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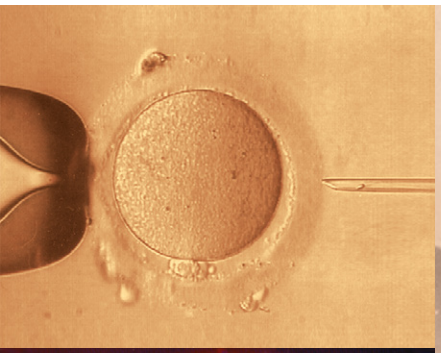

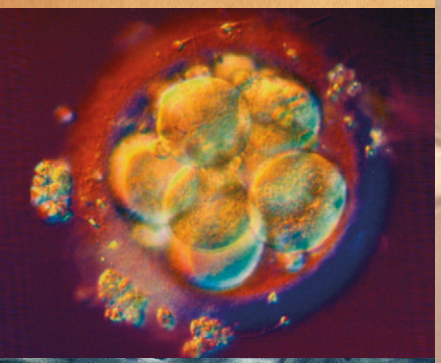

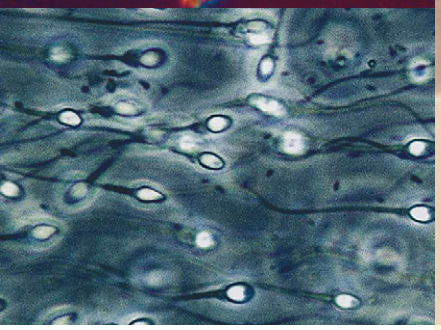

D.I.R-Annual 2011

Bühler K, Bals-Pratsch M, Blumenauer V, Dahncke W

Felberbaum R, Fiedler K, Gnoth C, Happel L, Krüssel JS

Kupka MS, Wendelken M

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Ladies and Gentlemen,
Dear Colleagues,

The German IVF-Registry is turning 30!

Not quite four years after the first birth following an IVF-treatment, in the year the first „German IVF-baby" was born, the then five active centers in Germany joined forces to document their activities in this new and in the eyes of many revolutionary field. They decided to make both their activities and their results accessible to the public. This way however, the Registry not only carried information about the results to scientists and into the interested public, it also transmitted transparency and lead to a less opaque perception of our field – showing that we are by no means secretly working on the creation of a homunculus.

Since 1996, when the results were first published in print, this annual has become a highly important resource for patients, doctors, politicians, as well as journalists. Even the highest courts of justice rely on the results to arrive at their decisions. More than 1.2 million cycles have been documented in our Registry since 1982. Since 1997 more than one million cycles have been recorded electronically – to this day unique and unsurpassed worldwide.

742 treatment cycles were reported in 1982 – in this 2011-edition, the total comes to 80,943 cycles. Yet we should bear in mind that before the introduction of the GMG (health system modernization act) 105,845 had been reported.

While in the year 1982, the average clinical pregnancy rate was 7%, in 2010 it is 29.3% after IVF or ICSI. Just for comparison: the natural conception rate in humans is between 27 to 30% – the rate after ART thus surely a clear indicator for the excellent quality reproductive medicine in Germany stands for.

Due to a variety of societal changes, the percentage of women age 35 and above undergoing IVF or ICSI has risen from 38.7% to 54.4%. Yet the great number of cases in the Registry also justifies the conclusion that in Germany, women between the age of 40 and 42 with good tubal reaction have a mean probability to achieve a pregnancy ranging from 22 to 23%.

Politically relevant is the result that there is no significant difference in the probability for achieving a pregnancy in a 6th cycle over the first three cycles for women under 35. Thus, the assumptions made in 1990 and 2003 – close to no probability at the age of 40 and no significant probability after the 3rd treatment cycle – no longer hold and politics in this country are obligated to react.

For years now, politics and politicians in this country have announced the expansion of financial support for couples suffering from fertility problems. Yet to this day, hardly any support has reached our patients. Instead, they are crushed between the various political fronts. What a disgrace for a country so desperately in need of more children! Only the federal states Saxony, Saxony-Anhalt and, starting in 2013, also Lower-Saxony have picked up on the idea and give financial support to couples, provided they have been living in the respective state and receive treatment there.

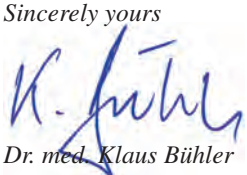
It seems wrong that location is the decisive factor for a couple's rate of co-payment.

A number of statutory health insurance companies have recently started to make use of the „GKV-Versorgungsstrukturgesetz" by offering special conditions to couples seeking fertility treatment. The resulting reduction of the 50% co-payment is highly appreciated by patients and centers alike.

We are grateful to all who, over the past 30 years, have contributed towards making the German IVF Registry into a world-wide unique and highly respected information resource and quality control instrument. Above all, our gratitude is extended to the teams in the centers for reproductive medicine. Only through their continuous, at time inevitably tedious collection of relevant data, a registry of this magnitude comes to life and is able sustain its outstanding quality. Our gratitude is also extended towards the team at the Ärztekammer Schleswig-Holstein. For the past 15 years, it has handled the registry management as well as the data evaluation in an outstanding manner.

We pay tribute to Professor F. Lehmann for founding the registry in 1982, and to its recent chairmen Professor H. Rjosk and Professor R. Felberbaum. Our recognition and thanks go to the members of the board, the advisory committee, and the board of trustees for their engagement and the spare time sacrificed to make the Registry into what it is today.

Sincerely yours



Dr. med. Klaus Bühler
Chairman

Annual 2011 – German IVF-Registry

K. Bühler, M. Bals-Pratsch,V. Blumenauer, W. Dahncke, R. Felberbaum,
K. Fiedler, C. Gnoth, L. Happel, J.-S. Krüssel, M. S. Kupka, M. Wendelken

Abstract: The German IVF-Registry (Deutsches IVF-Register, D·I·R) was established in 1982. Its main objective, from the beginning, was to lend transparency and openness to the newly established infertility treatment options.

By 1996 electronic data collection was implemented, allowing the online check for data completeness and plausibility as well as ensuring prospectivity. Since 1997, data entry has to be performed electronically. From 1998, participating in the German IVF-Registry has become mandatory by decree of the German Medical Association.

By the year 2011, the registry comprised 128 centers, with all 128 submitting their data to D·I·R: 80,934 treatment cycles were reported in 2011; 780,922 datasets are plausible, and 67,935 fulfill prospectivity. 53,076 oocyte retrievals led to an IVF or ICSI treatment, and in 48,166 of these "fresh" cycles, an embryo transfer (ET) was performed. In addition to these "fresh" cycles, 19,228 embryo transfers with cryopreserved thawed pro-nucleus-stage oocytes were recorded.

In 2011, the clinical pregnancy rate for IVF is 30.2% and for ICSI 28.3%. Generally we observe that in the data-collection-year the outcome of about 40% of all reported pregnancies is unclear. One year later this figure decreases to about 12.5–15%. From 1997 to 2011, a dramatic reduction of triplets results from the 20 % reduction of the number of embryos transferred.

More than one million cycles have been collected since the registry's establishment in 1982 and the births of 171,722 children have been reported to D·I·R since 1997. **J Reproduktionsmed Endokrinol 2012; 9 (6): 456–84.**

ART 2011 in Germany: Safe and Successful

In this 30th year after its founding, the German IVF-Registry (Deutsches IVF-Register [D·I·R]) again comprehensively publishes the data collected in the survey of reproductive treatments rendered in Germany in 2011.

A total of 49,696 women had been treated by means of extracorporeal fertilization (Assisted Reproductive Technique – ART) in 2011.

By comparison, 47,159 women had undergone this treatment in 2010.

By the year 2000, the General Directive for Assisted Reproduction ([Muster-] Richtlinie Assistierte Reproduktion) issued by the German Medical Association had been implemented Germany-wide and the participation in the D·I·R Registry was now obligatory for each center. As a consequence, the reported number of treated women dropped to 38,442. However, in 2003, just prior to the inauguration of the Health System Modernization Act ("Gesundheitssystem-Modernisierungsgesetz" [GMG]), the number had risen to 63,111. On an average, each of these women underwent 1.63 treatment cycles.

Plausibility and Prospectivity Remain High

80,943 treatment cycles were documented in the D·I·R Registry in 2011. The checks classified 97.5% as "plausible" already upon entry of the dataset. Thus, all the information requested in the D·I·R questionnaire was considered complete and seemed inherently consistent.

It goes without saying that it is impossible to verify all of the data comprehensively nor can every input error be caught by plausibility checks. Still, for the majority the inherent logic, in particular in reference to other items, can successfully be verified this way. Another key feature of the German IVF-Registry is the „prospective" data collection: a specific treatment cycle is entered into the system within the first 8 days after the treatment had been initiated. At this point, the result of the treatment is still unclear. This process of continuous and prospective data collection contributes greatly towards data quality. Moreover, the evaluation of the large number of cases allows for reliable conclusions as well as the comparison of treatment strategies.

While plausibility and prospectivity rates had declined for a few years due to the implementation of different data acquisition solutions, we see an increase to 97.5% and 86.1%, respectively, in 2011. Certainly, the recently introduced software solutions have added to this increase because they facilitate compliance with the criteria.

General Availability of ART Services

In 2011 the number of centers performing extracorporeal fertilization in Germany hast increased to 128. We of course see a concentration of centers offering these highly specialized treatments in the cities. However, the list of participants in the back of the yearbook does show that the area-wide and need-based coverage is warranted.

Number of Treatment Cycles Gradually Increases

The steady increase following the dramatic reduction in 2004 can partially be attributed to the clear increase of ICSI (intracytoplasmic sperm injection) treatments. The article on the parameters for sperm analysis (p. 458) uncovers the reasons behind this development. Looking at the European data it becomes quite obvious that the increase is by no means a specifically German trend. ICSI has very noticeably become the treatment of choice.

Correspondence: D·I·R committee's offices, c/o MRU-Consulting GbR, Torstraße 140, D-10119 Berlin, Phone 0049 303/9800 743, e-mail: d.i.r.geschaeftsstelle@mru-consulting.de, www.deutsches-ivf-register.de Contact: Monika Uszkoreit

D·I·R data management: D·I·R committee's offices, c/o Chamber of Physicians of Schleswig-Holstein, Bismarckallee 8–12, D-23795 Bad Segeberg, Phone 0049 4551/803-147, Fax 00 4551/803-180, e-mail: dir@aeksh.org

Contact: Wolfgang Dahncke, Manja Hüchstedt, Mirja Wendelken

This article is not peer reviewed.

The average pregnancy rate of 28.7% in so-called fresh-cycles (30.2%/transfer in an IVF-cycle and 28.3%/transfer in an ICSI-cycle) corresponds to the natural monthly fertility rate. Yet, we also see that cryopreservation of PN-cells followed by a thawing- and-transfer cycle has nominally as well and relatively increased considerably during the past five years. In 2006, 9,983 such cycles (≙19,9% of all cycles) were performed and in 2011 16,958 (≙ 25%).

Multiple Pregnancies Continually Decrease

The risk of bearing triplets has decreased noticeably over the years. While in 1997 an average of 2.49 (IVF) and 2.56 (ICSI) embryos had been transferred, we see a decline to 1.99 and 2.02 resp. in 2011. This decrease by approximately 20% leads to an 80% drop of triplets in all children born after ART. Comparing the number of multiple births after ART with the total number of multiples recorded by the German Federal Statistical Office shows that the reproductive fertility treatments account for 17.7% of all multiple births (2,101 of a total of 11,838).

Influence of Woman's Age Still Underestimated

For years, the age-related pregnancy and miscarriage rates have been a valuable and effective tool for the information of our patients. In our consultations we still notice a remarkable lack of knowledge about the extent of the reproductive window. Couples are still quite unaware of the continuously diminishing probability per month to achieve a pregnancy after the age of 32–33. In 1996, every third woman undergoing treatment was 35 years and older, in 2011 this applies to more than half of our female patients.

Embryo Quality the Most Crucial Factor

As might be expected, we can very clearly show again this year that the individual pregnancy probability is not only highly age-dependent. The probability also depends to a great degree on embryo quality. Up to the age of 40, transferring more than two embryos of "ideal" quality is of no advantage but on the contrary increases the risk of a higher grade multiple pregnancy – a condition to be avoided at all cost. Although under the present German legal parameters, the elective "single-embryo-transfer" is not an option, we will certainly strive for a further reduction of the rate of multiple pregnancies.

What's New – in Brief
The Bottom Line

- 1997 to 2011, a total of 172,993 children have been documented in the registry
- Averaged over all age groups, 36.1% of all embryo transfers in a conventional IVF cycle resulted in a pregnancy – intact ovarian function given
- In an ICSI cycle, in 33.6% of all transfers a pregnancy was achieved
- In a cryopreservation cycle (previously frozen and later thawed egg cells in the pronuclear stage) this probability was 19.7%
- Intact ovarian function given, the 2010 data show that for 23.7% of all embryo transfers a birth was documented
- Every second woman treated in 2011 was 35 years and older. In 1996 – only 15 years ago – this was true for merely every third woman
- The older the woman, the higher the risk of incurring a miscarriage. On the other hand, both egg cell reservoir and egg cell quality decrease with rising age.
- Total probability of pregnancy increases steadily with the number of treatment cycles and according to the number of the embryos transferred
- In comparison with previous years, the multiple birth rate was further reduced. Only 17.7% of all multiples born in Germany in 2011 can be attributed to assisted reproduction treatments (2,101 [D·I·R] of 11,838 (German Federal Office for Statistics)
- International comparison shows that in 2011, couples undergoing ART again have received treatment of outstanding quality
- The bottom line for patients:
  - Increase patients' awareness of the consequences of progressing age on the development of natural fecundity
  - Strive for good timing of the appropriate therapy
  - Don't wait too long and don't give up too soon

ART is Safe

Children born after ART show no difference in birth weight compared with non-ART children.

In 2011, serious complications during oocyte aspiration were documented in 0.27% of all treatment cases. This clearly indicates that extracorporeal fertilization is a safe method.

Quality of Data Increases Steadily

As was already pointed out earlier, the German IVF-Registry continuously performs quality verification of the reported data. Prospectivity as well as plausibility are checked when the data are first entered. However, in addition a great number of other parameters concerning the individual centers are checked: the number of first introduced and later-on deleted cycles; the ratio of cryo-thawed-cycles to the total number of fresh-cycles; cycle entry date and possibly a cluster at day 7 or 8; the normal distribution of the recorded duration of pregnancies – to name only a few.

Needless to say, the outcome quality of every center is evaluated as well. Based on close to a hundred items, an individual center profile is created and made available to the center.

In the graphic representation of the percentile curves that contain the results of all centers each center can determine its own position in relation to the others.

Decades ago already, this procedure was used in the German Perinatal Survey and proved highly reliable and effective. In case of extreme deviations, the Data-Management Department informs the Registry's board. According to the statutes, the board members are eligible to directly approach the specific center and request a statement. In addition, the IVF-commissions in the regional State Chambers of Physicians receive those

profiles, this way allowing for regional quality assurance according to the legal requirements.

This bundle of measures supports the high outcome quality in the field of reproductive medicine in Germany and allows for the continuous improvement of our Registry's impressive data quality.

♦ ♦ ♦

Indications for Reproductive Therapies in the Treatment of Male Subfertility Reconsidered

For several years, the number of ICSI-cycles in extracorporeal therapies has steadily increased and is meanwhile exceeding 75%. This trend can neither be explained by a principally better rate of fertilization, nor a higher transfer or pregnancy rate than achieved by a correctly indicated conventional IVF therapy.

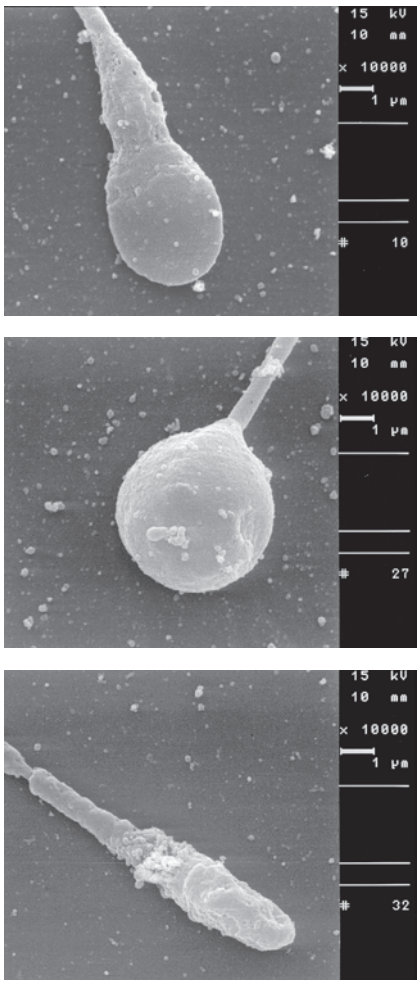
Fertilisation Failure is the Least Favorable Treatment Outcome

The data, published in the 2009 yearbook already proved that there is an impending fertilization failure of 40% in a classical IVF starting at a sperm density of < 25×10^6/ml in the native ejaculate and < 15×10^6/ml after sperm preparation and/or sperm progressive motility < 20% native and < 10% after preparation or an overall motility < 40% native and < 65% after preparation.

Fertilization failure is by far the least favorable outcome of a therapy cycle since the couple did not even incur the chance of achieving a pregnancy yet lost one of the limited number of cycles granted if insured in the German statutory health insurance system. Therefore, the incidence of fertilization failure should be avoided at all cost.

New WHO Reference Values are Insufficient Predictors for Male Fertility

The reference values recently published by the World Health Organization in the Laboratory Manual for the Examination of Processing of Human Semen (WHO 2010) have led to remarkable confusion in this country since parameters on the 5th percentile are frequently mistaken for the "standard values".



Diversity in appearance of human sperm cells (top: normal shape, center and bottom: abnormal morphology). [Reprint by courtesy of Prof. Dr. Dr. h.c. Hans Wilhelm Michelmann and Dr. Peter Schwartz, Göttingen.]

The reference values published in the 5th edition of the WHO Manual, however, do not lend themselves to the verification of an indication for reproductive treatment nor for the choice of the appropriate reproductive method since they apply to fertile men whose female partners had become pregnant spontaneously within the course of a year.

Commonly, the "normal" range for laboratory parameters is defined as the mean 95% of all values.

Beyond these limits, values for a significantly different population will be found. For sperm analysis parameters, a one-sided reference interval is much more reasonable since very high parameters will not have a negative effect on fertility. For statistical considerations, the 5th percentile was therefore defined as the lower reference value. Thus, 95% of the men who had become fathers had sperm analyses with semen volumes of > 1.5 ml, a total sperm count of > 39×10^6/ml, sperm concentration of > 15×10^6/ml, a progressive motility above 32% within an overall motility above 40%. More than 4% were normomorph. All this indicates that the reference limit drawn by the WHO Manual is for systematic-methodological reasons only. As a matter of fact, the WHO Manual explicitly states that it only very marginally touches on fertility. Moreover, in reproductive medicine sperm analyses are normally not performed for men who have only recently become fathers but rather for men in involuntarily childless couples.

