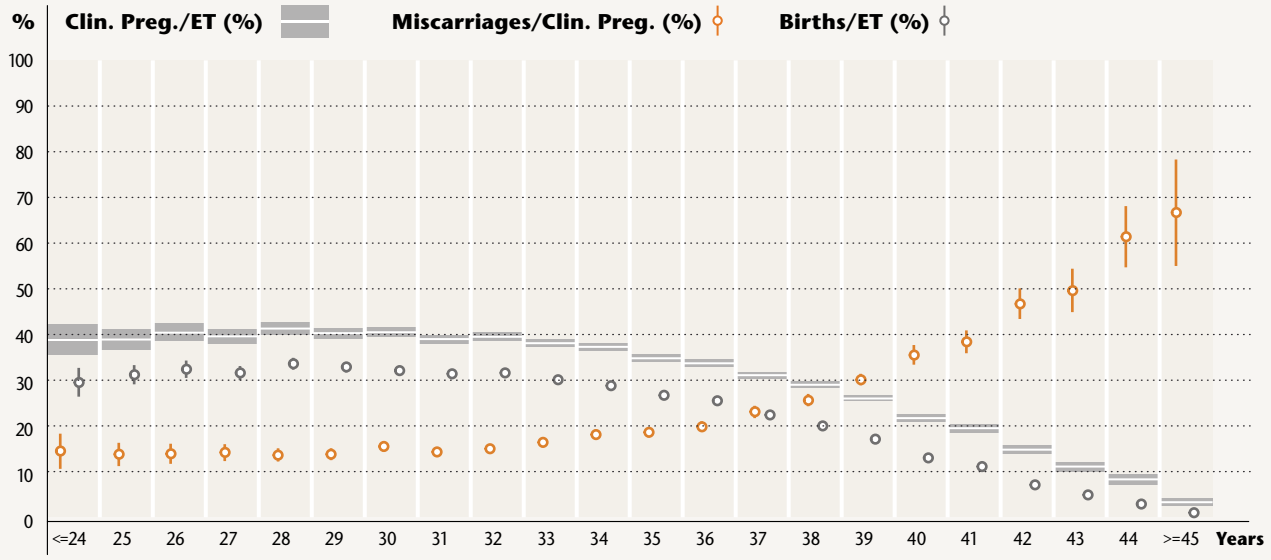
Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	9,391	28,508	38,598	4,353	3,781	2,782	1,955	1,103	798	**91,269**
Oocytes[1]	11.5	10.3	8.3	6.7	6.3	5.7	5.3	4.9	4.1	**8.9**
Insemination[1]	11.3	10.2	8.2	6.6	6.2	5.7	5.3	4.8	4.1	**8.8**
Transfer	7,209	22,671	31,189	3,442	3,002	2,164	1,507	814	570	**72,568**
ET/OPU %	76.8	79.5	80.8	79.1	79.4	77.8	77.1	73.8	71.4	**79.3**
Trans. Embr.[1]	1.59	1.56	1.59	1.60	1.61	1.63	1.62	1.66	1.55	**1.59**
CP	3,071	8,889	10,091	850	629	364	193	84	20	**24,191**
CP/OPU %	32.7	31.2	26.1	19.5	16.6	13.1	9.9	7.6	2.5	**26.5**
CP/ET Upper Confidence Limit*%	43.8	39.9	32.9	26.2	22.5	18.4	14.5	12.5	5.0	**33.8**
CP/ET %	**42.7**	**39.3**	**32.4**	**24.8**	**21.0**	**16.9**	**12.8**	**10.4**	**3.5**	**33.4**
CP/ET Lower Confidence Limit*%	41.5	38.6	31.9	23.3	19.6	15.3	11.2	8.3	2.0	**33.1**
CP/ET %: 2 Embr. Transf. + min. 2 2PN Surplus	48.7	46.4	40.0	34.7	28.4	24.6	16.4	15.8	8.1	**41.7**
CP/ET %: 1 Embr. Transf. + min. 3 2PN Surplus	45.2	40.0	35.0	33.6	26.0	18.1	10.9	19.6	0.0	**37.2**
Misc./CP Upper Confidence Limit*%	15.3	16.4	24.3	39.9	43.2	55.1	53.7	73.4	94.0	**21.5**
Misc./CP %	**14.1**	**15.6**	**23.5**	**36.7**	**39.4**	**50.0**	**46.6**	**63.1**	**75.0**	**21.0**
Misc./CP Lower Confidence Limit*%	12.8	14.8	22.6	33.5	35.6	44.9	39.6	52.8	56.0	**20.5**
Births/ET Upper Confidence Limit*%	35.3	31.8	23.7	15.8	12.6	8.7	7.6	4.4	1.7	**25.0**
Births/ET %	34.2	31.2	23.2	14.6	11.5	7.6	6.4	3.2	0.9	**24.7**
Births/ET Lower Confidence Limit*%	33.1	30.6	22.7	13.5	10.3	6.5	5.2	2.0	0.1	**24.4**

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 – 2022

Prospective Data

ICSI 2018 – 2022



n	820	1,850	2,395	3,525	5,015	6,751	8,805	10,491	11,971	12,953	13,504	14,312	14,021	14,195	14,593	19,887	8,754	7,402	5,689	3,842	2,442	1,917	ET
%	38.8	38.9	40.4	39.6	41.3	40.3	40.5	39.0	39.5	38.1	37.3	34.8	33.7	31.1	29.0	26.0	21.7	19.5	14.8	11.1	8.3	3.3	CP/ET
n	242	577	774	1,109	1,682	2,215	2,825	3,284	3,776	3,888	3,876	3,812	3,569	3,179	2,915	3,383	1,134	820	404	186	71	19	Birth

Age in Years	<= 29	30 – 34	35 – 39	40	41	42	43	44	>=45	Total
OPU	25,187	70,268	93,748	10,985	9,356	7,303	5,038	3,271	2,656	**227,812**
Oocytes[1]	12.3	11.1	8.8	7.0	6.5	5.9	5.4	4.7	3.9	**9.4**
Insemination[1]	9.6	8.7	6.9	5.6	5.3	4.7	4.3	3.8	3.2	**7.4**
Transfer	20,356	57,724	77,008	8,754	7,402	5,689	3,842	2,442	1,917	**185,134**
ET/OPU %	80.8	82.1	82.1	79.7	79.1	77.9	76.3	74.7	72.2	**81.3**
Trans. Embr.[1]	1.63	1.62	1.62	1.63	1.62	1.62	1.64	1.62	1.60	**1.62**
CP	8,182	22,313	23,461	1,888	1,438	839	423	202	63	**58,809**
CP/OPU %	32.5	31.8	25.0	17.2	15.4	11.5	8.4	6.2	2.4	**25.8**
CP/ET Upper Confidence Limit* %	40.9	39.1	30.9	22.5	20.4	15.7	12.1	9.4	4.1	**32.1**
CP/ET %	**40.3**	**38.7**	**30.5**	**21.7**	**19.5**	**14.8**	**11.1**	**8.3**	**3.3**	**31.8**
CP/ET Lower Confidence Limit* %	39.6	38.3	30.2	20.8	18.6	13.9	10.1	7.2	2.5	**31.6**
CP/ET %: 2 Embr. Transf. + min. 2 2PN Surplus	45.6	44.9	38.2	27.7	28.0	22.4	19.0	13.5	9.5	**40.1**
CP/ET %: 1 Embr. Transf. + min. 3 2PN Surplus	39.9	39.3	33.1	25.8	24.6	16.7	13.9	15.6	15.9	**35.6**
Misc./CP Upper Confidence Limit* %	14.6	16.4	24.0	37.7	40.9	50.1	54.4	68.1	78.3	**21.1**
Misc./CP %	**13.8**	**16.0**	**23.5**	**35.5**	**38.4**	**46.7**	**49.6**	**61.4**	**66.7**	**20.7**
Misc./CP Lower Confidence Limit* %	13.1	15.5	23.0	33.4	35.9	43.3	44.9	54.7	55.0	**20.4**
Births/ET Upper Confidence Limit* %	33.1	31.0	22.2	13.7	11.8	7.8	5.5	3.6	1.4	**23.9**
Births/ET %	32.5	30.6	21.9	13.0	11.1	7.1	4.9	2.9	1.0	**23.7**
Births/ET Lower Confidence Limit* %	31.8	30.3	21.7	12.3	10.4	6.4	4.2	2.3	0.6	**23.5**

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 2022

Prospective Data

IVF 2022– Ø Avg. Patient Age: 35.6

	n	%	Fertilization %	Embryo exist. %	Transfer %	Clin. Preg. %
Performed IVF Treatm.	19,074	100.0				
Successful Fertilization*	17,212	90.2	100.0			
Freeze All Treated Oocytes	1,712	9.0	9.9			
Minimum 1 Embryo**	15,414	88.8	99.4	100.0		
ET Performed**	14,566	83.9	94.0	94.5	100.0	
Clin. Pregnancy	4,659	**24.4**	27.1	30.2	**32.0**	100.0
Birth	3,350	**17.6**	**19.5**	**21.7**	**23.0**	**71.9**
Miscarriage	1,059					22.7
Ectopic Pregnancy	74					1.6
Not Yet Recorded	179					3.8

ICSI 2022 – Ø Avg. Patient Age: 35.6

	n	%	Fertilization %	Embryo exist.%	Transfer %	Clin. Preg. %
Performed ICSI Treatm.	44,659	100.0				
Successful Fertilization*	41,505	92.9	100.0			
Freeze All Treated Oocytes	4,231	9.5	10.2			
Minimum 1 Embryo**	36,928	91.3	99.1	100.0		
ET Performed**	34,260	84.7	91.9	92.8	100.0	
Clin. Pregnancy	10,518	**23.6**	25.3	28.5	**30.7**	100.0
Birth	7,713	**17.3**	**18.6**	**20.9**	**22.5**	**73.3**
Miscarriage	2,283					21.7
Ectopic Pregnancy	117					1.1
Not Yet Recorded	411					3.9

IVF and ICSI in Natural Cycles 2022** – Ø Avg. Patient Age: 38.7

	n	%	Cycle %	Fertilization %	Embryo exist. %	Transfer %	Clin. Preg. %
Started Cycles	4,158	100.0					
No Oocyte Treatment	1,252	30.1					
Treatm. in Natural Cycles***	2,906	69.9	100.0				
ø Oocytes Retrieved	3.2						
Successful Fertilization*	2,290	55.1	78.8	100.0			
Freeze All Treated Oocytes	105	2.5	3.6	4.6			
Minimum 1 Embryo**	2,110	52.1	75.3	96.6	100.0		
ET Performed**	2,058	50.8	73.5	94.2	97.5	100.0	
Clin. Pregnancy	478	**11.5**	**16.4**	20.9	22.7	**23.2**	100.0
Birth	337	**8.1**	**11.6**	**14.7**	**16.0**	**16.4**	**70.5**
Miscarriage	115						24.1
Ectopic Pregnancy	3						0.6
Not Yet Recorded	24						5.0

**) Successful fertilization of at least one oocyte per cycle.*
***) %-rates up to fertilization adjusted by freeze all oocytes culture.*
****) Evaluation for "IVF and ICSI in Natural Cycles" if "Yes, without any ovarian stimulation" or "Yes, with mild ovarian stimulation (e.g. with CC, letrozole, low dose FSH/HMG)" was documented manually.*

Results of Thawing-Cycles, TESE, IVF and ICSI with Donor Sperm 2022

Prospective Data

Cryo Transfer Cycles 2022

	n	%	PN/Embryo %	Transfer %	Clin. Preg. %
Cryo Transfer Cycles	38,374	100.0			
Thawed PN/Embryo	37,940	98.9	100.0		
ET Performed	36,635	95.5	96.6	100.0	
Clin. Pregnancy	11,318	**29.5**	29.8	**30.9**	100.0
Birth	8,148	**21.2**	**21.5**	**22.2**	**72.0**
Miscarriage	2,573				22.7
Ectopic Pregnancy	104				0.9
Not Yet Recorded	500				4.4

TESE 2022 – Ø Avg. Patient Age: 34.7

	n	%	Fertilization %	Embryo %	Transfer %	Clin. Preg. %
Perf. ICSI/TESE Treatm.	2,206	100.0				
Successful Fertilization*	1,986	90.0	100.0			
Freeze All Treated Oocytes	185	8.4	9.3			
Minimum 1 Embryo**	1,719	85.1	95.4	100.0		
ET Performed**	1,537	76.1	85.3	89.4	100.0	
Clin. Pregnancy	482	**21.8**	24.3	28.0	**31.4**	100.0
Birth	347	**15.7**	**17.5**	**20.2**	**22.6**	**72.0**
Miscarriage	113					23.4
Ectopic Pregnancy	7					1.5
Not Yet Recorded	15					3.1

IVF and ICSI with Donor Sperm 2022– Ø Avg. Patient Age: 37.2

	n	%	Fertilization %	Embryo %	Transfer %	Clin. Preg. %
ART-Treatm. (donor sperm)	2,610	100.0				
Successful Fertilization*	2,457	94.1	100.0			
Freeze All Treated Oocytes	209	8.0	8.5			
Minimum 1 Embryo**	2,233	93.0	99.3	100.0		
ET Performed**	2,121	88.3	94.4	95.0	100.0	
Clin. Pregnancy	699	**26.8**	28.4	31.3	**33.0**	100.0
Birth	520	**19.9**	**21.2**	**23.3**	**24.5**	**74.4**
Miscarriage	168					24.0
Ectopic Pregnancy	3					0.4
Not Yet Recorded	8					1.1

In the analysis "IVF and ICSI with Donor Sperm 2022" due to an error in one of the data collection programs, this evaluation could only access the data from 116 centers (potentially missing 15 centers). Therefore, this analysis should be considered preliminary.

