

# Controlled Ovarian Stimulation Should Not Be Recommended for Male Infertility Treated With IUI

**Yan Tang**

Zhongshan People's Hospital <https://orcid.org/0000-0002-9969-7797>

**Qian-Dong He**

Zhongshan People's Hospital

**Ting-Ting Zhang**

Zhongshan People's Hospital

**Jing-Jing Wang**

Zhongshan People's Hospital

**Si-Chong Huang**

Zhongshan People's Hospital

**Yun Ye (✉ [bigbig.g@126.com](mailto:bigbig.g@126.com))**

Zhongshan People's Hospital

---

## Research

**Keywords:** Intra-uterine insemination, Controlled ovarian stimulation, Clinical pregnancy, Live birth, Multiple pregnancy

**Posted Date:** November 9th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-101961/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

**Version of Record:** A version of this preprint was published on March 19th, 2021. See the published version at <https://doi.org/10.1186/s12958-021-00730-3>.

# Abstract

**Background:** Some studies stated that intra-uterine insemination (IUI) with controlled ovarian stimulation (COS) might increase the chance of pregnancy, while others suggested that IUI in natural cycle (NC) should be the treatment of first choice. Whether it is necessary to use COS at the same time, when IUI is applied to treat male infertility solely? There is still no consensus.

**Objective:** To investigate the efficacy of IUI with COS in male infertility solely?

**Methods:** 544 IUI cycles from 280 couples who sought medical care for male infertility from January 2010 to February 2019 were divided into two groups: group NC-IUI and group COS-IUI. Besides, the COS-IUI group was further divided into two subgroups according to the number of pre-ovulatory follicles on the day of HCG: cycles with monofollicular development (1 follicle group) and cycles with at least two pre-ovulatory follicles ( $\geq 2$  follicles group). The outcome of IUI, including clinical pregnancy rate, live birth rate, spontaneous abortion rate, ectopic pregnancy rate and multiple pregnancy rate were compared.

**Results:** The clinical pregnancy rate, live birth rate, early spontaneous abortion rate, and ectopic pregnancy rate were comparable between NC-IUI group and COS-IUI group. Similar results were observed among NC-IUI group, 1 follicle group and  $\geq 2$  follicles group. However, when it comes to the multiple pregnancy rate, a trend toward higher multiple pregnancy rate was observed in the COS-IUI group compared that in the NC-IUI group (10.5% (2/19) vs. 0 (0/42),  $P=0.093$ ), furthermore, a significant difference was found between NC-IUI group and  $\geq 2$  follicles group (0 vs. 20%,  $P=0.034$ ).

**Conclusion:** For male infertility, since in cycles with COS, especially in those with at least two pre-ovulatory follicles cycles, the multiple pregnancy rate increased without substantial gain in overall pregnancy rate, COS in IUI should not be recommended. If COS is required, one stimulated follicle and one health baby should be the goal considering the safety both for mothers and fetuses.

## Introduction

Infertility, which is defined as failure to achieve pregnancy within 12 months of unprotected intercourse or therapeutic donor insemination in women younger than 35 years or within 6 months in women older than 35 years, affects approximately 15% of couples (1). Male factor infertility is solely responsible in about 20% of infertile couples and contributes in another 30–40% (2, 3).

Intra-uterine insemination (IUI) is an effective and frequently used fertility treatment for couples with male infertility and unexplained infertility because it is less invasive, less stressful, more acceptable and more cost-effective (4–9). In IUI, a small volume of prepared semen, removing those ingredients which might interfere with fertilization, such as the dead and immotile spermatozoa, debris, white cells and seminal plasma, is injected directly into the uterine cavity around the expected time of ovulation. The rationale of this procedure includes bypassing the cervical barrier, increasing the density of normal motile spermatozoa, and bringing the spermatozoa closer to the released oocyte (6, 10).

IUI can be performed with or without controlled ovarian stimulation (COS). However, is COS beneficial for the outcome of IUI, which is still under debate. Some studies stated that IUI with COS might increase the chance of pregnancy (11, 12), while others suggested that IUI in natural cycle (NC) should be the treatment of first choice (4, 13–15). Whether it is necessary to use COS at the same time, when IUI is applied to treat male infertility solely? There is still no consensus. Therefore, we performed a retrospective study to investigate the efficacy of IUI with COS in male infertility. To the best of our knowledge, the present study includes the largest number of couples with male infertility to date in whom the outcome of IUI were analyzed between NC and COS cycles.