Normal Sperm Parameters do not Prove Male Fertility

Arguments are provided by a prospective Dutch multicenter study on the chances of spontaneous conception in subfertile couples, lacking a relevant female sterility factor. With 3,345 subjects in the study's database, it nearly approximates the WHO collective. From an extended analysis drawn from the study we know that even with sperm concentrations above 40×10^6/ml and an ideal progressive motility of 50%, the probability to conceive spontaneously within one year is at best 65%. Despite seemingly "normal sperm analysis parameters", fertility of these men compared to proven fertile men was reduced to at least 50%.

Based on the lower limiting values of the "old" WHO 1999 (sperm concentration of 20×10^6ml, 25% forward progression), fertility is reduced to less than a quarter. Relative to the 5th percentile of the WHO 2010, the probability of reaching an ongoing stable pregnancy within one year is only 31.53%. This means that 70% of the couples with women not showing a relevant fertility-related factor will not get pregnant for another year. The rate for spontaneous conception per cycle is a mere 3.11%. Fertility of these men is reduced to less than 1/8th of the normal rate.

Duration of Subfertility as Indicator for ART

Sperm analysis thus discloses the degree of fertility reduction in men in subfertile partnerships but lacking a relevant female sterility factor. Since in this collective even "ideal values" do not exclude

the possibility of male subfertility, indication for reproductive treatment is given and can therefore be deducted from the mere duration of involuntary childlessness. The choice of treatment then depends on the results of the sperm preparation and forward progression count. This way, and only this way, the risk of incurring a complete or incomplete fertilization failure can be reduced to a minimum. As can be seen from the current as well as past yearbooks, German IVF-centers have been exemplary in doing so.

References: Please inquire relevant references with the office of the D·I·R Registry.

♦ ♦ ♦

IVF-Labs – Where are we Headed

What the future in our IVF-labs might hold in store for us can be viewed from various angles: what will be new in the future but also where we are headed!

Let Us First Dwell on the Past

Recent introductions into our labs include: new culture media, especially for day-5-culture, optimized techniques for the vitrification of oocytes and embryos, smaller incubators and reduced oxygen atmosphere, quality management leading to certified and accredited labs. Here and there pregnancy rates might have increased due to these innovations – the big breakthrough, however, was not among them.

If future development is seen under the aspect of success rates, then the major benefit – from the patients' point of view – will certainly lie in the improvement of lab quality in centers with low success rates. In the context of global success rates of 20–25% per treatment cycle we need to acknowledge that according to the 2010 D·I·R figures, 40 of the 100 largest IVF-centers – after all – display a pregnancy rate per transfer of under 25%. A fact that cannot be neglected since new lab techniques and sophisticated procedures do require a certain quality level in order to allow for their integration into the routine and result in the expected added gain.

Morphokinetics Increasingly Important

The challenge of identifying those embryos with the highest implantation potential in a treatment cycle is still top of the list of all future aspects. In the years to come, morphokinetics, i. e. the morphological assessment of embryos over time, will play an increasingly dominant role. If supplemented with simple and physiologically significant diagnostic methods – apart from array-CGH mainly with improved metabolomic concepts – and in combination with vitrification, the elective "single embryo transfer" will inevitably prevail, thus leading to a further reduction of the rate of multiples.

Economics Enters the IVF-Lab

The future in and of the IVF-Labs however will also be determined by economic aspects. Internationally, lab conglomerates have been entering the scene and the acquisition of IVF-centers by investors is by no means something new. Inevitably this development will lead to new concepts: central IVF-laboratories and the standardized critical evaluation and selection of the embryos to be transferred via electronic communication systems will enter our every day lives.

Many interesting challenges lie ahead, challenges that require a certain openness to change as well as reconsideration of traditional approaches.

♦ ♦ ♦

Acknowledgements

Our sincere gratitude goes to Prof. Dr. rer. nat. Markus Montag, Heidelberg, for his invited article "IVF-Labs – Where are we Headed". We thank Monika Uszkoreit for her translation of the German texts into English.

Outcome of ART 2011

centers for IVF-, ICSI- and cryo-transfer treatments

Participating IVF centers	n = 128
Data received until deadline (August 21, 2012)	n = 128
Documented treatment cycles	n = 80,943 (100.00 %)
Plausibel	n = 78,922 (97.50 %)
Prospective (all cycles)	n = 67,935 (86.08 %)
Prospective (IVF, ICSI, IVF/ICSI)	n = 45,078 (84.93 %)
Number of treated women*	n = 49,696
Treatment cycles per women (mean)	1.63

*) Base quantity: all women with specified age; implausible treatment cycles are also included.

Number of IVF centers 1982 - 2011

for IVF-, ICSI- and cryo-transfer treatments

	1982	1986	1990	1994	1996	1998	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
IVF	5	28	53	66	66	86	100	107	112	114	118	117	120	118	117	119	121	124
ICSI	0	0	0	32	59	85	98	108	112	116	120	117	120	118	120	119	124	128
Cryo	0	0	0	19	35	63	77	95	97	101	112	109	109	112	112	117	120	125
Total					71	86	102	108	112	116	120	117	121	118	120	121	124	128

*) Electronic data processing in D.I.R was implemented in 1996, therefore no data is available for the previous years.

Number of treatment cycles 1982 - 2011 (plausible cycles)

IVF, ICSI, IVF/ICSI, cryo-transfer

	1982	1986	1990	1994	1998	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
IVF	742	3,806	7,343	16,175	16,763	28,945	28,506	23,936	28,058	11,848	11,098	11,082	11,362	11,264	11,585	11,278	11,341
ICSI				5,856	23,578	15,752	24,897	37,692	51,389	25,339	25,532	28,015	31,452	34,333	36,712	38,320	40,641
IVF/ICS					424	790	695	678	987	446	590	672	798	834	873	985	1,094
Cryo				499	4,616	9,457	12,195	14,923	14,265	16,883	14,471	14,926	16,566	17,646	17,866	18,939	19,228
none *					67	6,562	7,507	9,802	11,133	4,928	4,539	4,600	5,137	5,825	5,946	6,404	6,618
Total**	742	4,201	8,653	23,684	45,459	61,531	73,819	87,044	105,854	59,448	56,232	59,295	65,316	69,902	72,984	75,928	78,922

Since 1999 all started treatment cycles are documented.
*) No treatment: aborted treatments before oocyte culture.
**) The value 'total' includes very few cases of GIFT. They are omitted due to their steady decrease.

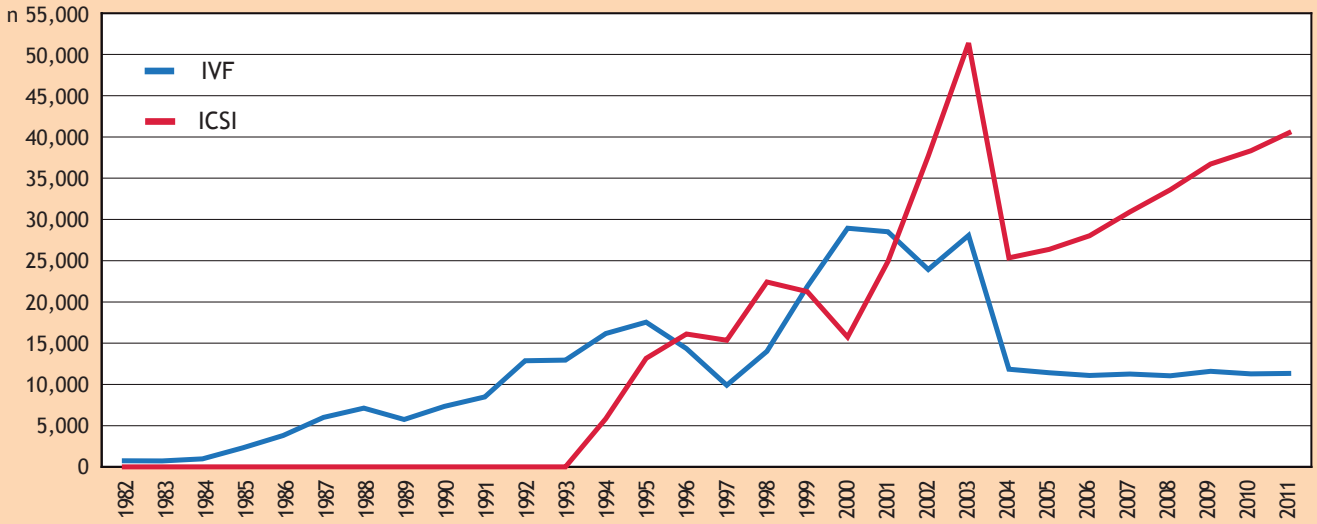
Number of treatment cycles 2011 (prospective cycles)

IVF, ICSI, IVF/ICSI, cryo-transfer

	IVF	ICSI	IVF/ICSI	Cryo-transfer	No treatment	Total
n	9,524	34,637	917	16,958	5,899	67,935
%	14.02	50.99	1.35	24.96	8.68	100.00

Number of cycles with ovum pick-up (OPU) 2011

IVF, ICSI*



	1982	1986	1990	1996	1998	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
IVF	742	3,806	7,343	14,344	14,024	28,945	28,506	23,936	28,058	11,848	11,410	11,082	11,362	11,048	11,585	11,278	11,341
ICSI				16,108	22,420	15,752	24,897	37,692	51,389	25,339	26,370	28,015	31,452	33,591	36,712	38,320	40,641
Total**	742	3,806	7,343	30,452	37,933	45,487	54,098	62,306	80,434	37,633	38,382	39,769	43,612	45,461	49,170	50,583	53,076

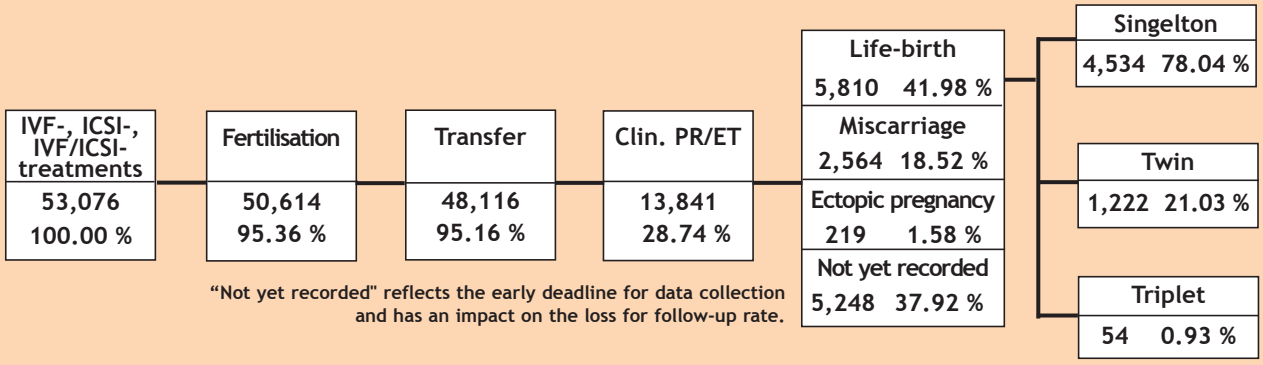
*) OPU with IVF- or ICSI-oocyte culture.

**) The value for IVF/ICSI is enclosed in "total", for instance in 2011: 1,094 OPU.

Prospectively and retrospectively collected data were used.

Statistics in short 2011 for IVF, ICSI and IVF/ICSI

German IVF Registry, status: August 21, 2012



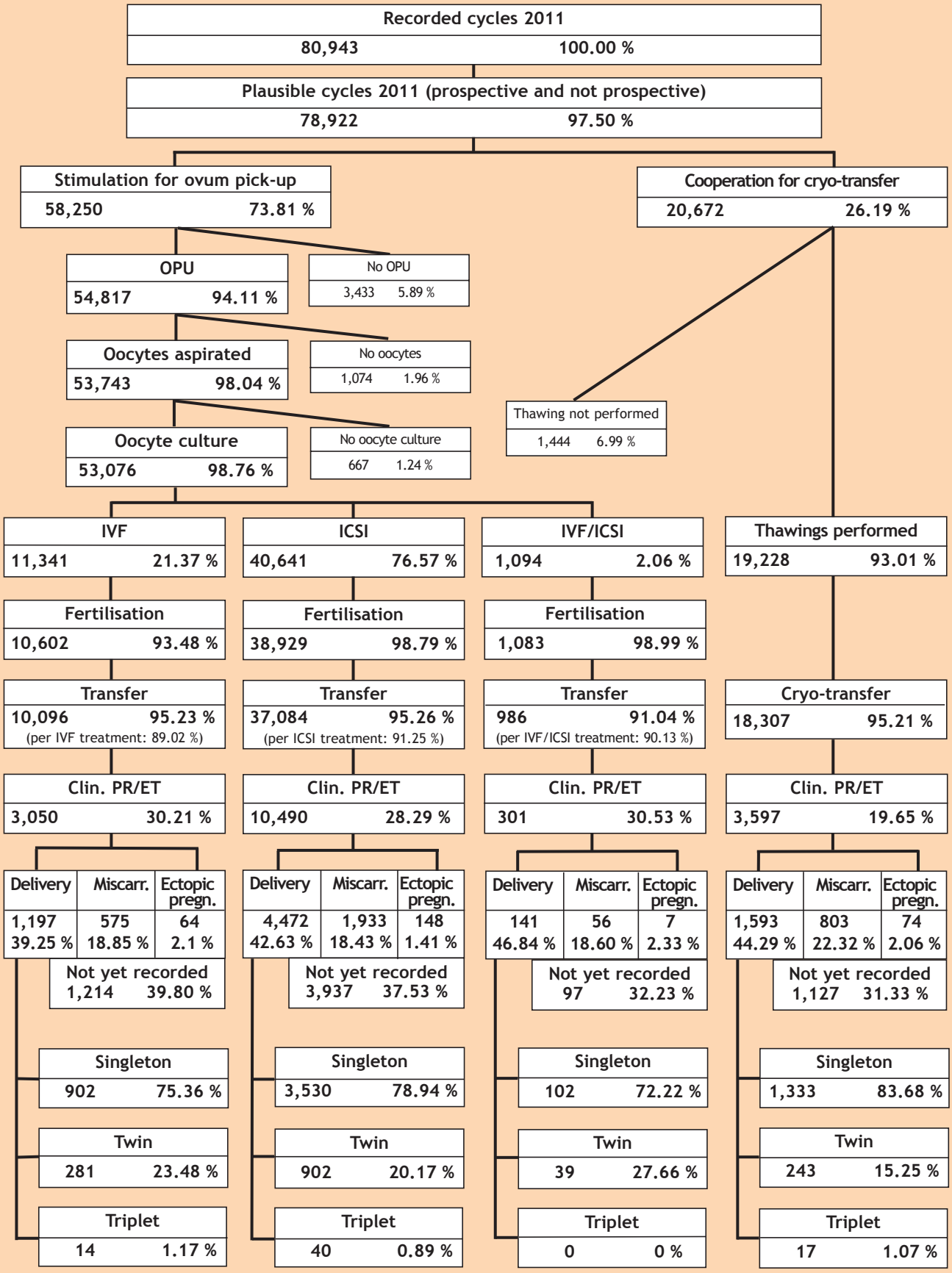
"Not yet recorded" reflects the early deadline for data collection and has an impact on the loss for follow-up rate.

Prospectively and retrospectively collected data were used.

D.I.R. statistics in short 2011

German IVF Registry

status: August 21, 2012



D.I.R. statistics in short 2010 (update to annual 2010)

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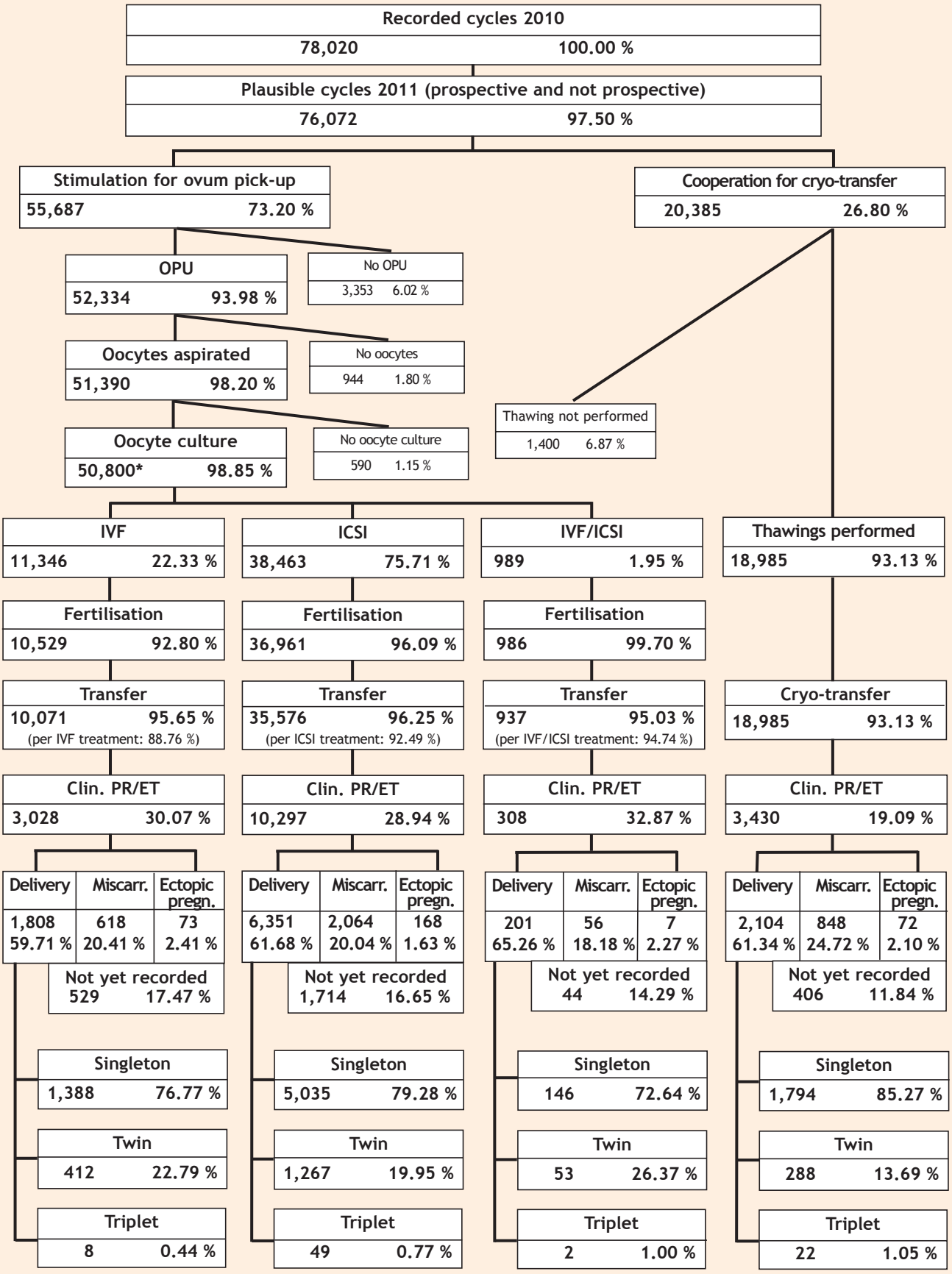


*) 2 GIFT-cases are enclosed

Clinical pregnancies, miscarriages, ectopic pregnancies and still births 2010

2010	IVF		ICSI		IVF/ICSI		Cryo-transfer	
	n	%	n	%	n	%	n	%
Treatment cycles	11,346		38,463		989		18,985	
Clin. pregnancies	3,028	100.00	10,297	100.00	308	100.00	3,430	100.00
not aviable (n. a.)	529	17.47	1,714	16.65	44	14.29	406	11.84
Deliveries	1,808	59.71	6,351	61.68	201	65.26	2,104	61.34
Miscarriages	618	20.41	2,064	20.04	56	18.18	848	24.72
Induced abortions and fetal reductions*	36 (39)	1.19	129 (161)	1.25	4 (5)	1.30	35 (40)	1.02
Ectopic pregnancies	73	2.41	168	1.63	44	14.29	72	2.10
Children	2,328		7,908		268		2,520	
Dead newborns **	26	1.12	69	0.87	3	1.12	16	0.63
Malformations	15	0.64	73	0.92	3	1.12	18	0.71
Baby-take-home rate ***		15.94		16.52		20.34		11.09
		16.72[1]		17.30[1]		21.27[1]		11.23[1]
		17.73[2]		19.19[2]		23.97[2]		12.61[2]

Prospectively and retrospectively collected data were used.

