

Congenital malformations in children after in vitro fertilization in the Czech Republic in 1995 – 1999

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Objective:

To study the frequency of registered congenital malformations (CM) in children after in vitro fertilization (IVF) and to compare it to that in spontaneously conceived children.

Design:

A retrospective study of a material from Czech IVF and CM Registers, covering the 1995 – 1999 period.

IVF outcomes

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
<i>year</i>	<i>abortions</i>	<i>spontaneous abortions</i>	<i>ectopic pregnancy</i>	<i>induced abortions</i>	<i>all births</i>	<i>live births</i>	<i>stillbirths</i>	<i>deliveries</i>
1995	50	40	5	5	127	126	1	92
1996	99	71	15	13	680	679	1	501
1997	128	100	15	13	1328	1323	5	969
1998	134	110	12	12	1750	1745	5	1271
1999	30	24	2	4	1241	1235	6	909
1995-1999	441	345	49	47	5126	5108	18	3742

Naturally conceived outcomes

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
<i>year</i>	<i>abortions</i>	<i>spontaneous abortions</i>	<i>ectopic pregnancy</i>	<i>induced abortions</i>	<i>all births</i>	<i>live births</i>	<i>stillbirths</i>	<i>deliveries</i>
1995	61540	10531	1471	49538	96270	95971	299	95252
1996	59863	10225	1545	48093	90083	89767	316	89167
1997	56845	10292	1537	45016	89602	89334	268	88721
1998	55520	11018	1543	42959	89079	88790	289	88067
1999	52073	11149	1534	39390	88533	88236	297	87377
1995-1999	285841	53215	7630	224996	453567	452098	1469	448584

IVF outcomes

		<i>spontaneous abortions</i>	<i>ectopic pregnancy</i>	<i>induced abortions</i>		[(2)+(3)]/	(8)/	
<i>year</i>	<i>abortions</i>					[(2)+(3)+(8)]	[(2)+(3)+(8)]	
1995	100,0	80,0	10,0	10,0		32,85	67,15	100,0
1996	100,0	71,7	15,2	13,1		14,65	85,35	100,0
1997	100,0	78,1	11,7	10,2		10,61	89,39	100,0
1998	100,0	82,1	9,0	9,0		8,76	91,24	100,0
1999	100,0	80,0	6,7	13,3		2,78	97,22	100,0
1995-1999	100,0	78,2	11,1	10,7		9,53	90,47	100,0

Naturally conceived outcomes

		<i>spontaneous abortions</i>	<i>ectopic pregnancy</i>	<i>induced abortions</i>		[(2)+(3)]/	(8)/	
<i>year</i>	<i>abortions</i>					[(2)+(3)+(8)]	[(2)+(3)+(8)]	
1995	100,0	17,1	2,4	80,5		11,19	88,81	100,0
1996	100,0	17,1	2,6	80,3		11,66	88,34	100,0
1997	100,0	18,1	2,7	79,2		11,76	88,24	100,0
1998	100,0	19,8	2,8	77,4		12,48	87,52	100,0
1999	100,0	21,4	2,9	75,6		12,68	87,32	100,0
1995-1999	100,0	18,6	2,7	78,7		11,94	88,06	100,0

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
<i>abortions</i>	<i>spontaneous abortions</i>	<i>ectopic pregnancy</i>	<i>induced abortions</i>	<i>all births</i>	<i>live births</i>	<i>stillbirths</i>	<i>deliveries</i>

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between IVF and NC

Spontaneous abortions and ectopic pregnancies

		<i>gestation</i>	<i>age</i>
NC	Mean	8,76	27,22
	Std. Deviation	3,84	6,29
	N	60845	60845
IVF	Mean	9,88	29,98
	Std. Deviation	5,42	4,65
	N	394	394

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between IVF and NC

Births - total

		<i>gestation</i>	<i>birth weight</i>	<i>age</i>
NC	Mean	39,45	3333	25,31
	Std. Deviation	1,81	543,47	4,79
	N	453567	453567	453567
IVF	Mean	37,15	2760	30,16
	Std. Deviation	3,20	797,07	4,20
	N	5126	5126	5126

NC Naturally conceived

IVF In vitro fertilization

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between NC and CM

Births - total

		<i>gestation</i>	<i>birth weight</i>	<i>age</i>
NC	Mean	39,45	3333	25,31
	Std. Deviation	1,81	543	4,79
	N	453567	453567	453567
CM	Mean	38,87	3195	25,40
	Std. Deviation	2,45	666	4,90
	N	11960	11960	11960