**) Successful fertilization of at least one oocyte per cycle.*
***) %-rates up to fertilization adjusted by freeze all oocytes culture.*

Culture According to the "German Compromise" and Impact on Therapy Outcome – Fresh Cycles 2022

Prospective and Retrospective Data

Number of centers choosing >=3 x 2PN for extended culture: n=137

Oocyte Treatment (All) - Culture >= 3 x 2PN
32,842

Oocyte Treatment - Culture >= 3 x 2PN for Transfer on Day 4-6
24,369

Number of Transfer Cycles with SET Day 4-6		Number of Transfer Cycles with DET Day 4-6	
15,171	Mean age woman: 34.6	8,963	Mean age woman: 35.7
CP/ET (doc. and outcome known)*		**CP/ET (doc. and outcome known)***	
5,440	36.9%	3,531	39.6%
Outcome unknown		**Outcome unknown**	
25	0.2%	50	0.6%

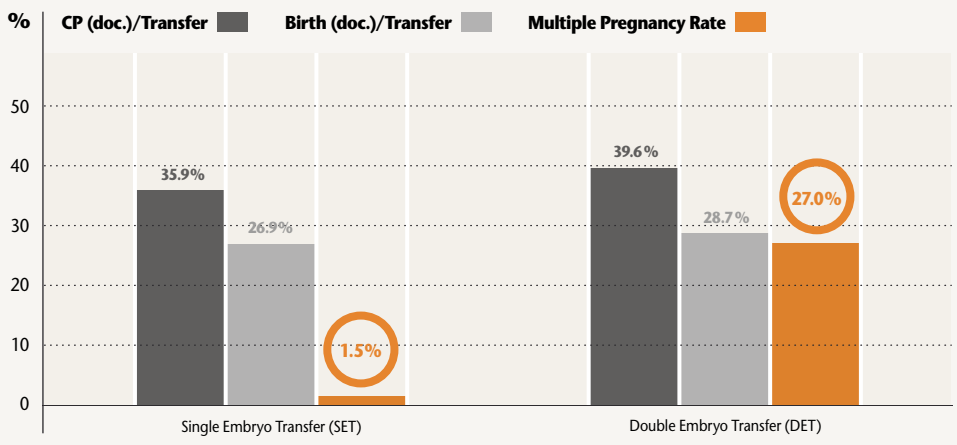
Miscarriage	1,106	20.3%	Miscarriage	794	22.5%
EP	59	1.1%	EP	41	1.2%
Not yet Recorded	198	3.6%	Not yet Recorded	124	3.5%
Birth (doc.)	**4,077**	**74.9%**	**Birth (doc.)**	**2,572**	**72.8%**
	per Transfer	26.9%		per Transfer	28.7%

Births	**n**	**%**	**Births**	**n**	**%**
Singletons	4,014	98.5	Singletons	1,878	73.0
Twins	63	1.5	Twins	678	26.4
Triplets	0	0.0	Triplets	16	0.6
Quadruplets	0	0.0	Quadruplets	0	0.0

Multiple Pregnancy Rate	**1.5%**	**Multiple Pregnancy Rate**	**27.0%**

**) please note: documented clinical pregnancies (7,269) per transfer with outcome known (28,293) on other days than 4-6: 25.7%*

Comparison SET and DET "German Compromise" Fresh Cycles 2022



SET versus DET:
The likelihood of birth after DET increases by a factor of 1.07.
A multiple birth after DET likely increases by factor 17.5.
For an increase in the birth rate of not even 2 percentage points, the risk of multiples is raised by nearly 18 times!

Culture According to the "German Compromise" and Impact on Therapy Outcome – Thawing Cycles Embryos 2022

Prospective and Retrospective Data

Number of centers transfering previously cryopreserved embryos: n=136

Thawing total
39,474

Thawing Embryos
19,300

Transfer Single ET
15,468

CP/ET (doc. and outcome known)
4,925 — 31.9%

Outcome unknown
50 — 0.3%

Miscarriage	1,180	24.0%
EP	42	0.9%
Not yet Recorded	207	4.2%
Birth (doc.)	**3,498**	**71.0%**
	per Transfer	22.6%

Births	**n**	**%**
Singletons	3,445	98.5
Twins	53	1.5
Triplets	0	0.0
Quadruplets	0	0.0

Multiple Pregnancy Rate 1.5%

Transfer Double ET
2,889

CP/ET (doc.)
1,058 — 36.8%

Outcome unknown
17 — 0.6%

Miscarriage	267	25.2%
EP	5	0.5%
Not yet Recorded	49	4.6%
Birth (doc.)	**738**	**69.8%**
	per Transfer	25.5%

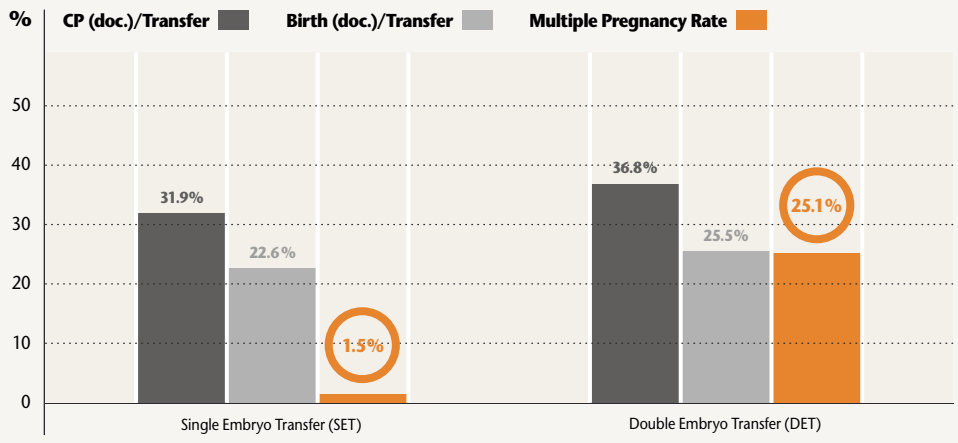
Births	**n**	**%**
Singletons	625	84.7
Twins	181	24.5
Triplets	4	0.5
Quadruplets	0	0.0

Multiple Pregnancy Rate 24.3%

Compared to thawing 2PNs:

	SET (n)	CP/Transfer (%)	Births/Transfer (%)	MBR (%)	DET (n)	CP/Transfer (%)	Births/Transfer (%)	MBR (%)
Transfers (outcome kown)	9,223	28.0	20.4	2.2	9,281	30.6	22.2	19.9
Transfers d2/3	2,589	17.3	11.7	1.3	5,298	25.7	18.2	14.9
Transfers d5/6	5,978	33.0	24.4	2.0	3,285	38.6	28.5	25.1
others	656	25.0	19.1	5.6	698	30.8	23.2	18.5

Comparison SET and DET "German Compromise" Thawing Cycles Embryos 2022



SET versus DET:
The likelihood of birth after DET increases by a factor of 1.13.
A multiple birth after DET likely increases by factor 16.5.
For an increase in the birth rate of not even 3 percentage points, the risk of multiples is raised by more than 16 times!

Pregnancies Cumulative 2020 – 2022 as a Function of Female Age

IVF, ICSI, Cryo Cycles – Prospective Data

Age Group <= 29	Transfers	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle with Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cum. CP	Cumulative Pregnancy Rate in %
1st Transfer	9,768	4,136	42.3	2,344	919	39.2	5,055	**41.7**
2nd Transfer	2,715	1,068	39.3	4,563	1,607	35.2	7,730	**63.8**
3rd Transfer	1,295	479	37.0	2,561	883	34.5	9,092	**75.1**
4th Transfer	603	215	35.7	1,247	420	33.7	9,727	**80.3**
>4 Transfers	432	160	37.0	1,211	354	29.2	10,241	**84.6**

Age Group 30-34	Transfers	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle with Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cum. CP	Cumulative Pregnancy Rate in %
1st Transfer	26,699	10,630	39.8	5,987	2,269	37.9	12,899	**39.5**
2nd Transfer	7,863	2,833	36.0	12,238	4,177	34.1	19,909	**60.9**
3rd Transfer	4,295	1,519	35.4	6,893	2,309	33.5	23,737	**72.6**
4th Transfer	2,027	693	34.2	3,637	1,179	32.4	25,609	**78.3**
>4 Transfers	1,680	529	31.5	3,770	1,125	29.8	27,263	**83.4**

Age Group 35-39	Transfers	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle with Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cum. CP	Cumulative Pregnancy Rate in %
1st Transfer	30,672	9,891	32.2	5,281	1,758	33.3	11,649	**32.4**
2nd Transfer	11,071	3,049	27.5	11,145	3,376	30.3	18,074	**50.3**
3rd Transfer	5,936	1,649	27.8	6,488	1,831	28.2	21,554	**60.0**
4th Transfer	2,787	730	26.2	3,630	942	26.0	23,226	**64.6**
>4 Transfers	2,541	655	25.8	4,188	1,013	24.2	24,894	**69.2**

Age Group >= 40	Transfers	CP (Fresh Cycles)	CP (Fresh Cycles) in %	Cryo Cycle with Transfer	CP (Cryo Cycles)	CP/ET (Cryo Cycles) in %	Cum. CP	Cumulative Pregnancy Rate in %
1st Transfer	10,490	1,793	17.1	2,045	464	22.7	2,257	**18.0**
2nd Transfer	4,057	646	15.9	2,875	525	18.3	3,428	**27.3**
3rd Transfer	2,066	321	15.5	1,610	269	16.7	4,018	**32.1**
4th Transfer	986	129	13.1	888	157	17.7	4,304	**34.3**
>4 Transfers	1,140	145	12.7	1,026	176	17.2	4,625	**36.9**

Follow-up clinical pregnancies until Dec. 31st, 2023.

Here again, we present cumulative chances after several cycles depending on age. Patients under 34 years of age have around an 80% chance of becoming pregnant with four transfers.

In patients between 35 and 39 years of age, 2 out of 3 patients achieve pregnancy with four transfers.

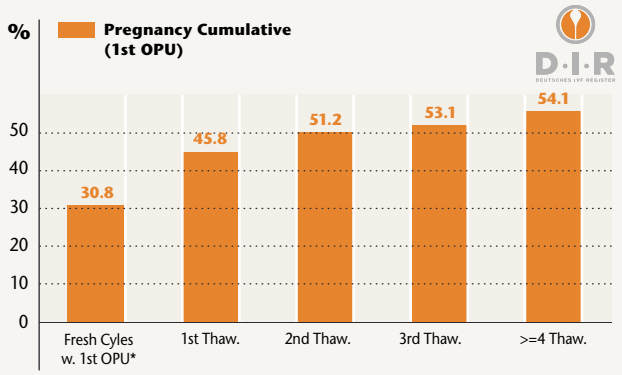
In patients aged 40 and over, the chances increase to "only" a third. So even in a cumulative view, the age of our patients plays a decisive role.

These figures can help assess the chances during counselling.

Live Births Cumulative 2018 – 2021 Based on First OPU

IVF, ICSI, Cryo Cycles – Prospective Data

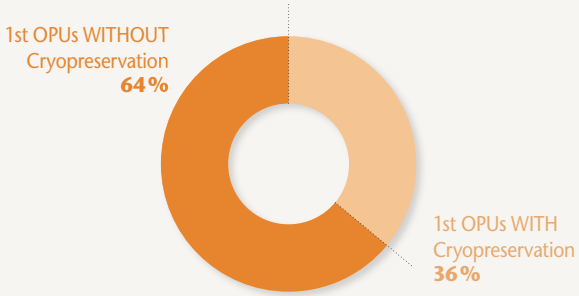
This evaluation presents cumulative probability of having a child per aspiration. Other evaluations present cumulative probability of pregnancies with regard to transfers.
After first aspiration, the chance of birth in Germany is just over 30 %. Subsequent thawing transfers can increase birth rate to more than 50 %.
And this is after only one aspiration for oocyte retrieval!
The relatively small percentage increase after the 3rd transfer is due to the small number of those having 4 or more transfers from one puncture.



2018 – 2021 (Total)	1st OPU*	Thawings Based on 1st OPU	Live Births	Live Births/OPU / Live Births/FET (%)	Live Births Cumulative	Live Births/OPU Cumulative (%)
Fresh Cyles with 1st OPU*	41,658		12,828	30.8	12,828	**30.8**
1st Thawing		28,462	6,242	22.8	19,070	**45.8**
2nd Thawing		11,794	2,276	20.8	21,346	**51.2**
3rd Thawing		4,331	784	20.3	22,130	**53.1**
>= 4 Thawings		2,387	404	20.3	22,534	**54.1**

Follow-up births until Dec. 31st, 2022.
**) Cycles without fresh transfer (freeze all) and cycles without cryopreservation were excluded. Sample sizes: 1st OPU = 131,717; 1st OPU without freeze all = 115,669; Cycles without cryopreservation = 41,658; Cycles with Cryopreservation = 74,011.*

1st OPU without Freeze All: Ratio Cycles with and without Cryopreservation

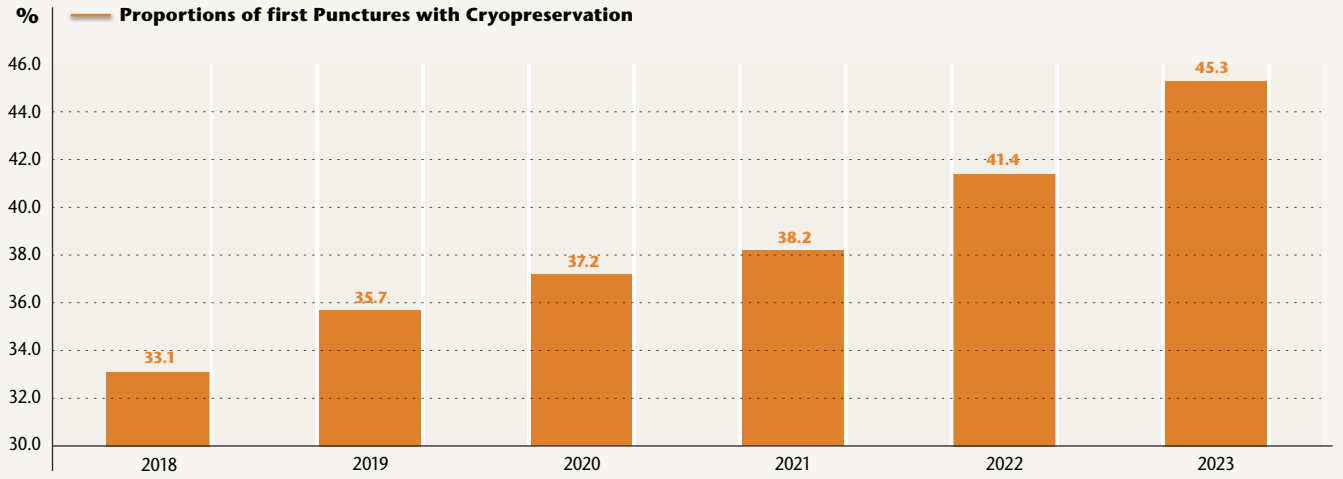


In the years 2018–2021, only 36 % of all first oocyte retrieval with transfer were also cryopreserved. This is certainly partly due to the fact that the costs are not covered by public health insurance.