*) Number of cycles, in which an induced abortion/fetal reduction was documented. Detailed data cannot be given. Number of embryos are given in brackets.

**) Number of dead newborns corresponding to the number of children

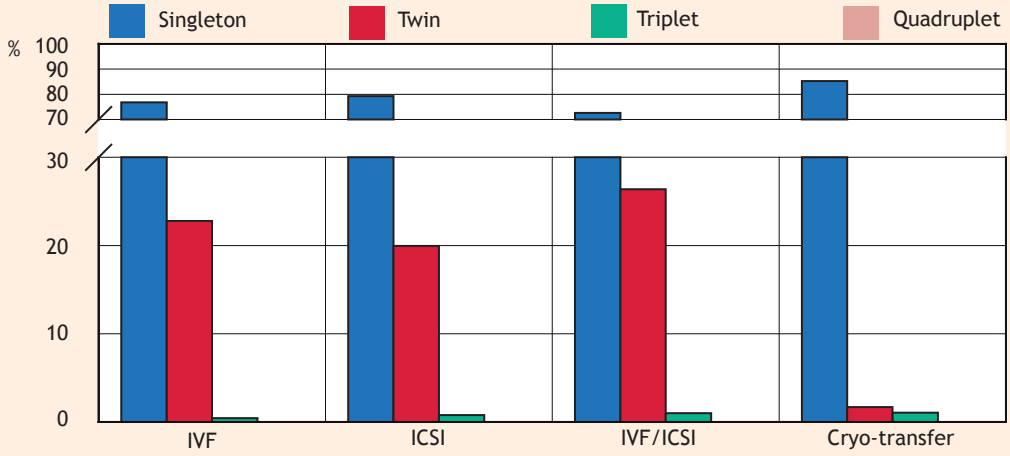
***) Number of deliveries in correlation to the number of treated cycles given in percent.

1) Total number of treatment cycles reduced for those cycles with unknown pregnancy outcome.

2) For cycles with unknown pregnancy outcome the probable rate for deliveries was calculated (delivery per pregnancy) and added to the reported number of deliveries.

Delivery rate/transfer for patients with 2 embryos transferred and at least 2 2PN stages in abundance: IVF 23.30 %, ICSI 23.81 %, IVF/ICSI 24.87 %

Multiple deliveries 2010



Prospectively and retrospectively collected data were used.

	IVF			ICSI			IVF/ICSI			Cryo-transfer		
	n	%	%	n	%	%	n	%	%	n	%	%
Clin. PR/ET	3,028	100.00		10,297	100.00		308	100.00		3,430	100.00	
Deliveries	1,808	59.71	100.00	6,351	61.68	100.00	201	65.26	100.00	2,104	61.34	100.00
Singleton	1,388	45.84	76.77	5,035	48.90	79.28	146	47.40	72.64	1,784	52.01	85.27
Twin	412	13.61	22.79	1,267	12.30	19.95	53	17.21	26.37	288	8.40	1.69
Triplet	8	0.26	0.44	49	0.48	0.77	2	0.65	1.00	22	0.64	1.05
Quadruplet	-	-	-	-	-	-	-	-	-	-	-	-
n. a.	529	17.47		1,714	16.64		44	14.29		406	11.84	
Miscarriages	618	20.41		2,064	20.04		56	18.18		848	24.72	
Ectopic Pregn.	73	2.41		168	1.63		7	2.27		72	2.10	

Deliveries as a function of the number of embryos transferred and age groups 2000 - 2010 - IVF, ICSI, IVF/ICSI, cryo-transfer

Age of woman		Singleton		Twin		Triplet		Quadruplet		Total
		n	%	n	%	n	%	n	%	n
Up to 24 years	1 embryo	119	100.00	0	-	0	-	0	-	119
	2 embryos	1,517	77.20	440	22.39	8	0.41	0	-	1,965
	3 embryos	269	68.45	103	26.21	19	4.83	2	0.51	393
	Total	1,905	76.91	543	21.92	27	1.09	2	0.08	2,477
25 - 29 years	1 embryo	1,041	98.30	18	1.70	0	-	0	-	1,059
	2 embryos	13,737	75.92	4,282	23.67	73	0.40	2	0.01	18,094
	3 embryos	2,543	69.03	934	25.35	204	5.54	3	0.08	3,684
	Total	17,321	75.85	5,234	22.92	277	1.21	5	0.02	22,837
30 - 34 years	1 embryo	2,427	98.14	46	1.86	0	-	0	-	2,473
	2 embryos	27,481	77.87	7,667	21.73	141	0.40	1	0.00	35,290
	3 embryos	7,098	70.92	2,508	25.06	396	3.96	6	0.06	10,008
	Total	37,006	77.47	10,221	21.40	537	1.12	7	0.01	47,771
35 - 39 years	1 embryo	2,574	98.24	46	1.76	0	-	0	-	2,620
	2 embryos	19,654	83.64	3,788	16.12	55	0.23	1	0.00	23,498
	3 embryos	9,443	76.83	2,577	20.97	268	2.18	2	-	12,290
	Total	31,671	82.46	6,411	16.69	323	0.84	3	0.01	38,408
40 and older	1 embryo	442	98.44	7	1.56	0	-	0	-	449
	2 embryos	2,032	92.15	169	7.66	3	0.14	1	0.05	2,205
	3 embryos	2,148	87.21	305	12.38	10	0.41	0	-	2,463
	Total	4,622	90.33	481	9.40	13	0.25	1	0.02	5,117

Total number of deliveries 2000 - 2010: 116,610

Prospectively and retrospectively collected data were used.

Deliveries as a function of the number of embryos transferred 2000 - 2010 - IVF, ICSI, cryo-transfer

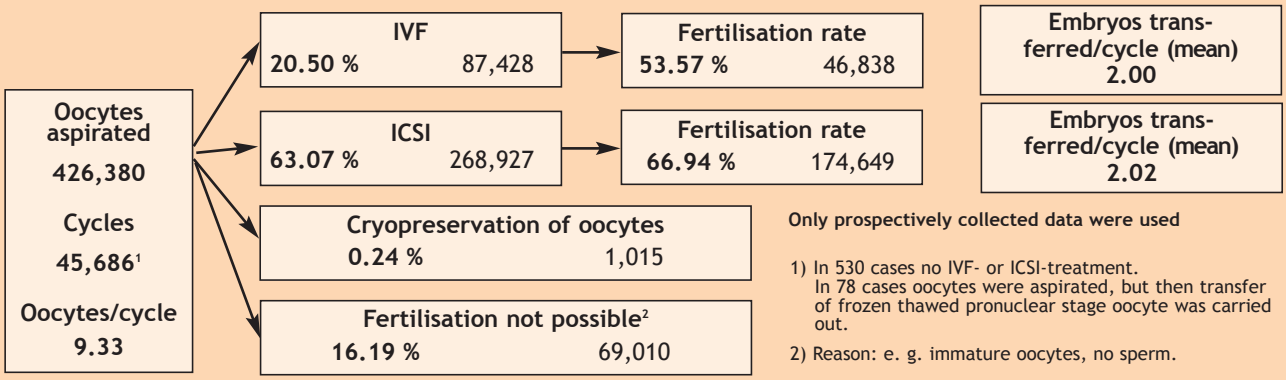
IVF	Singleton		Twin		Triplet		Quadruplet		Total
	n	%	n	%	n	%	n	%	n
1 embryo	1,724	98.51	26	1.49	0	-	0	-	1,750
2 embryos	16,223	76.56	4,888	23.07	78	0.37	1	0.00	21,190
3 embryos	5,588	71.12	1,916	24.39	347	4.42	6	0.08	7,857
Total	23,535	76.42	6,830	22.18	425	1.38	7	0.02	30,797

ICSI	Singleton		Twin		Triplet		Quadruplet		Total
	n	%	n	%	n	%	n	%	n
1 embryo	3,206	98.56	47	1.44	0	-	0	-	3,253
2 embryos	37,034	79.21	9,558	20.44	157	0.34	3	0.01	46,752
3 embryos	11,174	74.59	3,354	22.39	446	298	6	0.04	14,980
Total	51,414	79.12	12,959	19.94	603	0.93	9	0.01	64,985

Cryo-transfer	Singleton		Twin		Triplet		Quadruplet		Total
	n	%	n	%	n	%	n	%	n
1 embryo	1,609	97.52	41	2.48	0	-	0	-	1,650
2 embryos	10,136	86.19	1,584	13.47	40	0.34	0	-	11,760
3 embryos	4,491	79.26	1,077	19.01	97	1.71	1	0.02	5,666
Total	16,236	85.11	2.702	14.16	137	0.72	1	0.01	19,076

Prospectively and retrospectively collected data were used.

Fertilisation rate IVF and ICSI 2011



Only prospectively collected data were used

1) In 530 cases no IVF- or ICSI-treatment.
In 78 cases oocytes were aspirated, but then transfer of frozen thawed pronuclear stage oocyte was carried out.

2) Reason: e. g. immature oocytes, no sperm.

Embryos transferred/cycle (mean*) and children IVF, ICSI 1997 - 2011

(prospective and non-prospective data)

		1997	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
IVF	Embryos transf.	2.49	2.29	2.25	2.19	2.17	2.15	2.11	2.08	2.06	2.06	2.03	2.01	1.99
	Children/transfer	0.21	0.23	0.24	0.22	0.23	0.23	0.24	0.25	0.25	0.24	0.24	0.22	0.15
	Children/delivery	1.31	1.28	1.27	1.26	1.26	1.25	1.23	1.23	1.24	1.24	1.22	1.24	1.26
ICSI	Embryos transf.	2.56	2.39	2.30	2.21	2.17	2.15	2.11	2.09	2.08	2.08	2.06	2.05	2.02
	Children/transfer	0.22	0.23	0.24	0.22	0.23	0.23	0.24	0.24	0.24	0.23	0.23	0.22	0.15
	Children/delivery	1.29	1.26	1.23	1.23	1.23	1.22	1.22	1.20	1.21	1.22	1.21	1.21	1.22
Cryo-trans-fer	Embryos transf.	2.34	2.25	2.20	2.14	2.12	2.14	2.10	2.10	2.07	2.07	2.05	2.04	2.02
	Children/transfer	0.10	0.12	0.12	0.12	0.12	0.12	0.14	0.14	0.14	0.14	0.14	0.14	0.10
	Children/delivery	1.14	1.16	1.16	1.16	1.16	1.17	1.16	1.16	1.16	1.15	1.16	1.16	1.18

Distribution of indications for IVF and ICSI 2011

IVF

Female factor \ Male factor	Normal	%	Reduced semen quality	%	Other**	%	Total	%
Normal	978	10.27	708	7.43	568	5.96	2,254	23.67
Tubal infertility	1,407	14.77	486	5.10	447	4.69	2,340	24.57
Endometriosis	455	4.78	242	2.54	222	2.33	919	9.65
Hyperandrogenism	202	2.12	110	1.15	106	1.11	418	4.39
Ovulatory dysfunction	362	3.80	206	2.16	176	1.85	744	7.81
Psychological impact	8	0.08	1	0.01	1	0.01	10	0.10
Other*	605	6.35	536	5.63	940	9.87	2,081	21.85
n. a.	27	0.28	8	0.08	723	7.59	758	7.96
Total	4,044	42.46	2,297	24.12	3,183	33.42	9,524	100.00

ICSI

Female factor \ Male factor	Normal	%	Red. semen quality	%	Azoo-spermia	%	Other**	%	Total	%
Normal	627	1.81	10,082	29.11	869	2.51	2,713	7.83	14,291	41.26
Tubal infertility	483	1.39	1,717	4.96	49	0.14	547	1.58	2,796	8.07
Endometriosis	209	0.60	1,296	3.74	55	0.16	557	1.61	2,117	6.11
Hyperandrogenism	102	0.29	1,164	3.36	52	0.15	347	1.00	1,665	4.81
Ovulatory dysfunction	179	0.52	1,838	5.31	87	0.25	379	1.09	2,483	7.17
Psychological impact	1	0.00	21	0.06	2	0.01	15	0.04	39	0.11
Other*	483	1.39	4,594	13.26	270	0.78	3,105	8.96	8,452	24.40
n. a.	19	0.05	144	0.42	34	0.10	2,597	7.50	2,794	8.07
Total	2,103	63.07	20,856	60.21	1,418	4.09	10,260	29.62	34,637	100.00

*) Infertility factors “sperm antibodies” and “cervical factor” are enclosed.
**) Infertility factor “impaired sperm function” and “impaired sperm-mucus-interaction” are enclosed.

Only prospectively collected data were used.

Outcome of IVF, ICSI and cryo-transfer 2011

prospective cycles

IVF 2011

	n	%	Fertilis. %	Embryo present %	Transfer %	Clin. preg. %
IVF	9,524	100.00				
Successful fertilisation*	8,904	93.49	100.00			
At least one embryo present	8,472	88.95	95.15	100.00		
Performed ET	8,470	88.93	95.13	99.98	100.00	
Clin. pregnancy	2,582	27.11	29.00	30.48	**30.48**	100.00
Delivery	1,027					39.78
Miscarriage	485					18.78
Ectopic pregnancy	58					2.25
n. a.	1,012					39.19

ICSI 2011

	n	%	Fertilis. %	Embryo present %	Transfer %	Clin. preg. %
ICSI	34,637	100.00				
Successful fertilisation*	33,170	95.76	100.00			
At least one embryo present	31,560	91.12	95.15	100.00		
Performed ET	31,551	91.09	95.12	99.97	100.00	
Clin. pregnancy	8,937	25.87	26.94	28.32	**28.33**	100.00
Delivery	3,877					43.38
Miscarriage	1,681					18.81
Ectopic pregnancy	125					1.40
n. a.	3,254					36.41

ICSI 2011 - sperm retrieval by TESE or cryo-TESE

	n	%	Fertilis. %	Embryo present %	Transfer %	Clin. preg. %
ICSI	2,143	100.00				
Successful fertilisation*	1,971	91.97	100.00			
At least one embryo present	1,866	87.07	94.67	100.00		
Performed ET	1,866	87.07	94.67	100.00	100.00	
Clin. pregnancy	449	20.95	22.78	24.06	**24.06**	100.00
Delivery	182					40.53
Miscarriage	94					20.94
Ectopic pregnancy	2					0.45
n. a.	171					38.08

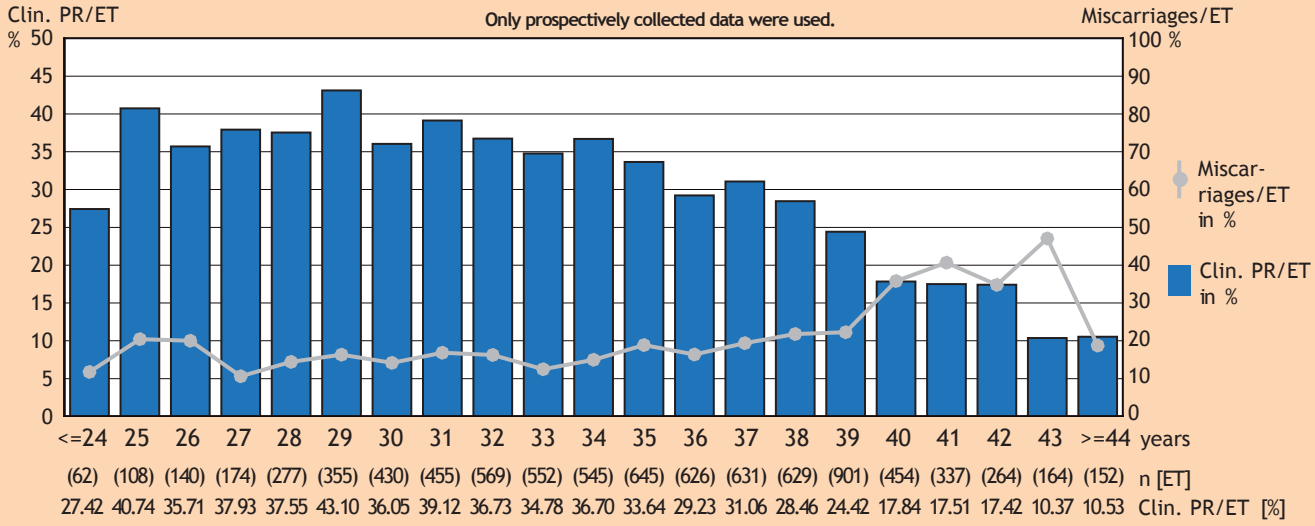
ET from cryo-preserved 2PN 2011

	n	%	PN %	Transfer %	Clin. preg. %
Thawing cycles	16,958	100.00			
Thawed PN present	15,843	93.42	100.00		
Performed ET	15,581	91.88	98.35	100.00	
Clin. pregnancy	3,105	18.31	19.60	**19.93**	100.00
Delivery	1,385				44.61
Miscarriage	702				22.61
Ectopic pregnancy	65				2.09
n. a.	953				30.69

*) Successful fertilisation of at least one oocyte per cycle.

