ART Registry of Japan,2008

Contents

Summary

Assisted Reproductive Technology (ART) — such as In-Vitro Fertilization (IVF), IntraCytoplasmic Sperm Injection (ICSI) and Frozen Embryo Replacement (FER) — is a core element for infertility treatment that is used to assist women to become pregnant. ART usually involves aspirating eggs from a woman's ovaries, fertilizing them in the laboratory and then transferring embryo(s) back into a woman's uterus. Since the first treatment, in 1978 in the United Kingdom, numerous treatments had undertaken in the clinical field. It is important to validate the safety of this technology because it is a medical treatment of a human fundamental part as birth of the life. In 1990, Japan Society of Obstetrics & Gynecology (JSOG) started reporting the outcome of ART treatments and in 2007 came to create a reporting system through the Internet, known as ART online registry. ART online registry is the main website of the present data on women who underwent ART treatments from 2007.

Increased use of ART treatments
There were 190,613 ART treatment cycles reported in Japan in 2008. This is an approximate 15% increase over 2007 reported treatments. All women used their own eggs or embryos and approximately 32 % of all cycles used frozen thawed embryos.

Treatment outcomes and number of babies
Of the 190,613 treatment cycles, 17.1% resulted in a clinical pregnancy and 10.7% resulted in a live birth delivery (the birth of at least one live born baby). There were 20,422 live deliveries resulting in 21,704 live born babies.

Multiple births
From 2008, JSOG has recommends that one embryo is used for Embryo Transfer (ET) and a maximum of two embryos for those over 35-years-old or who have failed ART treatments more than once.
Multiple birth rate for ART treatment cycles in 2008 was 6.51% compared to that of 11.0% in 2007. The decrease in treatment cycles is due to Single Embryo Transfer (SET) where only one embryo maybe transferred to uterus. More importantly, the decrease in the multiple birth rate has been achieved while clinical pregnancy rate remains stable around 27% per embryo transfer cycle.

Acknowledgments

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Japan Society of Obstetrics &Gynecology
Registration and investigation subcommittee

Director
Hidekazu Saito, MD, PhD

Commissioner
Osamu Ishihara, MD, PhD
Koji Kugu,MD,PhD
Rintarou Sawa, MD, PhD
Naotake Tsuda,MD,PhD
Kouji Banno, MD, PhD
Hideya Sakakibara , MD, PhD
Fumiki Hirahara, MD, PhD
Taizou Hori, MD, PhD
Yoh Watanabe, MD, PhD

Statistical analysis
Akira Kuwahara, MD, PhD
Ryuichiro Araki,PhD
Akira Nakashima,MD
Hirohiko Tani,MD

Collaborator
Tetsurou Sakumoto, MD, PhD
Aritoshi Nakaza, B.S

Introduction to the 2008 JSOG Report

In Japan, there are 609 clinics registered to Japan Society of Obstetrics & Gynecology (JSOG) for assisted reproductive technology （ART） practice including in-vitro fertilization(IVF), intracytoplasmic sperm injection (ICSI) and frozen embryo replacement(FER). It has been mandatory for registered ART clinics to report their cycle-based clinical data via web-based registry since 2007. Pooling the data from all clinics made it possible to provide an overall national demography that could not be obtained by examining data from an individual clinic.

The data for this national report were gathered from the 609 fertility clinics. The 190,613 treatment cycles are performed at these reporting clinics in 2008, resulted in 20,422 cycles of live births (deliveries of one or more living infants) and 21,704 live infants.

This report consists of graphs and charts based on 2008 data. These figures are organized according to a type of ART procedures used. In one of the procedures, the embryos that develop in vitro are transferred back to the woman in the same cycle (fresh embryo transfer cycle). In the other, the embryos or eggs are frozen (cryopreserved) to transfer for next cycles (frozen thawed embryo transfer cycle). This report was laid out in order to contrast the above two procedures.

In Japan, ART procedures are used only for a woman’s own eggs or embryos in officially married couples. Then there is no description about ART using donor eggs or embryos in this report.

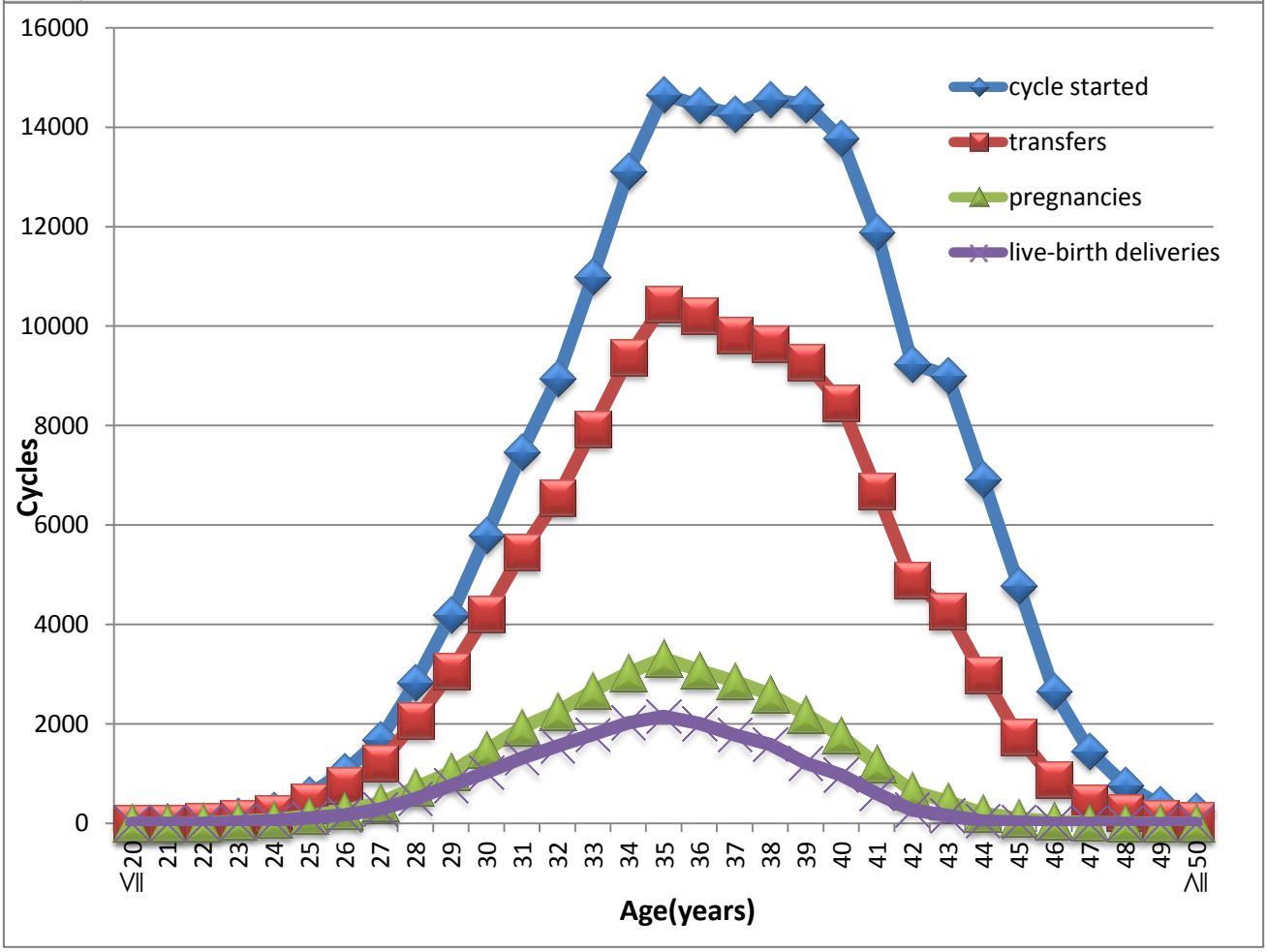
Overview of ART treatment in 2008

How does the age distribution show for the women who are treated by ART procedures?

In Japan, it has been mandatory for registered ART clinics to report their treated cycle based clinical data via web-based registry since 2007. This mandate has made the data available for analysis.
In 2008, 190,613 ART cycles in total were reported to the registry of JSOG. The patient's own eggs or embryos were used in all cycles. 121,395 cycles were able to carry out embryo transfer and 32,511 cycles achieved pregnancy. Finally 20,422 cycles resulted in live births. Figure 1 showed distribution of cycle started, transfers, pregnancies and live-birth deliveries in each age. The percentage at cycle started were about 6% in women younger than age 30, about 62% in women aged 30-39, and approximately 32% in women aged 40 or older.

Figure 1

Age Distribution of Women Treated by ART Procedures, Japan JSOG, 2008

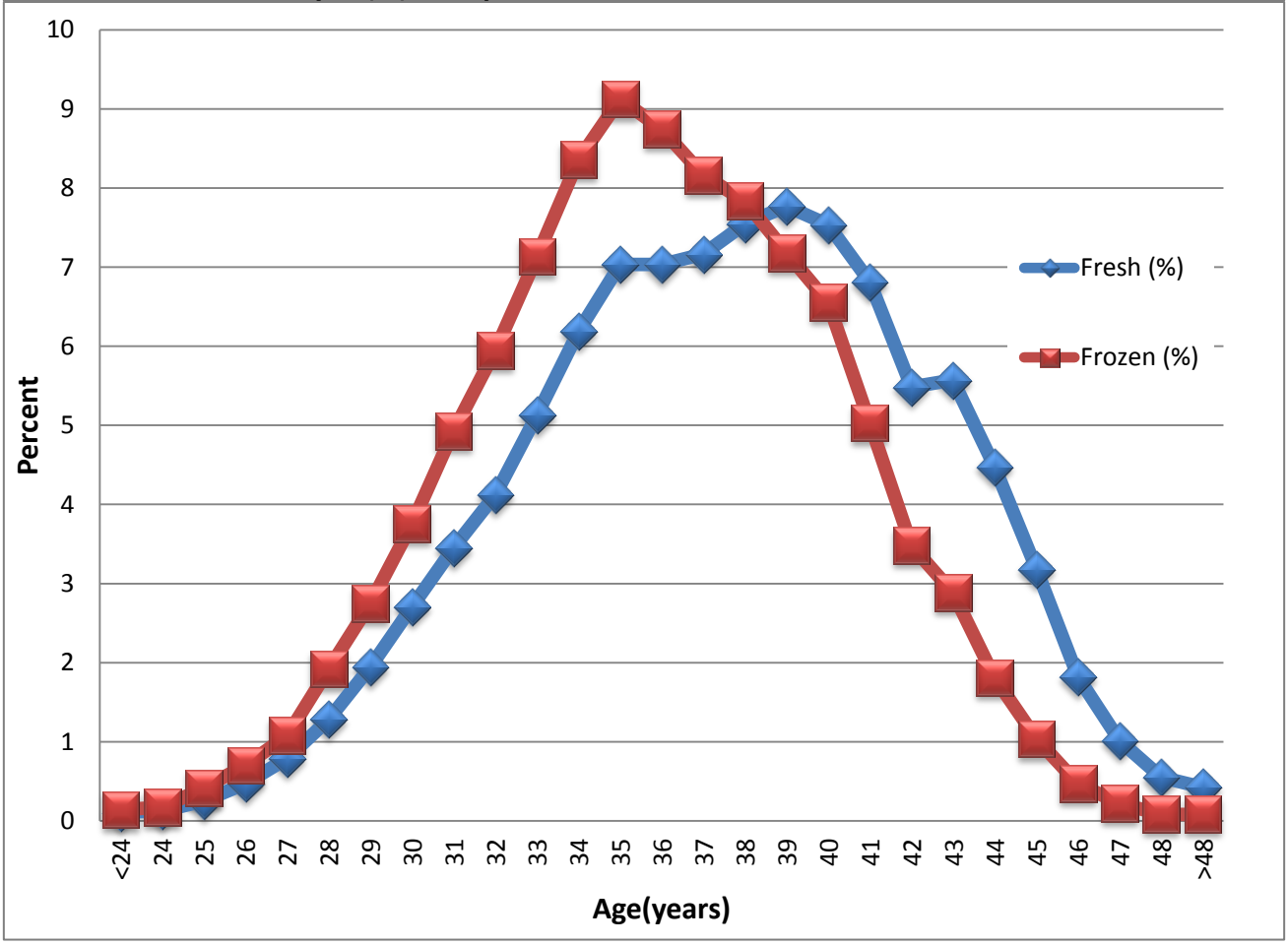


Are there any differences in the age distribution between the women who are transferred fresh embryos and frozen thawed embryos?

Figure 2 presents the distribution in percentage according to the age of the women who were transferred fresh and frozen thawed embryo(s) in ART procedure.
The peak for fresh embryo transfer group was 39 years old. This means that women transferred fresh embryo(s) tend to shift to higher in age than those transferred frozen/thawed embryo(s).