NC **Naturally conceived**

CM **Congenital malformations**

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between IVF and NC

Births - singletons

		<i>gestation</i>	<i>birth weight</i>	<i>age</i>
NC	Mean	39,52	3354	25,29
	Std. Deviation	1,72	524	4,78
	N	443670	443670	443670
IVF	Mean	38,88	3265	30,49
	Std. Deviation	2,23	609	4,36
	N	2430	2430	2430

NC **Naturally conceived**

IVF **In vitro fertilization**

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between NC and CM

Births - singletons

		<i>gestation</i>	<i>birth weight</i>	<i>age</i>
NC	Mean	39,52	3354	25,29
	Std. Deviation	1,72	524	4,78
	N	443670	443670	443670
CM	Mean	38,99	3229	25,35
	Std. Deviation	2,40	639	4,90
	N	11562	11562	11562

NC **Naturally conceived**

CM **Congenital malformations**

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between IVF and NC

Births - twins

		<i>gestation</i>	<i>birth weight</i>	<i>age</i>
NC	Mean	36,38	2422	26,39
	Std. Deviation	2,94	601	4,89
	N	9690	9690	9690
IVF	Mean	35,83	2369	29,90
	Std. Deviation	3,03	627	4,07
	N	2486	2486	2486

NC **Naturally conceived**

IVF **In vitro fertilization**

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between NC and CM

Births - twins

		<i>gestation</i>	<i>birth weight</i>	<i>age</i>
NC	Mean	36,38	2422	26,39
	Std. Deviation	2,94	601	4,89
	N	9690	9690	9690
CM	Mean	35,32	2207	27
	Std. Deviation	3,76	673	5,00
	N	440	440	440

NC **Naturally conceived**

CM **Congenital malformations**

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between IVF and NC

Abortions and births

	NC	IVF		NC	IVF
previous number of					
<i>spontaneous abortions</i>					
0	239842	354		83,9	80,3
1	36746	62		12,9	14,1
2+	9253	25		3,2	5,7
	285841	441		100,0	100,0
<i>induced abortions</i>					
0	163351	401		57,15	90,93
1+	122490	40		42,85	9,07
	285841	441		100,00	100,00
<i>live births</i>					
0	73306	365		25,65	82,77
1+	212535	76		74,35	17,23
	285841	441		100,00	100,00

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between NC and CM

Abortions and births

	NC	CM		NC	CM
previous number of					
<i>spontaneous abortions</i>					
0	239842	10564		83,9	81,0
1	36746	1482		12,9	11,4
2+	9253	992		3,2	7,6
	285841	13038		100,0	100,0
<i>induced abortions</i>					
0	163351	10354		57,15	79,41
1+	122490	2684		42,85	20,59
	285841	13038		100,00	100,00
<i>live births</i>					
0	73306	6542		25,65	50,18
1+	212535	6496		74,35	49,82
	285841	13038		100,00	100,00

DESCRIPTIVE STATISTICS

DISTRIBUTION DIFFERENCES between IVF and NC

Births

	NC	IVF		NC	IVF
Deliveries of					
<i>singletons</i>	443670	2430		98,90	64,94
<i>twins</i>	4845	1243		1,08	33,22
<i>triplets</i>	69	66		0,02	1,76
<i>quadruplets</i>	0	3		0,00	0,08
total	448584	3742		100,00	100,00
All births					
<i>premature</i>	15482	1332		3,41	25,99
<i>hypertrophic</i>	9106	326		2,01	6,36
<i>hypotrophic</i>	9575	382		2,11	7,45
<i>normal</i>	419404	3086		92,47	60,20
total	453567	5126		100,00	100,00