Outcome as a function of woman's age

IVF - 2011

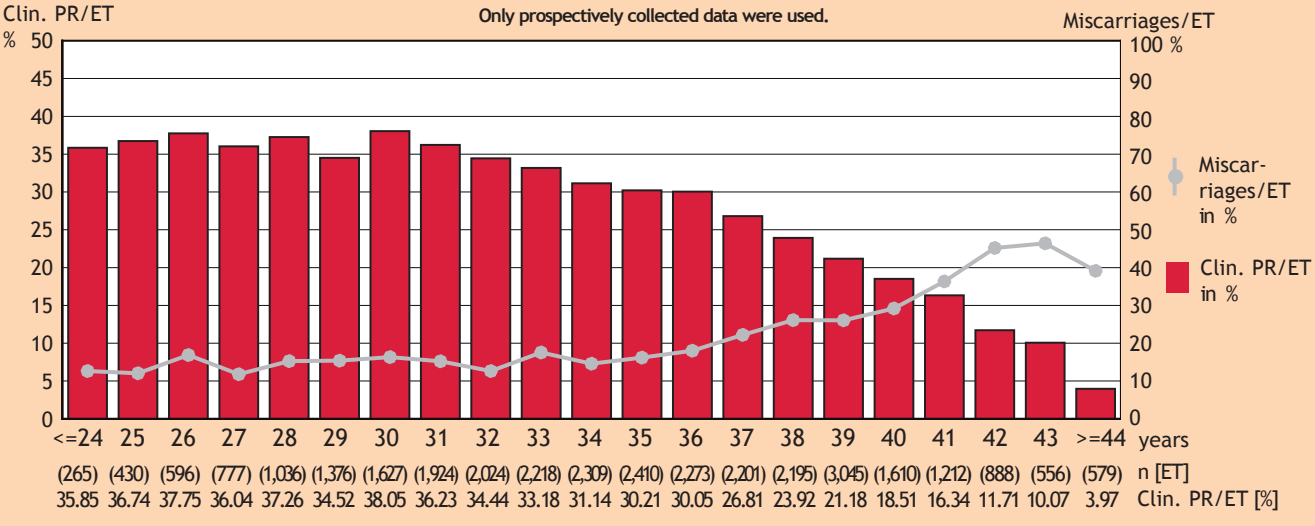


Age in years	OPU	Oocytes (mean)	Insemin. (mean)	ET	ET/OPU %	Transf. Emb. (mean)	Clin. preg.	Clin. PR/ OPU %	Clin. PR/ ET %	Clin. PR/ ET % "ideal" *
<= 29	1,255	11.21	11.01	1,116	88.92	1.95	434	34.58	38.89	42.64
30 - 34	2,813	10.14	9.93	2,551	90.69	1.97	934	33.20	36.61	40.35
35 - 39	3,841	8.16	7.98	3,432	89.35	2.01	995	25.90	28.99	33.73
>= 40	1,614	5.97	5.86	1,370	84.88	2.06	218	13.51	15.91	21.71
Total**	9,524	8.78	8.59	8,470	88.93	2.00	2,582	27.11	30.48	36.14

*) "Ideal": 2 embryos were transferred and at least 2 2PN stages in abundance. **) One case with unknown documentation of age is enclosed.

Outcome as a function of woman's age

ICSI - 2011



Age in years	OPU	Oocytes (mean)	Injection (mean)	ET	ET/OPU %	Transf. Emb. (mean)	Clin. preg.	Clin. PR/ OPU %	Clin. PR/ ET %	Clin. PR/ ET % "ideal" *
<= 29	4,821	12.22	9.73	4,480	92.93	1.99	1,619	33.58	36.14	39.07
30 - 34	10,860	10.89	8.74	10,102	93.02	2.00	3,468	31.93	34.33	38.00
35 - 39	13,327	8.62	6.92	12,124	90.97	2.03	3,171	23.79	26.15	30.72
>= 40	5,628	6.35	5.11	4,844	86.07	2.05	678	12.05	14.00	19.48
Total**	34,637	9.46	7.59	31,551	91.09	2.00	8,937	25.80	28.33	33.66

*) "Ideal": 2 embryos were transferred and at least 2 2PN stages in abundance. **) One case with unknown documentation of age is enclosed.

Clinical pregnancy rate as a function of the number of embryos transferred and age groups 2011

IVF	1 Embryo		2 Embryos		3 Embryos		Total	
	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %
Up to 24 years	5	0.00	55	29.09	2	50.00	62	27.42
25 - 29 years	108	22.22	890	41.69	56	39.29	1,054	39.56
30 - 34 years	306	21.24	2,027	38.83	218	37.61	2,551	36.61
35 - 39 years	560	17.68	2,286	31.06	586	31.74	3,432	28.99
40 - 44 years	317	6.62	603	15.09	401	25.44	1,321	16.20
45 years and older	21	4.76	15	6.67	13	15.38	49	8.16
Total	1,317	15.95	5,876	33.63	1,277	31.01	8,470*	30.48

ICSI	1 Embryo		2 Embryos		3 Embryos		Total	
	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %
Up to 24 years	25	20.00	222	38.29	18	27.78	265	35.85
25 - 29 years	368	21.20	3,520	37.67	327	36.70	4,215	36.16
30 - 34 years	1,119	20.73	7,866	36.50	1,117	32.68	10,102	34.33
35 - 39 years	2,010	14.03	7,689	28.66	2,425	28.25	12,124	26.15
40 - 44 years	1,183	7.19	1,934	16.39	1,450	18.62	4,567	14.71
45 years and older	106	1.89	88	1.14	83	3.61	277	2.17
Total	4,811	14.22	21,320	31.92	5,420	26.72	31,551*	28.32

Cryo-transfer	1 Embryo		2 Embryos		3 Embryos		Total	
	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %
Up to 24 years	21	9.52	100	12.00	20	35.00	141	14.89
25 - 29 years	313	13.10	1,405	24.48	417	22.06	2,161	22.12
30 - 34 years	921	13.14	3,500	23.00	1.094	25.32	5,558	21.72
35 - 39 years	1,114	10.68	3,419	20.47	1.183	23.84	5,740	19.20
40 - 44 years	417	9.35	1,006	16.90	493	16.63	1,922	15.19
45 years and older	11	0.00	27	14.81	21	4.76	59	8.47
Total	2,797	11.51	9,457	21.52	3,228	22.96	15,680**	19.85

*) In one case the age is unknown.
**) Embryos transferred plus 2PN stages; in 99 cases uncalculable.

Only prospectively collected data were used.

Clinical pregnancy rate as a function of the embryo quality 2011

IVF, ICSI, IVF/ICSI

Quality		<= 29 years		30 - 34 years		35 - 39 years		>= 40 years		Total	
Ideal	Non-ideal	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %	ET	Clin. PR/ET %
0	1	85	7.06	255	7.84	480	5.42	299	2.34	1,119	5.27
0	2	337	23.44	794	16.25	926	13.61	279	7.89	2,336	15.24
0	3	30	16.67	114	12.28	238	9.24	144	10.42	526	10.65
1	0	424	23.82	1,178	23.51	2,094	17.10	1,329	7.67	5,025	16.68
1	1	588	34.18	1,253	30.65	1,400	25.86	452	11.50	3,693	27.05
1	2	30	20.00	118	27.97	244	22.95	165	13.94	557	21.19
2	0	3,758	40.39	7,835	40.11	7,639	37.71	1,903	17.66	21,135	37.27
2	1	63	34.92	218	38.53	466	27.68	321	19.00	1,068	27.71
3	0	277	41.52	882	35.83	2,056	32.20	1,315	21.14	4,530	30.31
Total		5,596	36.68	12,653	34.79	15,556	27.97	6,214	14,42	40,019*	29.24

*) In 30 cases quality is unknown.

Only prospectively collected data were used.

Clinical pregnancy rate as a function of the embryo quality 2011

Cryo-transfer

Quality		After IVF		After ICSI	
Ideal	Non-ideal	ET	Clin. PR/ET %	ET	Clin. PR/ET %
0	1	133	4.51	507	5.72
0	2	310	9.35	997	11.43
0	3	73	10.96	321	13.08
1	0	464	17.03	1,595	12.35
1	1	467	19.06	1,320	18.03
1	2	105	17.14	325	20.31
2	0	1,446	25.80	4,544	25.09
2	1	168	24.40	448	24.33
3	0	403	22.33	1,217	27.28
Total*		3,569	20.54	11,274	20.11

*) In 24 cases the previous method of treatment was IVF/ICSI; in 714 cases the previous method of treatment was unknown.

Only prospectively collected data were used.

Miscarriage rates as a function of woman's age and the number of embryos transferred 2011

IVF, ICSI, IVF/ICSI

Age in years	1 Embryo		2 Embryos		3 Embryos		Total	
	Clin. preg.	Miscarriage/ clin. preg. %	Clin. preg.	Miscarriage/ clin. preg. %	Clin. preg.	Miscarriage/ clin. preg. %	Clin. preg.	Miscarriage/ clin. preg. %
<= 24	5	0.00	102	12.75	6	16.67	113	12.39
25 - 29	104	15.38	1,728	14.29	142	21.83	1,974	14.89
30 - 34	299	20.07	3,743	14.59	459	16.99	4,501	15.20
35 - 39	389	26.48	2,998	19.68	881	22.93	4,268	20.97
40 - 44	106	37.74	420	36.43	377	33.95	903	35.55
45 =>	3	66.67	2	50.00	5	20.00	10	40.00
Total	906	24.39	8,994	17.23	1,871	23.57	11,771*	18.79

*) In two cases the age is unknown.

Cryo-transfer

Age in years	1 Embryo		2 Embryos		3 Embryos		Total	
	Clin. preg.	Miscarriage/ clin. preg. %	Clin. preg.	Miscarriage/ clin. preg. %	Clin. preg.	Miscarriage/ clin. preg. %	Clin. preg.	Miscarriage/ clin. preg. %
<= 24	2	0.00	12	33.33	7	28.57	21	28.57
25 - 29	41	14.63	344	21.74	92	21.74	478	21.13
30 - 34	121	19.83	805	20.50	277	18.41	1,207	19.97
35 - 39	119	21.01	700	23.00	282	25.89	1,102	23.59
40 - 44	39	33.33	170	28.82	82	35.37	292	31.51
45 =>	-	-	4	25.00	1	100.00	5	40.00
Total	322	21.12	2,035	22.36	741	23.75	3,105*	22.61

*) In seven cases the number of embryos transferred is unknown.

Only prospectively collected data were used.

Clinical pregnancy rates as a function of the stimulation protocol

IVF, ICSI 2011

- IVF -

	u-FSH	rec-FSH	hMG only	rec-LH and rec-FSH	rec-FSH and hMG	Other*	n. a.	Total
Short GnRHa	4	283	453	17	143	10	4	914
Transfer rate (%)	25.00	92.23	93.82	88.24	89.51	90.00	100.00	92.23
Clin. PR/ET (%)	0.00	28.35	29.18	20.00	20.31	22.22	25.00	27.28
Long GnRHa	63	1,907	788	219	591	46	31	3,645
Transfer rate (%)	87.30	89.88	88.07	81.28	91.37	89.13	93.55	89.19
Clin. PR/ET (%)	27.27	35.47	28.67	30.34	30.37	34.15	48.28	32.85
Without GnRH-analogues	13	279	219	46	126	65	153	901
Transfer rate (%)	92.31	88.53	93.61	89.13	91.27	80.00	77.12	88.90
Clin. PR/ET (%)	33.33	33.20	32.68	34.15	24.35	21.15	27.12	30.13
Antagonists	39	2,282	798	252	339	326	28	4,064
Transfer rate (%)	89.74	90.32	87.59	79.37	85.84	84.97	82.14	88.24
Clin. PR/ET (%)	25.71	33.77	26.47	24.50	20.27	16.25	13.04	29.17
Total	119	4,751	2,258	534	1,199	447	216	9,524

- ICSI -

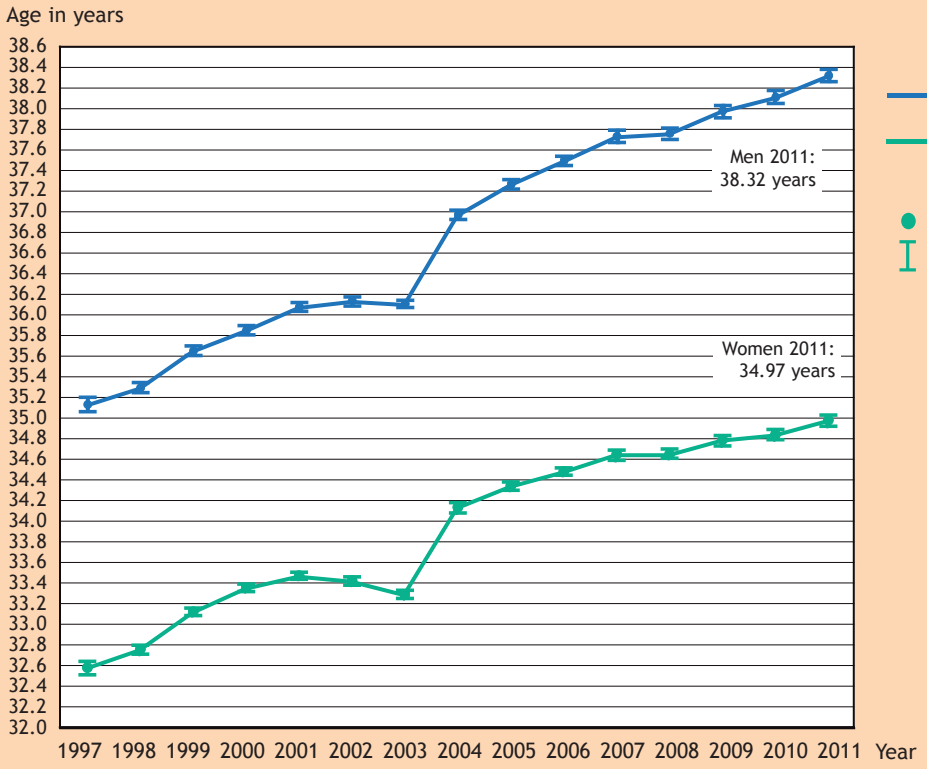
	u-FSH	rec-FSH	hMG only	rec-LH and rec-FSH	rec-FSH and hMG	Other*	n. a.	Total
Short GnRHa	66	984	1,061	82	386	118	9	2,706
Transfer rate (%)	90.91	94.41	92.27	87.80	90.16	92.37	88.89	92.50
Clin. PR/ET (%)	13.33	22.93	20.53	18.06	15.23	10.09	25.00	20.00
Long GnRHa	179	7,193	2,674	880	2,435	190	89	13,640
Transfer rate (%)	96.09	93.67	92.93	88.98	94.37	92.63	95.51	93.39
Clin. PR/ET (%)	27.33	33.51	27.89	28.10	29.55	22.16	16.47	31.01
Without GnRH-analogues	32	1,097	567	178	597	287	657	3,415
Transfer rate (%)	93.75	91.70	89.95	85.96	90.62	83.28	74.73	87.37
Clin. PR/ET (%)	23.33	32.50	31.37	25.49	26.80	14.64	18.94	27.13
Antagonists	138	8,210	2,614	1,018	1,668	1,125	103	14,876
Transfer rate (%)	90.58	91.08	87.95	85.66	90.77	85.42	87.38	89.62
Clin. PR/ET (%)	21.60	31.17	25.18	26.72	22.72	15.71	16.67	27.59
Total	415	17,484	6,916	2,158	5,068	1,720	858	34,637

*) E. g. U-FSH and hMG, Clomifen/rec-FSH, Clomifen/hMG etc.

Only prospectively collected data were used.

Average age of women and men

1997 - 2011 - IVF, ICSI, IVF/ICSI



Men

Women

: Mean

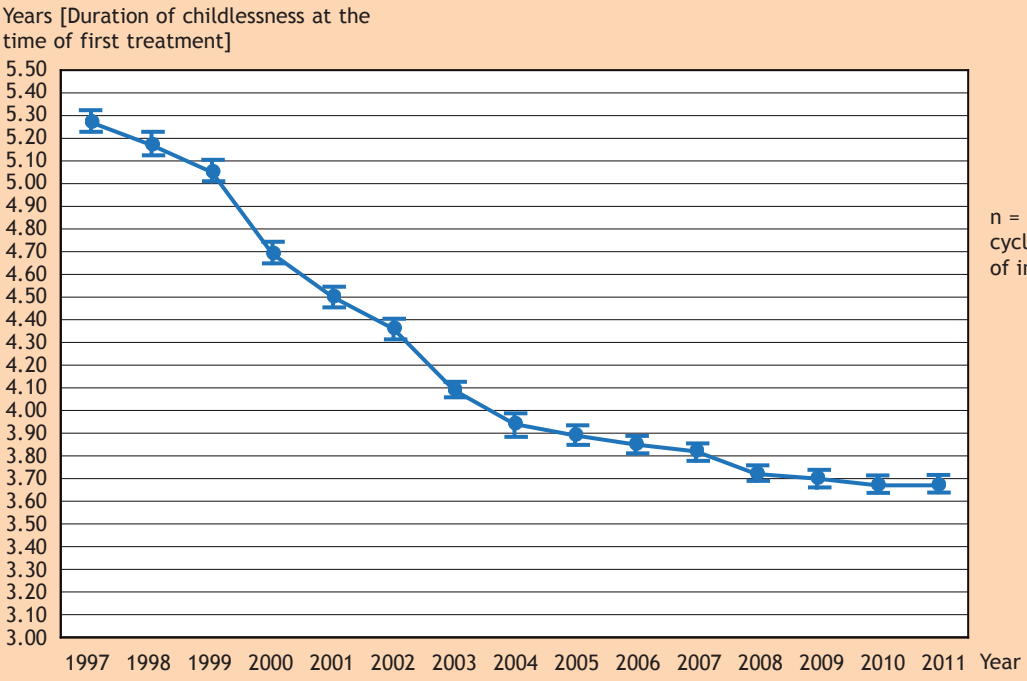
: 95 % confidence interval (e.g: in 1997, the CI for women with a mean age between 32.51 and 32.65 years shows a probability of 95%)

n = 663,076 cycles with plausible age documentation

Prospectively and retrospectively collected data were used.

Duration of childlessness at the time of first treatment

1997 - 2011 IVF, ICSI, IVF/ICSI

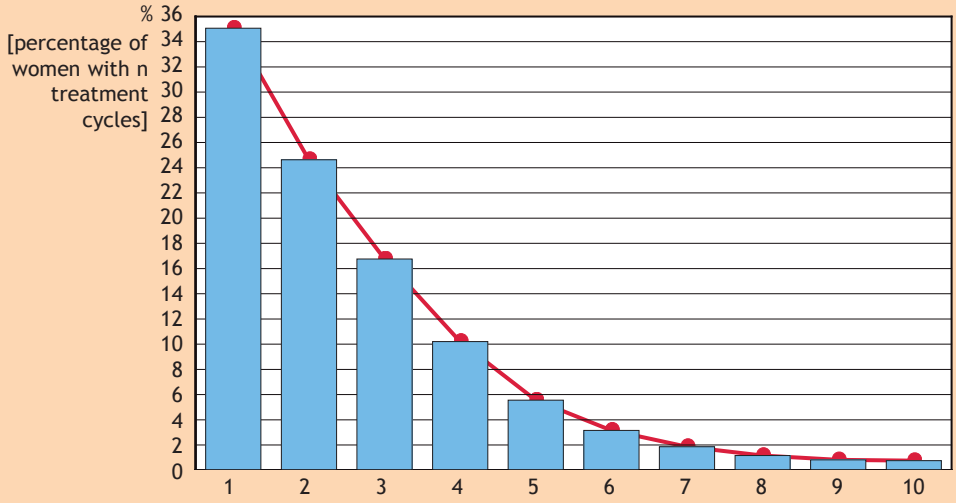


n = 321,588 first treatment cycles with known duration of infertility

Prospectively and retrospectively collected data were used.

Number of treatment cycles per woman

1997 - 2011 IVF, ICSI, IVF/ICSI, cryo-transfer



n = 376,303 women

Prospectively and retrospectively collected data were used.