## Materials And Methods

### Patients

A retrospective study was performed by reviewing the clinical data of 544 IUI cycles from 280 couples who sought medical care for male infertility at Center for Reproductive Medicine of Zhongshan People's Hospital from January 2010 to February 2019. Inclusion criteria were as follows: (1) couples were diagnosed as primary infertility or secondary infertility; (2) female partner has a normal fertility status, such as having regular menstrual cycles, normal uterine cavity, positive post-coital test, and so on; (3) at least one patent fallopian tube assessed by hysterosalpingography / transvaginal real-time three-dimensional hysterosalpingo-contrast sonography and/or laparoscopy. Couples were excluded if the female partner had bilateral tubal pathology, endometriosis, irregular cycles, polycystic ovarian syndrome, or other endocrine disorders. Of note, in our center, before 2014, the diagnosis of male infertility was defined as one or more of subnormal semen variables: sperm concentration  $< 20 \times 10^6/\text{mL}$ ; motility  $< 50\%$ ; normal morphology  $< 15\%$ , according to the World Health Organization (WHO) criteria (4th version). And since 2014, the diagnosis was changed as follows: total sperm  $< 39 \times 10^6/\text{ejaculation}$  or sperm concentration  $< 15 \times 10^6/\text{mL}$ ; progressive motility  $< 32\%$ ; normal morphology  $< 4\%$ , according to the current WHO criteria (5th version). All the diagnosis was based on at least two occasional semen analyses. The study protocol was approved by the institutional ethics committee of Zhongshan People's Hospital, and informed consent for their clinical data to be used for research purposes was obtained from all participants.

### Ovarian stimulation protocols and follicle monitoring

Ovarian stimulation drugs includes: clomiphene citrate (CC), letrozole (LE), HMG, urine follicle stimulating hormone (uFSH, Livzon, Zhuhai, China). The ovarian stimulation protocols were as follows: (1) CC 50–100 mg/d or LE 2.5–5 mg/d starting from day 3–5 of the menstrual cycle for 5 days; (2) HMG or uFSH 37.5–75 IU/day starting from days 3–5 for a variable duration depending on the response; (3) CC/LE combined with HMG/uFSH: CC 50–100 mg/day or LE 2.5–5 mg/d starting from day 3–5 for 5 days followed by addition of 37.5–75 IU HMG/uFSH for a variable duration depending on the response.

Follicle growth was monitored with the use of transvaginal ultrasound by gynecologists in the reproductive medicine center. In both NC and COS cycles, follicle development was monitored from day 8–10, and then repeated every 2 or 3 days based on the follicle size. Couples were advised to cancel the cycle if more than 3 dominant follicles > 16 mm were present. Ovulation was triggered by administering human chorionic gonadotrophin (hCG) 5000-10 000 IU or triptorelin (Diphereline, Ipsen) 0.1 mg. Insemination was performed 36–40 hours later.

## **Semen preparation and insemination**

On the day of IUI, semen was processed by density-gradient centrifugation or swim up method after liquefaction. The pre-wash and post-wash parameters of semen, such as volume, sperm concentration, progressive motility, normal sperm morphology were recorded. The volume of washed semen sample used for insemination was 0.5 mL. IUI was performed by a gynecologist in a room adjacent to the laboratory. After IUI, women had a bed rest for 30 minutes.

## **Luteal phase support and follow-up**

Luteal phase support consisted of 20 mg/d dydrogesterone (Duphaston; Abbott) was routinely used since the day of ovulation. If pregnancy was confirmed on Day 14–16 after IUI by measuring serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) levels, luteal phase support was continued up to 8 weeks' gestation. In women with positive  $\beta$ -hCG, a transvaginal ultrasound examination was performed 2 weeks later to confirm clinical pregnancy. The outcome of clinical pregnancy was subsequently recorded, including spontaneous abortion, ectopic pregnancy, multiple pregnancy and live birth. A live birth was defined as the birth of an infant after 28 weeks gestation with postnatal evidence of life.