However, there has been a constant annual increase in the proportion of first punctures with cryopreservation from 2018 (33.1 %) to 2023, now at 45.3 %. Every year, more is being preserved! We believe this is a positive development, as nearly 46 % of our patients have a child after two embryo transfers (see above).

This is certainly also related to improved freezing and thawing techniques (vitrification).

Annual development of the proportions of first punctures with cryopreservation, without Freeze All, 2018–2023



Positive Pregnancy Outcomes 2022

IVF, ICSI – Prospective and Retrospective Data

	Fresh Cycles		Cryo Cycles	
	n	%	n	%
Clinical Pregnancies	16,240	100.0	11,589	100.0
Outcome documented	15,572	95.9	11,037	95.2
Transfer	52,536		37,678	
Births	11,775		8,314	
Life-Birth-Rate/Birth	11,742	99.7	8,304	99.9
Life-Birth-Rate/ET	11,742	22.4	8,304	22.0
SET Good Prognosis Patient*				
Number of Transfers	3,394			
Life-Birth-Rate/ET	1,084	31.9		
Multiple Pregnancies	13	1.2		
DET Good Prognosis Patient*				
Number of Transfers	1,972			
Life-Birth-Rate/ET	714	36.2		
Number of Multiple Births	216	30.3		

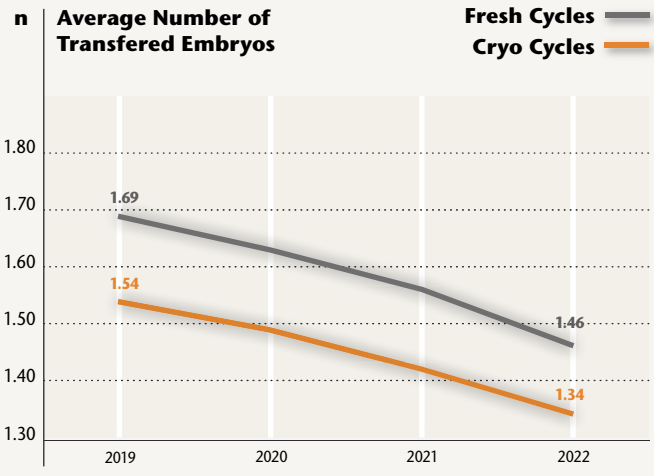
Loss of Pregnancy 2022

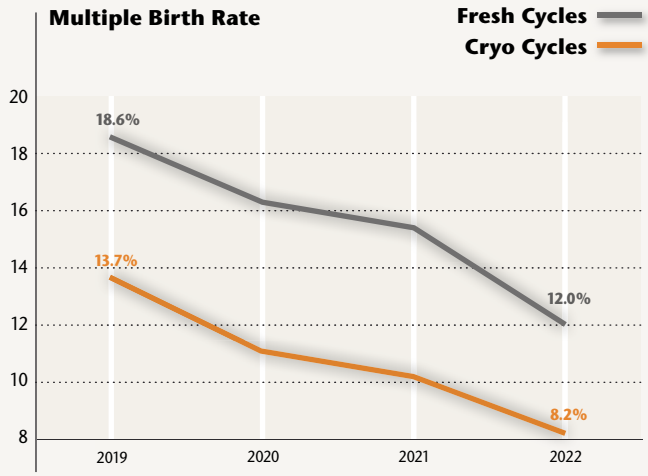
Prospective and Retrospective Data

	Fresh Cycles		Cryo Cycles	
	n	%	n	%
Clinical Pregnancies	16,240	100.0	11,589	100.0
Outcome documented	15,572	95.9	11,037	95.2
Miscarriages	3,594	22.1	2,541	21.9
Among those: Induced Abortions	268	7.5	156	6.1
Stillbirths	41	0.3	10	0.1

Embryos per Transfer[1] and Multiple Birth Rate 1997 – 2022

IVF, ICSI, Cryo – Prospective and Retrospective Data





		1997	[...]	2019	2020	2021	2022
Fresh Cycles	ø Number of Transf. Embryos	2.56	*For values from 1998 to 2018 see www.deutsches-ivf-register.de*	1.69	1.63	1.56	1.46
	Multiple Birth Rate	25.2		18.6	16.3	15.4	12.0
Cryo Cycles	ø Number of Transf. Embryos	2.34		1.54	1.49	1.42	1.34
	Multiple Birth Rate	11.6		13.7	11.1	10.2	8.2

The significant reduction in multiple births continues! This is thanks to the fact that more and more centers are transferring fewer embryos per embryo transfer. Single embryo transfer is also becoming increasingly popular in Germany.

In thawing cycles, the multiple birth rate is already well below 10 %! In the total fresh and thawing cycles, the multiple birth rate was 17.0 % in 2019, but in 2022 it has already fallen to 10.4 %!

**) Good prognosis patient in D·I·R: age <=35, fresh cycle, 1st cycle, oocytes retrieved >=8, 2PNs >=5, sperm collection anterograde*
1) Mean

Special Laboratory Evaluation: Cryopreservation and Blastocyst Culture – Reliable Procedures for High Treatment Success Rates

Does the preference for cryopreservation of 2PN cells in Germany affects pregnancy rates compared to FET of blastocysts? Are there differences compared to pregnancies achieved in fresh cycles? A special analysis by the D·I·R yields reassuring results.

In vitro fertilization involves the meeting of gametes and early embryonic development outside the body. The processes necessary for the successful execution of IVF, ICSI, and other reproductive techniques are typically monitored with lab-specific KPIs such as oocyte maturity, fertilization rates, degeneration rates, and developmental rates. The impact of culture duration and cryopreservation on treatment success and birth weight of children can only be determined with larger sample sizes. Therefore, these evaluations...

1. Miscarriage Rates in Fresh Cycles and FET

Premature termination of a pregnancy occurs in approximately 10-15% of spontaneous pregnancies.
Various factors can influence miscarriage rates, including the woman's age, causes of infertility, and comorbidities. The quality of embryos is also influenced by culture conditions and cryopreservation, both of which affect pregnancy and miscarriage rates.

In the D·I·R, clinical pregnancy is defined by the ultrasound detection of a gestational sac. In international literature, a later positive fetal heartbeat is often used as the basis for calculation.

Based on 44,043 fresh cycles and 28,313 FET with sonographically confirmed intrauterine gestational sacs, no differences in miscarriage rates were found between the two groups. 13.6% of pregnancies in fresh cycles and 14.5% in FET end before the sonographic detection of a gestational sac. Overall, 24.0% and 24.8% of documented pregnancies, respectively, result in miscarriage.

Tab1: Miscarriage Rates in Fresh Cycles and FET (2020–2022)

	Fresh Cycles				FET			
	n	%	%	%	n	%	%	%
CP (with Gestational Sac)	44,043	100.0		100.0	28,313	100.0		100.0
Misc. before HB	5,984	13.6			4,104	14.5		
CP with HB	38,059	86.4	100.0		24,209	85.5	100.0	
Misc. after HB	4,606		12.1		2,909		12.0	
Total Misc.	10,590			24.0	7,013			24.8

2. Cultivation Strategies in Fresh Cycles and FET

In fresh cycles, blastocyst culture has become standard as part of the "German middle way." The higher implantation rates per transferred embryo have paved the way for the single-embryo transfer.

The decision to transfer embryos at an early cleavage stage or to culture them to the blastocyst stage provides better opportunities to identify viable, developmentally competent embryos for transfer. Additionally, surplus 2 PN-stage embryos and blastocysts are cryopreserved. Day 2/3 embryos are only cryopreserved in exceptional cases. In other countries, embryos are almost exclusively frozen at the cleavage or blastocyst stages. Can comparable results be achieved in FET by cryopreserving 2 PN-stage oocytes?

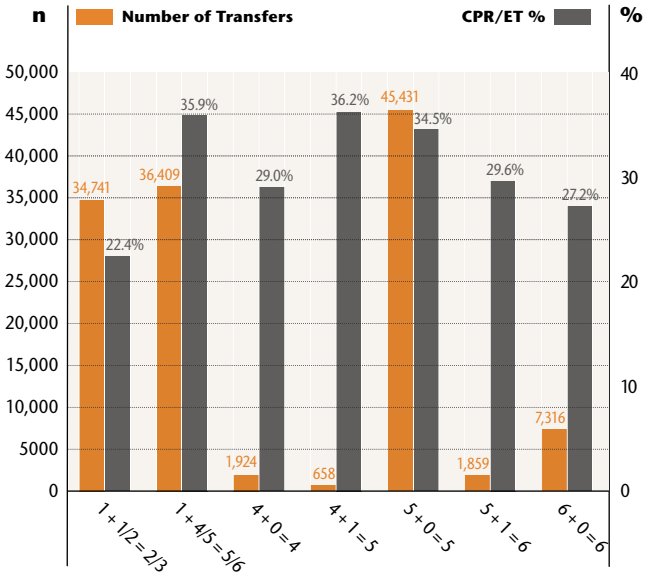
Pregnancy Rates According to Different Culture Strategies

The results of FET from the years 2020–2023 are analyzed based on the various culture durations before and after cryopreservation.

In FET, transfers most commonly occur after freezing at the 2 PN stage. Extended culture following thawing of 2 PN-stage embryos is slightly more common than transfer 1–2 days after thawing.

Cryopreserved blastocysts are most frequently transferred on the day of thawing. Freezing of 4- or 6-day-old embryos is less common. For transfers of day-6 embryos, it is important to consider that slowly developing embryos are often transferred a day earlier to achieve better synchrony with the endometrium. Details on this practice are not available to the D·I·R and are therefore not considered in the analysis.

When only a few 2 PN cells are cryopreserved, transfer typically occurs on day 2/3, as a longer culture would not provide additional selection criteria due to the limited number and/or quality of the embryos. This approach, however, may lead to lower pregnancy rates (22.4%) compared to cycles with better selection options.



Explanation of X-axis: Culture duration before cryopreservation + after thawing = total

Two approaches are preferred by German IVF centers for the transfer of day 5/6 embryos:

- Freezing on day 1 – extended culture after thawing – transfer at embryo age 5/6, and
- Freezing on day 5 – transfer on the day of thawing or at the latest the following day.

In FET, significantly more pregnancies are achieved with the extended culture to the blastocyst stage compared to the transfer of thawed blastocysts (35.9% vs. 34.5%, p=0.000148).

A plausible explanation for the difference: In fresh cycles, blastocysts of the best quality have already been transferred. In contrast, embryos are frozen at the 2 PN stage without prior quality assessment, meaning that after extended culture–especially in freeze-all cycles–the embryos with the best developmental potential are still available for transfer.

A longer culture duration of embryos is intended to reduce the miscarriage rate in both fresh and frozen cycles. However, in the data from 2020-2022 for Germany, this difference for transfers performed on days 2/3, 4, or 5/6 is only marginal.

	Fresh Cycles			**FET**		
Embryo age at transfer	D2/3	D4	D5/6	D2/3	D4	D5/6
All CP	16,547	3,612	23,806	5,655	1,439	19,663
All miscarriages	4,185	854	5,534	1,434	377	4,787
All miscarriages % of CP	**25.3**	**23.6**	**23.2**	**25.4**	**26.2**	**24.3**

3. Monozygotic Twins

Spontaneous monozygotic twins (MZT) are reported worldwide at a rate of 3-4 per 1,000 births. In Germany, during the study period of 2019-2022, 15 monozygotic twin births per 1,000 births were documented after fresh cycle ART treatment and 19 after FET.

Thus, FET show a significantly higher rate of monozygotic twinning (MZT) (p = 0.0022).

	Fresh Cycles			**FET**		
Embryo age at transfer	D2/3	D4	D5/6	D2/3	D4	D5/6
All SET	39,558	7,338	49,697	11,783	3,447	53,969
All births after SET	4,841	1,540	13,040	1,303	638	12,839
Monozygotic twins	62	24	204	23	21	241
Monozygotic twins/SET %	**1.3%**	**1.6%**	**1.6%**	**1.8%**	**3.3%**	**1.9%**

The frequently mentioned increased incidence of MZT after extended culture could not be confirmed in single-embryo transfers between 2020 and 2022 in the D·I·R. No differences were found in the MZT rate for births after short or extended culture in fresh cycles or FET (fresh p = 0.1859, FET p = 0.8547). The incidence of MZT after transfer of day 2/3 embryos was comparable in both fresh cycles and FET (p = 0.2320). Similarly, no significant difference was observed in MZT rates after transfer of day 5/6 embryos (p = 0.0592).

