SUCCESS RATES OF IVF CYCLES IN SANATORIUM HELIOS, 2014

First we would like to explain how we calculate our results. To understand whether they are objective and true, we would like to clarify our philosophy and practices. What we do is based upon long-term work, and experience gained in cooperation with the global leader in the field of IVF research, Australian company Genea, whose own exclusive licence we have proudly owned for nearly 13 years.

It is not true that all IVF centers operate in the same way. That they have the same procedures, use the same materials and devices, that their staff have had their training of the same quality, and that they produce embryos of the same quality. The price you pay for IVF is more or less similar everywhere in the Czech Republic. The health insurance companies also pay the same amount of money to all the centers. But your chance to fulfill your dream to get pregnant and to give birth to a healthy child, varies considerably, which can be clearly demonstrated on the data available on Czech IVF centers' websites.

Unfortunately at this time there is no independent databasis to objectively compare success rates of individual centers. The available data are always cumulative and even outdated. That is why we always try to explain and clarify our results and reveal our data as much as possible.

Our practices are different from those of other IVF centres, mostly because we ensure:

- monitoring of stimulations with three to four regular check ups (blood collection + ultrasound examination)
- correct timing of egg collection. Sometimes it is necessary to prolong or shorten the length of stimulation according to the check ups' results. Therefore, we work 7 days a week. Time to adapt to achieve optimal results.
- high quality using so called prolonged cultivation until the 5th-6th day of embryo development. In 2014, we increased its utilisation up to to 39.1% of good quality blastocyst (for the last 5 years, on average about 10%).
- transferring only one embryo, always after prolonged cultivation and at the phase of the cycle,
- PGS examination in more than half of IVF cycles, which helps to eliminate genetically defective embryos from further use. Thus we increase the success and reduce the time needed for a healthy pregnancy.
- in more than 70% of the cycles we freeze all quality blastocysts (ie. cryocycles), thereby increasing the chance of pregnancy with transfers in natural cycles.
SUCCESS RATES OF IVF CYCLES IN SANATORIUM HELIOS, 2014

IVF Cycles in Sanatorium Helios Brno in 2014

In 2014 we performed 502 oocyte pick ups, out of which 431 were infertility treatments with patients' own eggs.

The average age of our patients compared to 2013 increased again, up to 34.3 years (see chart).

Therefore it is not true that we only have young patients with good prospects of success. On the contrary, every year we have more and more patients with "poorer prognosis." They are older and have had multiple failed IVF cycles. More and more patients keep coming to us after failed IVF cycles in other centers. Older patients (35 and older) even slightly outweigh the younger ones.
SUCCESS RATES OF IVF CYCLES IN SANATORIUM HELIOS, 2014

Graph: Ratio of cycles with health insurance (71%) and private patients (29%). Private patients are those, who had already undergone all the cycles to which they are entitled from their health insurance, foreigners, patients older than the limits for health insurance coverage (over 40).

Graph: Ratio of cycles with fresh transfer – ie. Introduction of embryos in the cycle after stimulation (26%) and cryocycles (74%) – suitable embryos are frozen and transferred in another cycle.

Elaborated by RNDr. Kateřina Okénková, head of the IVF Laboratory
**SUCCESS RATES OF IVF CYCLES IN SANATORIUM HELIOS, 2014**

**IVF Cycles in Sanatorium Helios Brno in 2014**

<table>
<thead>
<tr>
<th></th>
<th>Younger (under 35)</th>
<th>Older (over 35)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of all the IVF patients</td>
<td>49,88 %</td>
<td>50,12 %</td>
<td>100 %</td>
</tr>
<tr>
<td>Average patient’s age (without egg donors and recipients)</td>
<td>30</td>
<td>38,5</td>
<td>34,3 let</td>
</tr>
<tr>
<td>Average IVF cycle</td>
<td>1,7</td>
<td>2,2</td>
<td>1,92</td>
</tr>
<tr>
<td>Average number of retrieved eggs</td>
<td>17,3</td>
<td>10</td>
<td>13,7</td>
</tr>
<tr>
<td>Average number of fertilized eggs</td>
<td>70,3 %</td>
<td>67,4 %</td>
<td>69,2 %</td>
</tr>
<tr>
<td>Average number of embryos with 7 and more cells on 3rd day of cultivation</td>
<td>69 %</td>
<td>66 %</td>
<td>68 %</td>
</tr>
<tr>
<td>Average number of blastocysts on 5th and 6th day</td>
<td>70,8 %</td>
<td>59 %</td>
<td>66 %</td>
</tr>
<tr>
<td>Average number of blastocysts suitable to use on 5th and 6th day</td>
<td>43,6 % (5,3)</td>
<td>31,8 % (2,14)</td>
<td>39,1 % (3,7)</td>
</tr>
<tr>
<td>Average number of transferred embryos</td>
<td>1,0</td>
<td>1,0</td>
<td>1,0</td>
</tr>
<tr>
<td>Average number of frozen (vitrified) embryos</td>
<td>3,1</td>
<td>1,3</td>
<td>2,2</td>
</tr>
</tbody>
</table>