Figure 2

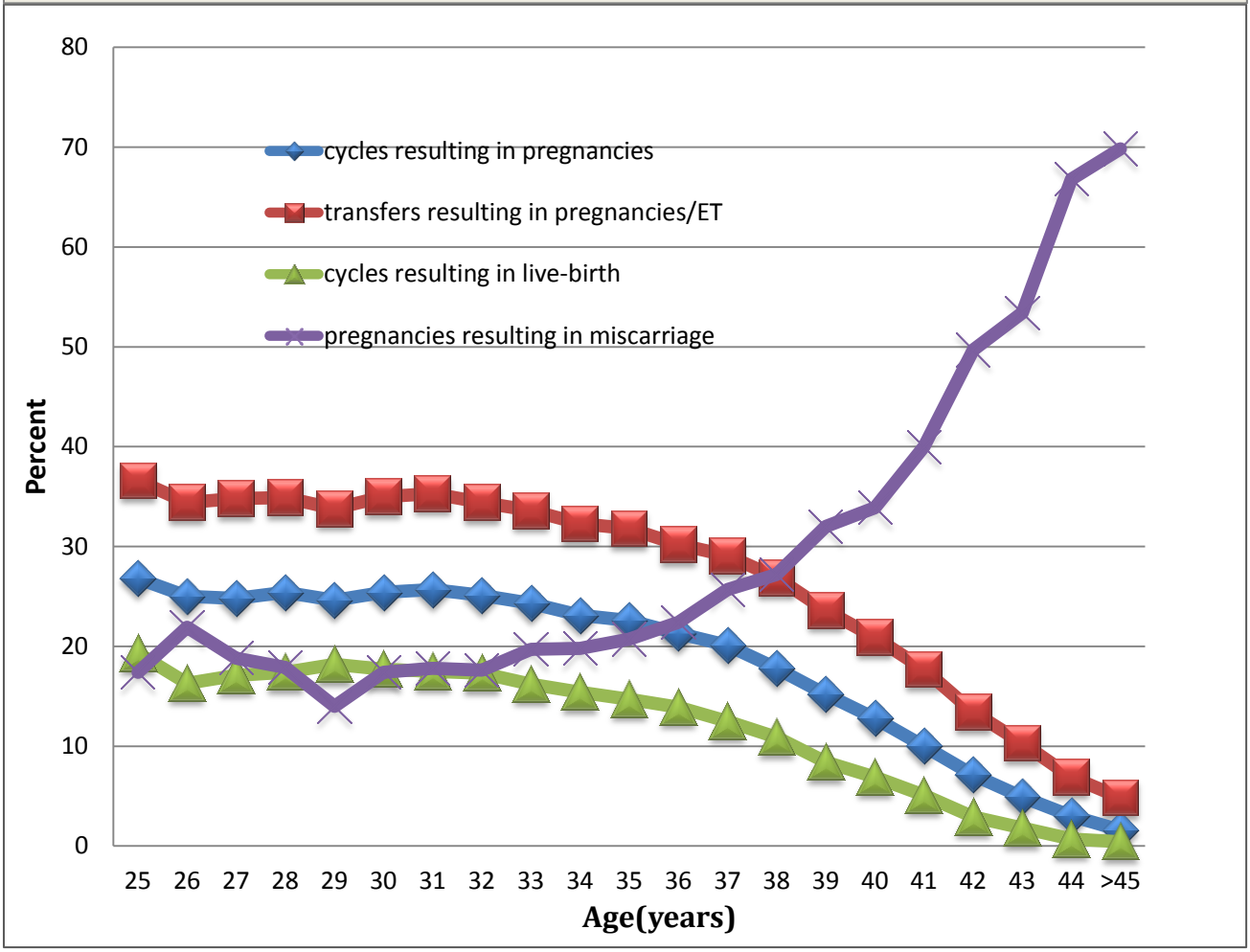
Age Distribution of women transferred fresh and frozen thawed embryo(s), Japan JSOG, 2008



How do the rates of pregnancy, birth and abortion vary by age?

The age of a woman is the most important factor affecting the chances of a live birth. This is because that it is difficult to achieve pregnancy and has the higher risk of miscarriage among the older woman. Figure 3 shows percentages of pregnancies, live births, and miscarriage for women with each age who were treated by ART procedures of fresh embryos in 2008. Among women in their 20's, percentages of pregnancy and live birth-remained steady. On the other hand, percentages of pregnancy and live birth gradually reduced from the early-30's onward. In addition, percentage of miscarriage continued to increase and it reaches approximately 32% at the age of 39. From the age of 45 onward, the rate of miscarriage resulted in twice every three times.

Figure3
Rates of Pregnancy, Birth and Abortion in Each Age, Japan JSOG, 2008



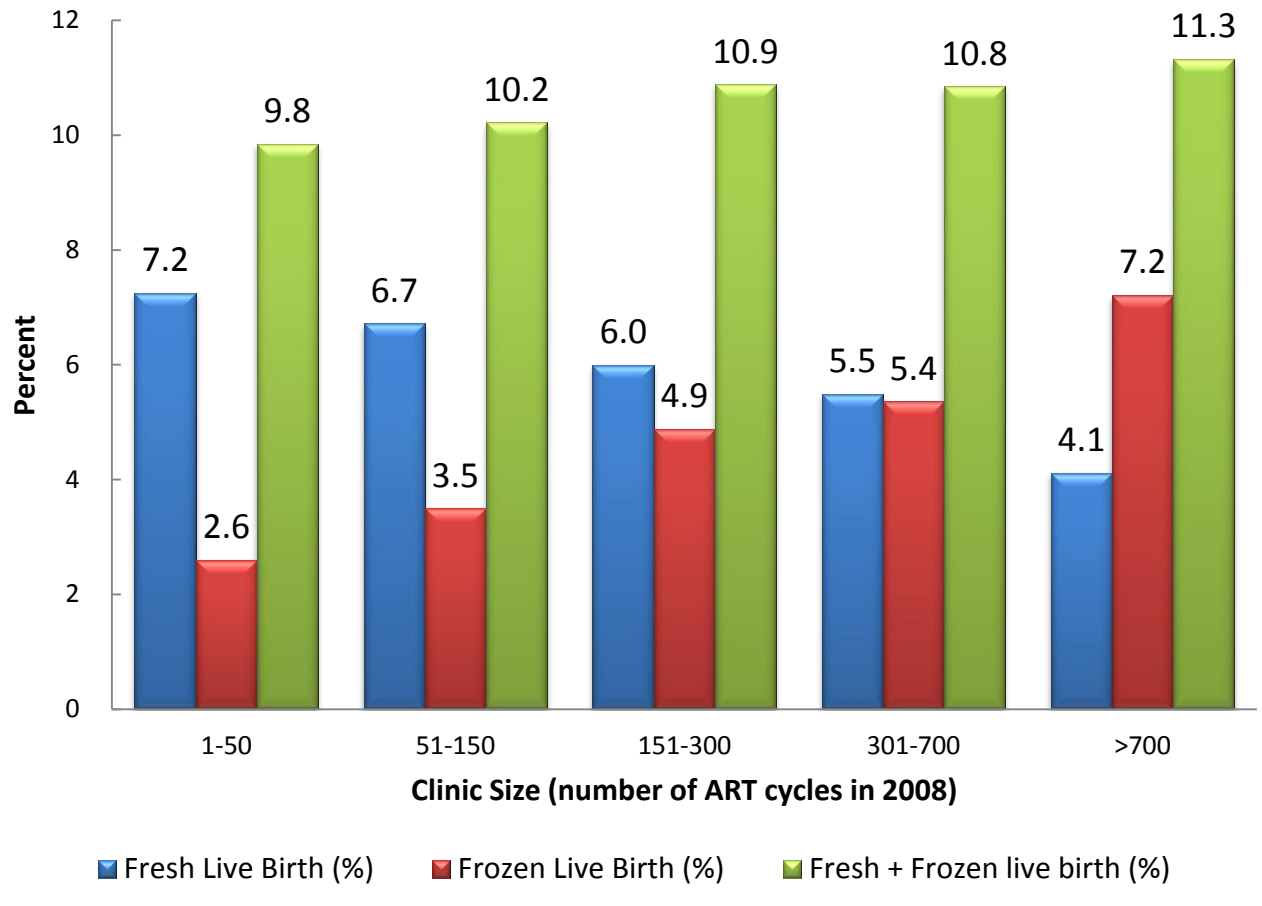
How is the clinic size related to rates of live births?

In Japan, a total of 607 fertility facilities exists. In Fig 4, each of the clinics were divided into five groups based on the number of ART cycles performed in 2008. Each percentage shows the rate of ART cycle that resulted in live birth in these groups. Percentages in each chart are calculated from the total number of the cycles treated by each group. Therefore they represent the characteristics of each group rather than each facility.

In 2008, total (fresh +frozen) percentages of live births were similar to each group regardless of the number of cycles performed. In group that performed small number of cycles, the percentage of live births transferred fresh embryo(s) was higher than frozen thawed embryo(s). On the contrary, in group that performed large number of cycles, the percentage of live birth transferred frozen thawed embryo(s) was higher than fresh embryo(s).

Figure 4

Rate of Live Birth per Clinic Size in Fresh and Frozen Thawed Embryo Transfer, Japan JSOG, 2008



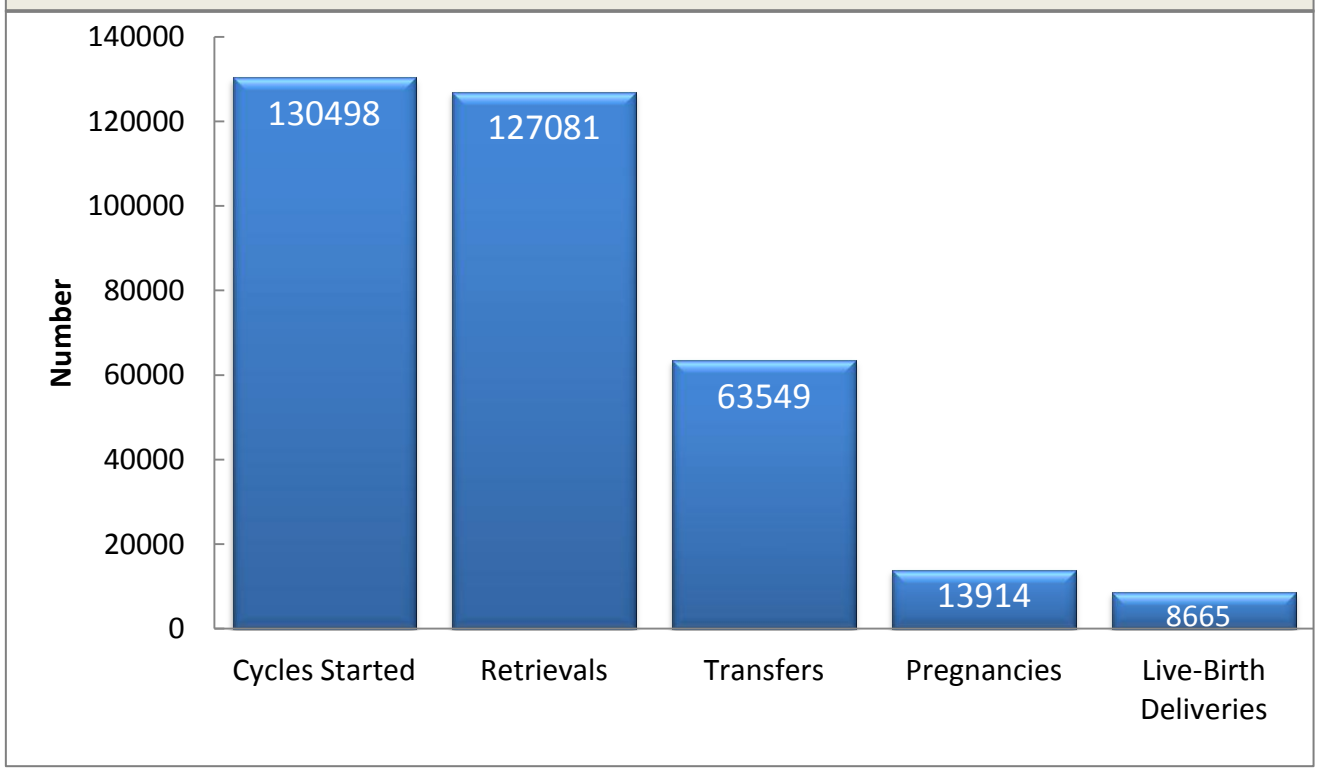
ART cycles transferring fresh embryo(s) in 2008

The numbers of cycles in each procedure of ART applied to fresh embryo transfer.

Figure 5 shows the result in each procedure of ART cycle applied to fresh embryo transfer.

- **Cycle started:**
the number of cycles in which women started to receive medication for stimulating the ovaries to develop multiple eggs or to monitor by ultrasound and/or blood samples for their ovaries without any stimulation.
- **Egg retrieval ：**
the number of cycles in which women were able to collect eggs by surgical procedure.
- **Transfer:**
the number of cycles in which women were able to transfer one or more of embryo(s) (Cycles of Gamete IntraFallopian Transfer (GIFT) and Zygote Intra-Fallopian Transfer (ZIFT) are included).
- **Pregnancy**
the number of cycles in which women became pregnant and confirmed one or more of gestational sac by ultrasound.
- **Live birth**
the number of cycles in which women delivered one or more live-born infants.
(The birth of twins, triplets, or more is counted as one live birth.)

Figure 5
Numbers of Cycles in Each Procedure of ART with Fresh Embryo Transfer, Japan JSOG, 2008

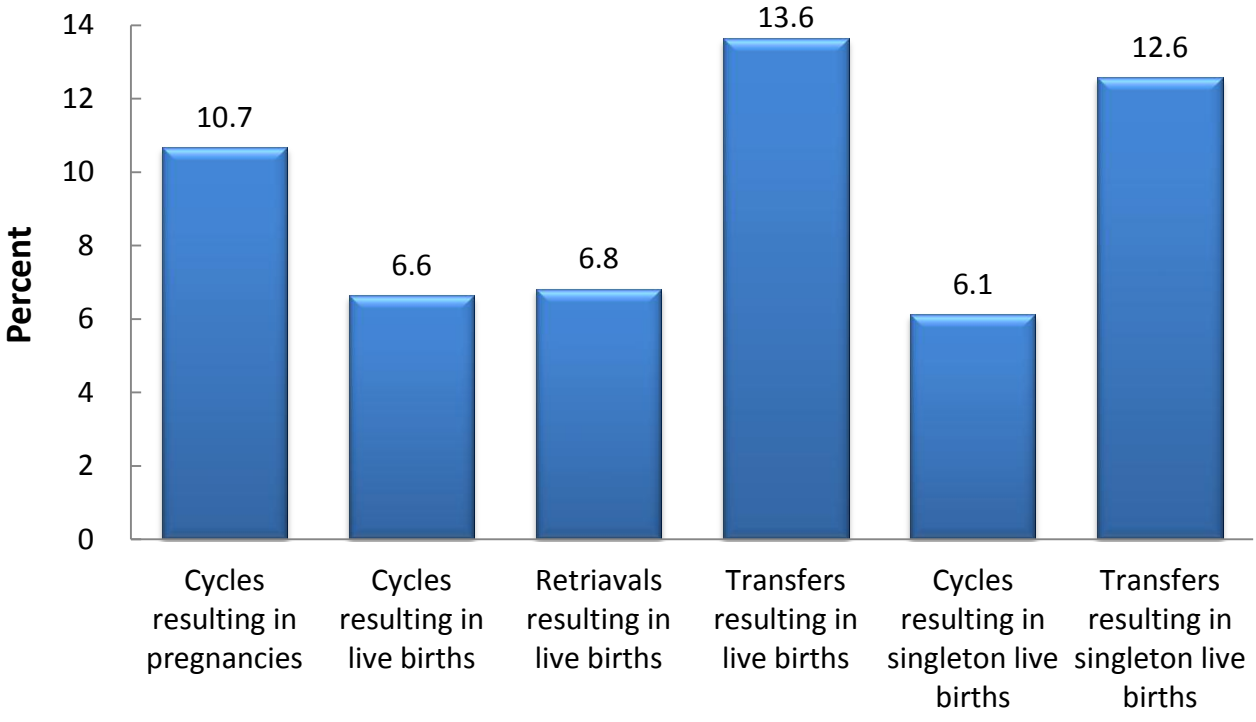


How is the success rate of ART with fresh embryo transfer cycle?