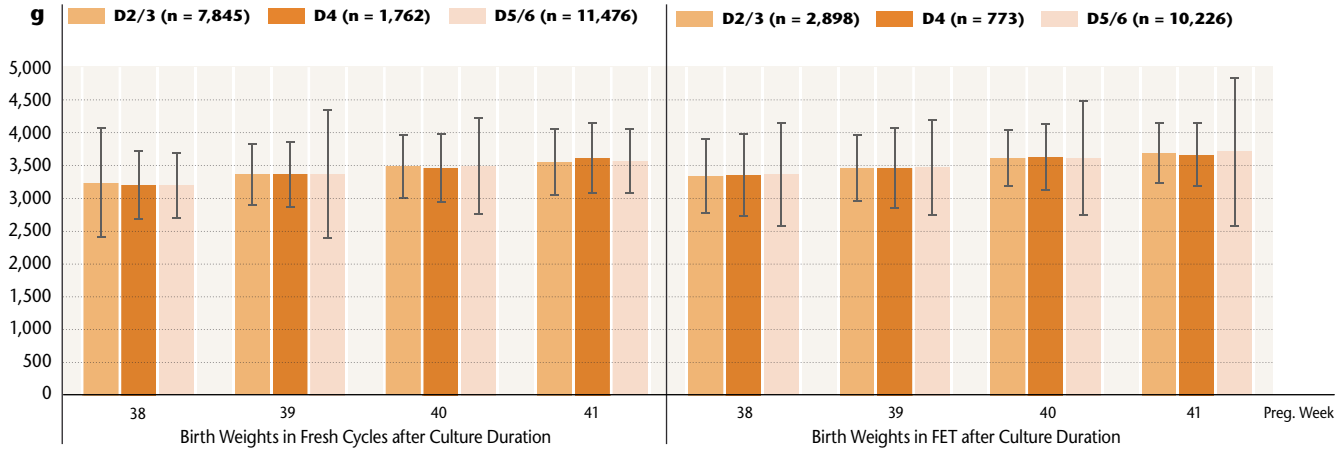
For the transfer of day 4 embryos, MZT occurred significantly more often in FET (p = 0.0154) than in fresh cycles, although this may be due to the small sample size.

4. Birth Weight and Culture Duration

The in vitro culture of oocytes and embryos can influence metabolism and development in various ways. For example, developmental differences are known to depend on the culture media and oxygen concentrations used. Additionally, methylation patterns of the embryonic DNA can vary.

There is very little and contradictory data regarding different culture durations. Does the culture duration affect the birth weight of the children?

To improve comparability, singleton births from the years 2020–2022 are considered separately according to gestational weeks and culture duration. No significant differences were found between the individual culture durations in either fresh cycles or FET. Significance tests were performed for all gestational weeks. The results were also the same for male



Several studies have shown that children born after cryopreservation tend to be slightly heavier on average compared to children born from fresh cycles. We also observe this trend in Germany. After fresh embryo transfer, babies were on average slightly lighter compared to those born after FET (girls 3.327g-3.458g, boys 3.462g-3.616g). The reason for this is unknown and requires further investigation.

In summary, the data analyzed are reassuring regarding treatment success and the health of the born children. However, it is important to continue observations and analyses to gain a more comprehensive understanding of the long-term effects of the applied methods.

Dipl.-Biologin Verona Blumenauer (Lead Author)
Dipl. Biologin Vera Baukloh
Dr. rer. medic. Martin Greuner

ICSI/ejaculated versus ICSI/TESE: Development of the Retrieved Oocytes 2020–2023

Prospective and Retrospective Data

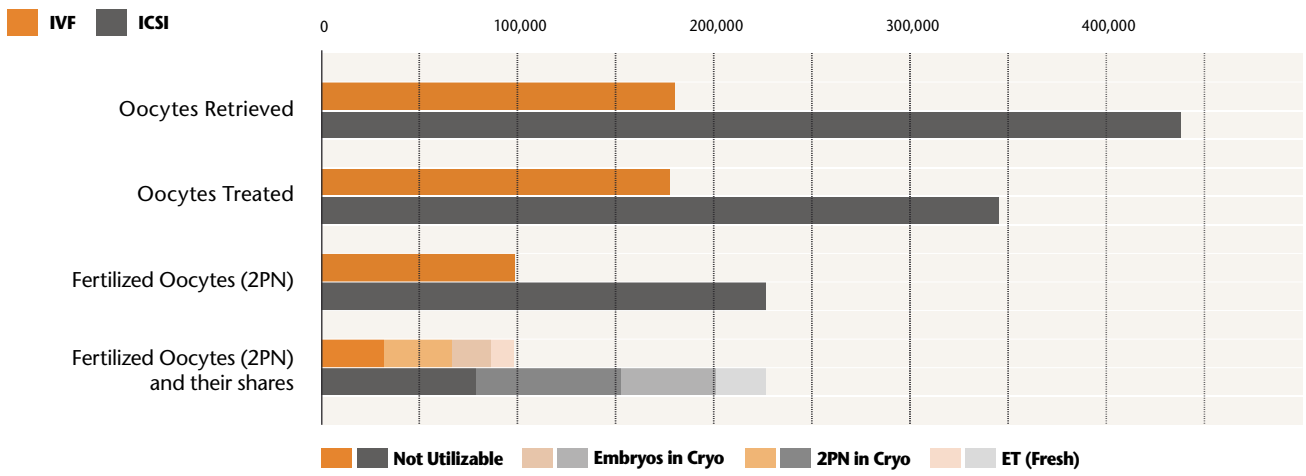
	ICSI with Ejaculated Sperm				ICSI after TESE*			
	n	%	%	%	n	%	%	%
Retrieved Oocytes	1,549,434	100.0			97,462	100.0		
Treated Oocytes	1,218,984	78.7	100.0		76,844	78.8	100.0	
Fertilized (2PN)	806,148	52.0	66.1	100.0	38,022	39.0	49.5	100.0
Cryopreserved 2PN	260,055			32.3	9,843			25.9
Transferred Embryos	196,800			24.4	9,887			26.0
Cryopreserved Embryos	75,022			9.3	3,799			10.0

**) There was no distinction made between fresh and thawed sperm.*

Evolution of Retrieved Oocytes (IVF or ICSI) 2023

IVF, ICSI – Prospective and Retrospective Data

	IVF	%			ICSI	%		
Oocytes Retrieved	179,944	100.0			437,934	100.0		
Oocytes Treated	177,623	98.7	100.0		345,189	78.8	100.0	
Fertilized Oocytes (2PN)	98,621	54.8	55.5	100.0	226,312	51.7	65.6	100.0
2PN Cryopreserved	35,379			35.9	74,245			32.8
transf. Embryos	19,788			20.1	48,143			21.3
Embr. Cryopreserved	11,269			11,4	25,184			11.1



Clinical Pregnancies (CP)/Fresh Transfer as a Function of Embryo Quality 2023

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	442	20.1	1,502	17.0	2,198	12.1	989	4.2	5,131	12.7
0	2	154	26.6	586	24.4	984	19.4	516	11.4	2,240	19.4
0	3	1	0.0	5	40.0	13	7.7	12	0.0	31	9.7
1	0	2,490	44.3	8,324	40.9	11,294	31.9	3,992	17.5	26,100	33.8
1	1	174	42.0	650	34.1	1,090	25.6	610	19.9	2,524	27.5
1	2	0	-	1	0.0	5	40.0	14	7.1	20	15.0
2	0	885	50.0	2,892	43.4	4,592	38.2	2,123	23.4	10,492	37.6
2	1	0	-	9	33.3	17	29.4	32	8.8	58	24.1
3	0	2	100.0	16	25.0	35	41.2	80	20.0	133	27.3
Total*		**4,150**	**42.2**	**13,994**	**37.8**	**20,240**	**30.2**	**8,371**	**17.2**	**46,755**	**31.2**

**) 26 transfers could not be allocated.*

Clinical Pregnancies (CP)/Frozen Transfer as a Function of Embryo Quality 2023

Cryo Transfer – Prospective Data

Quality		IVF		ICSI	
ideal	Not Ideal	ET	CP/ET %	ET	CP/ET %
0	1	845	16.6	2,043	16.4
0	2	329	15.3	955	18.8
0	3	5	0.0	25	4.0
1	0	8,490	31.0	17,705	33.2
1	1	428	27.5	1,060	29.7
1	2	2	50.0	26	20.0
2	0	2,020	34.5	4,816	34.3
2	1	6	33.3	28	21.4
3	0	25	36.0	81	25.9
Total**		**12,170**	**30.0**	**26,815**	**31.3**

***) 96 transfers could not be allocated.*

Children Born as a Function of Week of Gestation (WoG) and Birth Weight (BW) 2022

Prospective and Retrospective Data

IVF, ICSI, IVF/ICSI

Current WoG	20 - 26		27 - 31		32 - 37		38 - 41		>= 42		Total	% of total
Singletons (n and %)	43	0.5	122	1.3	1,546	16.3	7,697	81.2	75	0.8	**9,483**	**78.8**
Average Birth Weight (g)	674		1,314		2,723		3,397		3,532		**3,249**	
Twins (n and %)	72	2.9	166	6.7	1,892	76.5	340	13.8	2	0.1	**2,472**	**20.5**
Average Birth Weight (g)	695		1,325		2,410		2,786		2,700		**2,339**	
Triplets (n and %)	12	14.8	48	59.3	21	25.9	-	-	-	-	**81**	**0.7**
Average Birth Weight (g)	515		1,235		1,755		-		-		**1,274**	

Percentage of preterm deliveries in singleton pregnancies is 18.0%.
Percentage of preterm deliveries in twin pregnancies is 86.2%.
Percentage of preterm deliveries in triplets pregnancies is 100.0%.

Cryo Transfer

Current WoG	20 - 26		27 - 31		32 - 37		38 - 41		>= 42		Total	% of total
Singletons (n and %)	20	0.3	73	1.1	921	13.6	5,661	83.3	120	1.8	**6,795**	**85.1**
Average Birth Weight (g)	765		1,389		2,851		3,518		3,641		**3,399**	
Twins (n and %)	24	2.1	86	7.4	870	75.3	174	15.1	4	0.3	**1,156**	**14.5**
Average Birth Weight (g)	717		1,319		2,481		2,919		2,543		**2,428**	
Triplets (n and %)	-	-	15	45.5	18	54.5	-	-	-	-	**33**	**0.4**
Average Birth Weight (g)	-		1,204		2,016		-		-		**1,637**	

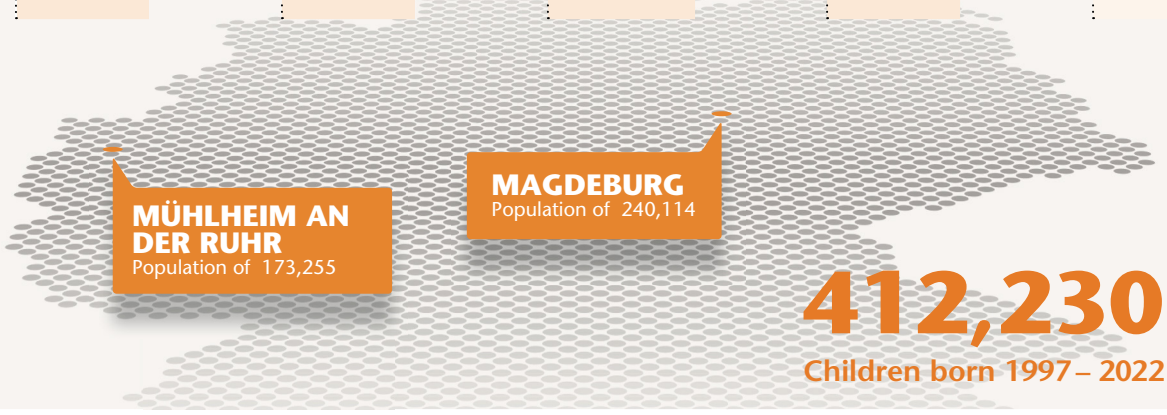
Percentage of preterm deliveries in singleton pregnancies is 14.9%.
Percentage of preterm deliveries in twin pregnancies is 84.8%.
Percentage of preterm deliveries in triplets pregnancies is 100.0%.

Children Born 1997 – 2022

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	14,580	67.2	6,800	31.3	321	1.5	8	0.0	21,709
2018	15,423	69.6	6,508	29.4	225	1.0	0	-	22,156
2019	16,467	70.7	6,560	28.2	273	1.2	0	-	23,300
2020	17,050	74.4	5,690	24.8	156	0.7	8	0.0	22,904
2021	18,547	76.0	5,702	23.4	165	0.7	0	-	24,414
2022	18,046	80.9	4,120	18.5	129	0.6	0	-	22,295
Total	**278,091**	**67.5**	**125,682**	**30.5**	**8,325**	**2.0**	**132**	**0.0**	**412,230**



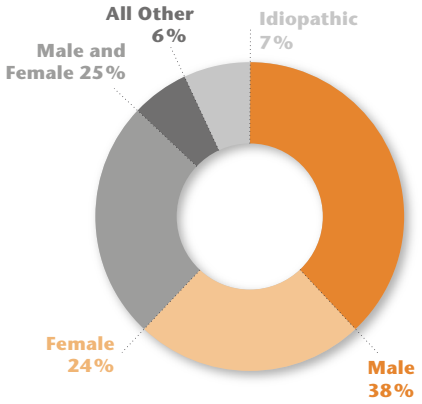
Distribution of Indications 2023

IVF and ICSI – Prospective Data

	Ø Age Pat.	Treatments	Transfers		Clin. Preg.	
	n	n	n	%	n	%*
No Information	34.9	1,655	1,385	83.7	432	31.2
Idiopathic	35.9	4,431	3,089	69.7	961	31.1
Male	35.2	23,958	18,558	77.5	6,056	32.7
Female	35.9	14,903	10,942	73.4	3,366	30.8
Male and Female	36.5	15,305	11,111	72.6	3,232	29.2
Single Woman	37.0	1,420	1,129	79.8	295	26.2
Lesbian Couple	35.7	716	541	75.6	209	38.9
Total	**35.8**	**62,388**	**46,755**	**75.0**	**14,551**	**31.2**