## **Statistical analysis**

The statistical analysis was performed with the Statistical Package for Social Sciences (SPSS, version 16.0 for Windows). A chi-square test was used to compare categorical data between groups. Mann-Whitney U-test was used to compare continuous variables between groups.  $P < 0.05$  was considered statistically significant.

## **Results**

280 couples completed 544 IUI cycles in total. Among them, 265 cycles (194 NC cycles and 71 COS cycles) were finished before 2014, account for 48.7%, the rest (201 NC cycles and 78 COS cycles) were performed after 2014. The mean  $\pm$  SD female age, male age and duration of infertility were  $30.9 \pm 4.8$  (years),  $33.1 \pm 5.7$  (years), and  $2.9 \pm 2.0$  (years), respectively. A total of 61 cycles resulted in pregnancy and 56 babies were delivered. The clinical pregnancy rate and live birth rate were 11.2% and 10.1%, respectively. Of the 61 pregnancies, 54 pregnancies resulted in the birth of single children ( $n = 53$ ) or twin ( $n = 1$ ), four pregnancies ended in spontaneous abortion, two pregnancies ended in ectopic pregnancy, and one heterotopic pregnancy, who underwent laparoscopic left salpingectomy at 7 weeks of gestation,

and delivered a live baby by cesarean section at 35 weeks of gestation. Neither high-order multiples occurred nor OHSS.

Table 1 showed the comparison of characteristics of patients and cycles between group NC-IUI and group COS-IUI, and except for the number of dominant follicles > 16 mm, no significant differences were found.

Table 1  
Characteristics of patients and cycles between group NC-IUI and group COS-IUI

Group	NC-IUI	COH-IUI	<i>P</i> -value
n	395	149	
Female age (y)	31.2 ± 4.8	30.8 ± 4.5	0.408
Male age (y)	33.5 ± 5.8	33.3 ± 5.3	0.840
Type of infertility (n (%))			0.137
Primary	246 (62.3)	103 (69.1)	
Secondary	149 (37.7)	46 (30.9)	
Duration of infertility (y)	2.9 ± 1.8	3.0 ± 2.4	0.602
No. of dominant follicles ≥ 16 mm	1.0 ± 0.1	1.5 ± 0.5	0.000*
Thickness of endometrium (mm)	9.8 ± 1.4	9.8 ± 1.6	0.951
TPMSC (post-wash, ×10 <sup>6</sup> )	18.2 ± 13.2	18.9 ± 12.2	0.299
normal morphology (post-wash, %)	6.3 ± 3.2	6.5 ± 3.6	0.839
Note: (1)* <i>P</i> < 0.05 was considered statistically significant;			
(2) TPMSC = total progressive motile sperm count.			

The clinical pregnancy rate of group NC-IUI per cycle was 10.6%, which was comparable to that of group COS-IUI (12.8%). And the outcome of clinical pregnancy, including live birth rate, spontaneous abortion rate, and ectopic pregnancy rate were also comparable between the two groups (Table 2). Although a trend toward higher multiple pregnancy rate was observed in the group COS-IUI (10.5% vs. 0), the difference did not reach statistical significance (*P* = 0.093) (Table 2). In order to eliminate the potential influence of repeated cycle data and different diagnostic criteria (WHO 4th version and WHO 5th version) on the results, only the first cycle were included and divided into two subgroups: the year before 2014 and the year after 2014. The pregnancy rate and live birth rate were compared between the group NC-IUI and group COS-IUI within each subgroup, and still no significant differences were shown (Fig. 1).