Figure 6 shows the success rate of six categories.

•Pregnancy rate per ART cycle started:
Only clinical pregnancies were counted. Cases where two or more number of gestational sacs are observed are counted as one pregnancy.
•Live birth rate per ART cycle started:
•Live birth rate per egg (oocyte) retrieval:
This rate is generally higher than that of live birth per ART cycle started. This excludes cancelled cycles for various reasons such as failure of ovarian response to stimulation, no collection of oocytes and so on.
•Live birth rate per embryo transfer:
This rate is the highest among analyzed categories for live birth rates. This excludes cancelled cycles due to failure of developing embryo.
•Singleton live birth rate per ART cycle started:
In Japan, SET is fundamentally performed. Therefore, there is no apparent difference between singleton live birth rate and live birth rate per cycle started. Singleton live births could possibly reduce the risk of prematurity, low birth weight, fetal disability and death.
•Singleton live birth rate per embryo transfer:
This rate is higher than that of singleton live birth rate per ART cycle started. The reason for the higher rate is mentioned in Live birth rate per embryo transfer.

Figure 6
Success Rate of Six Categories in ART with Fresh Embryo Transfer Cycle, Japan JSOG, 2008

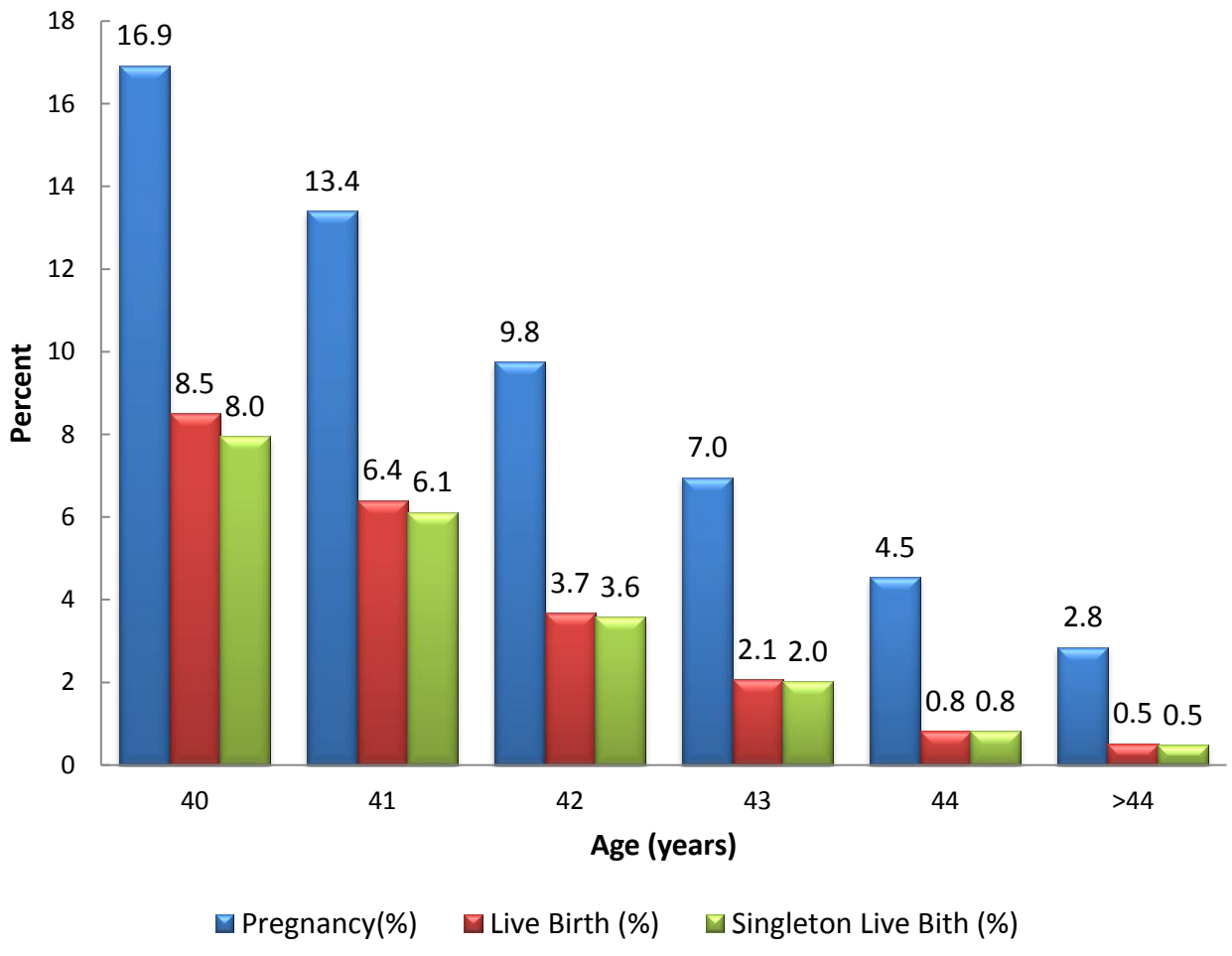


How is the rate of pregnancy, live birth, and singleton live birth for women in the age of 40 and older?

The rate of pregnancy, live birth, and singleton live birth decreased gradually from early-30's onward as shown in Figure 3. Figure 7 shows the rate of pregnancy, live birth, and singleton live birth per cycle started in women aged 40 and older. The rate of three categories is lower and decreases as the age progresses.

Figure 7

Rate of Pregnancy, Live Birth, and Singleton Live Birth for Women in the Age of 40 and Older, Japan JSOG, 2008

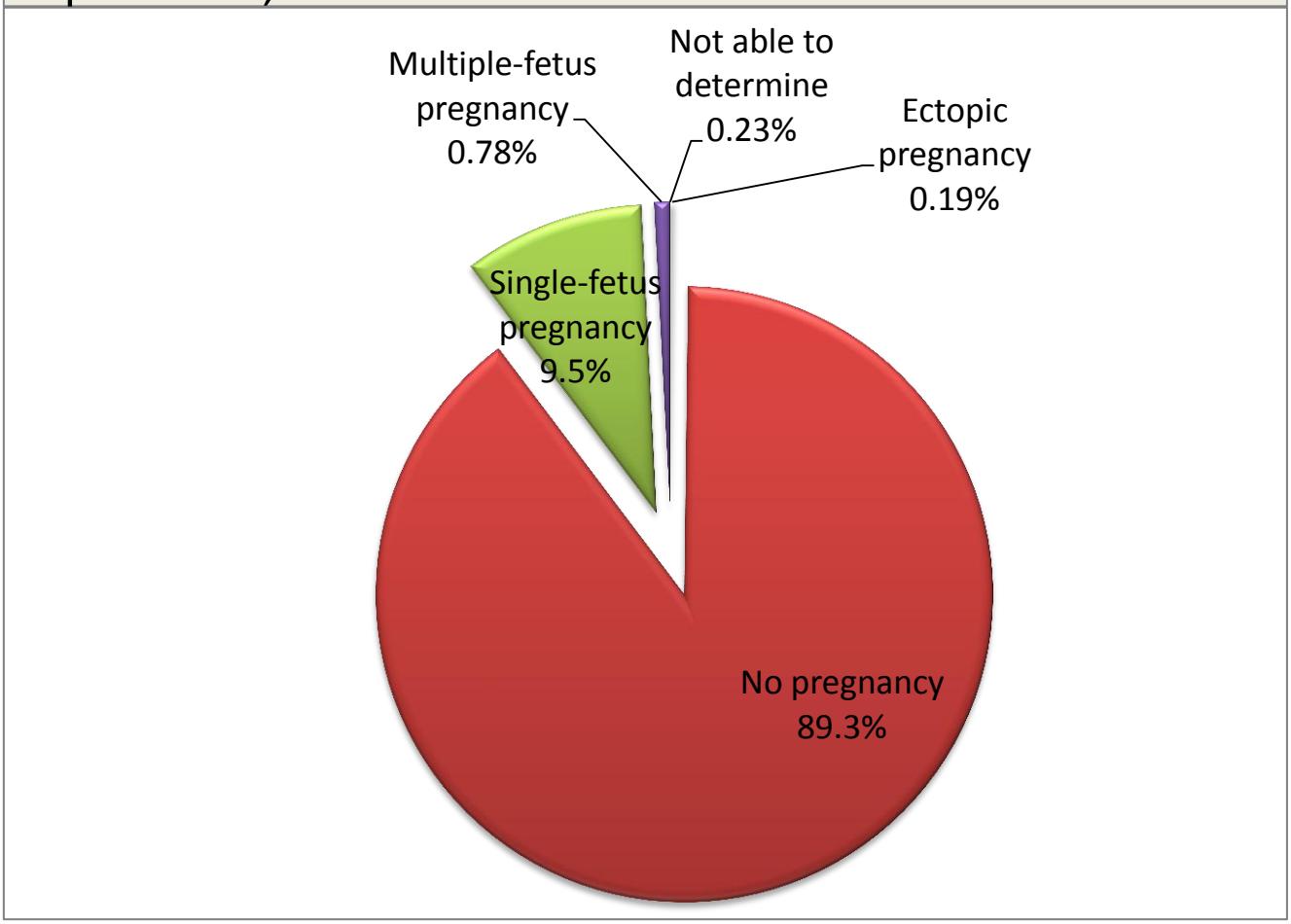


How is the pregnancy rate of ART cycles in fresh embryo transfer?

Figure 8 shows the pregnancy rate per cycle started. Approximately 10.5% resulted in clinical pregnancy. Most of them (9.5%) are singleton pregnancy. Multiple pregnancy rate is 0.78% as considerably low.

Figure 8

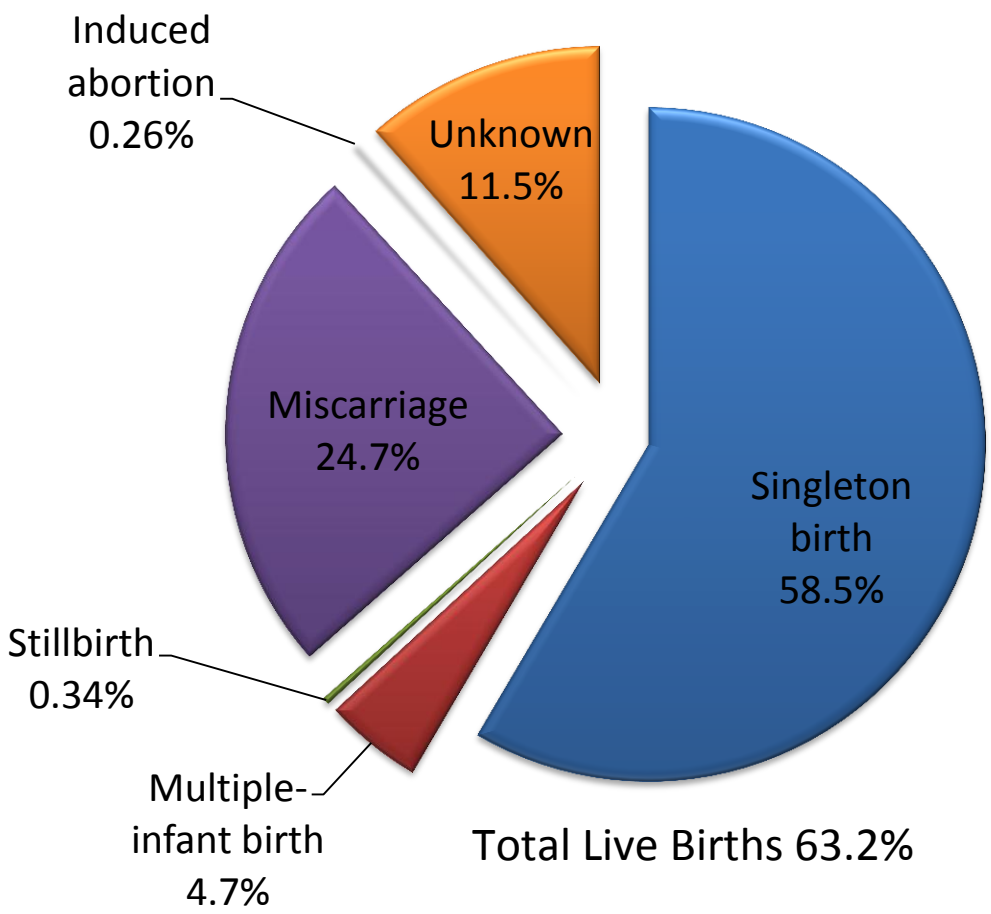
Pregnancy Rate of ART Cycles in Fresh Embryo Transfer, Japan JSOG, 2008



How is live birth rate after fresh embryo transfer?

Figure 9 shows the outcomes of pregnancies after fresh embryo transfer in 2008. Approximately 63% of the pregnancies resulted in a live birth. About 26% of pregnancies were unsuccessful by miscarriage, stillbirth and induced abortion. From 2008, JSOG has recommended SET to avoid the risk of prematurity, low birth weight, fetal disability and death. Thus, multiple-infant birth is suppressed to less than 8%.