*Chart: characteristics and partial results of IVF cycles - divided by younger (under 35 years) and older patients (35 years and more)*
Why we always do prolonged cultivation and never transfer embryos earlier than on 5th day of their development

- In natural cycles an egg is released and gets into the fallopian tube, where it meets sperm. The fertilized egg then moves in the fallopian tube towards the uterus.

- 1st, 2nd, and 3rd day of its development the embryo is still in the fallopian tube. On the 4th day the embryo gets into the phase of compact morula and heads closer to the uterus.

- In natural cycles embryos get to the uterus on 5th day of their development. This is why we do prolonged cultivation until 5th day, we try to imitate natural conditions of a woman's body to increase the odds of the implantation of the embryo to maximum.

- Prolonged cultivation is a technical term. In fact, it would rather be called "standard" cultivation and a cultivation to day 3 should be called "reduced".

- It is not true that two or three day old embryos colud do better in the uterus then in a culture dish. An embryo definitely does not belong into the uterus at this stage of development. Physiologically, it is still in the fallopian tube.

- During its journey towards the uterus, the egg/embryo needs various energy sources, types of amino acids and oxygen concentration. All this has impact on the viability of the embryo. Therefore, also the media in which embryos are cultured, are referred to as sequential. Embryos at different stages of development need various conditions for their proper development and growth.

- If the embryology laboratory is equipped with good facilities and if they know the quality of their cultivation, they can never claim to have the same success rates with transfers of three-day-old embryos and blastocysts.

- This is the main reason why we always do prolonged cultivation and we transfer embryos in the blastocyst stage (day 5 or 6 of development).
**Embrons on 3rd day of development versus 5 and 6 day old ones**

Aside from physiology and developmental stage embryos suitable for insertion into the uterus, another important factor for natural selection of embryos is prolonged cultivation. In many cases, eggs get fertilizes, but the embryos cease to evolve much earlier than they would implant into the uterus and pregnancy could be detected by a pregnancy test.

It is evident that **on average about 30% of embryos, that properly develop on the third day, would get transferred unnecessarily, since they do not result in good quality embryos** (blastocysts).

The graph also shows that although many embryos grow to the blastocyst stage, they are not of quality suitable for use (ET, freezing, PGD / PGS examination). **On average, nearly 30% blastocyst are of poor quality.**

For older patients this difference is even more significant.

![Graph: Comparison of development and quality of embryos on 3rd and 5th + 6th day of cultivation](image)

**Therefore we always do prolonged cultivation to:**

1/ assess the quality and proper embryo development

2/ introduce embryos into the uterus at the correct time
**Success rates of single embryo transfer**

Some patients have 1 transfer within one year, another patients have 2, 3, or even 4. For objective calculation of an overall success rate of IVF cycles we cannot count all the transfers and patients together. Some patients have more chances (transfers), others less.

To be able to evaluate our success of IVF objectively, we selected all the patients (except for recipients of donor eggs), who had an egg collection in 2014, and **just one single embryo transfer** – a fresh transfer or a cryoembryotransfer.

In this group we evaluated:

- overall success (biochemical and clinical pregnancy with cardiac events at one single embryo transfer)
- success after PGS-aCGH (biochemical and clinical pregnancy with cardiac events at one single embryo transfer after examination PGS)
- success rates for after fresh transfer (transfer in the cycle after stimulation) - biochemical and clinical pregnancy with cardiac events on one single embryo transfer, and success cryoembryotransfer (thawed embryo transfer) - biochemical and clinical pregnancy with cardiac events per one single embryo transfer
Why we transfer only one embryo

By following our long-term statistics, we found that success does not increase with the number of transferred embryos at the same time, but with the number of transfers (reps). It depends both on the quality of the embryo and of the endometrium. But whether one or two embryos are transferred does not show any significant effect on the final result.