Table 2  
Comparison of pregnancy outcome between group NC-IUI and group COS-IUI

Group	n	Clinical pregnancy (n (%))	Live birth (n (%))	Early spontaneous abortion (n (%))	Ectopic pregnancy (n (%))	Multiple pregnancy (n (%))
NC-IUI <sup>a</sup>	395	42 (10.6)	38 (9.6)	2 (4.8)	2 (4.8)	0 (0)
COS-IUI <sup>b</sup>	149	19 (12.8)	17* (11.4)	2 (10.5)	1* (5.3)	2* (10.5)
1 follicle <sup>b1</sup>	75	9 (12.0)	8 (10.7)	1 (11.1)	0 (0)	0 (0)
≥ 2 follicles <sup>b2</sup>	74	10 (13.5)	9* (12.2)	1 (10.0)	1* (10.0)	2* (20.0)
<i>P</i> -value (a vs. b)		0.542	0.527	0.582	1.000	0.093
<i>P</i> -value (b1 vs. b2)		0.811	0.802	1.000	1.000	0.474
<i>P</i> -value (a vs. b1)		0.688	0.832	0.449	1.000	/
<i>P</i> -value (a vs. b2)		0.427	0.527	0.481	0.481	0.034**
Note: (1) * in which there was one heterotopic pregnancy;						
(2) ** <i>P</i> < 0.05 was considered statistically significant.						

Then, the COS cycles were further divided into two subgroups according to the number of pre-ovulatory follicles on the day of HCG: cycles with monofollicular development (1 follicle) and cycles with at least two pre-ovulatory follicles (≥ 2 follicles). No significant differences were found in the clinical pregnancy rate, live birth rate, early spontaneous abortion rate and ectopic pregnancy rate between these two groups. Similar results were observed in the comparison between NC group and 1 follicle group. So did between NC group and ≥ 2 follicles group. However, when it comes to the multiple pregnancy, two multiple pregnancies (one twin and one heterotopic pregnancy) occurred in ≥ 2 follicles group, while no multiple pregnancy was found neither in NC group nor in 1 follicle group. A significant difference was found between NC-IUI group and ≥ 2 follicles group (0 vs. 20%, *P* = 0.034). These results are shown in Table 2.

## Discussion

Male infertility has become a global health issue. It has been reported that there had been a decline in semen counts over the previous 50 years (16). According to the results from Agarwal A's research (17), at least 30 million men worldwide are infertile with the highest rates in Africa and Eastern Europe. For a long time, IUI has been considered as the first-line treatment for male infertility. And the published pregnancy rates with IUI in NC cycles vary from 0-20.5%; while in stimulated cycles vary from 3.9–13.6% per cycle (4). In our study, the pregnancy rate and live birth rate per cycle in the NC-IUI group were 10.6% and 9.6%, respectively, while in the COS-IUI group were 12.8% and 11.4%, respectively, which was slightly higher than the former, but no statistically significant differences were observed. When only the first cycle were included and were further divided into two subgroups: the year before 2014 and the year after 2014, to eliminate the potential influence of repeated cycle data and different diagnostic criteria (WHO 4th version and WHO 5th version) on the results, similar results were shown. Besides, the cumulative live birth rate was also compared between those who used NC always and those who use NC or COS randomly (19.9% vs. 19.3%,  $P=1.000$ , data were not shown). Therefore, we advocate that for male infertility, IUI with COS did not significantly increase the pregnancy rate and live birth rate regardless of the diagnostic criteria for male infertility, which is consistent with other studies (4, 13–15, 18). Furthermore, two recent systematic reviews (10, 19) also suggested that IUI with or without COS for male infertility has no significant differences in pregnancy rate and live birth rate. However, in the study of Guzick DS. et al. (20), discordant results were shown. Their results showed that for unexplained infertility or male infertility, the pregnancy rate was nearly twice in IUI with superovulation as high as that in IUI without superovulation (33% vs. 18%). This might be explained by their intense stimulation with 150 IU HMG as an initiated dose.

As it has also been suggested that COS could overcome subtle ovulation disorders that cannot be detected by routine testing (15, 21), and to some extent, multifollicular growth is associated with increased pregnancy rates, IUI with COS is always preferred. However, of note, when undertaking IUI with COS, unlike in vitro fertilization, which can choose single embryo transfer, the number of oocytes released and fertilized in vivo can be controlled only to a limited extent, therefore, increased incidence of multiple pregnancies was an inherent drawback of this treatment strategy.