*) CPR/ET for outcomes known

Shares of Indications (Cycles) 2023



IVF

Male Factor	Normal		Red. Semen Quality		Unknown		Other***		Total****	
Female Factor	n	%	n	%	n	%	n	%	n	%
Normal	3,098	13.0	637	2.7	82	0.3	533	2.2	4,350	18.2
Tubal Pathology	2,667	11.2	426	1.8	69	0.3	481	2.0	3,643	15.2
Endometriosis	2,460	10.3	403	1.7	86	0.4	473	2.0	3,422	14.3
Hyperandrog./PCO	675	2.8	90	0.4	21	0.1	151	0.6	937	3.9
Ovulatory Dysf.	802	3.4	204	0.9	34	0.1	204	0.9	1,244	5.2
Psychogen. Factors	31	0.1	1	0.0	0	0.0	6	0.0	38	0.2
Age	1,521	6.4	240	1.0	40	0.2	211	0.9	2,012	8.4
Other**	5,543	23.2	951	4.0	139	0.6	1,140	4.8	7,773	32.5
No Information	438	1.8	12	0.1	2	0.0	30	0.1	482	2.0
Total**	**17,235**	**72.1**	**2,964**	**12.4**	**473**	**2.0**	**3,229**	**13.5**	**23,901**	**100.0**

ICSI

Male Factor	Normal		Red. Semen Quality		Azoospermia		Unknown		Other***		Total****	
Female Factor	n	%	n	%	n	%	n	%	n	%	n	%
Normal	4,557	8.1	7,993	14.3	1,171	2.1	185	0.3	1,998	3.6	15,904	28.4
Tubal Pathology	1,157	2.1	1,738	3.1	69	0.1	43	0.1	834	1.5	3,841	6.9
Endometriosis	1,585	2.8	2,303	4.1	133	0.2	73	0.1	997	1.8	5,091	9.1
Hyperandrog./PCO	542	1.0	982	1.8	104	0.2	25	0.0	381	0.7	2,034	3.6
Ovulatory Dysf.	767	1.4	1,682	3.0	147	0.3	42	0.1	789	1.4	3,427	6.1
Psychogen. Factors	33	0.1	56	0.1	3	0.0	1	0.0	23	0.0	116	0.2
Age	1,658	3.0	2,553	4.6	241	0.4	79	0.1	1,073	1.9	5,604	10.0
Other**	7,268	13.0	6,923	12.4	651	1.2	235	0.4	3,501	6.2	18,578	33.1
No Information	1,106	2.0	137	0.2	119	0.2	0	0.0	92	0.2	1,454	2.6
Total**	**18,673**	**33.3**	**24,367**	**43.5**	**2,638**	**4.7**	**683**	**1.2**	**9,688**	**17.3**	**56,049**	**100.0**

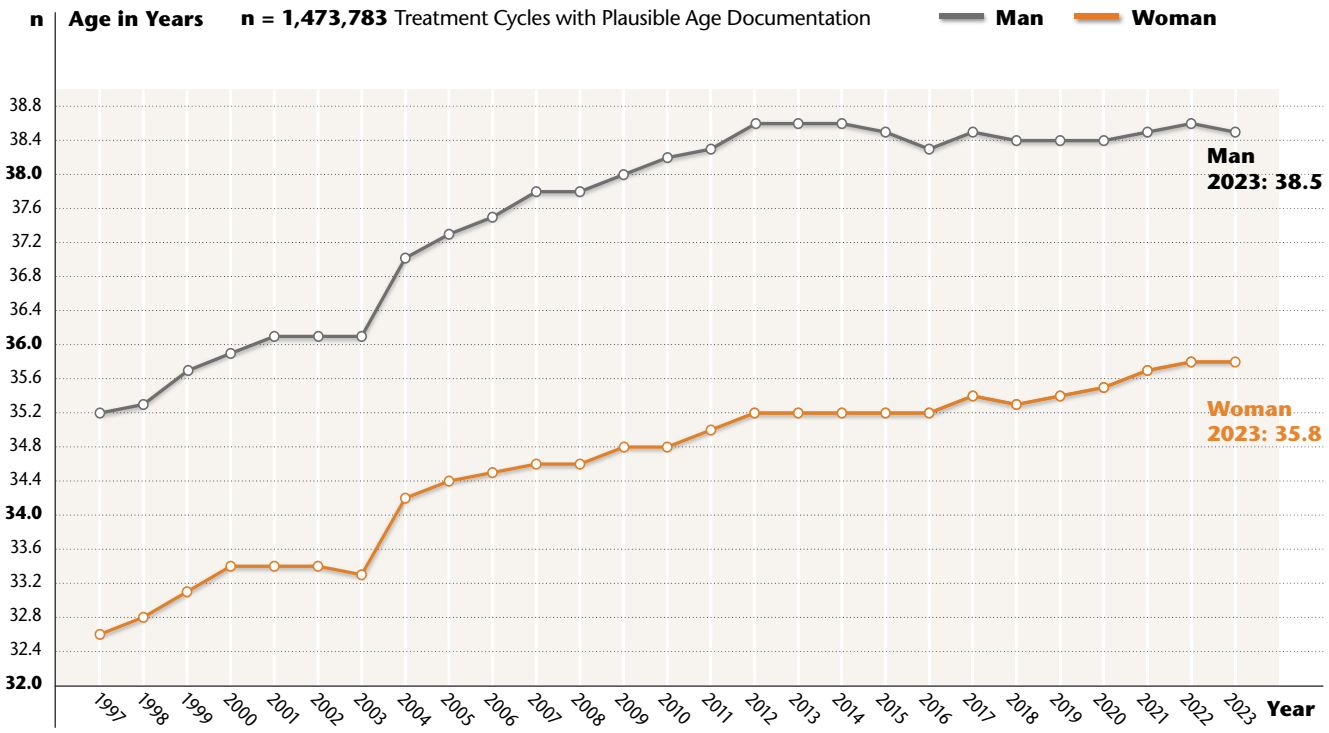
**) This includes the following indications: diminished ovarian reserve, medical freezing, single women, genetic testing (polar body analysis, trophectoderm biopsy for PGT-A, PGT-SR, PGT-M), lesbian couple, social freezing, uterine or cervical factor, others.

***) This includes following indications: anejaculation, medical freezing, preimplantation genetic testing, CBAVD, pathological function test, psychogenic disturbances, retrograde ejaculation, urogenital malformation, failed or bad fertilization rate in conventional ivf-procedure, condition after genital cancer, condition after severe genital infection, condition after vasectomy, others.

****) Multiple answers per cycle permitted.

Mean Age for Women and Men 1997 – 2023

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



Social Freezing 2020 – 2023

Fresh Cycles – Prospective and Retrospective Data

	2020	2021	2022	2023
No. of Centers	106	114	117	119
Recorded Cycles	1,637	2,284	2,439	3,700
Plausible Cycles	1,601	2,240	2,398	3,646
Plausible Cycles %	97.8	98.1	98.3	98.5
Number of Patients	1,210	1,633	1,808	2,755
Ø-Age of Patients	35.7	35.8	35.6	35.4
Ø Number of treatments / patient	1.3	1.4	1.3	1.3
OPU	1,486	2,105	2,209	3,393
Oocytes Aspirated	1,443	2,049	2,140	3,326
Avg. Oocytes Aspirated / Cycle	10.5	10.8	11.0	10.9
Freeze All MII	1,271	1,845	1,950	3,114
Share (%) of Cycles with Cryo-preserved from Retrieved Oocytes	76.3	76.6	76.9	76.5

Either therapy or patient are marked as social freezing.
Follow up social freezings: up to now, only a few pregnancies and births out of former social freezing cycles are recorded.

Clinical Pregnancy Rate as a Function of Stimulation 2023

Prospective Data

Total	recFSH	hMG	recFSH & recLH	recFSH & hMG	Long-Acting recFSH	hrFSH	Antiestrogen +/- Gonadotropin	Other*	No Info	Total
Stimulations (n)	24,495	9,426	21,380	4,726	1,913	1,193	4,885	2,645	1,816	72,479
Transfers (n)	16,025	5,954	14,193	2,925	1,088	805	2,280	1,923	991	46,184
Transfer (%)	65.4	63.2	66.4	61.9	56.9	67.5	46.7	72.7	54.6	63.7
CP (n)	5,610	1,640	4,494	792	266	301	456	601	317	14,477
CP/ET (%)	35.0	27.5	31.7	27.1	24.4	37.4	20.0	31.3	32.0	31.3
CP/Stim, (%)	22.9	17.4	21.0	16.8	13.9	25.2	9.3	22.7	17.5	20.0
Ø-Age of Patients	34.2	37.3	35.9	36.4	37.2	33.9	38.6	35.7	35.9	35.7

Short GnRHa	recFSH	hMG	recFSH & recLH	recFSH & hMG	Long-Acting recFSH	hrFSH	Antiestrogen +/- Gonadotropin	Other*	No Info	Total	Share (%) from total
Stimulations (n)	259	278	562	243	15	8	72	45	107	1,589	2.2
Transfers (n)	158	162	357	163	8	6	20	30	86	990	2.1
Transfer (%)	61.0	58.3	63.5	67.1	53.3	75.0	27.8	66.7	80.4	62.3	
CP (n)	47	34	90	38	4	1	2	9	35	260	1.8
CP/ET (%)	29.7	21.0	25.2	23.3	50.0	16.7	10.0	30.0	40.7	26.3	
CP/Stim, (%)	18.1	12.2	16.0	15.6	26.7	12.5	2.8	20.0	32.7	16.4	
Ø-Age of Patients	36.5	38.2	36.8	37.7	37.5	34.8	39.3	37.6	34.2	37.1	

Long GnRHa	recFSH	hMG	recFSH & recLH	recFSH & hMG	Long-Acting recFSH	hrFSH	Antiestrogen +/- Gonadotropin	Other*	No Info	Total	Share (%) from total
Stimulations (n)	1,788	1,513	2,682	820	192	34	52	240	224	7,545	10.4
Transfers (n)	1,381	1,100	1,986	594	123	21	33	188	150	5,576	12.1
Transfer (%)	77.2	72.7	74.0	72.4	64.1	61.8	63.5	78.3	67.0	73.9	
CP (n)	475	342	587	178	28	7	3	44	42	1,706	11.8
CP/ET (%)	34.4	31.1	29.6	30.0	22.8	33.3	9.1	23.4	28.0	30.6	
CP/Stim, (%)	26.6	22.6	21.9	21.7	14.6	20.6	5.8	18.3	18.8	22.6	
Ø-Age of Patients	34.7	37.1	36.0	36.1	37.4	36.6	38.5	36.2	36.5	36.0	

GnRH-Antagonists	recFSH	hMG	recFSH & recLH	recFSH & hMG	Long-Acting recFSH	hrFSH	Antiestrogen +/- Gonadotropin	Other*	No Info	Total	Share (%) from total
Stimulations (n)	19,440	6,492	16,261	3,300	1,509	1,061	3,104	2,108	1,299	54,574	75.3
Transfers (n)	12,955	4,116	10,798	2,010	881	721	1,579	1,546	692	35,298	76.4
Transfer (%)	66.6	63.4	66.4	60.9	58.4	68.0	50.9	73.3	53.3	64.7	
CP (n)	4,616	1,123	3,512	526	214	267	303	500	227	11,288	78.0
CP/ET (%)	35.6	27.3	32.5	26.2	24.3	37.0	19.2	32.3	32.8	32.0	
CP/Stim, (%)	23.7	17.3	21.6	15.9	14.2	25.2	9.8	23.7	17.5	20.7	
Ø-Age of Patients	34.1	37.3	35.8	36.3	37.3	33.8	38.7	35.5	35.8	35.6	

8,178 stimulations (11.3 %) have been realized without Analoga or Antagonists, resulting in 3,977 transfers (48.6 %) and 1,135 clinical pregnancies (28.5% CP/ET).

593 stimulations (0.8 %) could not been allocated to a specific protocol, resulting in 343 transfers (57.8 %) and 88 clinical pregnancies (25.7 % CP/ET).