Figure 9
Outcomes of Pregnancies after Fresh Embryo Transfer, Japan JSOG, 2008

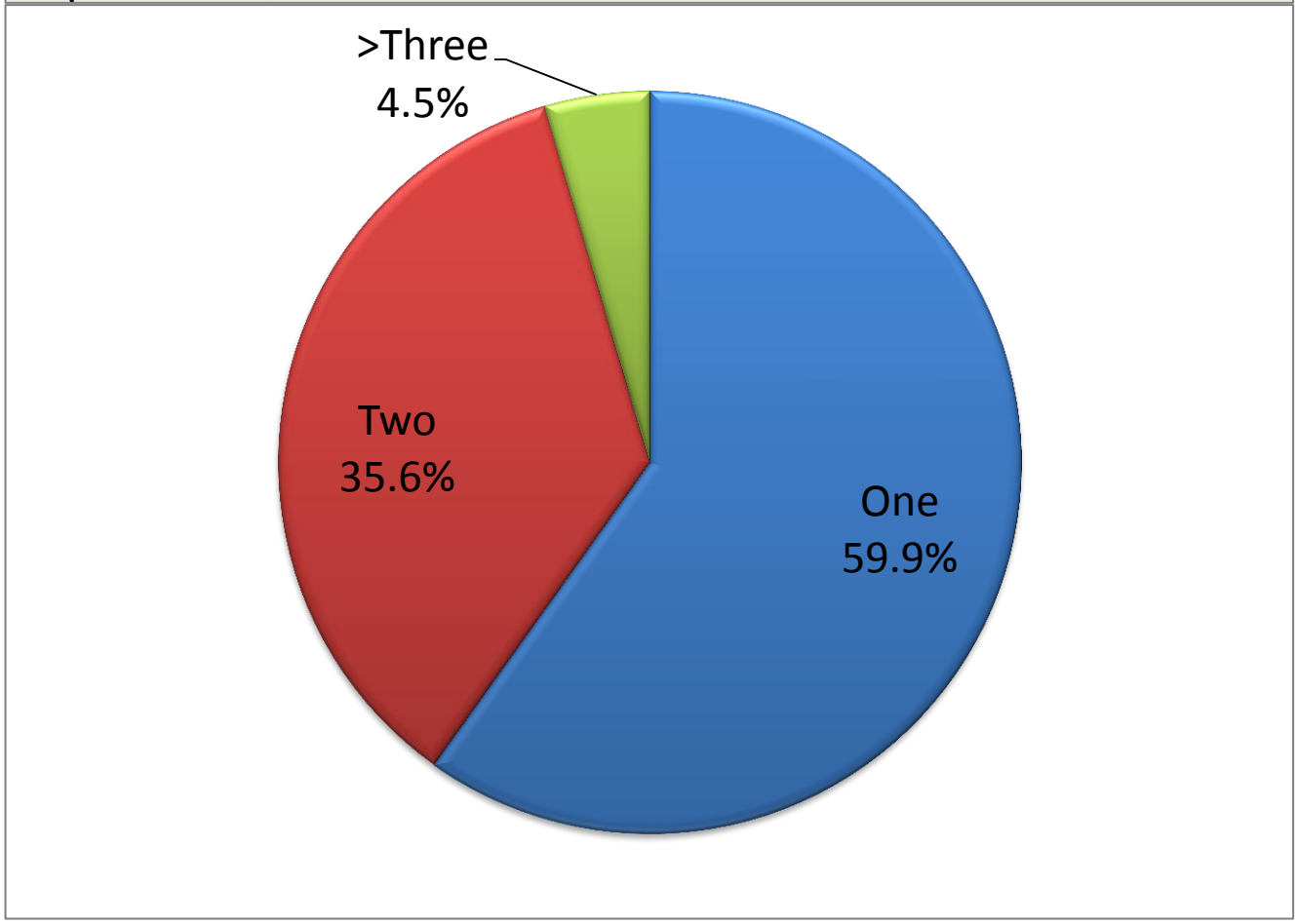


How many embryos are transferred in an ART procedure?

In Figure 5, approximately 49% of cycles were able to apply fresh embryo transfer in 2008. About 60% of these cycles were SET and approximately 36% of cycles are transferred two embryos as shown in Figure 10. Complying SET and double embryos transfers (DET) led to the low multiple pregnancy rate shown in Figure 8.

Figure 10

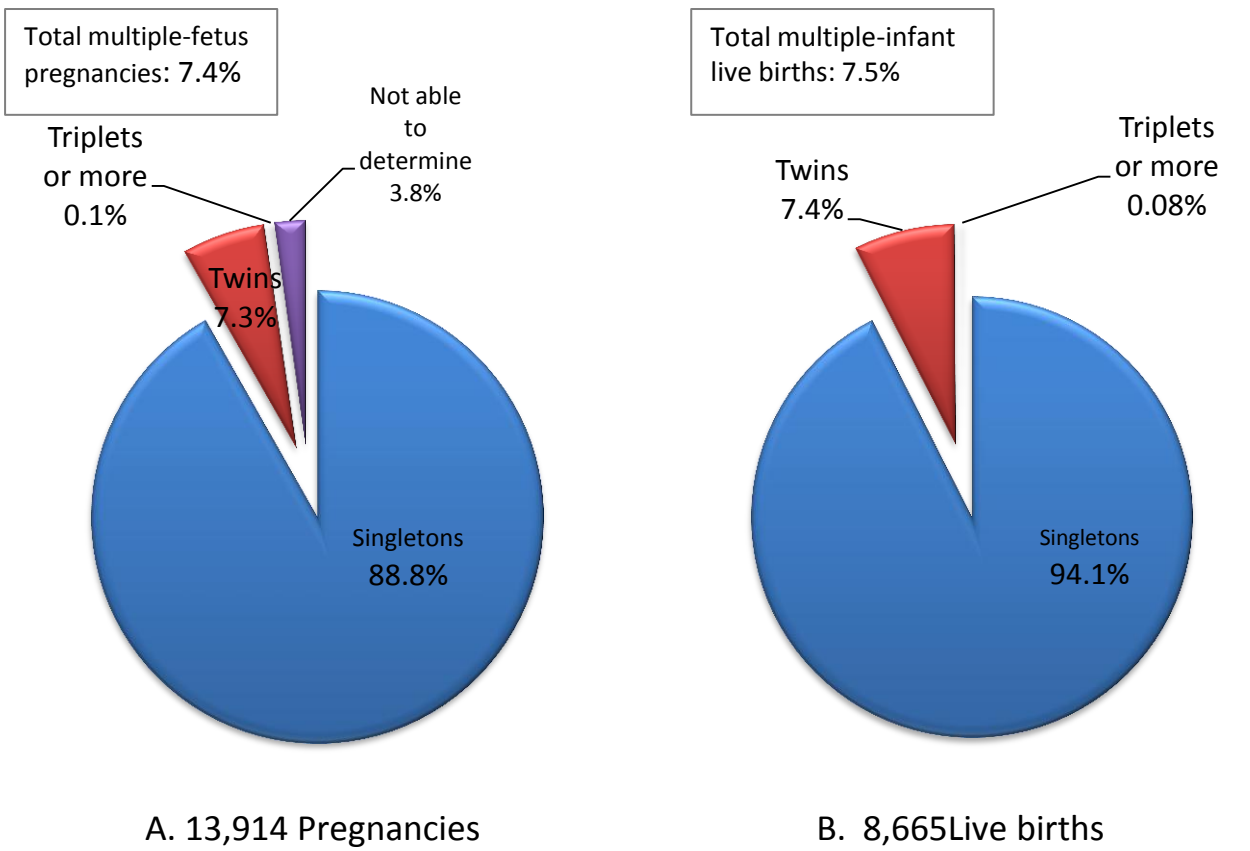
Number of Transferred Embryo(s) in Fresh ART Cysles, Japan JSOG, 2008



How many multiple pregnancy or multiple-infant birth are implicated in ART cycle with fresh embryo transfer?

Multiple pregnancy and infant births implicate risk for both mothers and infants. These risks include higher rates of caesarean section, prematurity, low birth weight, and infant disability or death.
In Figure 11, chart A shows the detail of 13,914pregnancies and 88.8% were singleton pregnancy, 7.3% were twins, and 0.1% were triplets or more. Chart B shows the similar rate of live birth as shown in chart A. Only 7.4% of these live births resulted in more than two infants. Therefore, the compliance of SET resulted in high singleton birth rate and lower rates of multiple pregnancy and multiple infant birth.

Figure 11
Rate of Multiple Pregnancy or Multiple-Infant Birth after Fresh Embryo Transfer, Japan JSOG, 2008



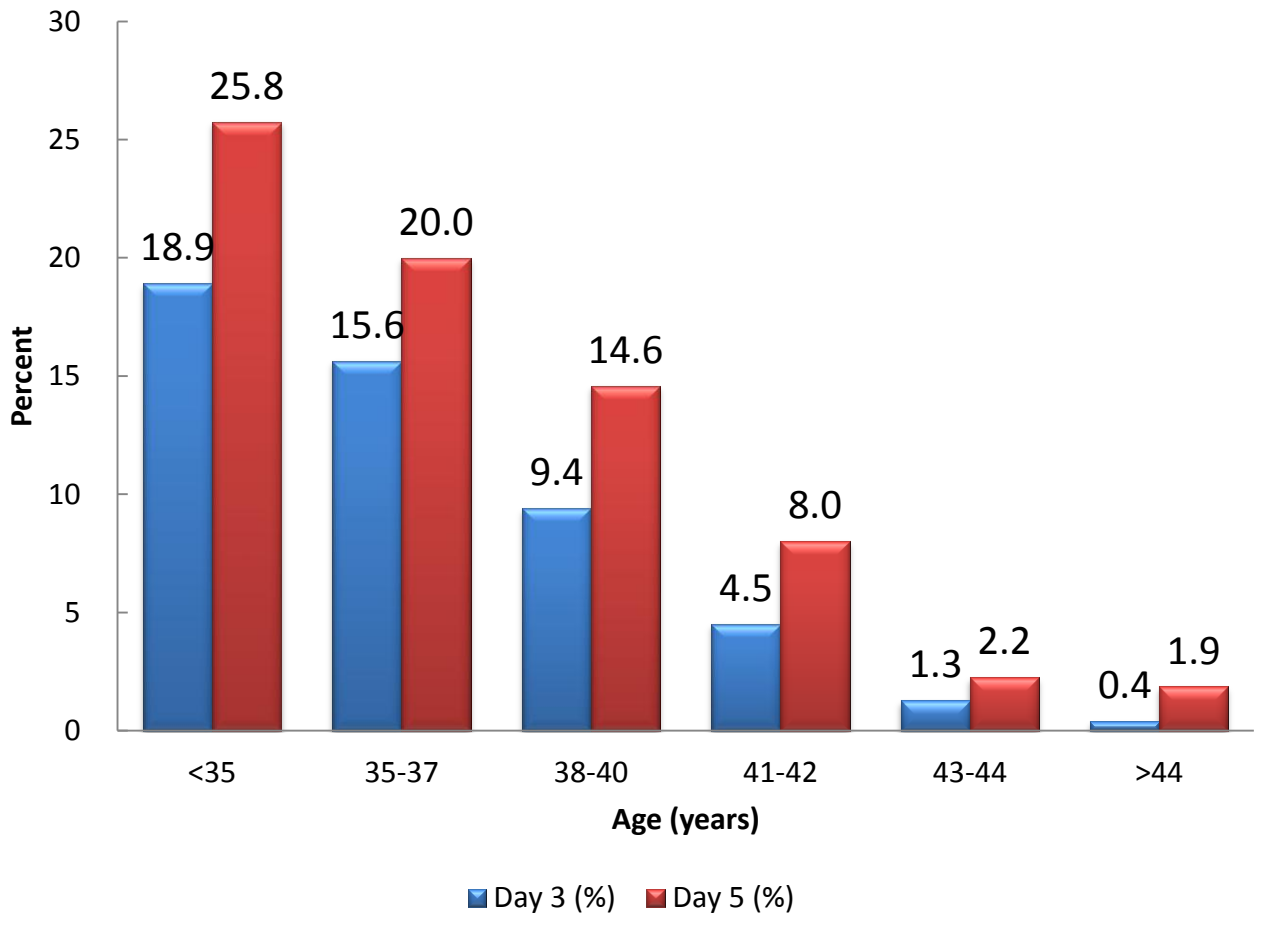
A. 13,914 Pregnancies

B. 8,665Live births

When is appropriate time to transfer embryo(s)?

Figure 12 shows the comparison between the live birth rates of embryo transfers on day 3 and day 5. In all age groups, rate of live birth was higher in day 5 embryo transfer than that in day 3 transfer. However, all of the cycles are not completed in processing of day 5 embryo transfer due to arrest of developing embryos. Such the cases are excluded from the group of day 5 embryo transfer. Therefore, the cases completed day 5 embryo transfer have a good quality of embryo(s).
For interpreting this figure, it is important to consider above-mentioned concepts.

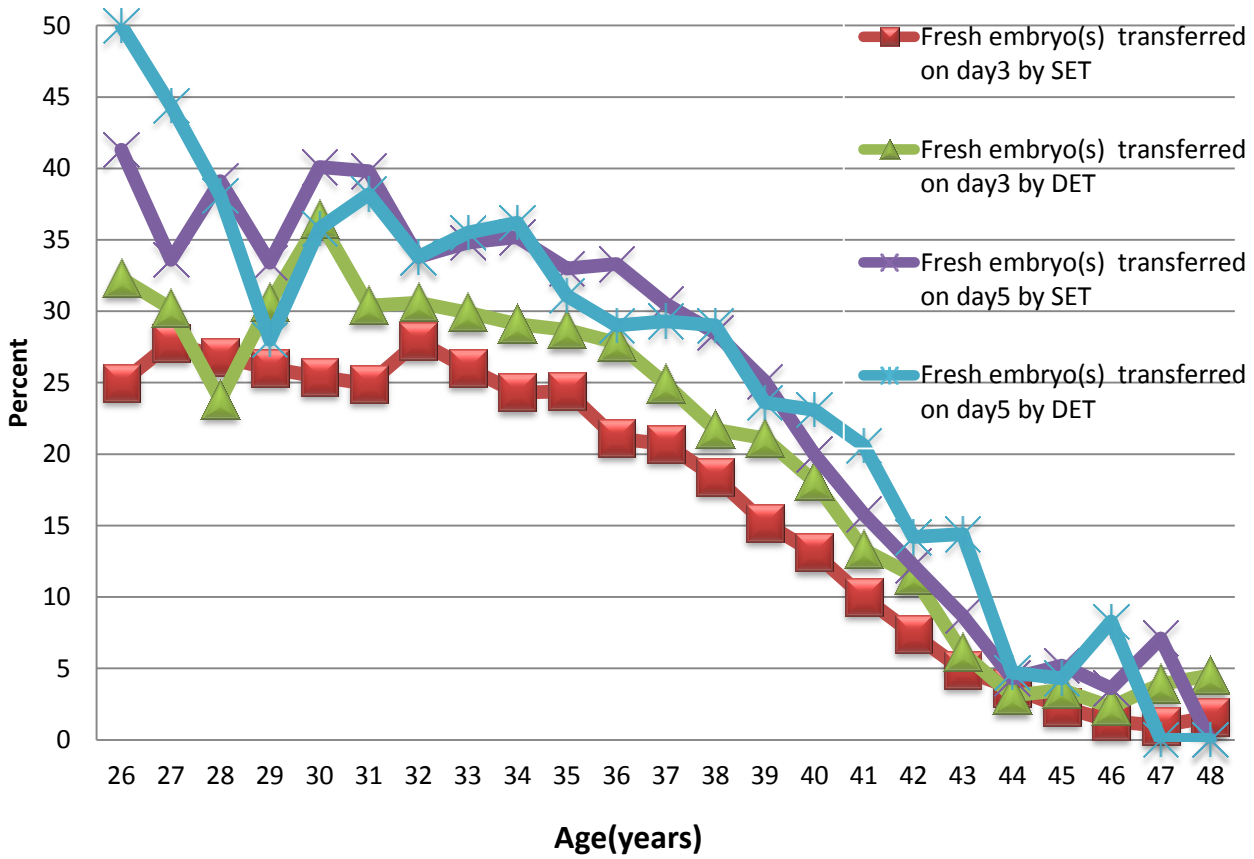
Figure 12
Live Birth Rate of Embryo Transfers on Day 3 and Day 5 in Each Age, Japan JSOG, 2008



Which is recommended for number of embryo(s) and timing of transfer?