Compared with singleton pregnancy, multiple pregnancy is related to a lot of pregnancy complications, including increased risks of miscarriage, pre-eclampsia, growth retardation, and preterm delivery (22). In addition, the rates of caesarean section and perinatal mortality rates were also higher in the multiple pregnancy. These are unacceptable. Therefore, the aim of fertility treatment is shifting from focusing on pregnancy rate to the birth of healthy singletons (23). A meta-analysis from van Rumste et al. (24) showed that the absolute pregnancy rate increased from 8.4–15% in IUI with COS when multifollicular growth was achieved as compared to monofollicular stimulation, while the multiple pregnancy rates increased from 3.7–17% per conceived cycle. They advocated that IUI with COS should not aim for more than two follicles, one stimulated follicle should be the goal if safety is the primary concern, whereas two follicles may be accepted after careful patient counseling.

In our study, two patients who received IUI with COS (both with HMG protocol, 2 follicles were generated) resulted in multiple pregnancies (one twin and one heterotopic pregnancy). A trend toward higher multiple

pregnancy rate was observed in the COS-IUI group, when compared to that in the NC-IUI group (10.5% (2/19) vs. 0 (0/42)), but the difference did not reach statistical significance ( $P=0.093$ ). However, when we further compared the multiple pregnancy rates between NC-IUI group and  $\geq 2$  follicles group, a significant difference was found (0 vs. 20%,  $P=0.034$ ). Besides, no differences were found between 1 follicle group and  $\geq 2$  follicles group, which was also 0 vs. 20%, and we contributed this to the small sample size. Few literatures report on multiple pregnancy of IUI with or without COS in male infertility.

## Conclusions

To the best of our knowledge, the present study included the largest number of couples with male infertility to date in whom the outcome of IUI, including clinical pregnancy, spontaneous abortion, ectopic pregnancy, multiple pregnancy and live birth, were analyzed between NC and COS cycles. The results showed that except for the multiple pregnancy rate, no significant differences were found in the clinical pregnancy rate, live birth rate, early spontaneous abortion rate, and ectopic pregnancy rate. The finding of the current study suggested that for male infertility, since in cycles with COS, especially in those with at least two pre-ovulatory follicles cycles, the multiple pregnancy rate increased without substantial gain in overall pregnancy rate, COS in IUI should not be recommended. If COS is required, one stimulated follicle and one health baby should be the goal considering the safety both for mothers and fetuses.

## Declarations

### Acknowledgments

None.

### Authors' contributions

YT conceived and designed the study. TTZ, JJW and SCH extracted the data. YT performed the statistical analysis. YT, QDH and YY wrote the manuscript. YT and YY revised the manuscript. All authors read and approved the final version of the manuscript.

### Funding

This study was supported by the Zhongshan Science and Technology Program Project (2015B1023).

### Availability of data and materials

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Ethics approval and consent to participate

The study protocol was approved by the institutional ethics committee of Zhongshan People's Hospital, and informed consent for their clinical data to be used for research purposes was obtained from all participants.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