*) *e.g. uFSH, uFSH and hMG etc.*

Ovarian Hyperstimulation Syndrome (OHSS) as a Function of Stimulation Protocol and Age Cohort 2023

IVF, ICSI, IVF/ICSI – Prospective Data

	Stimulations Started	%	Oocytes Retrieved	OHSS III (WHO)	OHSS III/Cycles %
Short GnRHa	**1,589**	**2.2**	**6.8**	**0**	**0.0**
< = 29 Years	84		10.7	0	0.0
30 – 34 Years	336		8.7	0	0.0
35 – 39 Years	711		6.5	0	0.0
> = 40 Years	458		5.1	0	0.0
Long GnRHa	**7,545**	**10.5**	**9.0**	**66**	**0.9**
< = 29 Years	489		12.0	8	1.6
30 – 34 Years	2,100		10.3	33	1.6
35 – 39 Years	3,566		8.7	22	0.6
> = 40 Years	1,390		6.9	3	0.2
GnRHa-Antagonists	**54,574**	**75.9**	**9.6**	**96**	**0.2**
< = 29 Years	5,282		12.7	16	0.3
30 – 34 Years	16,474		11.3	39	0.2
35 – 39 Years	22,846		9.1	34	0.1
> = 40 Years	9,972		6.2	7	0.1
No Analoga / no Antagonists	**8,178**	**11.4**	**7.8**	**13**	**0.2**
< = 29 Years	672		12.2	0	0.0
30 – 34 Years	2,204		10.3	2	0.1
35 – 39 Years	3,441		7.4	7	0.2
> = 40 Years	1,861		4.1	4	0.2
Total*	**71,886**	**100.0**	**9.3**	**175**	**0.2**

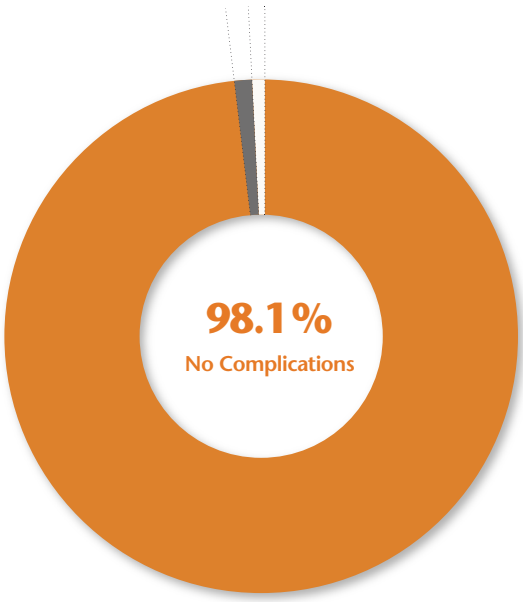
**) in 593 cycles, the protocol could not be reliably determined*

Complications as a Function of Ovum Pick-up (OPU) 2023

IVF, ICSI, IVF/ICSI, Prospective Data

Total OPU´s		**68,089**	**100.0%**
No Information		731	1.1%
No Complications		66,836	98.1%
Complications		**522**	**0.8%**

Complications	n	%
Vaginal Bleeding	335	64.2
Intraabdom. Bleeding	77	14.8
Intestinal Tract Injury	4	0.8
Peritonitis	29	5.6
Other	77	14.8
Total	**522**	**100.0**

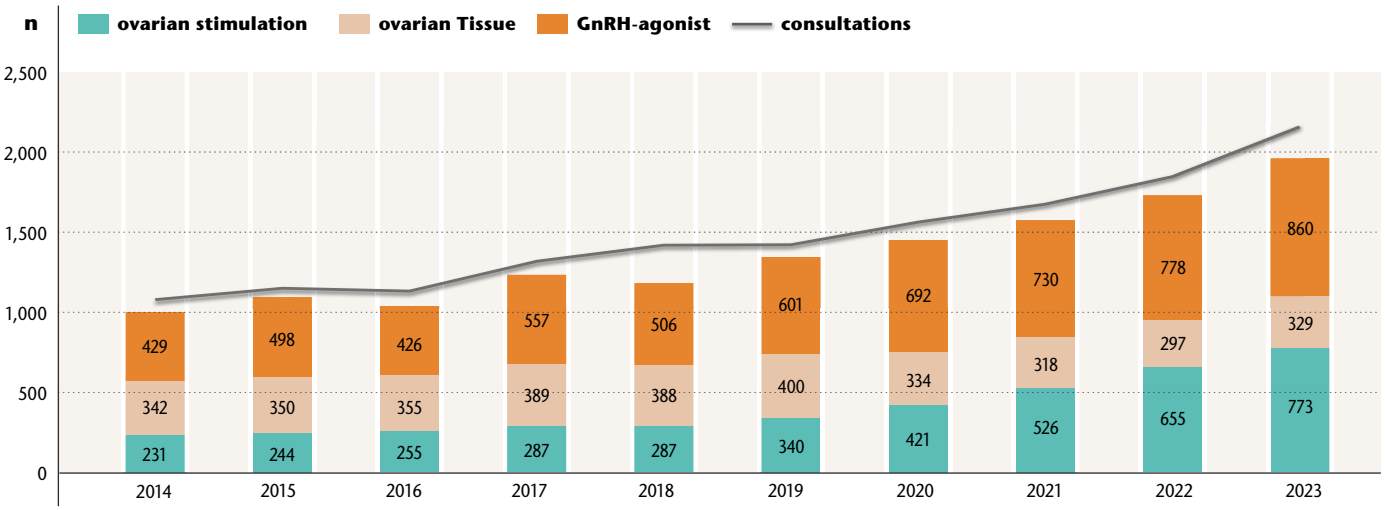


FertiPROTEKT
Netzwerk für fertilitätsprotektive Maßnahmen

The *Ferti*PROTEKT Register – Development of Fertility-Protective Measures Over the Past Decade

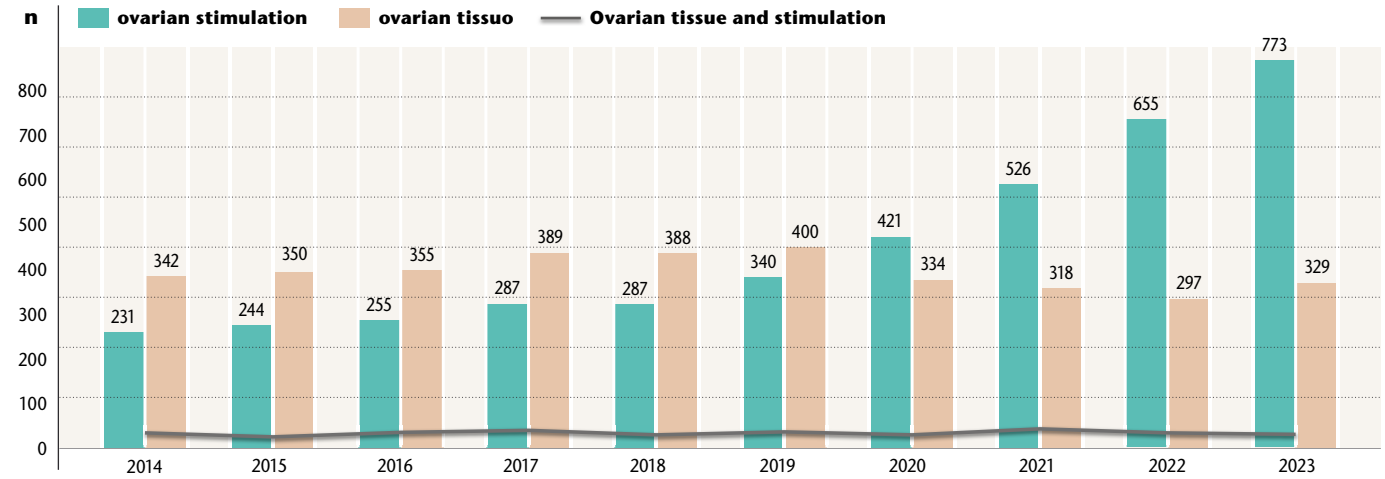
The *Ferti*PROTEKT network was founded in 2006 and registry data has been collected since 2007. A scientific data analysis of the first decade from 2007 to 2013 was published internationally in 2015 (von Wolff et al., Reprod Biomed Online, 2015, 31: 605-612). Now that the second decade (2014 to 2023) has been completed, the board of FertiPROTEKT e.V. has decided to present the data collected here.

Consultations and Interventions 2014–2023



The interventions documented in the *Ferti*PROTEKT Netzwerk e.V. show a steady increase in the number of consultations and the overall number of fertility preservation measures.

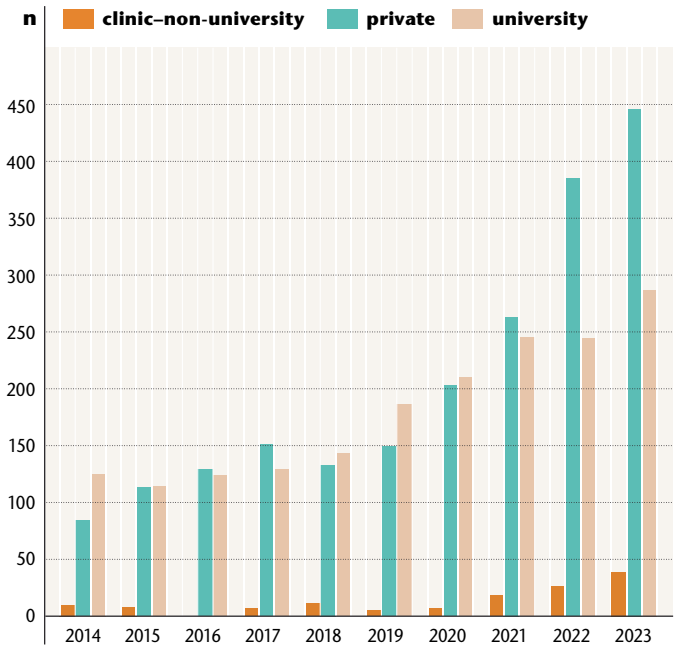
Ovarian Stimulation and Cryopreservation of Ovarian Tissue 2014–2023



The number of ovarian stimulations has increased significantly since 2019, while the number of ovarian tissue cryopreservations has decreased slightly since 2020. Combinations of both are rarely performed.

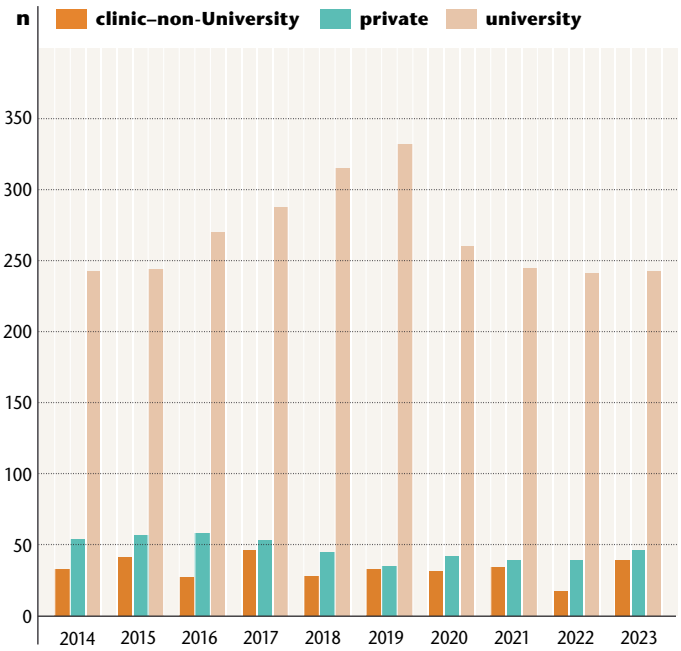
Ovarian tissue cryopreservation is mainly carried out at university hospitals (see next page) and has shown a significant decline since 2020. Possible reasons for this are, e.g. the coronavirus pandemic (2020), the publication of the first cryopreservation guideline by the responsible authorities (GBA) in 2021, which initially only took into account the cryopreservation of eggs; and the publication of the second cryopreservation guideline (2021), which allowed the invoicing of ovarian tissue cryopreservation, however, not by the university clinics that are mainly offering this method.

Ovarian Stimulation by Center Category 2014–2023



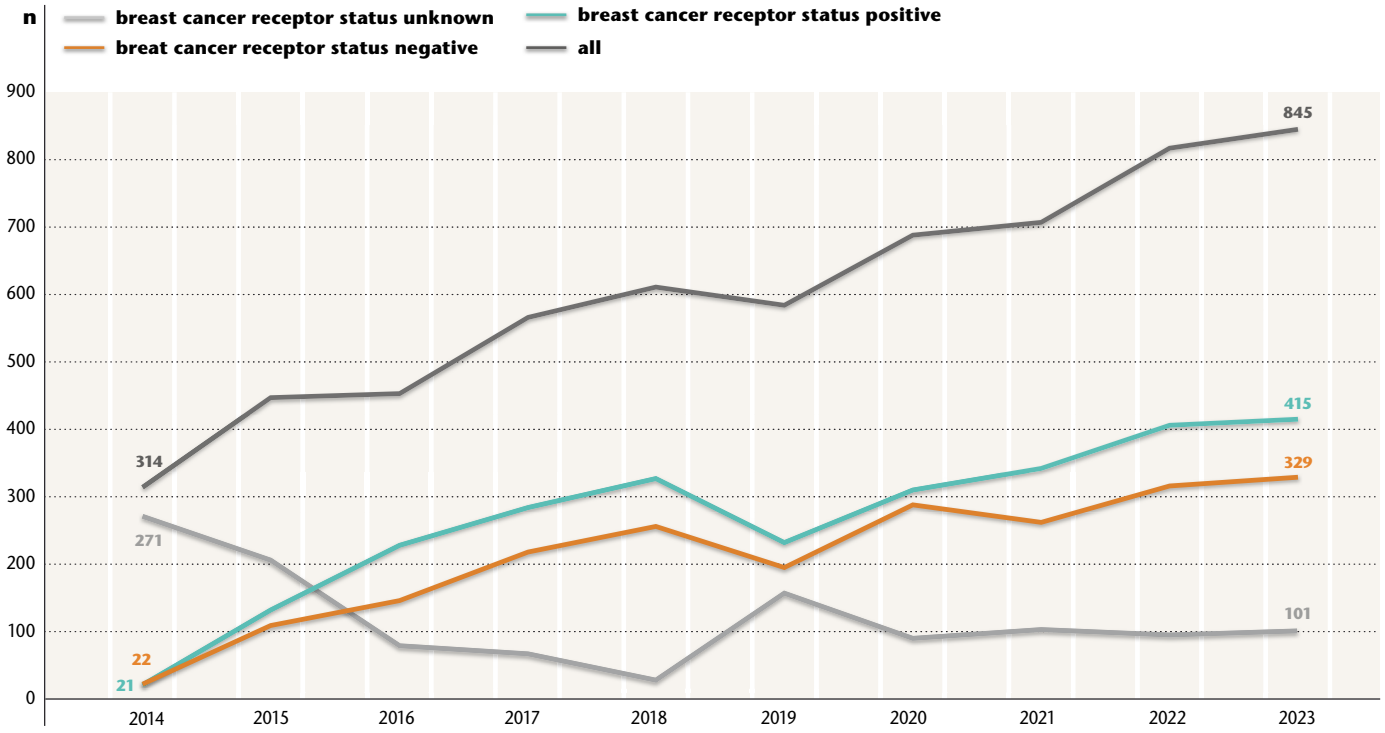
Ovarian stimulation is increasing, particularly in private centres, which is presumably due to the reimbursement policy.