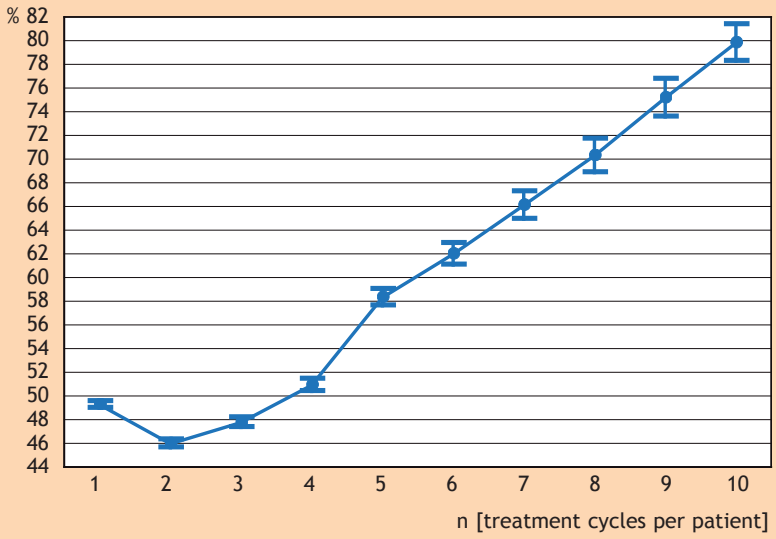
Total probability per woman for pregnancy

1997 - 2011 IVF, ICSI, IVF/ICSI, cryo-transfer

Total probability per woman for pregnancy as a function of the number of treatment-cycles

n = 376,303 women

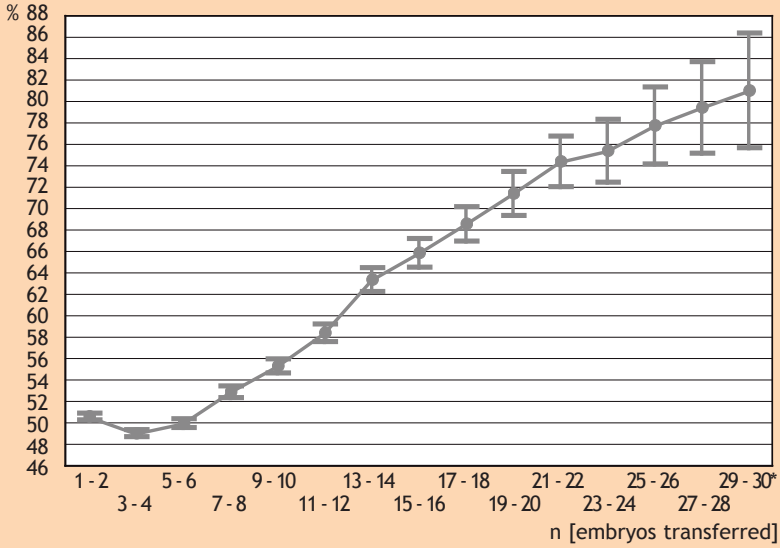
In 10 treatment cycles (n = 1,755) there is an 80% probability for a pregnancy.



Total probability per woman for pregnancy as a function of the number of the sum of embryos transferred

n = 376,303 women

With 29-30 embryos transferred, there is an 81% probability for a pregnancy.

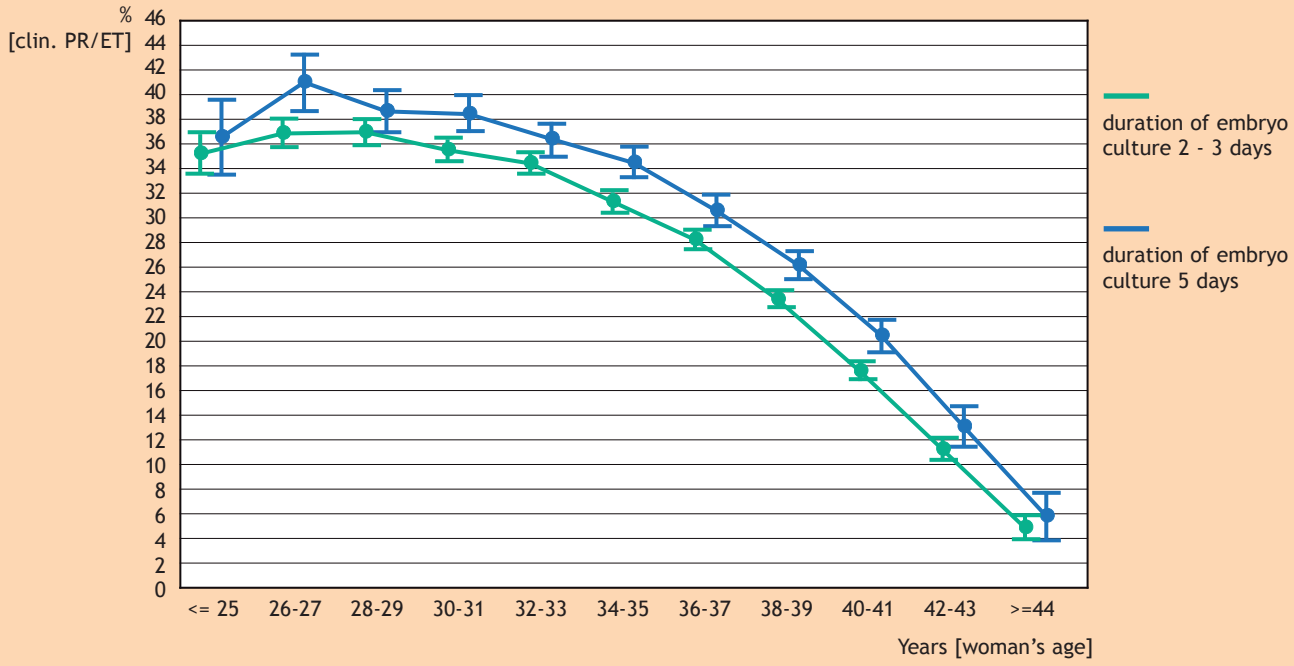


Prospectively and retrospectively collected data were used.

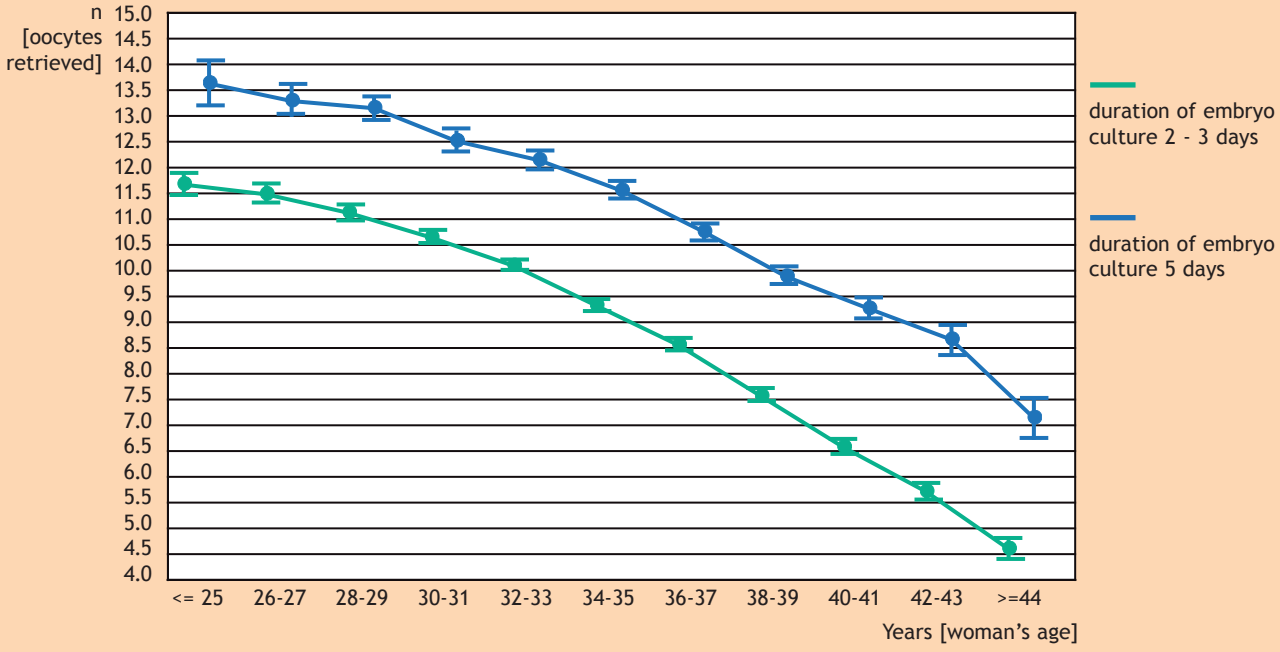
Clinical pregnancy rate as a function of the number of oocytes retrieved and the duration of embryo culture

2007 - 2011 IVF, ICSI, IVF/ICSI

Clinical pregnancy rate (Clin. PR/ET)



Number of oocytes retrieved



n = 208.620 treatment cycles (the 5 days-culture has been increasing from 15 % to 21 % in the period mentioned above)

Note: The higher pregnancy rate in 5 days-cultures can be explainied by the higher number of oocytes retrieved.

Prospectively and retrospectively collected data were used.

All children born 1997 - 2011

prospective and retrospective data

IVF, ICSI, IVF/ICSI

	Singleton		Twin		Triplet		Quadruplet		Total
	n	%	n	%	n	%	n	%	n
2001 *	6,798 (6,774)	60.89 (61.04)	3,956 (3,919)	35.43 (35.31)	411 (405)	3.68 (3.65)	0 (0)	- -	11,165 (11,098)
2002 *	7,746 (7,724)	62.59 (62.78)	4,256 (4,210)	34.39 (34.22)	366 (362)	2.96 (2.94)	8 (7)	0.06 (0.06)	12,376 (12,303)
2003 *	10,723 (10,688)	62.13 (62.78)	5,960 (5,866)	34.53 (34.22)	552 (533)	3.20 (2.94)	24 (24)	0.14 (0.14)	17,259 (17,111)
2004 *	5,368 (5,352)	63.69 (62.46)	2,826 (2,801)	33.53 (34.28)	234 (223)	2.78 (3.11)	0 (0)	- -	8,428 (8,376)
2005 *	5,527 (5,515)	63.84 (63.90)	2,936 (2,906)	33.91 (33.44)	183 (179)	2.11 (2.66)	12 (11)	0.14 (0.13)	8,658 (8,611)
2006 *	5,906 (5,894)	65.50 (64.05)	2,922 (2,890)	32.41 (33.75)	189 (174)	2.10 (2.08)	0 (0)	- -	9,017 (8,958)
2007 *	6,663 (6,628)	64.56 (64.69)	3,504 (3,471)	33.95 (33.88)	150 (143)	1.45 (1.40)	4 (4)	0.04 (0.04)	10,321 (10,246)
2008 *	6,696 (6,672)	64.09 (64.34)	3,528 (3,481)	33.77 (33.57)	216 (209)	2.07 (2.02)	8 (8)	0.08 (0.08)	10,448 (10,370)
2009 *	7,253 (7,217)	65.89 (66.02)	3,560 (3,523)	32.34 (32.23)	186 (183)	1.69 (1.67)	8 (8)	0.07 (0.07)	11,007 (10,931)
2010 *	6,767 (6,724)	64.42 (64.62)	3,554 (3,507)	33.83 (33.70)	183 (175)	1.74 (1.68)	0 (0)	- -	10,504 (10,406)
2011 *	4,671 (4,645)	63.64 (63.95)	2,498 (2,457)	34.03 (33.82)	171 (162)	2.33 (2.23)	0 (0)	- -	7,340 (7,264)

*) Values in brackets refer to live births. Added values of all years (1997 - 2011) observed revealed the following results: singleton 92,314 (88,946), twin 50,242 (49,637), triplet 5,074 (4,818), quadruplet 88 (85); total: 147,618 (146,486)

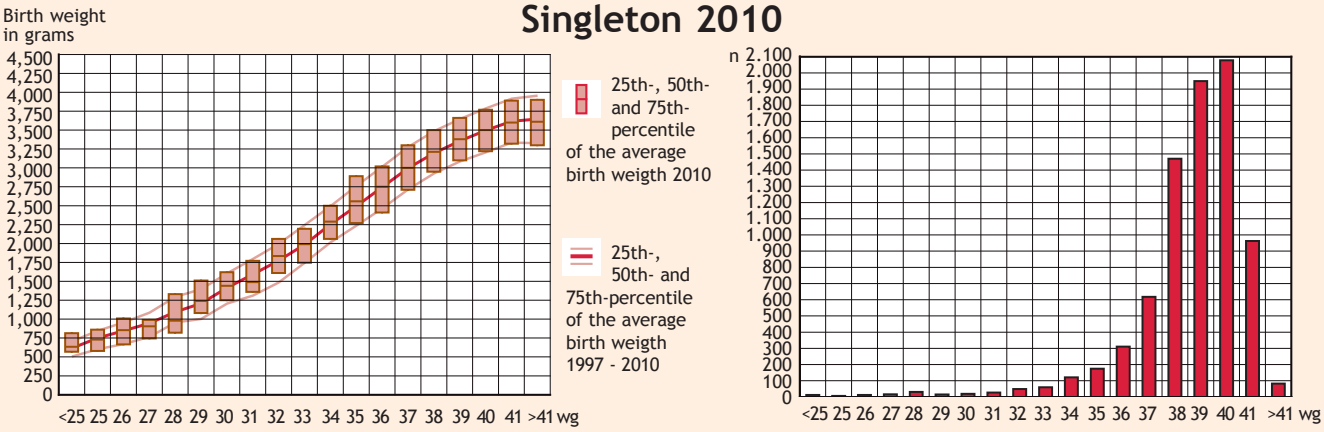
Total (IVF, ICSI, IVF/ICSI, cryo-transfer)

	Singleton		Twin		Triplet		Quadruplet		Total
	n	%	n	%	n	%	n	%	n
2001 *	7,795 (7,764)	62.20 (62.33)	4,288 (4,248)	34.21 (34.10)	450 (444)	3.59 (3.56)	0 (0)	- -	12,533 (12,456)
2002 *	8,930 (8,902)	63.84 (64.02)	4,662 (4,615)	33.33 (33.19)	387 (382)	2.77 (2.75)	8 (7)	0.06 (0.05)	13,987 (13,906)
2003 *	11,922 (11,887)	63.16 (63.48)	6,334 (6,237)	33.55 (33.31)	597 (578)	3.16 (3.09)	24 (24)	0.13 (0.13)	18,877 (18,726)
2004 *	6,891 (6,869)	65.63 (65.81)	3,336 (3,306)	31.77 (31.68)	273 (262)	2.60 (2.51)	0 (0)	- -	10,500 (10,437)
2005 *	7,038 (7,020)	65.76 (65.93)	3,440 (3,408)	32.14 (32.01)	213 (209)	1.99 (1.96)	12 (11)	0.11 (0.10)	10,703 (10,648)
2006 *	7,419 (7,402)	66.87 (67.14)	3.450 (3.417)	31.10 (30.99)	222 (202)	2.00 (1.83)	4 (4)	0.04 (0.04)	11,095 (11,025)
2007 *	8,407 (8,364)	66.35 (66.45)	4,076 (4,043)	32.17 (32.12)	183 (176)	1.44 (1.40)	4 (4)	0.03 (0.03)	12,670 (12,587)
2008 *	8,444 (8,416)	65.79 (66.07)	4,142 (4,084)	32.27 (32.06)	240 (230)	1.87 (1.81)	8 (8)	0.06 (0.06)	12,834 (12,738)
2009 *	9,016 (8,969)	67.32 (67.42)	4,152 (4,114)	31.00 (30.92)	216 (213)	1.61 (1.60)	8 (8)	0.06 (0.06)	13,392 (13,304)
2010 *	8,619 (8,566)	66.18 (66.35)	4,156 (4,105)	31.91 (31.80)	249 (239)	1.91 (1.85)	0 (0)	- -	13,024 (12,910)
2011 *	6,054 (6,022)	65.34 (65.61)	2,990 (2,943)	32.27 (32.07)	222 (213)	2.40 (2.32)	0 (0)	- -	9,266 (9,178)

*) Values in brackets refer to live births. Added values of all years (1997 - 2011) observed revealed the following results: singleton 110,920 (100,472), twin 56,506 (55,855), triplet 5,475 (5,306), quadruplet 92 (89); total: 172,993 (171,722)

Childrens birth weight (bw) and week of gestation (wg) 2010*

Singleton 2010

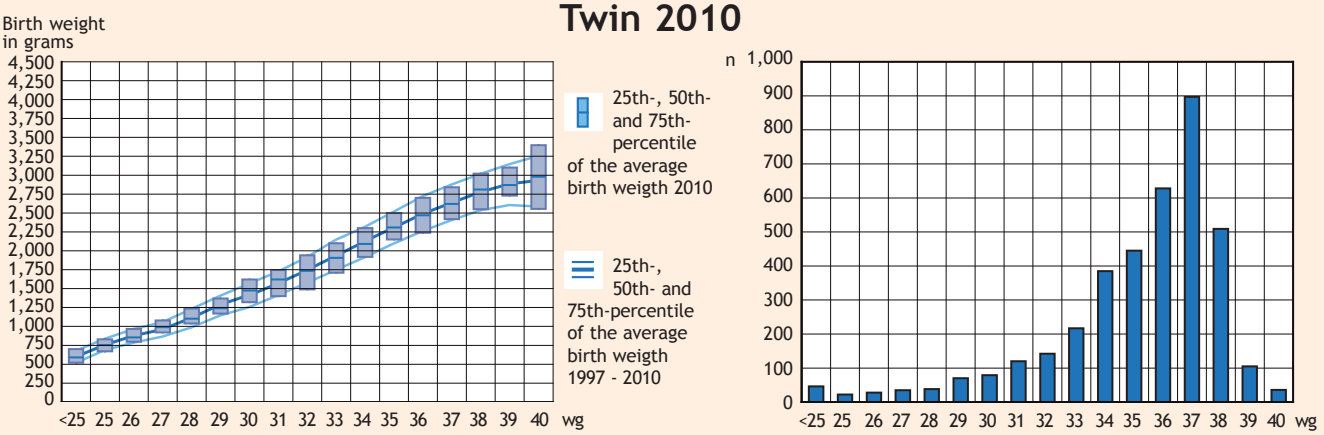


wg	< 25	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	> 41	total
n	12	7	12	16	31	15	19	27	49	60	121	174	311	618	1,470	1,949	2,078	963	83	8,015
bw Q 25	568	580	667	745	820	1,080	1,250	1,360	1,610	1,745	2,060	2,270	2,410	2,710	2,950	3,100	3,220	3,320	3,300	2,980
bw median	635	730	855	905	980	1,240	1,440	1,490	1,835	1,990	2,290	2,557	2,750	3,000	3,212	3,380	3,500	3,600	3,610	3,320
bw Q 75	815	860	1,010	990	1,330	1,510	1,620	1,770	2,060	2,195	2,500	2,890	3,020	3,300	3,500	3,650	3,660	3,770	3,890	3,650

Percentiles 2010: p25 = 38th wg., p50 = 39th wg., p75 = 40th wg.; Percentiles 1997 - 2010: p25 = 38th wg., p50 = 39th wg., p75 = 40th wg.