### Author details

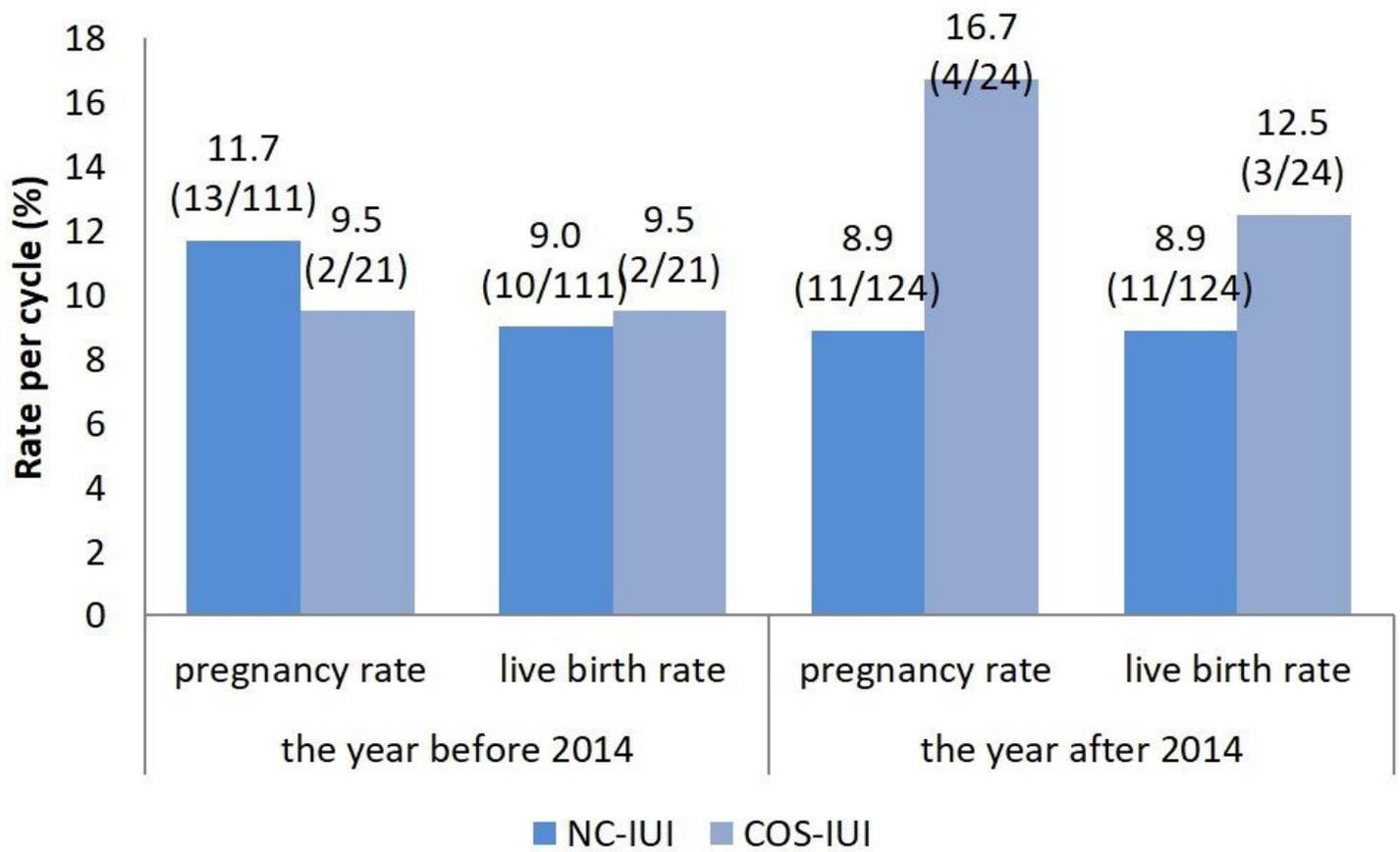
<sup>1</sup>Center for Reproductive Medicine, Department of Gynecology and Obstetrics, Zhongshan People's Hospital, No. 2, Sunwen East Road, Shiqi District, Zhongshan 528400, Guangdong Province, China.

## References

1. Infertility Workup for the Women's Health Specialist: ACOG Committee Opinion, Number 781. *OBSTET GYNECOL* 2019;133:e377-84.
2. Diagnostic evaluation of the infertile male: a committee opinion. *FERTIL STERIL* 2015;103:e18-25.
3. Sharlip ID, Jarow JP, Belker AM, Lipshultz LI, Sigman M, Thomas AJ *et al.*. Best practice policies for male infertility. *FERTIL STERIL* 2002;77:873-82.
4. Goverde AJ, McDonnell J, Vermeiden JP, Schats R, Rutten FF, Schoemaker J. Intrauterine insemination or in-vitro fertilisation in idiopathic subfertility and male subfertility: a randomised trial and cost-effectiveness analysis. *LANCET* 2000;355:13-8.
5. Keck C, Gerber-Schafer C, Breckwoldt M. Intrauterine insemination as first line treatment of unexplained and male factor infertility. *Eur J Obstet Gynecol Reprod Biol* 1998;79:193-7.
6. Kandavel V, Cheong Y. Does intra-uterine insemination have a place in modern ART practice? *BEST PRACT RES CL OB* 2018;53:3-10.
7. Cohlen BJ. Should We Continue Performing Intrauterine Inseminations in the Year 2004? *GYNECOL OBSTET INVES* 2005;59:3-13.
8. Kim Y, Park C, Ku S. Indications of Intrauterine Insemination for Male and Non-Male Factor Infertility. *SEMIN REPROD MED* 2014;32:306-12.
9. Tournaye H. Male factor infertility and ART. *ASIAN J ANDROL* 2012;14:103-8.
10. Cissen M, Bendsorp A, Cohlen BJ, Repping S, de Bruin JP, van Wely M. Assisted reproductive technologies for male subfertility. *Cochrane Database Syst Rev* 2016;2:D360.
11. Huang S, Wang R, Li R, Wang H, Qiao J, Mol BWJ. Ovarian stimulation in infertile women treated with the use of intrauterine insemination: a cohort study from China. *FERTIL STERIL* 2018;109:872-8.