The cycles of fresh embryo transfer are divided into four groups based on the number of embryos (i.e. SET and DET) and their developmental stages. The pregnancy rate is then compared to four groups by age. As shown in Figure 13, the rate in the group of day 5 (mostly blastocyst) tended to be higher than that of day 3 (early embryos). In the day 3 transfer groups, the rate for DET shows 5% higher by age than that for SET. The differences of pregnancy rate between these two groups decrease with advancing age. On the other hand, there is no apparent difference between SET and DET in day 5 transfer as compared with these of day 3.

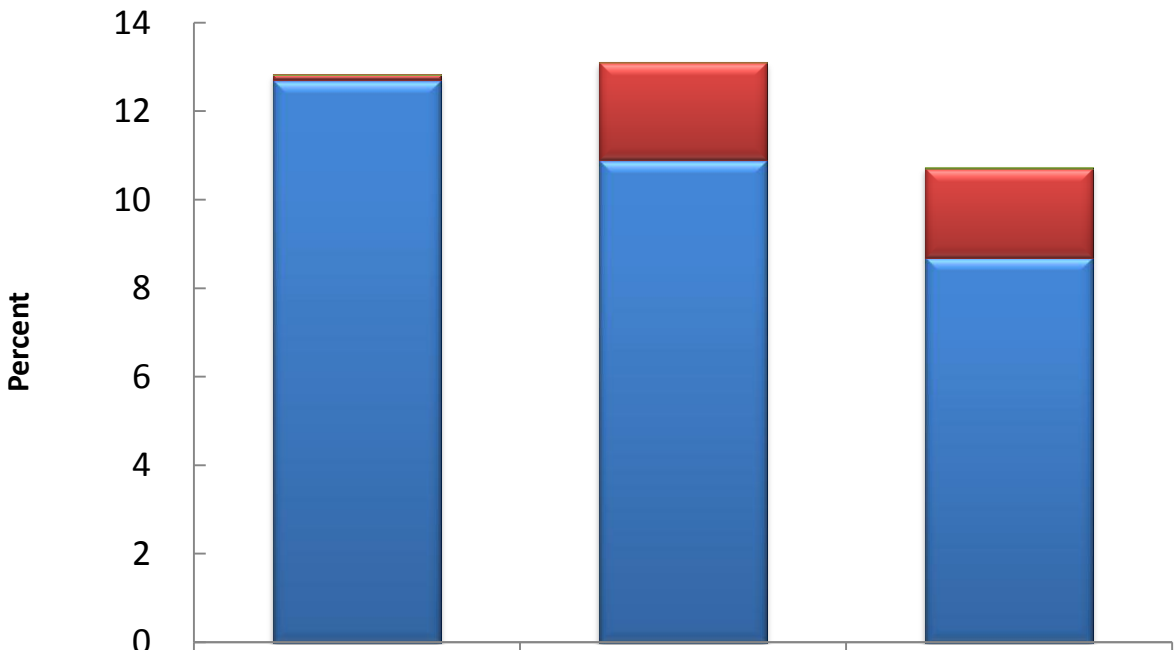
Figure 13
Pregnancy Rate of Single and Double Embryo Transfer on Day 3 and/or Day 5 in Each Age of Fresh Embryo Transfer Cycle, Japan JSOG, 2008



Is it more effective to transfer multiple embryos for achieving pregnancy?

Figure 14 shows the result for live birth rate based on the number of embryos in fresh transfer cycle. There are no apparent differences in the live birth rates between SET, DET and more. However, the rate of multiple birth obviously increased on DET or more. On selecting and transferring good quality embryo(s), it is possible that live birth rate might be equal between SET and DET. When embryos could not develop in good quality, multiple embryo transfer might not always result in success. In other words, SET could be better procedure than DET depending on the quality of embryos to be transferred.

Figure 14
Rate of Live Birth and Multiple-Infant Birth Based on Transferred Number of Embryo(s), Fresh Embryo Transfer Cycle, Japan JSOG, 2008



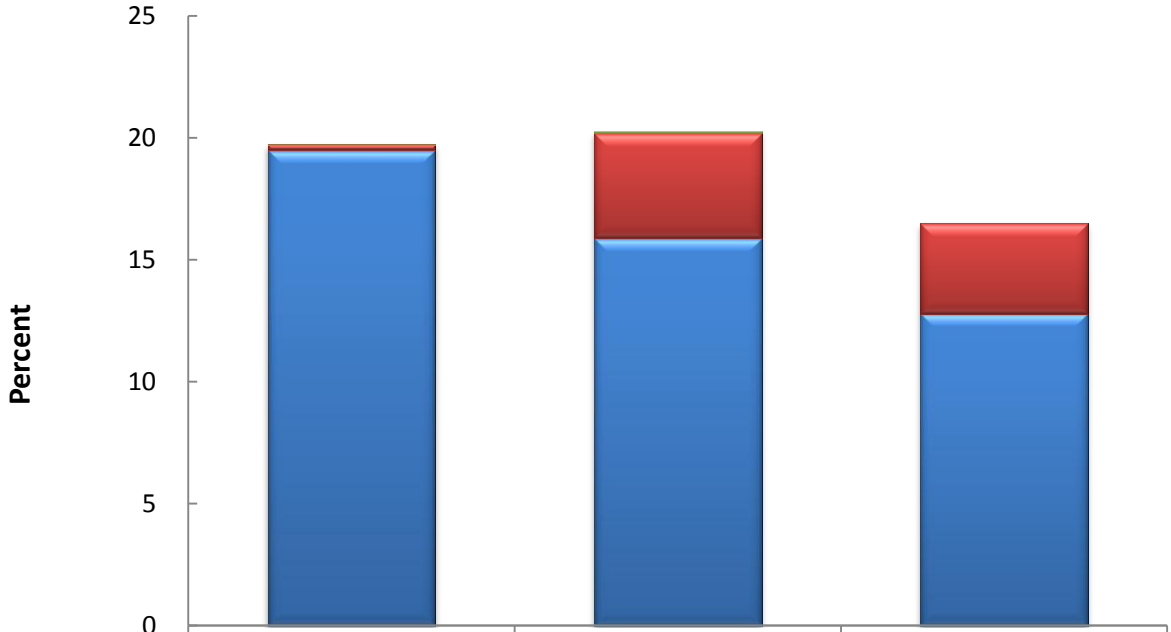
	1	2	>3
Triplets (%)	0.008	0.013	0.035
Twins (%)	0.13	2.2	2.0
Singletons (%)	12.7	10.9	8.7

Number of Embryos Transferred

Is live birth rate dependent on transferred number of good quality embryo(s) for women with the age of 35 or under?

Figure 15 shows the result for live birth rate based on the number of embryos in fresh transfer cycle for the age of 35 or under. The relationship between the number of embryos, the rates of live birth and multiple birth involves many factors such as age and the quality of embryos to be transferred.
In Figure 15, it is indicated that the high rate of multiple infant birth is more apparent in DET and more as compared with that in Figure 14. And, the live birth rates between SET and DET showed almost similar to each other. The rate of multiple infant birth increased in case of more than two embryos transferred. This shows the same tendency as the case in Figure 14 that includes all ages.

Figure 15
Rate of Live Birth and Multiple-Infant Birth Based on Transferred Number of Embryo(S) for Women with the Age of 35 or under, Fresh Embryo Transfer Cycle, Japan JSOG, 2008



	1	2	>3
Triplets (%)	0.008	0.052	0.00
Twins (%)	0.22	4.3	3.7
Singletons (%)	19.5	15.9	12.8

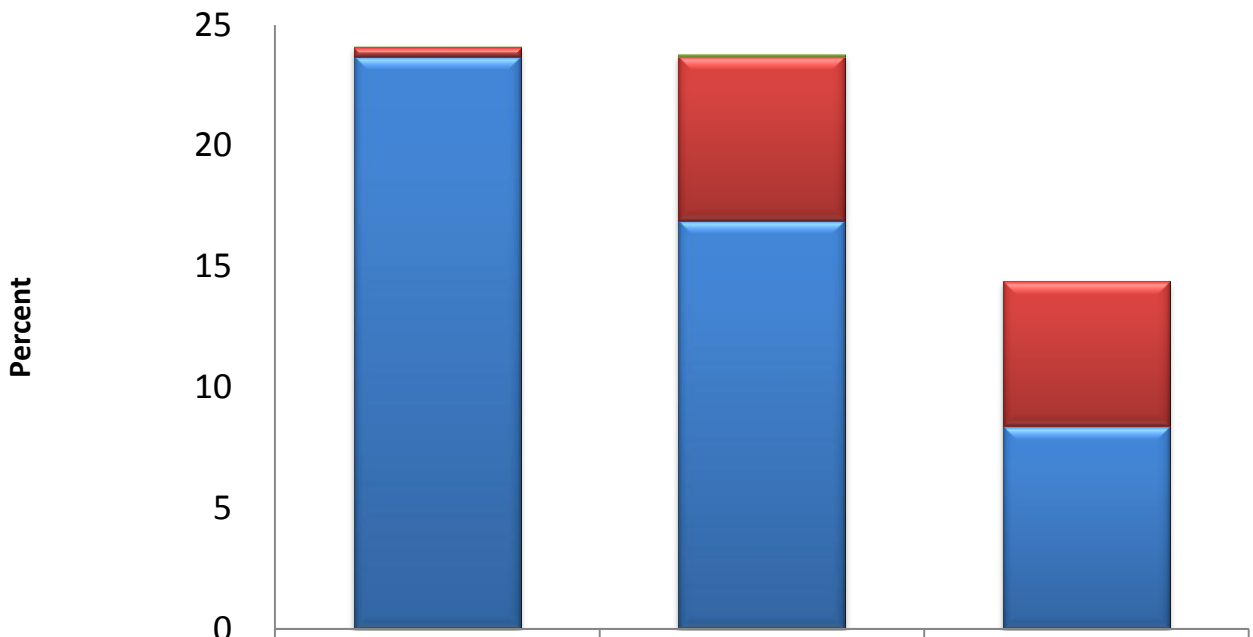
Number of Embryos Transferred

Is live birth rate dependent on transferred number of good quality embryo(s) on day 5 for women with the age of 35 or under?

Figure 16 shows the results for the rates of live birth and multiple infant birth based on the number of embryo(s) on day 5 in women with the age of 35 or under. In comparison with Figure 14 and 15, the live birth rate resulted higher shown in Figure 16. Similarly, the multiple infant birth rate in Figure 16 indicated higher compared with these two figures. In Japan, SET is fundamentally encouraged for women with the age of 35 or under in consideration of the risk for multiple infant birth. Figure 16 proves this encouragement.

Figure 16

Rate of Live Birth and Multiple-Infant Birth Based on Transferred Embryo(s) on Day 5 for Women with the Age of 35 or under, Fresh embryo Transfer Cycle, Japan JSOG, 2008



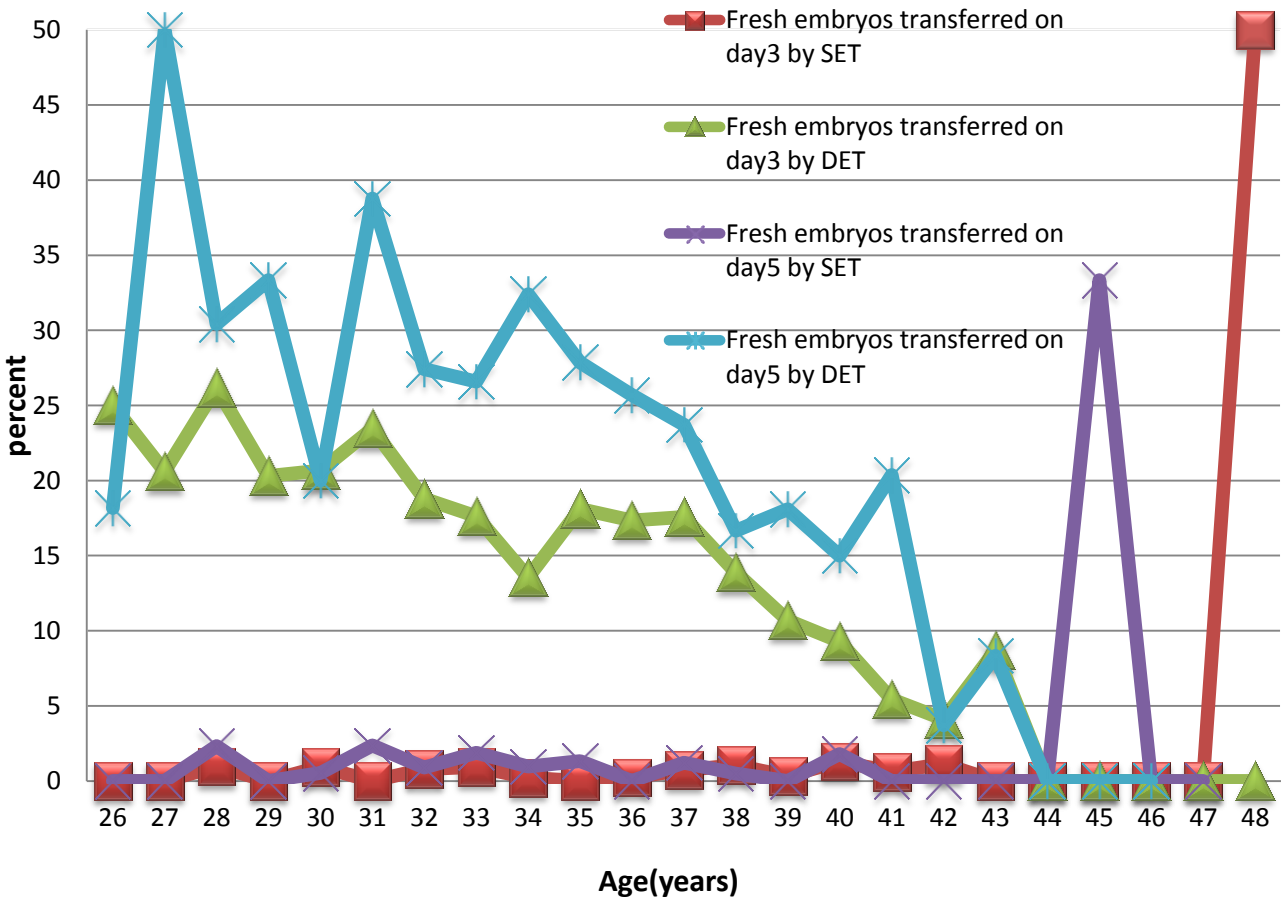
	1	2	>3
Triplets (%)	0.02	0.08	0.00
Twins (%)	0.39	6.8	6.0
Singletons (%)	23.7	16.9	8.4

Number of Embryos Transferred

Which has more risk for multiple infant birth rate based on number of embryo(s) and time of transfer?