Percentage of children born before completion of 37th wg: 18.37 %

Twin 2010



wg	<25	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	total**
n	46	22	28	35	38	70	79	120	142	217	385	445	628	897	509	105	36	3,813
bw Q 25	520	670	797	920	1,040	1,170	1,320	1,400	1,490	1,710	1,920	2,150	2,240	2,420	2,550	2,730	2,555	1,990
bw median	590	752	855	990	1,103	1,240	1,475	1,620	1,735	1,906	2,090	2,310	2,470	2,620	2,810	2,870	2,980	2,400
bw Q 75	700	830	967	1,080	1,235	1,370	1,620	1,745	1,940	2,100	2,300	2,500	2,700	2,840	3,020	3,100	3,397	2,720

Percentiles 2010: p25 = 34th wg., p50 = 36th wg., p75 = 37.th wg.; Percentiles 1997 - 2010: p25 = 34th wg., p50 = 36th wg., p75 = 37th wg.

Percentage of children born before completion of 37th wg: 82.66 %

*) Data contain 11 cases wg > 40

Triplet 2010

wg	24	25	26	27	28	29	30	31	32	33	34	35	total**
n	7	0	6	9	18	9	15	17	43	27	40	20	214
bw Q 25	470	-	890	950	840	1,200	1,240	1,390	1,460	1,780	1,800	1,900	1,320
bw median	570	-	1,150	950	1,027	1,560	1,455	1,490	1,675	2,150	1,967	2,018	1,672
bw Q 75	600	-	1,870	990	1,240	1,670	1,560	1,610	1,784	2,370	2,105	2,330	1,975

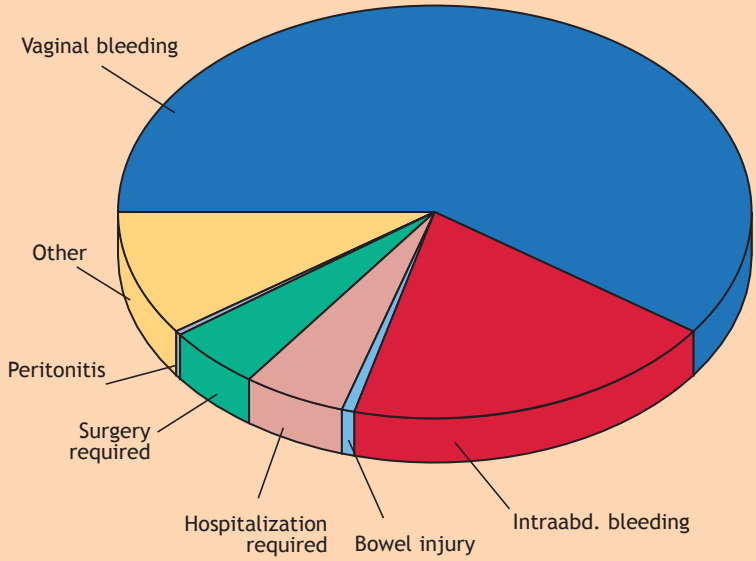
Percentiles 2010: p25 = 30th wg., p50 = 32th wg., p75 = 34th wg.; Percentiles 1997 - 2010: p25 = 30th wg., p50 = 32th wg., p75 = 33th wg.

Percentage of children born before completion of 37th wg: 98.60 %

**) Date contain 3 cases wg > 35

*) Children with plausible birth weight and week of gestation; prospectively and retrospectively collected data were used.

Complications as a function of ovum pick-up 2011



Total OPUs	46.583	100,00 %
n. a.	0	-
No complications	46,277	99.34
Complications	306	0,66

Complication	n	%
Vaginal bleeding	183	59.80
Intraabdom. bleeding	59	19.28
Bowel injury	2	0.65
Peritonitis	1	0.33
Hospitalization required	16	5.23
Surgery required	15	4.90
Other	30	9.80
Total	306	100.00

Only prospectively collected data were used.

OHSS after embryo transfer as a function of the stimulation protocol IVF, ICSI, IVF/ICSI 2011

	Stimulation	%	Oocytes retrieved	OHSS III/ST	%
Short GnRH	3,649	8.09	8.06	3	0.08
FSH only	1,347		9.39	2	0.15
hMG only	1,523		7.67	0	-
FSH and hMG	624		6.60	1	0.16
Other	142		6.39	0	-
n. a.	13		5.54	0	-
Long GnRH	17,674	39.21	10.55	74	0.42
FSH only	9,615		11.46	40	0.42
hMG only	3,529		9.32	1	0.03
FSH and hMG	3,241		9.91	31	0.96
Other	1,164		8.74	2	0.17
n. a.	125		9.22	0	-
Without analogues	4,354	9.66	8.19	6	0.14
FSH only	1,438		10.07	4	0.28
hMG only	793		8.81	1	0.13
FSH and hMG	771		9.09	1	0.13
Other	538		6.44	0	-
n. a.	814		4.56	0	-
Antagonists	19,401	43.04	8.86	54	0.28
FSH only	11,068		10.39	45	0.41
hMG only	3,451		7.15	4	0.12
FSH and hMG	2,282		7.11	3	0.13
Other	2,468		6.19	1	0.04
n. a.	132		5.98	1	0.76
Total	45,078	100.00	9.40	137	0.30

Only prospectively collected data were used.

Therapy decisions against outcome of previous treatment cycle

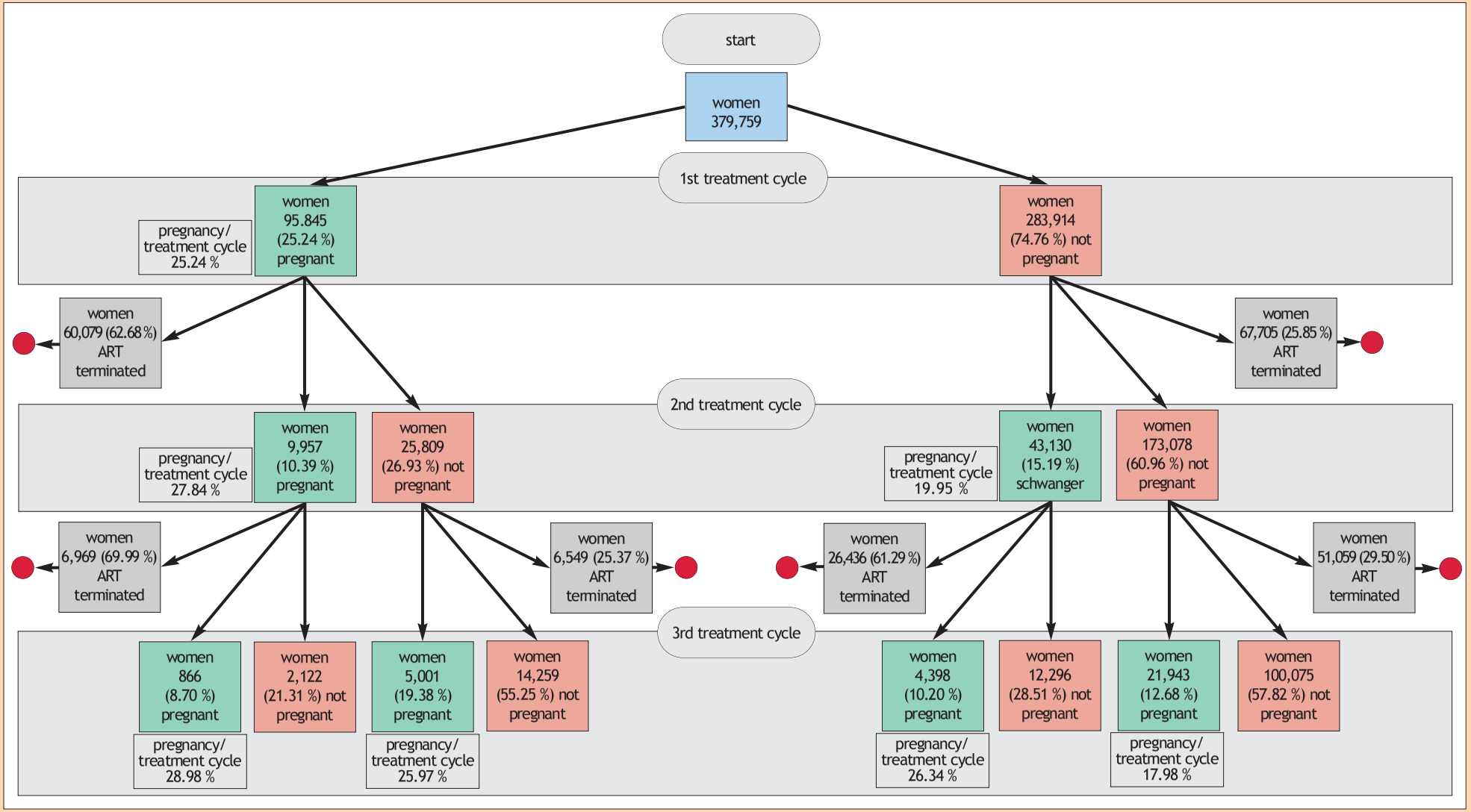
1997 - 2011, IVF, ICSI, IVF/ICSI, cryo-transfer

number of women getting pregnant in the n-th treamtment cycle

number of women *not* getting pregnant in the n-th treamtment cycle

women not undergoing another treatment cycle (● end point)

Note: A previous ART-pregnancy increases the probability for consecutive pregnancies.



Centers reporting to the German IVF Registry
in 2011

Kinderwunschzentrum Dresden
Praxisklinik Dr. med. H.-J. Held
Dr. med. Hans-Jürgen Held
Prager Straße 8 a
01069 Dresden
Tel. 0351/50 14 00-0, Fax -50 14 00-28
info@ivf-dresden.de
www.ivf-dresden.de

Gynäkologische Endokrinologie und Reproduktionsmedizin der Universitätsfrauenklinik Dresden
Dr. med. Constanze Reisenbüchler,
Dr. med. Katja Keller,
Dr. med. Jennifer-Lucia Wacker,
Prof. Dr. med. Wolfgang Distler,
Dr. rer. nat. Gudrun Keck
Fetscherstraße 74
01307 Dresden
Tel. 0351/458-3491, Fax -458-5351
wolfgang.distler@uniklinikum-dresden.de
www.uniklinikum-dresden.de/gyn

Zentrum für Reproduktionsmedizin, Gynäkologische Endokrinologie und Sexualmedizin,
UFK Leipzig
Prof. Dr. med. Henry Alexander,
Dr. med. Gabriele Pretzsch,
Dr. med. D. Marx,
Dipl.-Biol. Wolfgang Weber
Liebigstraße 20 a
04103 Leipzig

Kinderwunschzentrum Leipzig-Chemnitz
Dr. med. Fayez Abu Hmeidan,
Dr. med. Petra Jogschies,
Dörte Geistert,
Laila Shugair
Goldschmidtstraße 30
04103 Leipzig
Tel. 0341/141 200, Fax -141 2081
info@ivf-leipzig.de
www.ivf-leipzig.de

Kinderwunschzentrum Praxisklinik City Leipzig, Überörtliche BAG
Dr. med. Astrid Gabert,
Dr. med. Katharina Bauer,
Dr. med. Georg Saager,
Petersstraße 1
04109 Leipzig
Tel. 0341/215 855-0, Fax -215 855-17
info@ivf-city-leipzig.de
www.praxisklinik-city-leipzig.de

Universitätsklinikum Halle (Saale)
Zentrum für Reproduktionsmedizin und Andrologie
Univ.-Prof. Dr. med. Hermann M. Behre,
Dr. med. Petra Kaltwaßer,
Dr. med. Solveig Köller,
Dr. rer. nat. Ewald Seliger
Ernst-Grube-Straße 40
06120 Halle/Saale
Tel. 0345/557-2747, Fax -557-4788
ZRA@uki-halle.de
www.medizin.uni-halle.de/zra/

Reproduktionsmedizinisches Zentrum Jena/Erfurt
PD Dr. med. habil. Heidi Fritzsche,
Dipl. med. Jens-Peter Reiher,
Dr. med. Angela Hoffmann
Markt 4
07743 Jena
Tel. 03641/829 610, Fax -829 681
Dr.H.Fritzsche@t-online.de
www.kinderwunschnet.de

Universitätsfrauenklinik Jena
Prof. Dr. med. Jürgen Weiss,
Dr. rer. nat. Ines Hoppe
Bachstraße 18
07743 Jena
Tel. 03641/933 529, Fax -933 191
ines.hoppe@med.uni-jena.de
www.uni-jena.de/ufk

Kinderwunschzentrum Leipzig-Chemnitz
Dr. med. Fayez Abu Hmeidan,
Dr. med. Petra Jogschies,
Dörte Geistert,
Laila Shugair
Jakobikirchplatz 4
09111 Chemnitz
Tel. 0371/503 4980, Fax -503 49881
info@ivf-chemnitz.de
www.ivf-chemnitz.de

Kinderwunschzentrum Praxisklinik City Leipzig, Überörtliche BAG
Dr. med. Astrid Gabert,
Dr. med. Katharina Bauer,
Dr. med. Georg Saager
Flemmingstraße 2 a
09116 Chemnitz
Tel. 037/433 130-0, Fax -433 130-17
info@kinderwunschzentrum-chemnitz.de
www.kinderwunschzentrum-chemnitz.de

Praxis für Fertilität
Kinderwunsch- und Endometriose-Zentrum Berlin
Dr. med. Gülden Halis,
Dr. med. David J. Peet
Friedrichstraße 79
10117 Berlin
Tel. 030/8321 190-0, Fax -8321 190-19
info@fertilitaet.de
www.fertilitaet.de

Kinderwunschzentrum am Potsdamer Platz
Dr. med. Hanadi Awwadeh,
Dr. med. Anja Mutz
Leipziger Platz 7
10117 Berlin
Tel. 030/200 89 50-0, Fax -200 89 50-99
info@Kinderwunsch-potsdamerplatz.de
www.kinderwunsch-potsdamerplatz.de

Praxisklinik Sydow am Gendarmenmarkt
Dr. med. Peter Sydow,
Dr. med. Carmen Sydow,
Dr. med. Ulrike Bergmann-Hensel
Kronenstraße 55 - 58
10117 Berlin
Tel. 030/206 267 20, Fax -206 267 218
info@praxisklinik-sydow.de
www.praxisklinik-sydow.de

GLC - Reproduktionsmedizin im Lützow Center
Dr. med. Detlef H. G. Temme & Kollegen
Wichmannstraße 5
10787 Berlin
Tel. 030/230 998 0, Fax -230 998 30
info@ivf-berlin.de
www.ivf-berlin.de

Kinderwunschzentrum Berlin
Endometriosezentrum Berlin
Akademische Lehrpraxis der Charité Universitätsmedizin
Frauenärztliche Gemeinschaftspraxis
Dr. med. Reinhard Hannen,
Dr. med. Christian F. Stoll
Landgrafenstraße 14
10787 Berlin
Tel. 030/263 983-0, Fax -263 983-99
info@kinderwunschzentrum.de
www.kinderwunschzentrum.de

Kinderwunschzentrum an der Gedächtniskirche
Dr. med. Matthias Bloechle,
Dr. med. Silke Marr
Rankestraße 34
10789 Berlin
Tel. 030/219 092-0, Fax -219 092-99
info@kinderwunsch-berlin.de
www.kinderwunsch-berlin.de

Kinderwunschzentrum FERA im Wenckebach-Klinikum
Dr. med. Andreas Jantke,
Dr. med. Anna Stegelmann
Wenckebachstraße 23
12099 Berlin
Tel. 030/76 00 701 30, Fax -76 00 701 60
kinderwunsch@fera-berlin.de
www.kinderwunsch-ivf-berlin.de

Kinderwunschzentrum am Innsbrucker Platz Berlin
Babette Remberg,
Dr. med. Susanne Tewordt-Thyselius,
Dr. rer. nat. Thomas Jeziorowski
Hauptstraße 65
12159 Berlin
Tel. 030/857 579 30, Fax -857 579 35
praxis@kinderwunschpraxis-berlin.de
www.kinderwunschpraxis-berlin.de

Zentrum für Reproduktionsmedizin Helle-Mitte
Dr. med. Muna Zaghloul-Abu Dakah,
Dr. med. Swetlana Hoffmann
Stendaler Straße 24
12627 Berlin
Tel. 030/992 779-0, Fax -992 779 22
info@berliner-kinderwunsch.de
www.berliner-kinderwunsch.de/

Fertility Center Berlin
Auf dem Gelände der DRK Kliniken Westend
Prof. Dr. med. Heribert Kentenich,
Dr. med. Gabriele Stief,
Dr. med. Andreas Tandler-Schneider,
Dr. med. Anette Siemann,
Dr. med. Marina Werling
Spandauer Damm 130
14050 Berlin
Tel. 030/233 208 110, Fax -233 208 119
info@fertilitycenter-berlin.de
www.fertilitycenterberlin.de

Kinderwunschzentrum Potsdam
Dr. med. Kay-Thomas Moeller,
Dr. med. Kathleen Linca,
Dr. med. Manzoor Nowshari
Babelsberger Straße 8
14473 Potsdam
Tel. 0331/231 892 92, Fax -231 892 93
info@kinderwunsch-potsdam.de
www.kinderwunsch-potsdam.de

Praxis für Fertilität Rostock
PD Dr. med. Heiner Müller,
Annette Busecke, Anja Bossow
Südring 81
18059 Rostock
Tel. 0381/4401-2030, Fax -4401-2031
info@ivf-rostock.de
www.ivf-rostock.de

MVZ Fertility Center Hamburg GmbH
Prof. Dr. med. Klaus Rudolf,
Dr. med. (IL) Robert Fischer,
Dr. med. Olaf G. J. Naether,
Dr. med. Kay Christian Löbbecke
Speersort 4
20095 Hamburg
Tel. 040/308 044 00, Fax -308 049 00
fch@kinderwunsch-hamburg.de
www.kinderwunsch-hamburg.de

Kinderwunschzentrum Altonaer Straße im Gynaekologicum Hamburg
Dr. med. Gerd Bispink,
Dr. med. Annick Horn,
Dr. med. Wolf Michel und Partner
Altonaer Straße 59
20357 Hamburg
Tel. 040/306 836-0, Fax -306 836-69
info@ivf-hamburg.de
www.ivf-hamburg.de

Kinderwunschzentrum Fleetinsel Hamburg
Dr. univ. Semsettin E. Koçak,
Dr. med. Peter List
Admiralitätsstraße 4
20459 Hamburg
Tel. 040-38605550, Fax -3860541
info@kinderwunschzentrum-hamburg.de
www.kinderwunschzentrum-hamburg.de

Endokrinologikum Hamburg
Prof. Dr. C. Keck,
PD Dr. M. Graf,
PD Dr. U. Knuth, Dr. M. Motamedi
Lornsenstraße 4 - 6
22767 Hamburg
Tel. 040/306 28-200, Fax -306 28-327
info@endokrinologikum.com
www.endokrinologikum.com