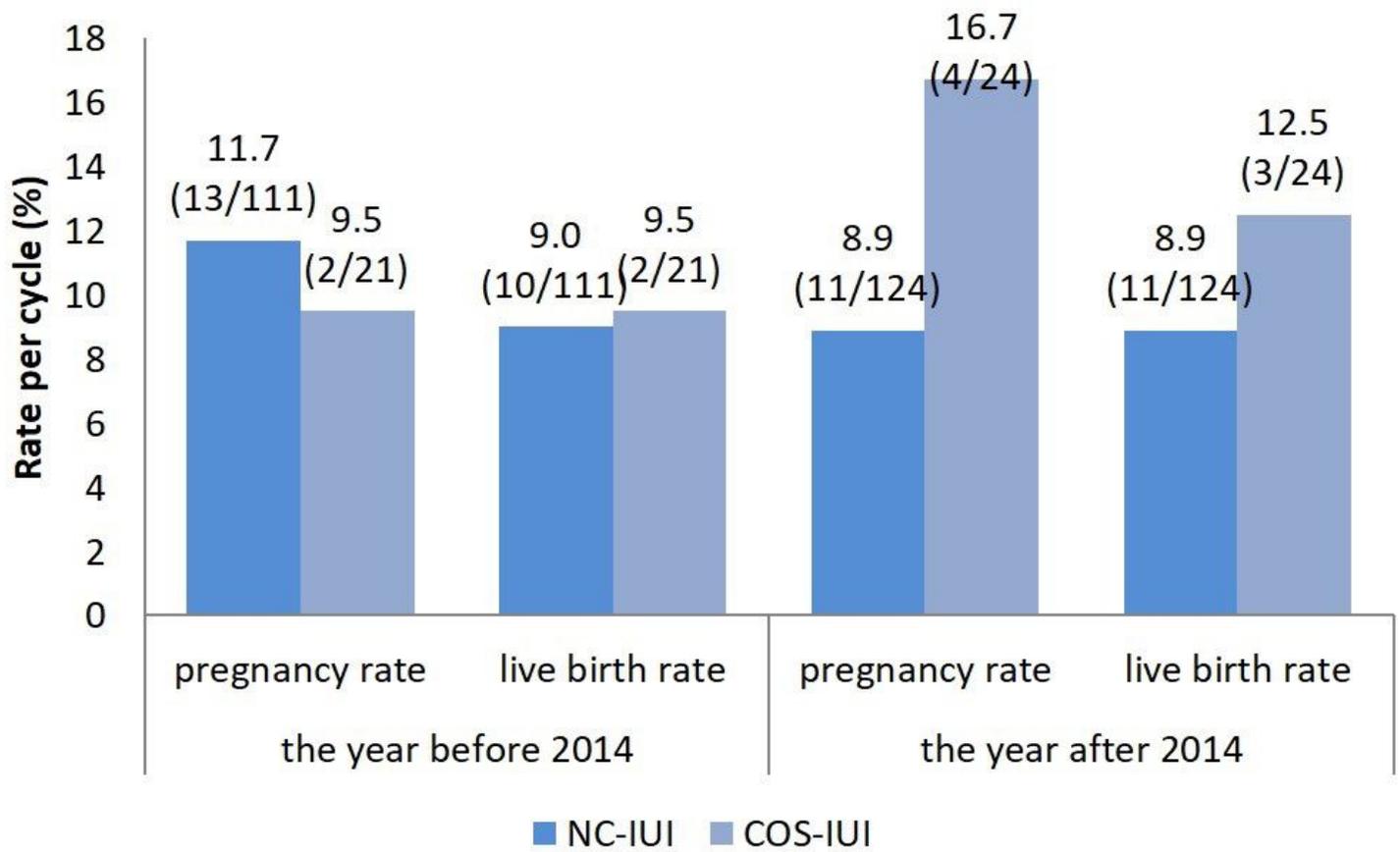
12. Liu J, Li T, Wang J, Wang W, Hou Z, Liu J. The impact of ovarian stimulation on the outcome of intrauterine insemination treatment: an analysis of 8893 cycles. *BJOG: An International Journal of Obstetrics & Gynaecology* 2016;123:70-5.
13. Cohlen BJ, Te VE, van Kooij RJ, Looman CW, Habbema JD. Controlled ovarian hyperstimulation and intrauterine insemination for treating male subfertility: a controlled study. *HUM REPROD* 1998;13:1553-8.
14. Francavilla F, Sciarretta F, Sorgentone S, Necozone S, Santucci R, Barbonetti A *et al.*. Intrauterine insemination with or without mild ovarian stimulation in couples with male subfertility due to oligo/astheno- and/or teratozoospermia or antisperm antibodies: a prospective cross-over trial. *FERTIL STERIL* 2009;92:1009-11.
15. Arici A, Byrd W, Bradshaw K, Kutteh WH, Marshburn P, Carr BR. Evaluation of clomiphene citrate and human chorionic gonadotropin treatment: a prospective, randomized, crossover study during intrauterine insemination cycles. *FERTIL STERIL* 1994;61:314-8.
16. Povey AC, Stocks SJ. Epidemiology and trends in male subfertility. *HUM FERTIL* 2010;13:182-8.
17. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. *REPROD BIOL ENDOCRIN* 2015;13.
18. Cohlen BJ, Vandekerckhove P, Te VE, Habbema JD. Timed intercourse versus intra-uterine insemination with or without ovarian hyperstimulation for subfertility in men. *Cochrane Database Syst Rev* 2000:D360.
19. Bendsdorp AJ, Cohlen BJ, Heineman MJ, Vandekerckhove P. Intra-uterine insemination for male subfertility. *Cochrane Database Syst Rev* 2007:D360.