The cycles of fresh embryo transfer are divided into four groups based on the number of embryos (i.e. SET and DET) and their developmental stages. The multiple infant birth rate is then compared according to four groups and age. As shown in Figure 17, the rate of multiple infant birth is about 1% in each age with SET of day 3 and day 5. In DET, the multiple infant birth rate for day 5 transfer is higher than that for day 3. In case with the age of 45 or more, the rate varies enormously due to the small size of group. It tends to be no significant difference of the rate based on number and developmental stage of embryo(s) with advancing age.

Figure 17
Multiple-Infant Birth Rate of Single and Double Embryo Transfer on Day 3 and Day 5 in Each Age of Fresh Embryo Transfer Cycle, Japan JSOG, 2008



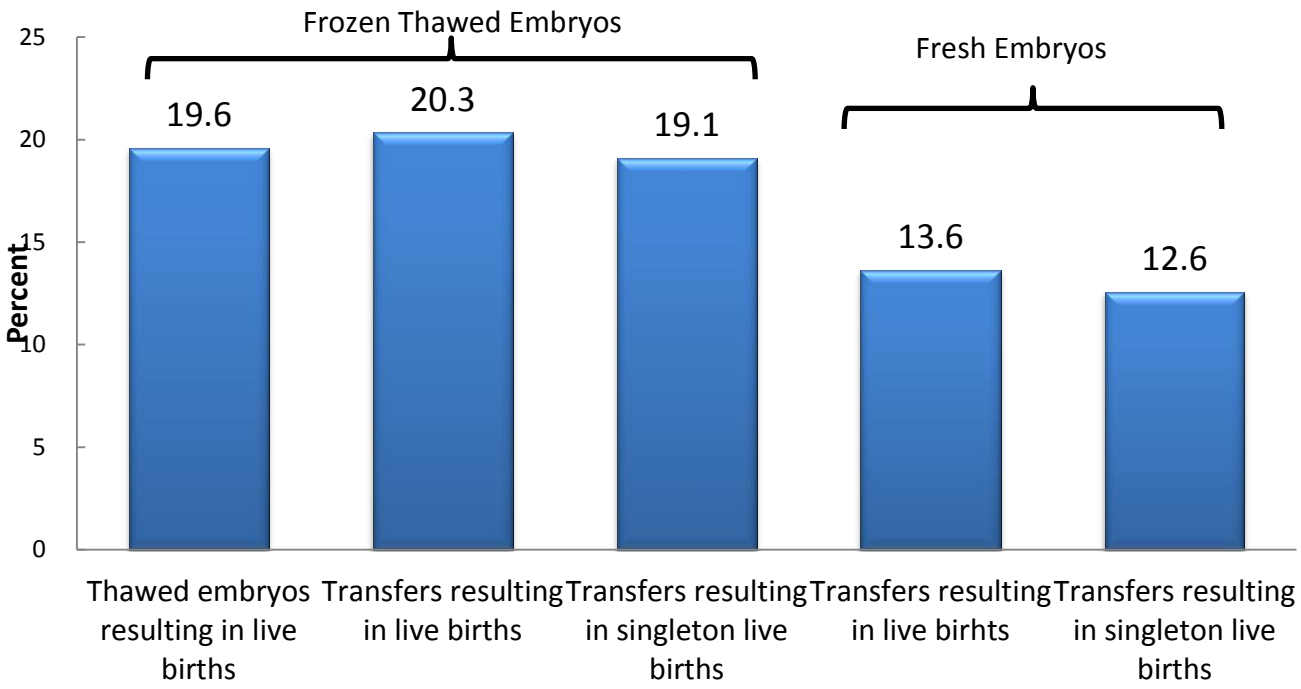
ART cycles transferring frozen thawed embryo(s) in 2008

What is the rate of live birth and singleton live birth in ART cycles with frozen thawed embryo transfer?

Frozen thawed embryos were used in approximately 32% (60,026 cycles) of all ART cycles performed in 2008. In Figure 18, the rates of live birth and singleton birth for frozen thawed embryo transfers were compared with those for fresh embryo transfers. It shows the rates for frozen thawed embryos are higher than those for fresh embryos. The fact that 96% of the treatment cycles were able to develop and transfer their own embryo(s) proves the high quality of freezing and thawing embryo processing technology of Japan. Moreover, the use of frozen thawed embryos leads to avoid the risk of going through the fertility drug stimulation and egg retrieval steps again; also, minimize the cost of the treatment.

Figure 18

Rates of Live Birth and Singleton Live Birth in Frozen Thawed and Fresh Embryo Transfers, Japan JSOG, 2008

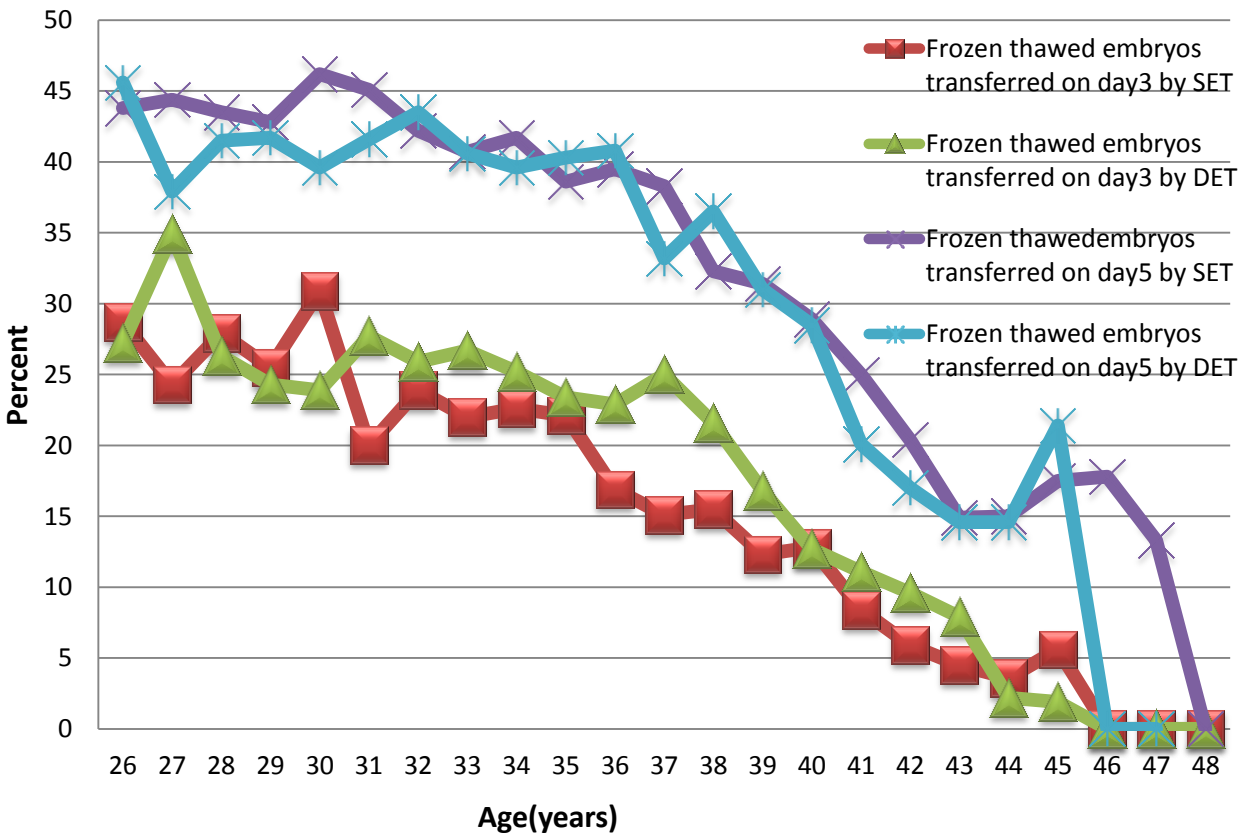


Which is recommended for number of embryo(s) and timing of transfer for frozen thawed embryo(s)?

The cycles of frozen thawed embryo transfer are divided into four groups based on the number of embryos (i.e. SET and DET) and their developmental stages. The pregnancy rate is then compared according to four groups and age. As shown in Figure 13, the rate in the group of day 5 (mostly blastocyst) tended to be higher than that of day 3 (early embryos). In terms of the number of transferred embryo(s), the difference of the pregnancy rate in the groups of day 3 and day 5 transfer was not apparent. Rather, it resulted the pregnancy rate of SET was higher than that of DET at some of the ages for the groups of day 5 transfer. The difference between transferred on day 3 and on day 5 of frozen thawed embryo(s) is greater than that of fresh embryo(s) (refer to Figure 13).

Figure 19

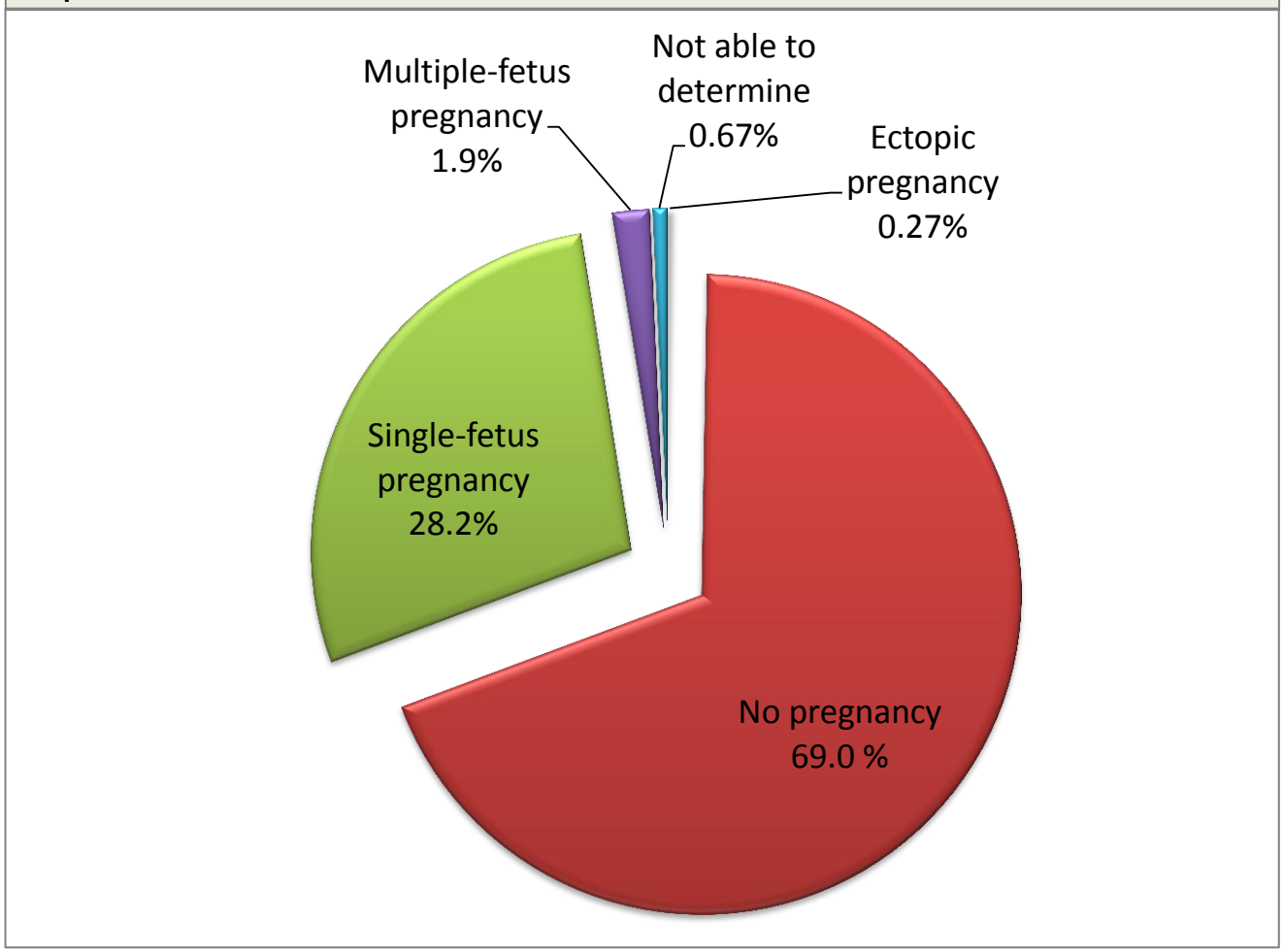
Pregnancy Rate of Single and Double Embryo Transfer on Day 3 and/or Day 5 in Each Age of Frozen Thawed Embryo Transfer Cycle, Japan JSOG, 2008



What is the pregnancy rate of frozen thawed embryo transfer in ART cycles?

In Figure 20, it shows the results of the pregnancy rate for frozen thawed embryo transfer in ART cycles of 2008. Approximately, 30% resulted in clinical pregnancy. Most of them (28.2%) are singleton pregnancy, and the frequency of multiple pregnancy is very low (1.9%). Compared with Figure 8, the pregnancy rate of frozen thawed embryo transfer is higher than that of fresh embryo transfer.