Universitäres Kinderwunschzentrum Lübeck
Ambulanzzentrum des UKSH gGmbH
Prof. Dr. med. Dr. h. c. mult. Klaus Diedrich,
Prof. Dr. med. Georg Griesinger, M.Sc.,
PD Dr. med. Askan Schultze-Mosgau
Ratzeburger Allee 160
23538 Lübeck
Tel. 0451/500-4418, Fax -500-5764
kinderwunsch@uk-sh.de
www.kinderwunsch-luebeck.de

fertilitycenterkiel
PD Dr. med. Sören von Otte,
Dr. med. Martin Völckers,
Dr. rer. nat. Heike Eckel
Prüner Gang 15
24103 Kiel
Tel. 0431/974 1333, Fax -974 1389
info@fertilitycenter.de
www.fertilitycenter.de

gyn-medicum Kinderwunschzentrum im UK-SH
Dr. Andreas Schmutzler,
Prof. Dr. Ali Salmassi
Arnold-Heller-Straße 3, Haus 24
24105 Kiel
Tel. 0431/597-2083, Fax -597-5352
schmutzler@email.uni-kiel.de
www.kinderwunschunikiel.de

Kinderwunsch Kiel
Dr. med. Kurt Brandenburg,
Dr. med. Angela Carstensen
Im Brauereiviertel 5
24118 Kiel
Tel. 0431/553 433, Fax -519 2745
info@kinderwunschkiel.de
www.kinderwunschkiel.de

Team Kinderwunsch Oldenburg
Dr. med. Saif ed-Din Jibril,
Dr. med. Gerhard Pohlig
Wilhelmstr. 5
26121 Oldenburg
Tel. 0441/248 9091, Fax -248 0611
tko@telemed.de
www.teamkinderwunsch.de

Tagesklinik Oldenburg
Zentrum für Kinderwunschbehandlung
Dr. med. Jörg Hennefründ,
Dr. med. Heike Boppert,
Dr. med. Michael Heeder
Achternstraße 21
26122 Oldenburg
Tel. 0441/922 700, Fax -922 7028
info@tagesklinik-oldenburg.de
www.tagesklinik-oldenburg.de

Zentrum für Fortpflanzungsmedizin Leer
Dr. med. Wolfgang von der Burg
Hafenstraße 6 d, Haus Singapore
26789 Leer
Tel. 0491/454 25-0, Fax -454 25-10
info@kinderwunschleer.de
www.kinderwunschleer.de

Kinderwunsch Bremen
Dr. med. Achim von Stutterheim,
Tanja Finger,
Dr. Anjarasoa Jung
Emmastraße 220
28213 Bremen
Tel. 0421/224 910, Fax -224 9122
info@kinderwunschbremen.de
www.kinderwunschbremen.de

BZF - Bremer Zentrum für Fortpflanzungsmedizin
Dr. med. Olaf Drost,
Prof. Dr. med. Ernst Heinrich Schmidt,
Dr. sc. Hum. Martin Pinteric
Gröpelinger Heerstraße 406 - 408
28239 Bremen
Tel. 0421/6102-1212, Fax -6102-1213
info@icsi.de
www.icsi.de

Team Kinderwunsch Hannover
Dr. med. Nabil Saymé,
Dipl.-Biol. T. Krebs
Brühlstraße 19
30169 Hannover
Tel. 0511/313 095, Fax -313 096
info@team-kinderwunsch-hannover.de
www.team-kinderwunsch-hannover.de

Medizinische Hochschule Hannover
Bereich Gynäkologische Endokrinologie und Reproduktionsmedizin, OE 6410
OÄ Dr. med. Cordula Schippert,
OA Dr. med. Guillermo-José Garcia-Rocha,
FÄ Dr. med. Christina Baßler,
AssÄ Dr. med. Wiebke Zempel
Carl-Neuberg-Straße 1
30625 Hannover
Tel. 0511/532-6099, Fax -532-6094
Schippert.Cordula@mh-hannover.de
www.mh-hannover.de/11327.html

Kinderwunschzentrum Langenhagen-Wolfsburg
Dr. med. Martina Müseler-Albers,
Dr. med. Klaus Bühler,
Horst Peter Arendt, Dr. med. Thilo Schill
Ostpassage 9
30853 Langenhagen
Tel. 0511/972 300, Fax -972 3018
praxis@kinderwunsch-langenhagen.de
www.kinderwunsch-langenhagen.de

Zentrum für Reproduktionsmedizin und Humangenetik
Dr. med. Franz-J. Algermissen,
Dr. med. Peter F. Justus,
Dr. med. Georg Wilke,
Dr. med. Notker Graf
Gartenstraße 18 - 20
31141 Hildesheim
Tel. 05121/206 79-0, Fax -206 79-11
praxis@kinderwunsch-hildesheim.de
www.kinderwunsch-hildesheim.de

Deutsche Klinik Bad Münder
Zentrum für Reproduktionsmedizin
MVZ wagnerstibbe GmbH
Dr. med. Elmar Breitbach,
Dr. med. Arvind Chandra,
Dr. med. Grita Hasselbach,
Dr. med. Natascha Peper
Hannoversche Straße 24
31848 Bad Münder
Tel. 05042/940-360, Fax -940-308
info@kinderwunsch.com
www.kinderwunsch.com

Zentrum für Kinderwunschbehandlung und pränatale Medizin
Dr. med. Dipl.-Biochem. Onno Buurman,
Dr. med. Michael Dumschat,
Dr. med. Ralf Menkhaus
Simeonsplatz 17
32423 Minden
Tel. 0571/972 60-0, Fax -972 60-99
info@kinderwunsch-minden.net
www.kinderwunsch.net

BIF - Bielefelder Institut für Fortpflanzungsmedizin
Prof. Dr. med. Joachim Volz,
Dr. med. Beate Harms
Teutoburger Straße 50
33604 Bielefeld

Bielefeld Fertility Center
Zentrum für Reproduktionsmedizin und Gynäkologische Endokrinologie
Paul A.Ebert,
Dr. med. Karl Völklein, Beata Szypajlo,
Dr. med. Wiebke Rübberdt,
Dr. med. Beate Harms
Werther Straße 266
33619 Bielefeld
Tel. 0521/101 005, Fax -101 079
praxis@kinderwunsch-bielefeld.de
www.kinderwunsch-bielefeld.de

MVZ für Reproduktionsmedizin
am Klinikum Kassel
Dr. med. Marc Janos Willi,
Dr. med. Oswald Schmidt
Prof. Dr. (UBsAs) Miguel Hinrichsen
Mönchebergstraße 41 - 43
34125 Kassel
Tel. 0561/980-2980, Fax -980-2981
info@ivf-kassel.de
www.ivf-kassel.de

RepKo – Reproduktionsmedizinisches
Kompetenzzentrum am Universitäts-
klinikum Gießen & Marburg GmbH
Prof. Dr. med. Peyman Hadji,
Dr. med. Volker Ziller,
Dr. med. Berna Seker-Pektas,
Dr. med. Christina Kliebe
Baldingerstraße
35043 Marburg
Tel. 06421/5861330, Fax -5867070
Haus 40 – Klinikstr. 33
35392 Gießen
Tel. 0641/98545207, Fax -98557099
www.repko-ukgm.de

Kinderwunschzentrum Mittelhessen
Dr. med. Amir Hajimohammad,
Berthold Oels
Sportparkstraße 9
35578 Wetzlar
Tel. 06441/200 2020, Fax -200 20299
info@ivf-mh.de
www.ivf-mh.de

gyn-medicum
Zentrum für Kinderwunsch
Dr. med. Monica Tobler,
Jana Rostek
Waldweg 5
37073 Göttingen
Tel. 0551/413 37, Fax -417 22
www.gyn-medicum.de

Kinderwunschzentrum Göttingen
Dr. med. Rüdiger Moltrecht,
Dr. med. Sabine Hübner,
Dr. med. Thomas Welcker,
Dr. med. Filiz Sakin-Kaindl,
Dr. med. Stephanie Mittmann,
Dr. med. Peter Schulzeck
Kasseler Landstraße 25 a
37081 Göttingen
Tel. 0551/998 88-0, Fax -998 88-99
info@kiwu-goettingen.de
www.kiwu-goettingen.de

Kinderwunschzentrum Magdeburg
Dr. med. Ingrid Nickel,
Dr. med. Evelyn Richter,
Dipl.-Biol. Katrin Pribbernow
Ulrichplatz 1
39104 Magdeburg
Tel. 0391/811 4090, Fax -852 0429
info@kiwumed.de
www.kinderwunschzentrum-magdeburg.de

Universitätsklinik für Reproduktionsmedizin
und Gynäkologische Endokrinologie
Prof. Dr. med. Jürgen Kleinstein,
Dr. med. Anke Britta Brössner
Gerhart-Hauptmann-Straße 35
39108 Magdeburg
Tel. 0391/671 7390, Fax -671 7389
juergen.kleinstein@med.ovgu.de
www.med.uni-magdeburg.de/krep.html

Kinderwunsch-Kö
Dr. Martina Behler, Fr. Tanja Emde
Dr. Suna Cukrucam, Dr. Giesa Rosiepen
Königsallee 63-65
40215 Düsseldorf
Tel. 0211/311 355-0, Fax -311 355-22
info@kinderwunsch-koe.de
www.kinderwunsch-koe.de

Interdisziplinäres Kinderwunschzentrum
Düsseldorf
Dr. med. Michael C. W. Scholtes,
Dipl. med. Kersten Marx,
PD Dr. med. Stefan Kißler,
Dr. med. Petra Hubert,
Dr. med. Selma Yildirim-Assaf
Völklinger Straße 4
40219 Düsseldorf
Tel. 0211/901 97-0, Fax -901 97-50
info@ivf-duesseldorf.de
www.kids4nrw.de

UniKiD Universitäres interdisziplinäres
Kinderwunschzentrum Düsseldorf
Prof. Dr. med. Jan-Steffen Krüssel,
PD Dr. med. Alexandra Hess,
Dres. med. Barbara Mikat-Drozdzynski,
Daniel Fehr, Tanja Freundl-Schütt,
Andrea Schanz, Sonja Schu,
Dres. rer. nat. Dunja Baston-Büst,
Jens Hirchenhain
Moorenstraße 5
40225 Düsseldorf
Tel. 0211/810-4060, Fax -811-6787
info@unikid.de
www.unikid.de

pro-Kindwunsch
Kinderwunschzentrum Niederrhein
Dr. med. Georg M. Döhmen,
Dr. med. Thomas Schalk
Von-Groote-Straße 175
41066 Mönchengladbach
Tel. 02161/496 86-0, Fax -496 86-19
info@pro-kindwunsch.de
www.pro-kindwunsch.de

green-ivf - Grevenbroicher Endokrino-
logikum & IVF-Zentrum
Dr. med. Jürgen Tigges,
Dr. med. Kerstin Friol,
PD Dr. med. Christian Gnoth
Rheydter Straße 143
41515 Grevenbroich
Tel. 02181/4915-13, Fax -4915-34
praxis@green-ivf.de
www.green-ivf.de

Bergisches Kinderwunschzentrum Remscheid
Dr. med. Johannes Luckhaus,
Dr. med. Anke Beerkotte
Elberfelder Straße 49
42853 Remscheid
Tel. 02191/791 92-0, Fax -791 92-39
mail@kinderwunsch-remscheid.de
www.kinderwunsch-remscheid.de

Kinderwunschzentrum Dortmund und Siegen
MVZ Ärzte Partnerschaft
Prof. Dr. med. Stefan Dieterle,
Dr. med. Andreas Neuer, Prof. Dr. med. Robert Greb
Olpe 19
44135 Dortmund
Tel. 0231-557545-0, Fax -55754599
info@ivf-dortmund.de
Hermelsbacher Weg 41
57072 Siegen
Tel. 0271/770 1810, Fax -770 18129
info@kinderwunschzentrum.org
www.kinderwunschzentrum.org

Vitro-Med Kinderwunschzentrum Bochum
Yvonne Giesner
Hellweg 2
44787 Bochum
Tel. 0234/610 654 03, Fax -685 479
info@vitro-med.de
www.vitro-med.de

novum - Zentrum für Reproduktionsmedizin
Essen - Duisburg
Prof. Dr. med. Thomas Katzorke,
Dr. med. Susanne Wohlers,
Najib N. R. Nassar,
Prof. Dr. med. Peter Bielfeld
Akazienallee 8 - 12
45127 Essen
Tel. 0201/294 29-0, Fax -294 29-14
Ärzteforum in der Tonhallenpassage
Friedrich-Wilhelm-Straße 71
47051 Duisburg
Tel. 0203/713 958-0, Fax -713 958-15
info@ivfzentrum.de
www.ivfzentrum.de

Reprovita - Kinderwunschzentrum
Recklinghausen
Dr. med. Cordula Pitone
Hertener Straße 29
45657 Recklinghausen
Tel. 02361/904 188-0, Fax -904 188-41
info@reprovita.de
www.reprovita.de

Kinderwunschpraxis Gelsenkirchen
Dr. med. Ute Czeromin,
Dr. med. Ina Walter-Göbel,
Dr. med. Kathrin Fißeler
Munscheidstraße 14
45886 Gelsenkirchen
Tel. 0209/167-1470, Fax -167-1471
info@kinderwunsch-gelsenkirchen.de
www.kinderwunsch-gelsenkirchen.de

Fertility Center Münsterland
Dr. med. Ulrich Hilland
Crispinusstraße 12
46399 Bocholt
Tel. 02871/239 43-43, Fax -239 43-44
praxis@fcm-net.de
www.fcm-net.de

Kinderwunschpraxis an der Promenade
Mempel & Stratmann
Dr. med. Andrea Mempel,
Susanne Stratmann,
Dr. rer. nat. Melanie Rickert-Föhring
Von-Vincke-Straße 14
48143 Münster
Tel. 0251/414 312-0, Fax -414 312-20
willkommen@kinderwunsch-promenade.de
www.kinderwunsch-promenade.de

MVZ Kinderwunsch- und Hormonzentrum
Münster GmbH
Dr. med. Dr. rer. nat. Lutz Belkien,
Dr. med. Caroline Niehoff,
Prof. Dr. med. Axel Kamischke
Hötteweg 5 - 7
48143 Münster
Tel. 0251/482 67-0, Fax -482 67-77
info@ivf-muenster.de
www.kinderwunschtherapie.de

Universitäres Kinderwunschzentrum Münster
PD Dr. med. Andreas Schüring
Klinik für Frauenheilkunde und Geburtshilfe
Univ.-Prof. Dr. med. Ludwig Kiesel
Centrum für Reproduktionsmedizin und Andrologie
Prof. Dr. med. Sabine Kliesch
Albert-Schweitzer-Campus 1, Gebäude D11
48149 Münster
Tel. 0251/8358 280
info-kinderwunsch@ukmuenster.de

Zentrum für Kinderwunschbehandlung Osnabrück
Irene Coordes,
Dr. med. Manfred Schneider
Rheiner Landstraße 93 - 95
49078 Osnabrück
Tel. 0541/404 500, Fax -404 5040
info@kinderwunsch123.de
www.kinderwunsch123.de

GMP Frauenheilkunde & Reproduktionsmedizin
Dr. med. Dieter Struller,
Dr. med. Christof Etien
Graf-Salm-Straße 10
50181 Bedburg, Erft
Tel. 02272/7778, Fax -7773
info@kinderwunsch-erft.de
www.kinderwunsch-erft.de

MVZ PAN Institut für Endokrinologie und Reproduktionsmedizin
Dr. med. Stefan Palm,
Dr. med. Dipl.-Biol. Irene Pütz,
Dr. med. Mirko Dannhof,
PD Dr. med. Dolores Foth
Zeppelinstraße 1
c/o PAN Klinik
50667 Köln
Tel. 0221/2776-229, Fax -2776-201
repro@pan-klinik.de
www.mvz-pan-institut.de

Kinderwunschzentrum Köln
Praxis und Klinik Schönhauserstraße
Dr. med. Markus Merzenich
Schönhauser Straße 3
50968 Köln
Tel. 0221-3403070
mmerzenich@kinderwunschzentrum-koeln.de
Kinderwunschzentrum
Eva Schwahn
Schönhauser Straße 3
50968 Köln
Tel. 0221/340 2280, Fax -340 6017
info@wunschkind-koeln.de
www.wunschkind-koeln.de

Universitäts-Frauenklinik für Gynäkologische Endokrinologie und Reproduktionsmedizin
Medizinische Fakultät der RWTH Aachen
Prof. Dr. med. Joseph Neulen,
Dr. med. Benjamin Rösing
Pauwelsstraße 30
52074 Aachen
Tel. 0241/808 8971, Fax -808 2518
gyn-endokrinologie@ukaachen.de
www.gyn-endokrinologie.ukaachen.de

Frauenarztpraxis mit Schwerpunkt Gynäkologische Endokrinologie und Reproduktionsmedizin an der Itertalklinik
Dr. med. Klaus Grunwald
Eisenhütte 23 - 25
52076 Aachen
Tel. 02408/958 499, Fax -958 477
kinderwunsch-aachen@t-online.de
www.kinderwunsch-aachen.de

Universitätsfrauenklinik Bonn
Abteilung für Gynäkologische Endokrinologie und Reproduktionsmedizin
Prof. H. van der Ven,
Prof. K. van der Ven,
Dr. U. Bohlen,
Prof. Dr. rer. nat. M. Montag,
Dr. M. Köster
Sigmund-Freud-Straße 25
53105 Bonn
Tel. 0228/287-19186 od. -19187, Fax -287-15795
Daniela.von_Kospoth@ukb.uni-bonn.de
www.kinderwunsch-uni-bonn.de

Praxisklinik für Gynäkologische Endokrinologie und Reproduktionsmedizin
Priv.-Doz. Dr. Dr. med. Gernot Prietl
Theaterplatz 18
53177 Bonn-Bad Godesberg
Tel. 0228/35 039 10, Fax -364 892
ivf@careme.de

Praxisklinik Trier – Zentrum für Gynäkologische Endokrinologie & Reproduktionsmedizin
Dr. med. Mohsen Satari,
Prof. Dr. med. Jürgen P. Hanker
Wissenschaftspark (WIP)
Max-Planck-Straße 15
54296 Trier
Tel. 0651/979 06-0, Fax -979 06-20
info@kinderwunsch-trier.de
www.kinderwunsch-trier.de

Kinderwunschzentrum - Universitätsmedizin Mainz
Univ.-Prof. Dr. med. Rudolf Seufert M.Sc.,
Fr. Priv.- Doz. Dr. C. Skala,
Fr. Dr. R. Gomez,
Fr. Dr. C. Heidner
Langenbeckstraße 1
55101 Mainz
Tel. 06131/173 929, Fax -176 215
seufert@uni-mainz.de
www.wunschkind-mainz.de

Kinderwunsch Zentrum Mainz
Dr. med. Robert Emig,
Dr. med. Silke Mettlin
Rheinstraße 4
Fort Malakoff Park
55116 Mainz
Tel. 06131/603 020, Fax -603 0210
arzt@kinderwunschzentrum-mainz.de
www.kinderwunschzentrum-mainz.de

Kinderwunschzentrum Mittelrhein
Dr. med. Josef Beran,
Dr. med. Birgit Müller,
Dr. med. Sebastian Hagelauer
Marktstraße 83
56564 Neuwied
Neustadt 8
56068 Koblenz
Tel. 02631/3968-0, Fax -3968-29
info@kinderwunsch-mittelrhein.de
www.kinderwunsch-mittelrhein.de

Zentrum für Reproduktionsmedizin
Prof. Dr. med. Dr. med. habil. Ernst Siebzehnrübl,
Dr. med. Anja Weidner
Hanauer Landstraße 328 - 330
60314 Frankfurt am Main
Tel. 069/426 077-0, Fax -426 077-10
anmeldung@ivf-ffm.de
www.ivf-ffm.de