- 1xET 1 embryo = Introduction of 1 embryo in 1 cycle
- 1xET 2 embryos = Introduction of 2 embryos at once in one cycle
- 2xET 1 embryo = 2 transfers in 2 cycles, in each with one introduced embryo

Graph: Comparing results from transfers of one or two embryos in 2006-2009. After introduction of two embryos, chances of pregnancy increase by about 2%. But increase of multiple pregnancies after introduction of two embryos was over 50%. If two embryos are divided into 2 transfers, the odds of getting pregnant rise by about 20%.
SUCCESS RATES OF IVF CYCLES IN SANATORIUM HELIOS, 2014

Why we transfer only one embryo

Graph: The results summarized in the graph show that the introduction of the SET does not decrease the cycles’ percentage of success. Percentage of clinical pregnancies increased linearly, and did not decrease below 50%. Clinical pregnancies (ASP+) in cycles of AR have increased since 2009 by 23%. Although the number of DET in this period was reduced from 63% (2009) to 1% (2013). The above mentioned show that success of AR cycles does not depend on the number of transferred embryos, but reflects the quality of cultivation and of the embryos.

Elaborated by RNDr. Kateřina Okénková, head of the IVF Laboratory
Why we transfer only one embryo

- Dividing embryos in multiple transfers increases the chances of pregnancy.
- Embryos do not interact together in a positive way. Neither they support each other.
- On the contrary, an embryo of lower quality, a fragmented embryo, might damage another healthy embryo (in the transfer of two embryos at once, we observed an increased percentage of abortions).
- According to current Czech legislation transfer of more than one embryo in the first two cycles of IVF means the loss of a possible fourth IVF cycle, paid by health insurance.
- If more than one embryo is transferred, there is a high risk of a multiple pregnancy. Such pregnancies are often risky and threaten both the mother and her children.

There is no logical argument why transfer more than one embryo. Such procedure should nowadays be standard to all IVF centres.
Does preimplementation genetic screening (PGS) increase success of IVF cycles?

Although blastocysts of good quality are produced (developmental stage of 5th and 6th day of embryo development), and both parents are genetically fine (having a normal karyotype), there may occur genetically faulty embryos. Such embryos may stop developing very early. These errors can also be the reason why embryos of good quality (in terms of development and morphology) do not implant in the womb, or a pregnancy occurs, but the embryo gets aborted very early. Concerning older women, there is a significantly larger number of chromosomally abnormal blastocysts compared to younger women. According to our results, among younger women (under 35) there is an average of about one-third of genetically abnormal embryos, while among women older than 35 there is indicated almost every other embryo a genetically abnormal after PGD / PGS aCGH testing. If embryos are after PGD / PGS tests reported as genetically abnormal, such genetically faulty embryos get excluded from further use, thus increasing the success rate and reducing time required for healthy pregnancies.
SUCCESS RATES OF IVF CYCLES IN SANATORIUM HELIOS, 2014

From the graphs it is clear that using the techniques of PGD / PGS increased success rate of IVF cycles in 2014 by 13% (biochemical pregnancies), and up to 19% of differences in clinical pregnancies with confirmed fetal heart activity versus IVF cycles without using these techniques.

Furthermore there is an obvious increase in success of frozen embryo transfers (FETs) versus fresh transfers in cycles after stimulation. Higher success rate of FETs is also to some extent due to the fact that all embryos after PGD / PGS after biopsy are frozen, and transferred in subsequent cycles. Impact on the success of FET is but natural-transfer in unstimulated cycle.

Given that prolonged cultivation, PGS blastocysts examination, their vitrification (freezing method) and transfer of one PGS examined embryo in a natural cycle, it is in our opinion and according to our experience, currently the most appropriate procedure of IVF. We perform increasingly more and more PGD / PGS cycles and FETs with a very high success rate.
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IVF cycles in Sanatorium Helios in 2010-2014

Graph: Numbers of OPUs, fresh transfers, frozen transfers (FET), and PGD and PGS cycles in 2010-2014
SUCCESS RATES OF IVF CYCLES IN SANATORIUM HELIOS, 2014

Comparison of Success Rates of Sanatorium Helios and European Average

(data taken from ESHRE website – European Society of Human Reproduction and Embryology) currently available data from ESHRE are from 2011.

Graph: Comparison of success rates of Sanatorium Helios and data presented by ESHRE

SUCCESS RATES OF IVF CYCLES IN 2014

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- In more than 70% of the cycles we freeze all quality blastocysts (ie. cryocycles), thereby increasing the chance of pregnancy with transfers in natural cycles.

We hope that not only our results demonstrate,
that Sanatorium Helios is the best choice for you.
Come and see yourself. We look forward to having you.

For the whole team of Sanatorium Helios

prim. MUDr. Pavel Texl