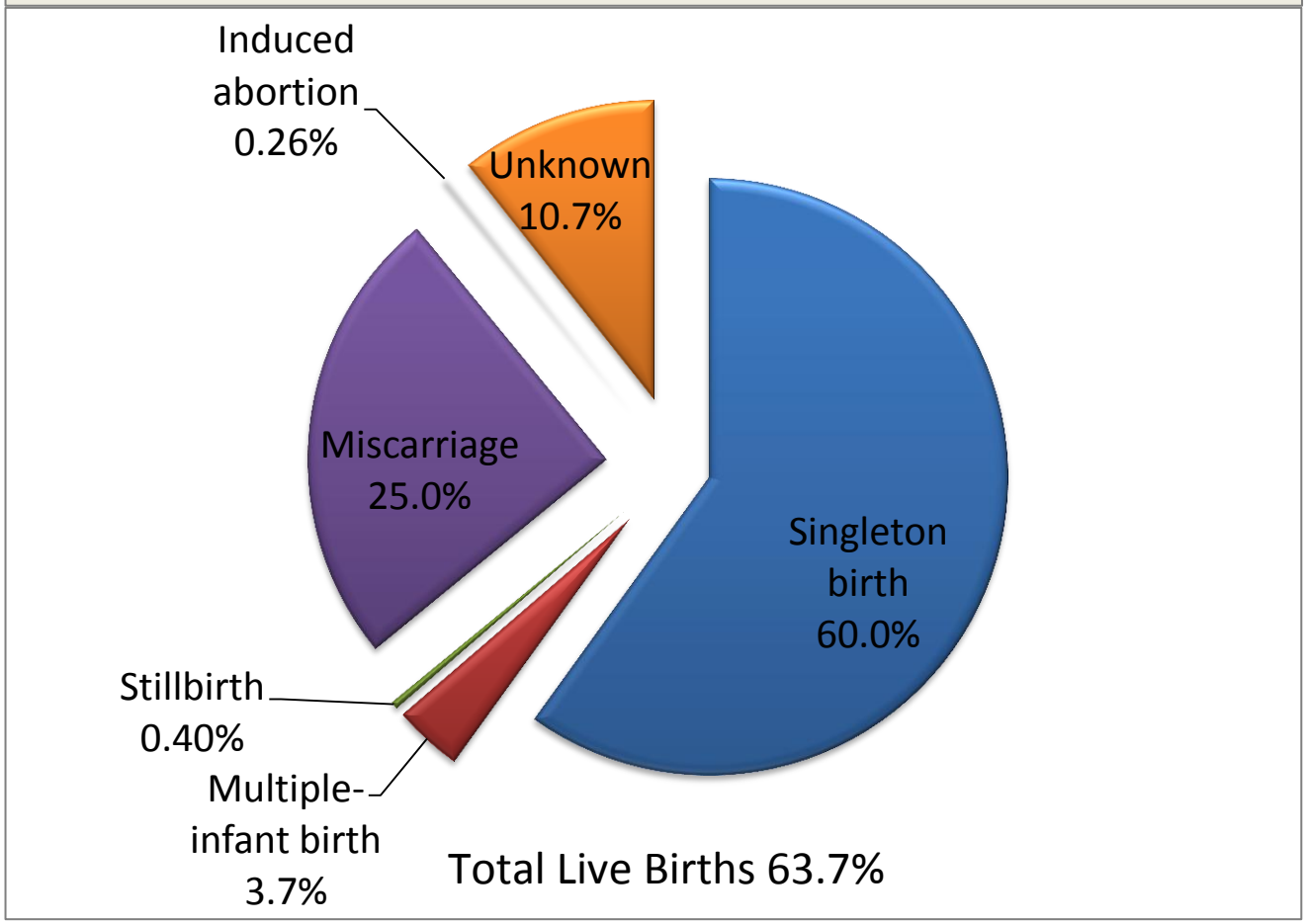
Figure 20
Results of ART Cycles for Frozen Thawed Embryos, Japan JSOG, 2008



What is the live birth rate of frozen thawed embryo transfer?

In Figure 21, it shows the rates of pregnancy after frozen thawed embryo transfer in 2008. Approximately 64% of the pregnancies resulted a live birth. About 26% of pregnancies resulted in miscarriage, stillbirth, induced abortion, and so on.
From 2008, JSOG has recommended SET to avoid the risk of prematurity, low birth weight, fetal disability and death. Thus, the rate of the multiple-infant birth is suppressed to less than 6 % that is lower than that of fresh embryo(s).

Figure 21
Outcomes of Pregnancies after Frozen Thawed Embryo Transfer, Japan JSOG, 2008

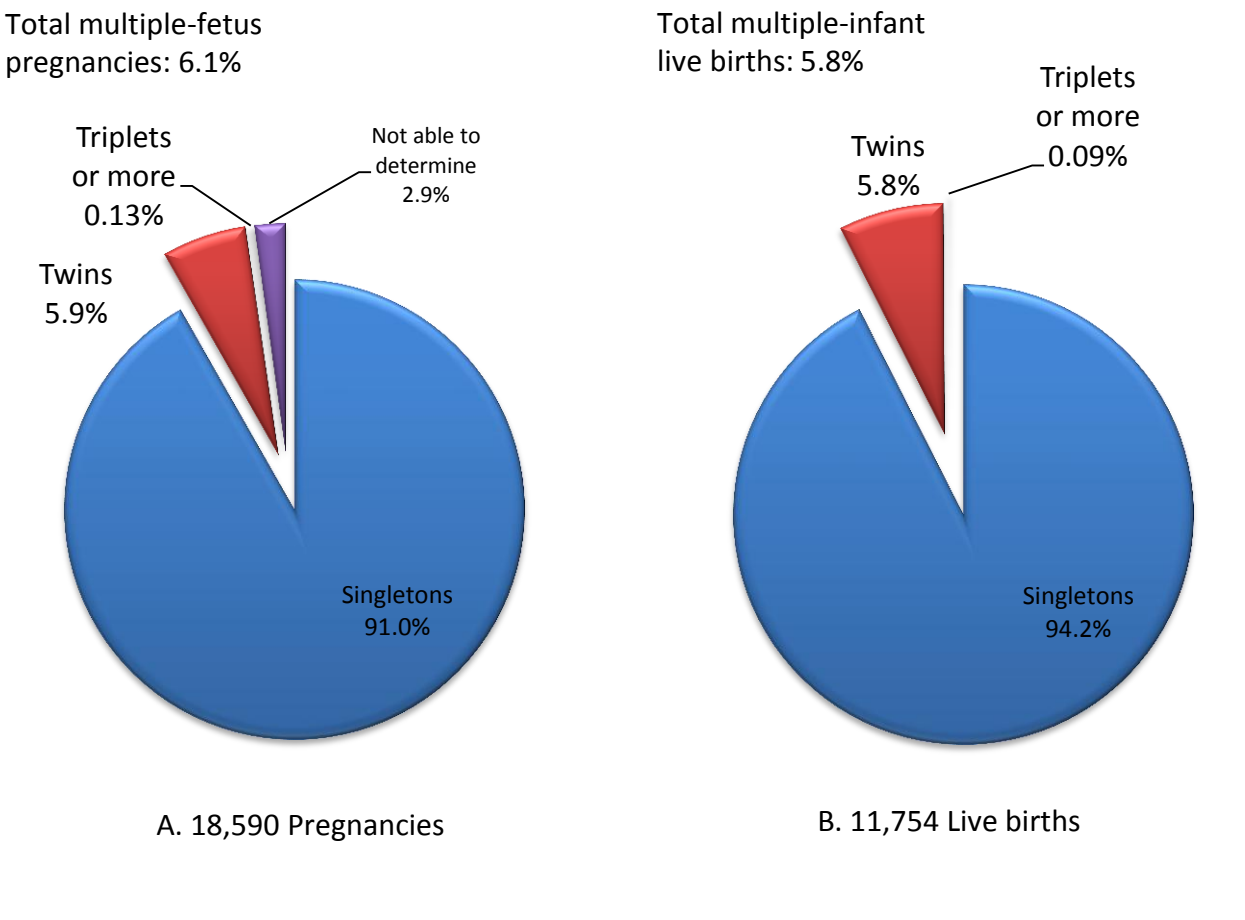


How many multiple pregnancy or multiple-infant birth are implicated in ART cycle with frozen thawed embryo transfer?

In figure 22, graph A shows the detail of 18,590 pregnancies: 91% were singleton pregnancy, 5.9% were twins, and 0.13% were triplets or more. Graph B shows the multiple infant birth rate is lower than that in graph A. Only 5.8% of these live births resulted in more than two infants. Furthermore, the rate of multiple pregnancy after frozen thawed embryo transfer is lower than that of fresh embryo transfer (refer to Figure 11).

Figure 22

Rate of Multiple Pregnancy or Multiple-Infant Birth after Frozen Thawed Embryo Transfer, Japan JSOG, 2008

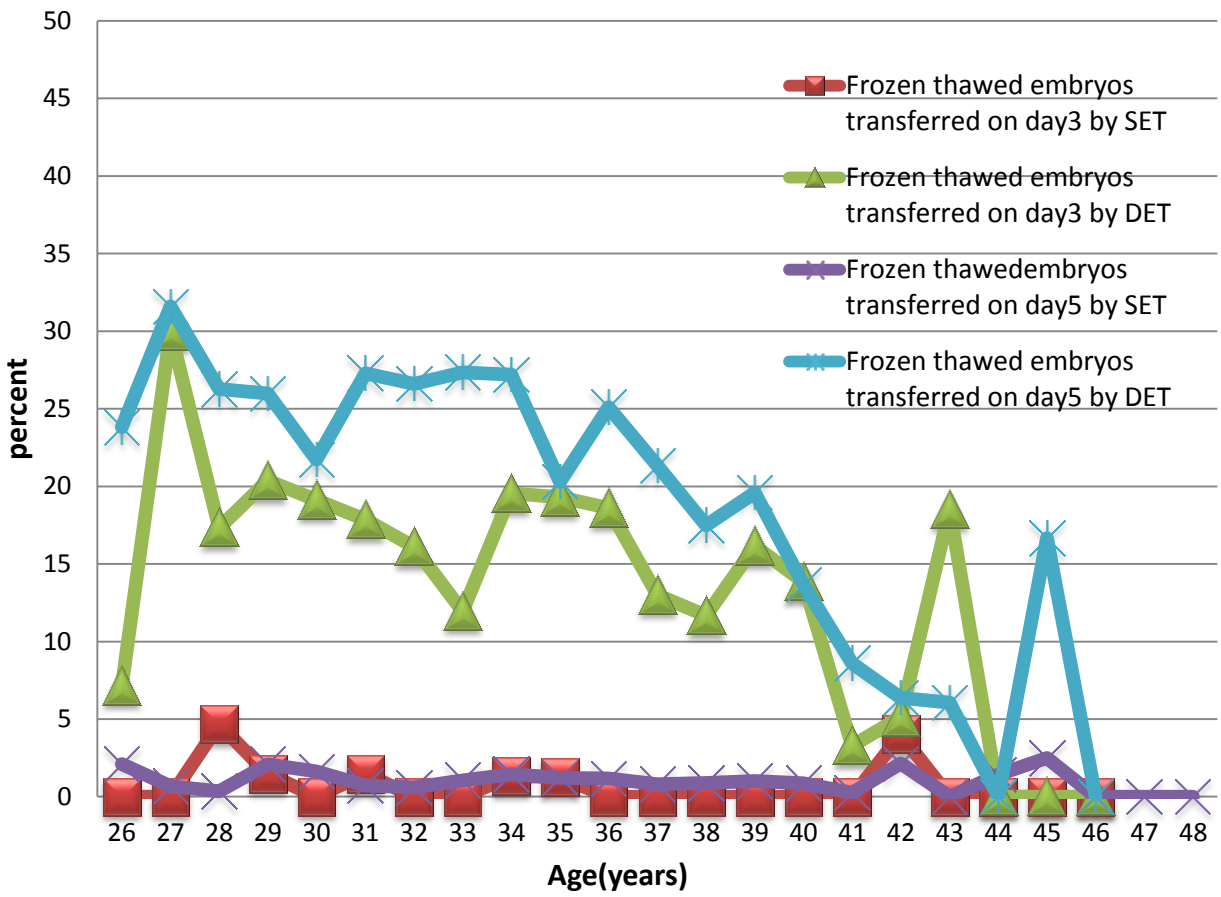


Which has more risk for multiple infant birth rate based on number of embryo(s) and time of frozen thawed embryo transfer?

The cycles of frozen thawed embryo transfer are divided into four groups based on the number of embryos (i.e. SET and DET) and their developmental stages The multiple infant birth rate is then compared according to four groups and age. The rate of multiple infant birth is about 1% in each age with SET of day 3 and day 5. In DET, the multiple infant birth rate for day 5 transfer is higher than that for day 3. In case with the age of 45 or more, the rate varies enormously due to the small size of group. It tends to be no significant difference of the rate based on number and developmental stage of embryo(s) with advancing age.