Kinderwunschzentrum Frankfurt am Main
Prof. Dr. med. Prof. h.c. Eberhard Merz,
Dr. med. Christine Molitor,
Dr. med. Marie-Theres Swayze,
Frau Ines Boehnisch
Steinbacher Hohl 2 - 26
60488 Frankfurt
Tel. 069/7601-3611, Fax -7601-3321
info@kinderwunschzentrum-frankfurt.de
www.kinderwunschzentrumfrankfurt.de

Fertilitätszentrum und Gynäkologische Endokrinologie
Klinik für Frauenheilkunde und Geburtshilfe
Johann-Wolfgang-Goethe-Universität
Prof. Dr. med. Inka Wiegratz,
Dr. med. Nicole Sänger,
Dr. med. Annette Bachmann,
Dr. Anna Michaelis
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Tel. 069/6301-5518, Fax -6301-4505
info.ivf@kgu.de
www.kgu.de/zfg/gyn

Kinderwunsch- und Endometriosezentrum am Büsing Park
Dr. med. Konstantin Manolopoulos,
Dr. med. Nadja Najjari
Herrnstraße 51
63065 Offenbach
Tel. 069/809 075 71, Fax -809 075 73
dr-manolopoulos@offenbach-kinderwunsch.de
www.offenbach-kinderwunsch.de

Kinderwunschzentrum Darmstadt
Prof. Dr. med. G. Leyendecker,
Dr. med. A. Bilgicyildirim,
Dr. med. M. Inacker,
Dr. med. J. Bratengeier,
Dr med. H Engelskirchen-Amran,
A. Weber-Lohrum,
Dr. rer. nat. Th. Stalf,
Dr. rer. nat. U. Mischeck,
Dr. rer. medic. B. Jackisch
Bratustraße 9
64293 Darmstadt
Tel. 06151/500 98-0, Fax -500 98-500
info@kwz-da.de
www.kinderwunschzentrum-da.de

MVZ Kinderwunschzentrum Wiesbaden GmbH
Dr. med. Martin Schorsch,
Dr. med. Thomas Hahn,
Dr. med. Geza Adasz,
Karin Schilberz,
Dr. med. Michael Amrani
Mainzer Straße 98 - 102
65189 Wiesbaden
Tel. 0611/976 32-0, Fax -976 32-10
info@kinderwunschzentrum-wiesbaden.de
www.kinderwunschzentrum-wiesbaden.de

Überregionales Kinderwunschzentrum IVF-Saar Saarbrücken-Kaiserslautern
Dr. med. Lars Happel,
Andreas Giebel,
Dr. med. Anette Russu,
Dr. med. Marika Otte
Dr. med. rer. medic. Martin Greuner
Europaallee 15
66113 Saarbrücken
Tel. 0681-93632-0, Fax -93632-10
Maxstraße 13
67659 Kaiserslautern
Tel. 0631/936 32-0, Fax: -936 32-10
zentrum@ivf-saar.de
www.ivf-saar.de

Klinik für Frauenheilkunde, Geburtshilfe und Reproduktionsmedizin
Universitätskliniken des Saarlandes
Prof. Dr. med. E.-F. Solomayer,
OA Peter Rosenbaum,
Prof. Dr. Dr. ME Hammadeh,
Dr. med. Kathrin Abel,
Dr. med. Michaela von Blohn
Kirrbergstraße 1
66421 Homburg
Tel. 06841/162 8213, Fax -162 8061
ivf@uks.eu
www.uniklinikum-saarland.de/einrichtungen/kliniken_institute/frauenklinik/

Kinderwunschzentrum Ludwigshafen
Dr. med. Tobias Schmidt,
Dr. med. Elena Hartschuh,
Dr. med. Claudia Schmidt,
Dr. rer. nat. Nicole Motzkus
Ludwigstraße 54 b
67059 Ludwigshafen
Tel. 0621/592 986 88, Fax -592 986 90
kontakt@kinderwunsch-lu.de
www.kinderwunschzentrum-ludwigshafen.de

Kinderwunschzentrum Mannheim
Prof. Dr. med. Marc Sütterlin,
Dr. med. Regine Schaffelder,
Dr. med. Julia Rehnitz,
Dr. med. Jade Mayer
Dr. sc. hum. Monika Gentili
Theodor-Kutzer-Ufer 1 - 3
68167 Mannheim
Tel. 0621/383-3638, Fax -383-3814
ivflabor@umm.de
www.umm.de/64.0.html

Viernheimer Institut für Fertilität
PD Dr. med. Stefanie Volz-Köster,
Dr. med. Christina Nell,
Dr. sc. Hum. Brigitte Hauff
Karl-Marx-Straße 43
68519 Viernheim
Tel. 06204/703 600, Fax -703 605
info@vif-kinderwunsch.de
www.vif-kinderwunsch.de

Abt. für Gynäkologische Endokrinologie und Fertilitätsstörungen
Universitätsklinikum Heidelberg
Prof. Dr. med. Thomas Strowitzki,
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Dr. med. Maren Goeckenjan,
Dr. med. Lisa-Maria Wallwiener,
Prof. Dr. rer. Nat Markus Montag
Voßstraße 9
69115 Heidelberg
Tel. 06221/567 910, Fax -564 099
thomas.strowitzki@med.uni-heidelberg.de
www.klinikum.uni-heidelberg.de/Kinderwunschambulanz.583.0.html

Kinderwunschzentrum Heidelberg
Dr. med. Waltraud Parta-Kehry,
Dr. sc. hum. Suat Parta,
Friederike Tesarz,
Dr. med. Daniela Seehaus,
Dr. med. Christina Thöne
Römerstraße 3
69115 Heidelberg
Tel. 06221/893 00-0, Fax -893 00-20
info@kwz-hd.de
www.kwz-hd.de

Kinderwunsch-Zentrum Stuttgart
Prof. Dr. med. Dieter H. A. Maas,
Dr. med. Friedrich Gagsteiger,
Dr. med. Christine Eberle,
Dr. med. Anja Bock-Skupin,
Dr. med. Nina Kircher
Friedrichstraße 45
70174 Stuttgart
Tel. 0711/997 806-0, Fax -997 806-10
info@kwz-stuttgart.de
www.kwz-stuttgart.de

Kinderwunsch-Zentrum Stuttgart
Praxis Villa Haag
Dr. med. Dieter B. Mayer-Eichberger
Herdweg 69
70174 Stuttgart
Tel. 0711/221 084, Fax -221 085
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www.kinderwunschpraxis.de

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Dr. med. Fred Maleika
Lessingstr. 9
70174 Stuttgart

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Univ.-Prof. Dr. med. Ute Fuchs
Dr. rer. nat. Silvia Harrer
Kornbergstraße 23
70176 Stuttgart
Tel. 0711/226 2728, Fax -226 2738
Prof.UteFuchs@t-oline.de
www.kinderwunsch-bw.de

Kinderwunschzentrum Ludwigsburg
Dr. med. Andreas Ott
Pflugfelder Straße 22
71636 Ludwigsburg
Tel. 07141/688 76-0, Fax -688 76-9
info@kiwu-lb.de
www.kiwu-lb.de

Praxis Dres. med. Göhring
Herr Dr. med. U. Göhring,
Frau Dr. med. I. Göhring,
Frau Dr. med. J. Rattenhuber
Hagellocher Weg 63
72070 Tübingen
Tel. 07071/946 63-0, Fax -946 63-99
info@kinderwunschpraxis.com
www.kinderwunschpraxis.com

IVF-Zentrum der Universitätsfrauenklinik Tübingen
Dr. med. Barbara Lawrenz
Calwerstraße 7
72076 Tübingen
Tel. 07071/298 3117 , Fax -292 250
barbara.lawrenz@med.uni-tuebingen.de
www.uni-frauenklinik-tuebingen.de

Kinderwunschzentrum Aalen
Dr. med. Rainer Rau,
Dr. med. Birgit Schröppel,
Dr. rer. nat. Roland Eid (Labor)
Weidenfelder Straße 1
73430 Aalen
Tel. 07361/620 21, Fax -620 26
info@kinderwunsch-aalen.de
www.kinderwunsch-aalen.de

IVF-Zentrum Esslingen
Dr. med. Johann Emil Costea
Dipl. Ing. Luminitza Costea
Dr. rer. nat. Michael Troge
Marktplatz 5/1
73728 Esslingen
Tel. 0711/310 591 60, Fax -310 591 61
IVFCostea@t-online.de
www.ivf-praxis.com

Centrum für Kinderwunsch Pforzheim
Verena Peuten
Zerrenner Straße 22 - 24
75172 Pforzheim
Tel. 07231/280 8280, Fax -280 82888
info@kinderwunsch-pforzheim.de
www.kinderwunsch-pforzheim.de

Kinderwunschzentrum Karlsruhe
Karlsruher IVF-Programm
Arbeitsgemeinschaft für Fortpflanzungsmedizin
Hans-Jürgen Gräber,
Dr. Frank Tetens,
Dr. med. Daniela Plathow,
Laborärzte Dr. Ehrfeld + Kollegen,
Humangenetik Dr. Schlüter, Dr. Schüler
Waldstraße 14
76133 Karlsruhe
Tel. 0721/824 6700, Fax -295 27
info@ivf-programm.de
www.ivf-programm.de

Kinderwunschzentrum Klinikum Mittelbaden
MVZ GmbH
Prof. Dr. med. Wolfgang Küpker,
Dr. med. Peter Hartmann,
Dr. med. Markus Knoll,
Dr. s.c. hum. Wolfgang Bernart (Dipl.-Biol.)
Engelstraße 39
76437 Rastatt
Tel. 07222/596 0282, Fax -596 0284
info@kinderwunschzentrum-mittelbaden.de
www.kinderwunschzentrum-mittelbaden.de

Kinderwunsch Bodensee
Dr. med. Andreas Heine,
Dr. med. Antje Hiemer,
Dr. Angela Panhans
Maggistraße 5
78224 Singen
Tel. 07731/912 999-0, Fax -912 999-99
info@endlichnachwuchs.de
www.endlichnachwuchs.de

Centrum für gynäkologische Endokrinologie und Reproduktionsmedizin Freiburg (CERF)-
Dr. med. Rudolf Weitzell,
Dr. med. Maria Thiemann,
PD Dr. med. Birgit Wetzka,
Prof. Dr. med. Franz Geisthövel
Bismarckallee 7 f
79098 Freiburg
Tel. 0761/207 43-0, Fax -321 11
info@kinderwunsch-hormone.de
www.kinderwunsch-hormone.de

Universitäts-Frauenklinik Freiburg
Endokrinologie und Reproduktionsmedizin
Dr. med. Stephanie Friebel,
Dr. med. Aida Hanjalic-Beck,
Dipl.-Biol. Elisabeth Halbe
Hugstetter Straße 55
79106 Freiburg
Tel. 0761/270-31500, Fax -270-29120
stephanie.friebel@uniklinik-freiburg.de
www.uniklinik-freiburg.de/frauenklinik/live/endokrinologie.html

Zentrum für Reproduktionsmedizin München
Gemeinschaftspraxis für Frauenheilkunde und Geburtshilfe
Dr. med. Walter Bollmann,
Dr. med. Thomas Brückner,
Dr. med. Ulrich Noss
Tal 11
80331 München
Tel. 089/242 295-0, Fax -242 295-60
info@ivf-bbn.de
www.ivf-bbn.de

Gynäkologische Endokrinologie und Reproduktionsmedizin der Uni München – Innenstadt
Ludwig-Maximilians-Universität
Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe, Klinikum der Universität München
Prof. Dr. med. Markus S. Kupka
Maistraße 11
80337 München
Tel. 089/5160-4214, Fax -5160-4918
nachricht@ivf-maistrasse.de
www.ivf-maistrasse.de

Hormonzentrum München
Dr. med. Helmut Lacher,
Dr. med. Jörg Puchta,
Dr. med. Silke Michna,
PD Dr. med. Hans-Ulrich Pauer
Westendstraße 193 - 195
80686 München
Tel. 089/547 041-0, Fax -547 041-34
info@hormonzentrum.de
www.hormonzentrum.de

Kinderwunsch Centrum München-Pasing
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Dr. med. Gottfried Krüsmann,
Prof. Dr. Dr. med. habil. Wolfgang Würfel,
Ina Laubert, Dr. med. Claudia Santjohanser,
Sabine Völker, Osama Meri,
Dr. med. Jan Krüsmann
Lortzingstraße 26
81241 München
Tel. 089/244 144-0, Fax -244 144-42
info@ivf-muenchen.de
www.ivf-muenchen.de

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Leitende Embryologin:
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Prinzregentenstraße 69
81675 München
Tel. 089/414 240-0, Fax -414 240-11
info@ivf-muenchen.com
www.ivf-muenchen.com

Kinderwunsch Centrum Chiemsee
Dr. med. Susann Böhm,
Dr. med. Matthias Lehnert,
Dr. med. Angelika Stahl
Hochriesstraße 21
83209 Prien am Chiemsee
Tel. 08051/5050, Fax -63499
info@kinderwunsch-chiemsee.de
www.kinderwunsch-chiemsee.de

Kinderwunschzentrum Augsburg
Dr. med. Klaus-Friedrich Hiller,
Dr. med. Thomas Bauer,
Dr. med. Harald Kraus,
Prinzregentenstraße 25/III
86150 Augsburg
Tel. 0821/502 7888, Fax -502 7878
info@ivf-augsburg.de
www.ivf-augsburg.de

KWK – KinderWunschKempten
Zentrum für Reproduktionsmedizin
Klinik für Frauenheilkunde und Geburtshilfe
- Klinikum Kempten Oberallgäu gGmbH
Prof. Dr. med. Ricardo Felberbaum,
OA Gerhard Allgayer,
Dr. med. Bettina Kollmannsberger,
Dipl.-Biol. Mohammad Kousehlar
Robert-Weixler-Straße 50
87439 Kempten
Tel. 0831/530-3393, Fax -530-3457
ricardo.felberbaum@klinikum-kempten.de
www.kinderwunsch-kempten.de

Praxis Frauenstraße Ulm GbR
Prof. Dr. med. Karl Sterzik,
Dr. med. Erwin Strehler
Frauenstraße 51
89073 Ulm
Tel. 0731/966 51-0, Fax -966 51-30
info@kinderwunsch-ulm.de
www.kinderwunsch-ulm.de

Universitätsfrauenklinik und Poliklinik Ulm
Zentrum für Reproduktionsmedizin und Gynäkologische Endokrinologie
PD Dr. med. Katharina Hancke
Prittwitzstraße 43
89075 Ulm
Tel. 0731/5005 8663, Fax -5005 8664
repromed.ufk@uniklinik-ulm.de
www.uni-ulm.de/klinik/ufk/

Kinderwunsch-Zentrum Ulm
Dr. med. Friedrich Gagsteiger,
Dr. med. Natalie Reeka,
Dr. med. Kerstin Eibner,
Dr. med. Nilofar Huzurudin
Einsteinstraße 59
89077 Ulm
Tel. 0731/151 590, Fax 0731-151 5915
info@kwz-ulm.de
www.kidz-ulm.de

Kinderwunsch und Frauen-Hormon Centrum
Dr. med. Joachim Neuwinger,
Dr. med. Barbara Munzer-Neuwinger,
Prof. Dr. med. Peter Licht
Agnesgasse 2-4
90403 Nürnberg
Tel. 0911/235 5500, Fax -235 5516
aerzte@kinderwunschcentrum-nuernberg.de
www.kinderwunschzentrum-nuernberg.de

Kinderwunschzentrum Erlangen
Dr. med. Jan van Uem,
Dr. med. Madeleine Haas
Michael-Vogel-Straße 1 e
91052 Erlangen
Tel. 09131/8095-0, Fax -8095-30
info@vanuem.com
www.kinderwunschzentrum-erlangen.de

Gemeinschaftspraxis der Frauenärzte
Dres. Hamori, Behrens, Hammel
Dr. med. Miklos Hamori,
Dr. med. Rolf Behrens,
Dr. med. Andreas Hammel
Nürnberger Straße 35
91052 Erlangen
Tel. 09131/895 20, Fax -205 410
info@ivf-erlangen.de
www.ivf-erlangen.de

Universitäts-Fortpflanzungszentrum Franken (UFF) des Univ.-Klinikums Erlangen
Prof. Dr. med. Matthias W. Beckmann
PD Dr. med. Andreas Müller,
Prof. Dr. rer. nat. Ralf Dittrich (Biologe)
Universitätsstraße 21 - 23
91054 Erlangen
Tel. 09131/85-33553, Fax -85-33552
fk-uff@uk-erlangen.de
www.reproduktionsmedizin.uk-erlangen.de

Kinderwunschzentrum Amberg
Dr. med. Jürgen Krieg
Prof. Dr. med. Anton Scharl
Mariahilfbergweg 7
92224 Amberg
Tel. 09621/381 519, Fax -381 941
info@kinderwunschzentrum-amberg.de
www.kinderwunschzentrum-amberg.de

KITZ Regensburg – KinderwunschTherapie im Zentrum Regensburg
Prof. Dr. med. Bernd Seifert,
Dr. med. Claudia Gaßner
Hemauerstraße 1
93047 Regensburg
Tel. 0941/992 577-0, Fax -992 577-23
info@kitz-regensburg.de
www.kitz-regensburg.de

Kinderwunschzentrum Profertilita
Prof. Bals-Pratsch, M. Sc.
Dr. Eder, M. Sc.
Hildegard-von-Bingen-Straße 1
93053 Regensburg
Tel. 0941/898 499 44, Fax -898 499 45
praxis@profertilita.de
www.profertilita.de

Kinderwunschzentrum Niederbayern
Dr. med. Hans-Joachim Kroiss,
Dr. med. Samuel Dadze-Arthur,
Dr. IM Tem. Elfriede Bernhardt
Stadtfeldstraße 50
94469 Deggendorf
Tel. 0991/297 993 32, Fax -297 993 31
praxis@ivf-bayern.de
dr.kroiss@ivf-bayern.de
www.kinderwunsch-niederbayern.de/

Klinik am Hofgarten
Dr. med. Stefan Todorow,
Dr. med. Erika Schwarz
Richard-Wagner-Straße 34 - 36
95444 Bayreuth
Tel. 0921/745 4440, Fax -745 44410
info@ivf-bayreuth.de
www.ivf-bayreuth.de

Zentrum für Reproduktionsmedizin, Medizinische Genetik und Pränataldiagnostik
Dr. med. Reinhard Mai,
Dr. med. Wolfgang Schmitt,
Dr. med. Lore Mulfinger
Juliuspromenade 7
97070 Würzburg
Tel. 0931/321 230, Fax -321 23-77
kontakt@drs-mai-schmitt-mulfinger.de
www.drs-mai-schmitt-mulfinger.de

Universitäts-Frauenklinik Würzburg
Zentrum für gynäkologische Endokrinologie und Reproduktionsmedizin
Prof. Dr. med. Ursula Zollner,
Dr. med. Michael Schwab,
Dr. rer. nat. Claudia Staib
Josef-Schneider-Straße 4
97080 Würzburg
Tel. 0931/201-25619, Fax -201-25406
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