20. Guzick DS, Carson SA, Coutifaris C, Overstreet JW, Factor-Litvak P, Steinkampf MP *et al.*. Efficacy of superovulation and intrauterine insemination in the treatment of infertility. National Cooperative Reproductive Medicine Network. *N Engl J Med* 1999;340:177-83.
21. ZIKOPOULOS K, KAPONIS A, ADONAKIS G, SOTIRIADIS A, KALANTARIDOU S, GEORGIU I *et al.*. A prospective randomized study comparing gonadotropin-releasing hormone agonists or gonadotropin-releasing hormone antagonists in couples with unexplained infertility and/or mild oligozoospermia. *FERTIL STERIL* 2005;83:1354-62.
22. Fauser BC, Devroey P, Macklon NS. Multiple birth resulting from ovarian stimulation for subfertility treatment. *LANCET* 2005;365:1807-16.
23. Min JK. What is the most relevant standard of success in assisted reproduction? The singleton, term gestation, live birth rate per cycle initiated: the BESST endpoint for assisted reproduction. *HUM REPROD* 2004;19:3-7.
24. van Rumste MM, Custers IM, van der Veen F, van Wely M, Evers JL, Mol BW. The influence of the number of follicles on pregnancy rates in intrauterine insemination with ovarian stimulation: a meta-analysis. *HUM REPROD UPDATE* 2008;14:563-70.

## Figures



**Figure 1**

Pregnancy rate per cycle and live birth rate per cycle in the NC-IUI group and the COS-IUI group stratified by the year of 2014 (only the first cycle included). (All P>0.05).



**Figure 1**

Pregnancy rate per cycle and live birth rate per cycle in the NC-IUI group and the COS-IUI group stratified by the year of 2014 (only the first cycle included). (All P>0.05).