Figure 23

Multiple-Infant Birth Rates of Single and Double Embryo Transfer on Day 3 and Day 5 in Each Age of Frozen Thawed Embryo Transfer Cycle, Japan JSOG, 2008



Appendix 1: Data used in this report

Outcome of ART cycles transferring fresh embryo(s), Japan JSOG, 2008

ART procedures	IVF-ET	Split	ICSI	ICSI(with TESE)	GIFT	**Others	Total
Cycles Started	57,719	7,582	61,529	2,239	137	1,292	130,498
Retrievals	55,863	7,484	60,152	2,228	133	1,221	127,081
Embryo transfers	28,609	4,594	28,547	1,284	114	401	63,549
Clinical pregnancies	6,808	1,083	5,691	243	14	75	13,914
Pregnancy rate per ET	23.80%	23.60%	19.90%	18.90%	12.30%	18.70%	21.90%
Pregnancy rate per retrieval	12.20%	14.50%	9.50%	10.90%	10.50%	6.10%	10.90%
Number of cycles with SET	17,626	2,811	16,883	596	17	115	38,048
Pregnancies with SET	4,082	650	3,196	118	2	16	8,064
Rate of SET	61.60%	61.20%	59.10%	46.40%	14.90%	28.70%	59.90%
Pregnancy rate with SET	23.20%	23.10%	18.90%	19.80%	11.80%	13.90%	21.20%
Miscarriages	1,576	242	1,452	72	9	21	3,372
Rate of miscarriage per pregnancy	23.10%	22.30%	25.50%	29.60%	64.30%	28.00%	24.20%
Ectopic pregnancies	135	13	103	1	0	2	254
Induced Abortions	23	3	7	1	0	1	35
Singleton pregnancies	6,304	976	5,060	214	10	67	12,361
Multiple pregnancies	513	77	409	16	2	5	1,022
Twin pregnancies	504	75	406	15	2	5	1,007
Triple or more pregnancies	9	2	3	1	0	0	15
Live births	4,296	703	3,473	148	4	41	8,665
Rate of live birth per ET	15.00%	15.30%	12.20%	11.50%	3.50%	10.20%	13.60%
Stillbirths	23	1	21	1	0	0	46
Infant live births	4,614	750	3,703	162	4	46	9,279
Singleton	3,935	651	3,222	138	4	36	7,986
Twin	338	48	233	12	0	5	636
Triple	1	1	5	0	0	0	7
Heterotopic pregnancies	1	0	0	0	0	0	1
Reductions for Multiple pregnancy	7	1	2	0	0	0	10
* Unknown cycles	755	121	635	20	1	10	1,542

***Besides Live-Birth, Stillbirth, Miscarriage, Ectopic pregnancy, and Induced abortion.**
****ZIFT is included in Others**

Outcome of ART cycle using frozen thawed embryo(s), Japan JSOG, 2008

ART procedures	Frozen/thawed embryo transfer	**Others	Total
Cycles Started	58,646	1,380	60,026
Retrievals			
Embryo transfers	56,494	1,300	57,794
Clinical pregnancies	18,194	396	18,590
Pregnancy rate per ET	32.20%	30.50%	32.20%
Pregnancy rate per retrieval			
Number of cycles with SET	38,389	766	39,155
Pregnancies with SET	12,913	255	13,168
Rate of SET	68.00%	58.90%	67.70%
Pregnancy rate with SET	33.60%	33.30%	33.60%
Miscarriages	4,507	96	4,603
Rate of miscarriage per pregnancy	24.80%	24.20%	24.80%
Ectopic pregnancies	164	1	165
Induced Abortions	46	1	47
Singleton pregnancies	16,563	345	16,908
Multiple pregnancies	1,086	31	1,117
Twin pregnancies	1,061	31	1,092
Triple or more pregnancies	25	0	25
Live births	11,527	227	11,754
Rate of live birth per ET	20.40%	17.50%	20.30%
Stillbirths	73	1	74
Infant live births	12,177	245	12,422
Singleton	10,836	209	11,045
Twin	663	18	681
Triple	5	0	5
Heterotopic pregnancies	0	0	0
Reductions for Multiple pregnancy	12	0	12
*Unknown cycles	1,877	70	1,947

*Besides Live-Birth, Stillbirth, Miscarriage, Ectopic pregnancy, and Induced abortion.
**ZIFT is included in Others

Appendix 2: JSOG data items

Data items from cycle start to pregnancy, Japan JSOG, 2008

Variable	*Data domain*
Patient ID number	unique ID for patient
Age at the time of the start of therapy	( ) years old
Cause of infertility	1.tubal dysfunction 2.endometriosis 3Antisperm antibody 4.male factor 5.unkown 6.others
Type of controlled ovarian stimulation	1.natural cycle 2.CC 3.CC+hMG or FSH 4.hMG or FSH 5.GnRHagonist+hMG or FSH 6.GnRHantagonist+hMG or FSH 7.others
Method of oocyto pick up	1.failed 2.endovaginal ultrasonography 3.laparoscopy 4.use of thawed egg or embryo 5.others
What type egg or embryo used for ART	1.fresh egg or embryo 2.frozen thawed embryo 3.frozen thawed egg
Therapeutic method	1.IVF-ET 2.GIFT 3.ICSI 4.IVF-ET+ICSI 5.thawed embryo 6.others
What type method to collect sperm	1.ejaculated sperm 2.TESE 3.other
Semen analysis	1.concentration( )*10~6/ml 2.motility ( )%
If check (1.fresh eggs or embryo) in (what type of egg or embryo used for ART),The input of following two items is necessary	
Number of eggs retrieved	number of eggs retrieved
Number of fertilized egg	number of fertilized egg
If check (2.frozen/thawed embryo) in (what type of egg or embryo used for ART),The input of following one item is necessary	
Number of thawed embryos	number of thawed embryos
If check (3.frozen/thawed eggs) in (what type of egg or embryo used for ART),The input of following two items is necessary	
Number of thawed eggs	number of thawed eggs
Number of fertilized egg with thawed egg	number of fertilized egg with thawed egg
Stage of embryo at embryo transfer	1.egg(unfertilized) 2.cleavage embryos 3.blastocysts 4.etcancellation 5.others
Number of egg or embryo at transfer	number of egg or embryo at transfer
Number of frozen egg or embryo	number of frozen egg or embryo
Luteal support	1.none 2.Progesterone(P) 3.hCG 4.hCG+P 5.Estrogen+P 6.others
Complications	1.none 2.bleeding 3.infection 4.OHSS(more than StageⅡ) 5.others
Having pregnancy or not	1.none 2.clinical pregnancy (Evidence by ultrasound of an intrauterine sac (with or without a fetal heart)
Use of governmental support system for ART	1. Yes 2. No

Data items from pregnancy to delivery, Japan ISOG, 2008

Variable	*Data domain*
Numbers of gestational sac	numbers of gestational sac ( )
Number of fetal hearts	number of fetal hearts( )
Outcome of pregnancy	1miscarriage 2.Ectopic pregnancy 3.heterotopic pregnancy 4.Elective termination of pregnancy (reason:) 5.livebirth 6.stillbirth 7 Selective reduction performed
Number of live birth	number of live birth( ) date (day/month/year)
Style of delivery	1.vagianl delivery 2.caesarean delivery 3.vaginal and caesarean delivery 4.unknown
Maternal complications of pregnancy	1.none 2.yes 3.unknown

findings of baby

	male or female	gestational age	Birth Weight	state of baby			Prognosis		
				livebirth or stillbirth	singleton or multiple	mulformation	under 7days	under 28days	death day
1	1.male 2.female 3.unknown	1.( )weeks 2.unknown	1.( )g 2.unknown	1.livebirth 2.stillbirth 3.unknown	1.singleton 2.multiple 3.unknown	yes ( ) No	1.survival 2.death 3.unknown	1.survival 2.death 3.unknown	Day /month /year
2	1.male 2.female 3.unknown	1.( )weeks 2.unknown	1.( )g 2.unknown	1.livebirth 2.stillbirth 3.unknown	1.singleton 2.multiple 3.unknown	yes ( ) No	1.survival 2.death 3.unknown	1.survival 2.death 3.unknown	Day /month /year
3	1.male 2.female 3.unknown	1.( )weeks 2.unknown	1.( )g 2.unknown	1.livebirth 2.stillbirth 3.unknown	1.singleton 2.multiple 3.unknown	yes ( ) No	1.survival 2.death 3.unknown	1.survival 2.death 3.unknown	Day /month /year
4	1.male 2.female 3.unknown	1.( )weeks 2.unknown	1.( )g 2.unknown	1.livebirth 2.stillbirth 3.unknown	1.singleton 2.multiple 3.unknown	yes ( ) No	1.survival 2.death 3.unknown	1.survival 2.death 3.unknown	Day /month /year

Terminology

Note: In Japan Society of Obstetrics & Gynecology (JSOG), the progression of pregnancy is defined by gestational age as follows:
Birth (delivery): deliveries that resulted in the birth of one or more live babies and/or stillborn babies at or after 22 gestational weeks.
Abortion (miscarriage): spontaneous or artificial loss of a clinical pregnancy that occurs before 22 completed weeks of gestational age (20 weeks post fertilization).
These two definitions for the progression of pregnancy in JSOG significantly differ from those of International Committee for Monitoring Assisted Reproductive Technology (ICMART).

Assisted reproductive technology (ART): all treatments or procedures that include the in vitro handling of both human oocytes and sperm, or embryos, for the purpose of establishing a pregnancy. This includes, but is not limited to, in vitro fertilization and embryo transfer, gamete intrafallopian transfer, zygote intrafallopian transfer, tubal embryo transfer, gamete and embryo cryopreservation, oocyte and embryo donation, and gestational surrogacy. ART does not include assisted insemination (artificial insemination) using sperm from either a woman's partner or a sperm donor.
Blastocyst: an embryo, five or six days after fertilization, with an inner cell mass, outer layer of trophectoderm and a fluid-filled blastocoele cavity.
Cancelled cycle: an ART cycle in which ovarian stimulation or monitoring has been carried out with the intention to treat, but did not proceed to follicular aspiration or, in the case of a thawed embryo, to embryo transfer.
Clinical pregnancy: a pregnancy diagnosed by ultrasonographic visualization of one or more gestational sacs or definitive clinical signs of pregnancy. It includes ectopic pregnancy. Note: Multiple gestational sacs are counted as one clinical pregnancy.
Clinical pregnancy rate: the number of clinical pregnancies expressed per 100 initiated cycles, aspiration cycles or embryo transfer cycles. Note: When clinical pregnancy rates are given, the denominator(initiated, aspirated or embryo transfer cycles) must be specified. Clinical pregnancy with fetal heart beat: pregnancy diagnosed by ultrasonographic or clinical documentation of at least one fetus with heart beat. It includes ectopic pregnancy.
Controlled ovarian stimulation (COS) for ART: Pharmacological treatment in which women are stimulated to induce the development of multiple ovarian follicles to obtain multiple oocytes at follicular aspiration.
Cryopreservation: the freezing or vitrification and storage of gametes, zygotes, embryos or gonadal tissue.
Birth rate : the number of deliveries expressed per 100 initiated cycles, aspiration cycles or embryo transfer cycles. When delivery rates are given, the denominator (initiated, aspirated or embryo transfer cycles) must be specified. It includes deliveries that resulted in the birth of one or more live babies and/or stillborn babies. Note: The delivery of a singleton, twin or other multiple pregnancy is registered as one delivery.
Ectopic pregnancy: a pregnancy in which implantation takes place outside the uterine cavity.

Embryo: the product of the division of the zygote to the end of the embryonic stage, eight weeks after fertilization. (This definition does not include either parthenotes - generated through parthenogenesis- nor products of somatic cell nuclear transfer.)
Embryo/fetus reduction: a procedure to reduce the number of viable embryos or fetuses in a multiple pregnancy.
Embryo transfer (ET): the procedure in which one or more embryos are placed in the uterus or fallopian tube.
•**Single embryo transfer (SET): only one embryo is placed in the uterus.**
•**Double embryo transfer (DET): two embryos are placed in the uterus.**
Embryo transfer cycle: an ART cycle in which one or more embryos are transferred into the uterus or Fallopian tube. **Fertilization:** the penetration of the ovum by the spermatozoon and combination of their genetic material resulting in the formation of a zygote.
Fetal death (stillbirth): death prior to the complete expulsion or extraction from its mother of a product of fertilization, at or after 22(according to the ICMART definition, this figure is 20) completed weeks of gestational age. The death is indicated by the fact that, after such separation, the fetus does not breathe or show any other evidence of life such as heart beat, umbilical cord pulsation, or definite movement of voluntary muscles.
Fetus: the product of fertilization from completion of embryonic development, at eight completed weeks after fertilization, until abortion or birth.
Frozen/thawed oocyte cycle: an ART procedure in which cycle monitoring is carried out with the intention of fertilizing thawed oocytes and performing embryo transfer.
Gamete Intra Fallopian Transfer (GIFT): an ART procedure in which both gametes (oocytes and spermatozoa) are transferred to the Fallopian tubes.
Gestational sac: a fluid-filled structure associated with early pregnancy, which may be located inside or outside the uterus (in case of an ectopic pregnancy).
In vitro fertilization (IVF): an ART procedure that involves extracorporeal fertilization.
Induced abortion: the termination of a clinical pregnancy, by deliberate interference that takes place before 22 (according to the ICMART definition, this figure is 20) completed weeks of gestational age (20(according to the ICMART definition, this figure is 18) weeks post fertilization). (or, according to the ICMART definition, if gestational age is unknown, of an embryo/fetus of less than 400 grams.)
Infertility (clinical definition): a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.
Intra Cytoplasmic Sperm Injection (ICSI): a procedure in which a single spermatozoon is injected into the oocyte cytoplasm.
Live birth: the complete expulsion or extraction from its mother of a product of fertilization, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life such as heart beat, umbilical cord pulsation, or definite movement of voluntary muscles, irrespective of whether the umbilical cord has been cut or the placenta is attached.
Live birth rate: the number of deliveries that resulted in at least one live born baby expressed per 100 initiated cycles, aspiration cycles or embryo transfer cycles. When delivery rates are given, the denominator (initiated, aspirated, or embryo transfer cycles) must be specified.
Low birth weight: Birth weight less than 2,500 grams.

Mild ovarian stimulation for IVF: a procedure in which the ovaries are stimulated with either gonadotropins and/or other compounds, with the intent to limit the number of oocytes obtained for IVF to fewer than seven.
Multiple pregnancy: pregnancy with two or more fetuses.
Multiple infant birth: birth with two or more neonates.
Natural cycle IVF: an IVF procedure in which one or more oocytes are collected from the ovaries during a spontaneous menstrual cycle without any drug use.
Ovarian Hyper Stimulation Syndrome (OHSS): an exaggerated systemic response to ovarian stimulation characterized by a wide spectrum of clinical and laboratory manifestations. It is classified as mild, moderate or severe according to the degree of abdominal distention, ovarian enlargement and respiratory, haemodynamic and metabolic complications.
Prematurity: a live birth or stillbirth that takes place after at least 22 (according to the ICMART definition, this figure is 20) but before 37 completed weeks of gestational age.
Spontaneous abortion/miscarriage: the spontaneous loss of a clinical pregnancy that occurs before 22(according to the ICMART definition, this figure is 20) completed weeks of gestational age (20(according to the ICMART definition, this figure is 18) weeks post fertilization) .
(or, according to the ICMART definition, if gestational age is unknown, the loss of an embryo/fetus of less than 400 grams.)
TESE: Testicular Sperm Extraction.
Birth/pregnancy rate with at least one live birth: the estimated total number of deliveries with at least one live born baby resulting from one initiated or aspirated ART cycle including all fresh cycles and all frozen/thawed ART cycles. This rate is used when all of the embryos fresh and/or frozen/thawed have been utilized from one ART cycles.
Note: The delivery of a singleton, twin or other multiple pregnancy is registered as one delivery.
Zygote: a diploid cell resulting from the fertilization of an oocyte by a spermatozoon, which subsequently divides to form an embryo.
Zygote Intra-Fallopian Transfer (ZIFT): a procedure in which zygote(s) is/are transferred into the Fallopian tube.
(Zegers-Hochschild F, Adamson GD, et al Hum Reprod. 2009 Nov;24(11):2683-7. Epub 2009 Oct 4.)

Reference

1. Centers for Disease Control and Prevention
http://www.cdc.gov/art/ARTReports.htm
2. Australia's national agency for health and welfare statistics and information
http://www.aihw.gov.au/publication-detail/?id=10737420465