Cryopreservation of Ovarian Tissue by Center Category 2014–2023



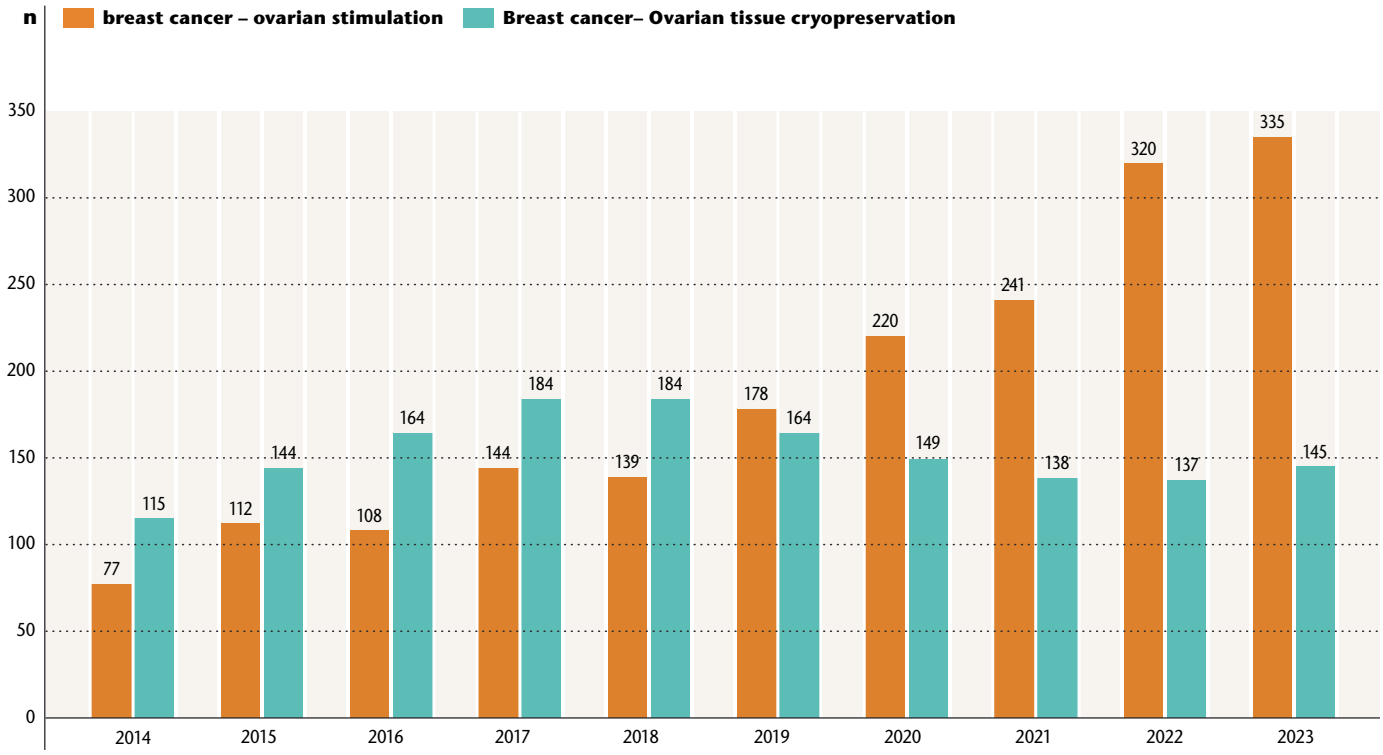
The cryopreservation of ovarian tissue is mainly carried out at university hospitals.

Consultations for Breast Cancer by Receptor Status 2014–2023



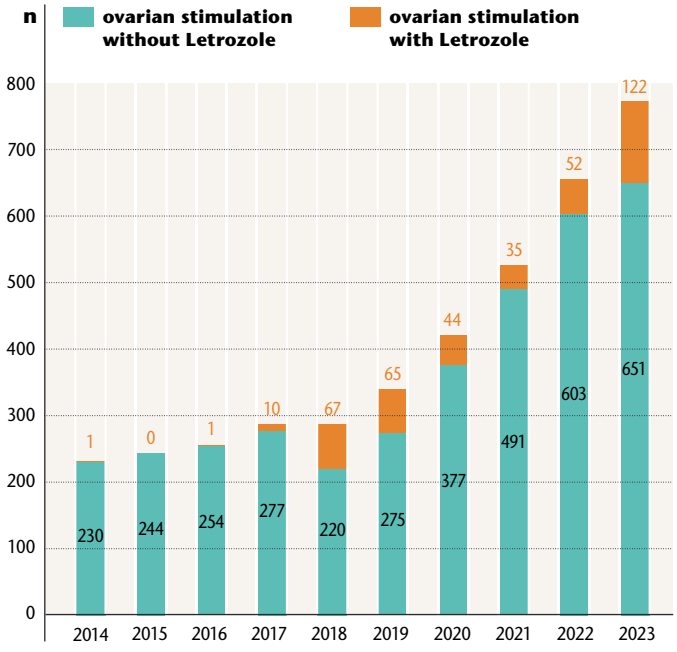
The increase in consultations for hormone receptor-positive and hormone receptor-negative breast cancer is largely the same.

Interventions for Breast Cancer 2014 – 2023



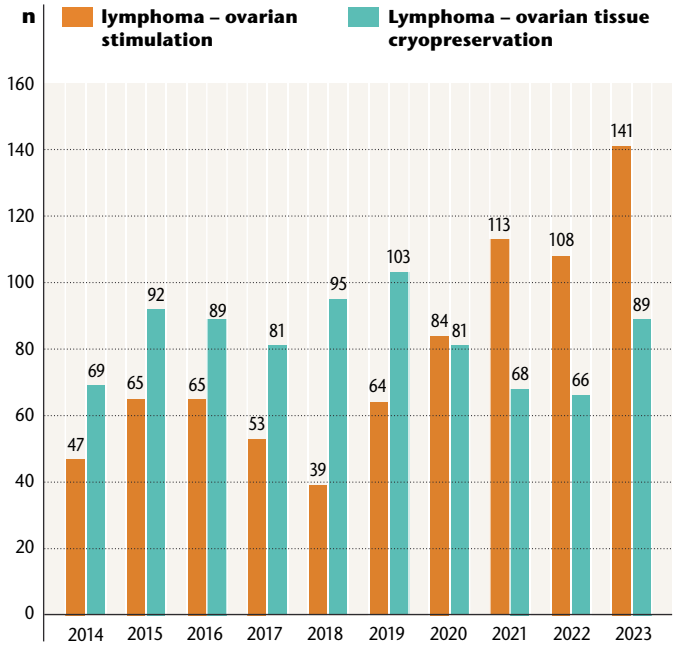
The number of ovarian stimulations has increased significantly in the recent years and now exceeds the number of cryopreservations of ovarian tissue.

Ovarian Stimulation with vs. Without Letrozole Concomitant Therapy 2014–2023



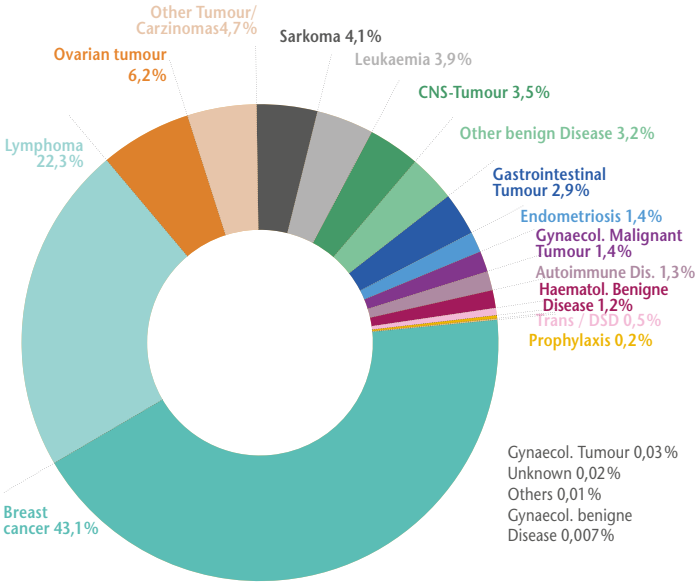
The proportion of ovarian stimulation with letrozole has increased in recent years.

Interventions for Lymphoma 2014 – 2023



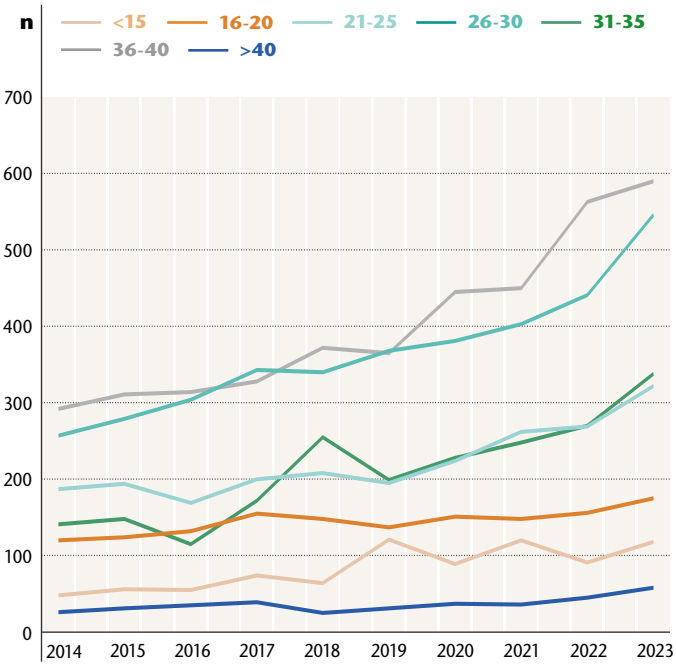
The number of ovarian stimulations has been increasing for 5 years, but cryopreservation of ovarian tissue is still frequently carried out.

Disease Spectrum at Consultation 2014–2023



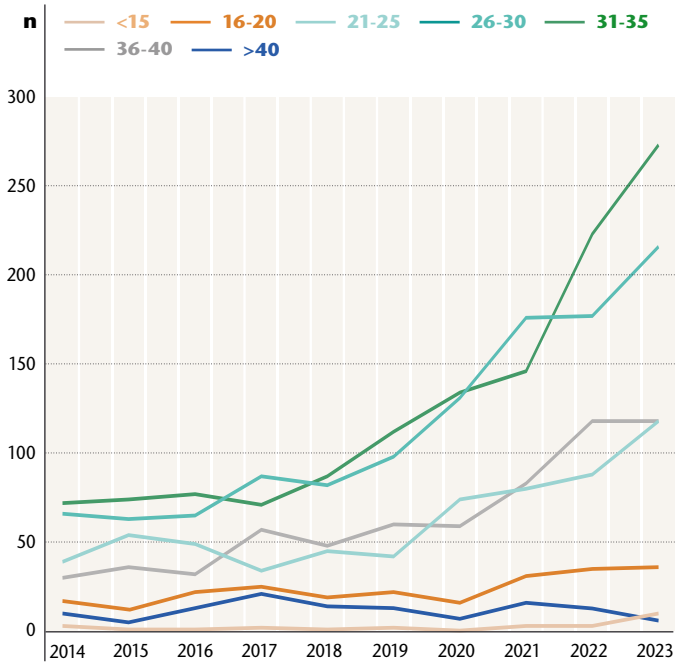
The most common underlying conditions are breast cancer and lymphomas, followed by ovarian tumors.

Consultations by Age Group 2014–2023



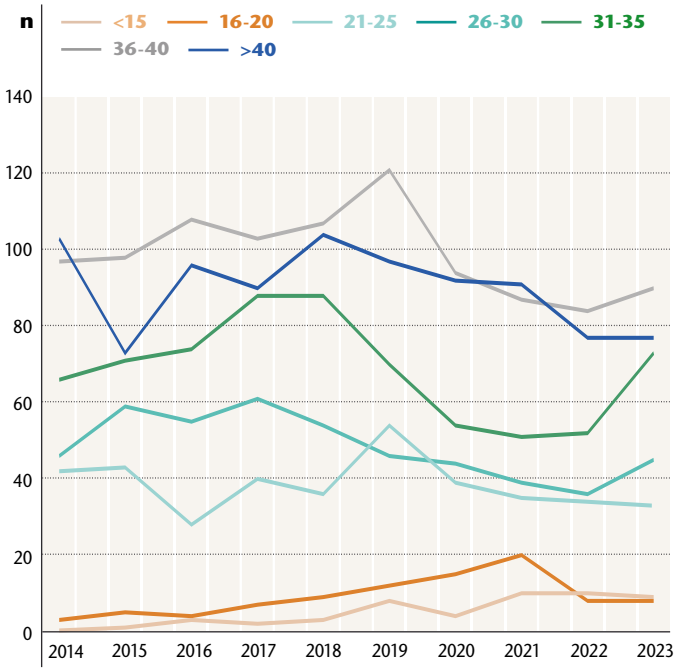
Most consultations are carried out with women aged 26-30 and 36-40. However, the number of consultations has approximately doubled in all age groups, including the very young female patients.

Ovarian Stimulation by Age Group 2014–2023



The strongest increase is seen in patients aged 26 to 35, but also in women aged 21 to 25 and 36 to 40.

Cryopreservation of Ovarian Tissue by Age Group 2014–2023



Cryopreservation of ovarian tissue shows no relevant change in the distribution between the different age groups.

DERI | Deutsches Register für Insemination

Today we are pleased to present for the second consecutive year the data we received on insemination treatments conducted and reported in Germany, both in the homologous and heterologous systems, within the framework of the German Insemination Registry (DERI).

Fortunately, the DERI has now grown to include 52 participating centres that document their treatments and submit them to DERI for evaluation.

This is a very positive development, demonstrating that an increasing number of centres in Germany, not only recognize the importance of cycle documentation for inseminations within the framework of quality assurance (alongside the long-established reporting of IVF/ICSI treatments to the D·I·R), but are also structurally capable of implementing digital documentation of insemination cycles.

The DERI registry data highlights a dramatic societal shift in the field of heterologous inseminations. Before the Sperm Donor Registry Act came into effect in 2018, nearly all treatments with donor sperm in Germany were provided to married or unmarried heterosexual couples. However, just six years later, this share has dropped to almost one-third of all treatments. Today, another third of donor sperm inseminations are performed for lesbian couples, and the remaining third for single women.

We continually receive positive feedback and grateful comments from patients and colleagues who base their treatment decisions on the transparent registry data or incorporate them into consultations.

The DERI is on a very good path, but its long-term sustainability and the quality of the data depend on each and every one of us. We, the leaders of reproductive medicine facilities, decide whether or not to participate in the DERI, whether the collected data will be comprehensive and representative, and whether the performance of our centres will be reflected on a European level or not.

Therefore, we appeal to the 92 German centres that have not yet reported any data: Please participate in the DERI!

Finally, we would like to express our special thanks to you, dear colleagues, who are already participating in the DERI and have made this data evaluation possible. We also thank Merck Healthcare for their continued financial support and Markus Kimmel for all his assistance.

If your centre would like to become part of the DERI in the future, please contact the DERI office directly at geschaeftsstelle@inseminationsregister.de (Markus Kimmel, Lise-Meitner-Str. 14, 40591 Düsseldorf) where we will be happy to provide you with the participation agreement and all necessary information.

With best regards,
The Board of AKDI with DERI: Dr. med. Andreas Hammel, Erlangen, Diplom-Psychologin, Constanze Bleichrodt, Munich, Dr. phil. Petra Thorn, Mörfelden, Dipl.-Ing. med. Biotech. Ann-Kathrin Klym, Berlin

Overview IUI-H Cycles 2018-2023 – (CoD September 2nd, 2024)

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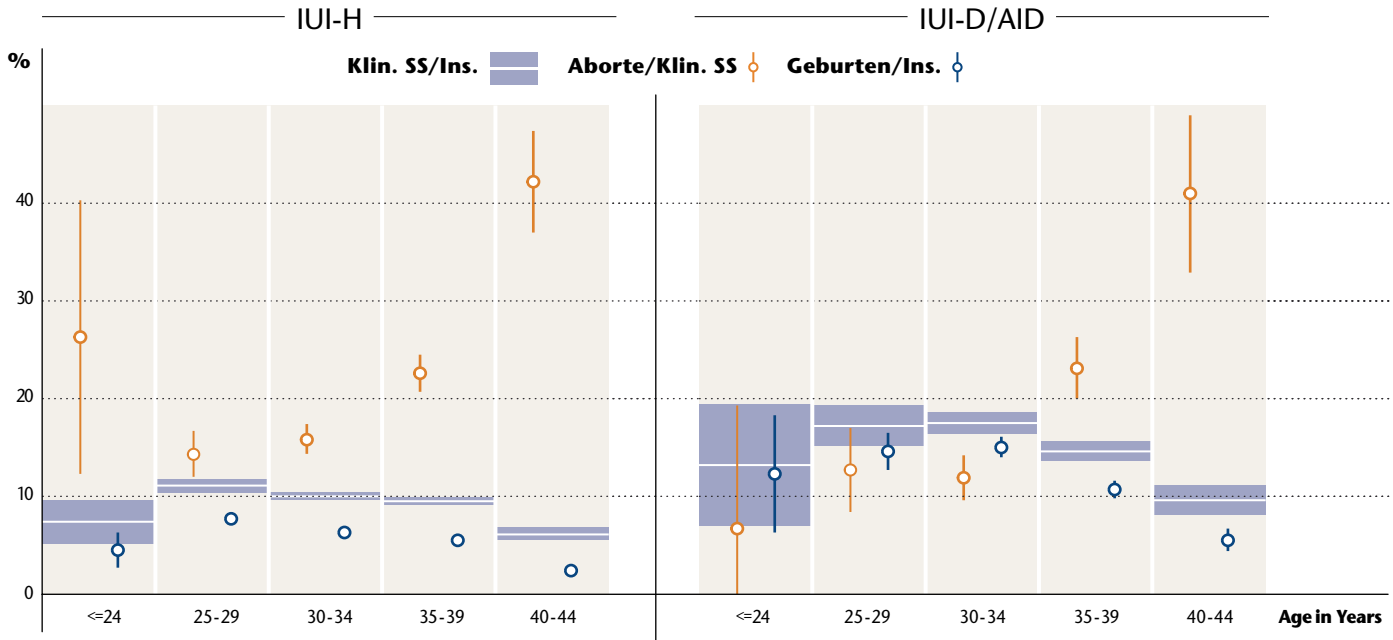
Year	2018	2019	2020	2021	2022	2023
Registry Participants IUI-H	39	40	44	45	43	47
Recorded Cycles IUI-H	11,982	12,253	13,299	14,083	14,902	15,483
Number of Patients IUI-H	5,674	5,662	5,752	5,984	6,450	6,998
Avg. Patient Age IUI-H	34.1	34.2	34.1	34.2	34.0	34.0
Inseminations IUI-H	10,512	10,617	10,663	11,561	12,593	13,721
Clinical Pregnancies IUI-H	940	977	1,035	1,088	1,229	1,360
Clin. Pregn. / Inseminations % IUI-H	9.0	9.3	9.8	9.5	9.8	10.0
Miscarriages IUI-H	182	185	210	200	266	
Miscarriages / Clin. Pregn. % IUI-H	19.4	18.9	20.3	18.4	21.6	
Births IUI-H	597	634	607	659	711	
Births / Inseminations % IUI-H	5.7	6.0	5.7	5.7	5.7	
Singletons / Births % IUI-H	92.5	93.5	94.1	95.3	95.5	
Twins / Births % IUI-H	7.0	6.0	5.8	4.6	4.4	
Number of Children IUI-H	645	678	645	691	744	

**) Adjusted by unknown outcomes*

Pregnancy Rate and Ongoing Pregnancy as a Function of Female Age 2018–2022

Plausible Cycles (CoD September 2nd, 2024)

DERI Deutsches Register für Insemination



	<=24	25-29	30-34	35-39	40-44	<=24	25-29	30-34	35-39	40-44	
n	524	7,739	22,027	19,611	5,689	116	1,331	4,477	4,823	1,508	Insem.
%	7.4	11.1	10.0	9.5	6.1	13.2	17.2	17.5	14.6	9.6	CP/Insem.
%	26.3	14.3	15.8	22.6	42.2	6.7	12.7	11.9	23.1	41.0	Misc./CP
n	23	590	1.387	1.075	133	14	194	671	514	83	Births
%	4.5	7.7	6.3	5.5	2.4	12.3	14.6	15.0	10.7	5.5	Births/ Insem.

In women aged 45 and older, 356 inseminations resulted in one pregnancy, one miscarriage, and thus no birth.

In women aged 45 and older, 91 inseminations took place, resulting in three pregnancies, two miscarriages, and one unknown pregnancy outcome.

Overview IUI-D/AID-Cycles 2017–2022 (CoD September 2nd, 2024)

DERI Deutsches Register für Insemination

Year	2018	2019	2020	2021	2022	2023
Registry Participants IUI-D/AID	35	35	43	44	44	47
Recorded Cycles IUI-D/AID	2,226	2,600	3,124	3,550	3,921	3,726
Number of Patients IUI-D/AID	950	1,040	1,231	1,429	1,645	1,675
Avg. Patient Age IUI-D/AID	34.4	34.6	34.7	34.8	34.6	34.7
Inseminations IUI-D/AID	1,971	2,241	2,485	2,677	2,972	3,025
Clinical Pregnancies IUI-D/AID	295	314	383	402	479	517
Clin. Pregn. / Inseminations % IUI-D/AID*	15.0	14.1	15.4	15.0	16.1	17.1
Miscarriages IUI-D/AID	42	64	69	72	99	
Miscarriages / Clin. Pregn. % IUI-D/AID	14.2	20.4	18.0	17.9	20.7	
Births IUI-D/AID	241	246	304	317	368	
Births / Inseminations % IUI-D/AID*	12.3	11.0	12.3	11.9	12.4	
Singletons / Births % IUI-D/AID	96.3	94.7	95.7	96.5	95.4	
Twins / Births % IUI-D/AID	3.3	5.3	4.3	2.8	4.6	
Number of Children IUI-D/AID	251	259	317	330	385	

**) Adjusted by unknown outcomes.*

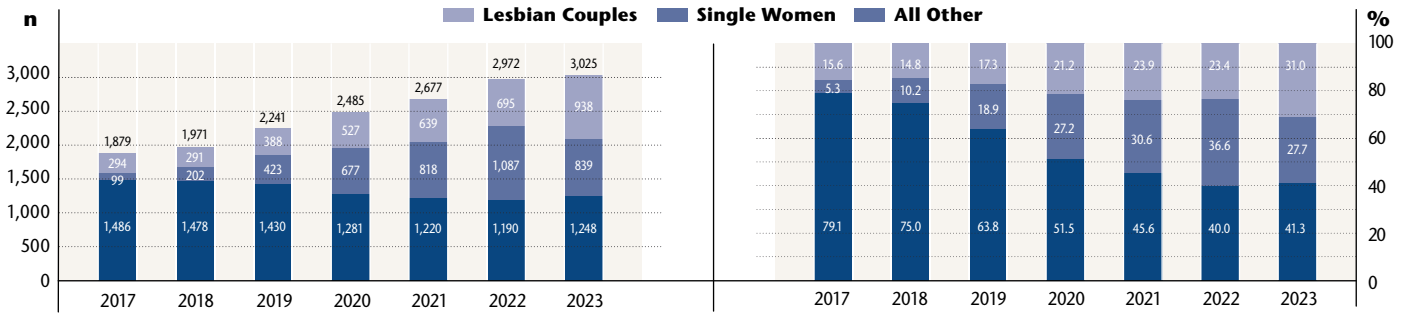
DERI Special Evaluations

DERI Deutsches Register für Insemination

IUI-D/AID: Development and Distribution of the Main Indications - Lesbian Couple, Single Woman, and All Others, 2017– 2023

Plausible Data (CoD September 2nd, 2024)

IUI-D/AID Inseminations — Number of all IUI-D/AID



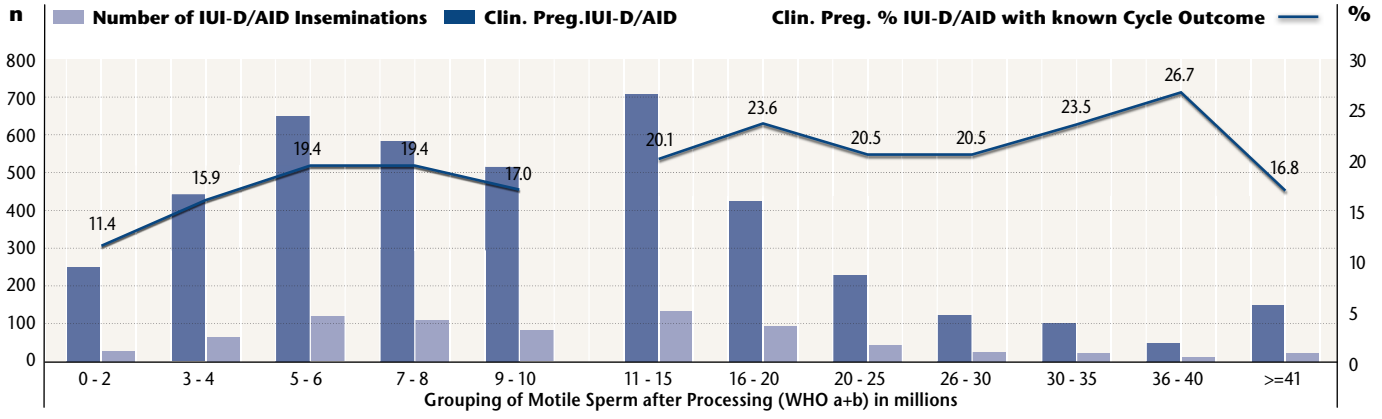
Jahre, Angaben jeweils n und %	2017	2018	2019	2020	2021	2022	2023
Number of IUI-D/AID Insem. for Lesbian Couples	294/15.6%	291/14.8%	388/17.3%	527/21.2%	639/23.9%	695/23.4%	938/31.0%
Number of IUI-D/AID Insem. for Single Women	99/5.3%	202/10.2%	423/18.9%	677/27.2%	818/30.6%	1,087/36.6%	839/27.7%
Number of all IUI-D/AID Inseminations	1,486/79.1%	1,478/75.0%	1,430/63.8%	1,281/51.5%	1,220/45.6%	1,190/40.0%	1,248/41.3%

IUI-D/AID: Pregnancy Rates 2018-2023 by Number of Motile Sperm after Processing (WHO a+b) (CoD September 2nd, 2024) – Age of Patient 25-35

DERI Deutsches Register für Insemination

Total IUI-D/AID Inseminations: 15,371
-> Subset with Indication of Number of Motile Sperm after Processing (WHO a+b): 7,253 (47.2% of all IUI-D/AID)
-> Subset and Evaluation Basis Patient Age 25-35: 4,205 (27.4% of all IUI-D/AID)

Grouping of Motile Sperm after Processing (WHO a+b)	0 - 2	3 - 4	5 - 6	7 - 8	9 - 10	11 - 15	16 - 20	20 - 25	26 - 30	30 - 35	36 - 40	>=41	Summe
Number of IUI-D/AID Insemseminations	249	442	651	583	515	708	425	230	124	102	48	149	**4,205**
Shares of IUI-D/AID Insemseminations	5.9	10.5	15.5	13.9	12.2	16.8	10.1	5.5	2.9	2.4	1.1	3.5	**100.0**
CP IUI-D/AID	27	65	119	109	82	134	95	44	24	23	12	23	**751**
CP % IUI-D/AID with known cycle outcome	11.4	15.9	19.4	19.4	17.0	20.1	23.6	20.5	20.5	23.5	26.7	16.8	**19.0**
Ø-Age of the Patient	31.6	31.8	31.8	32.1	31.6	31.6	31.9	31.7	32.3	32.0	31.1	32.1	**31.8**



The sum of the individual groups may differ from the total given because multiple entries are possible in different groups.

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