DESCRIPTIVE STATISTICS

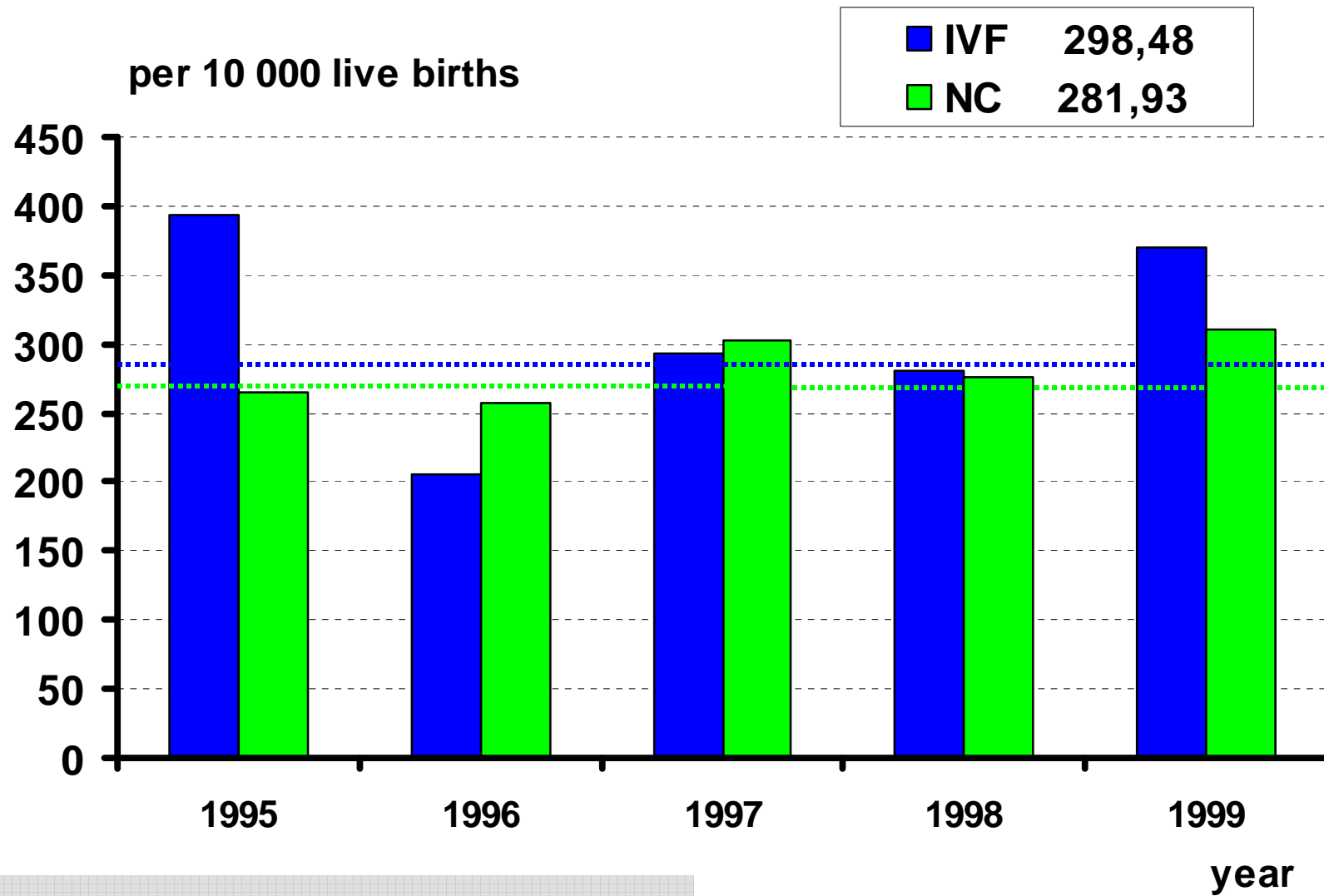
DISTRIBUTION DIFFERENCES between NC and CM

Births

	NC	CM		NC	CM
Deliveries of					
<i>singletons</i>	443670	11562		98,90	88,68
<i>twins, triplets, +</i>	4914	928		1,10	7,12
<i>unknown</i>	0	548		0,00	4,20
total	448584	13038		100,00	100,00
All births					
<i>premature</i>	15482	1006		3,41	7,72
<i>hypertrophic</i>	9106	954		2,01	7,32
<i>hypotrophic</i>	9575	669		2,11	5,13
<i>normal</i>	419404	10318		92,47	79,14
total	453567	13038		100,00	100,00

DESCRIPTIVE STATISTICS

Congenital malformations



NC Naturally conceived

IVF In vitro fertilization

DESCRIPTIVE STATISTICS

IVF methods

Assisted reproduction methods:

4 groups

IVF - **In - Vitro Fertilisation**

ICSI - **Intra Cytoplasmic Sperm Injection**

+ **MESA - Microchirurgical Epididymal Sperm Aspiration**

+ **TESE - Testicular Sperm Extraction**

+ **SUZI - SubZonal Insemination**

KET - **Kryo Embryo Transfer**

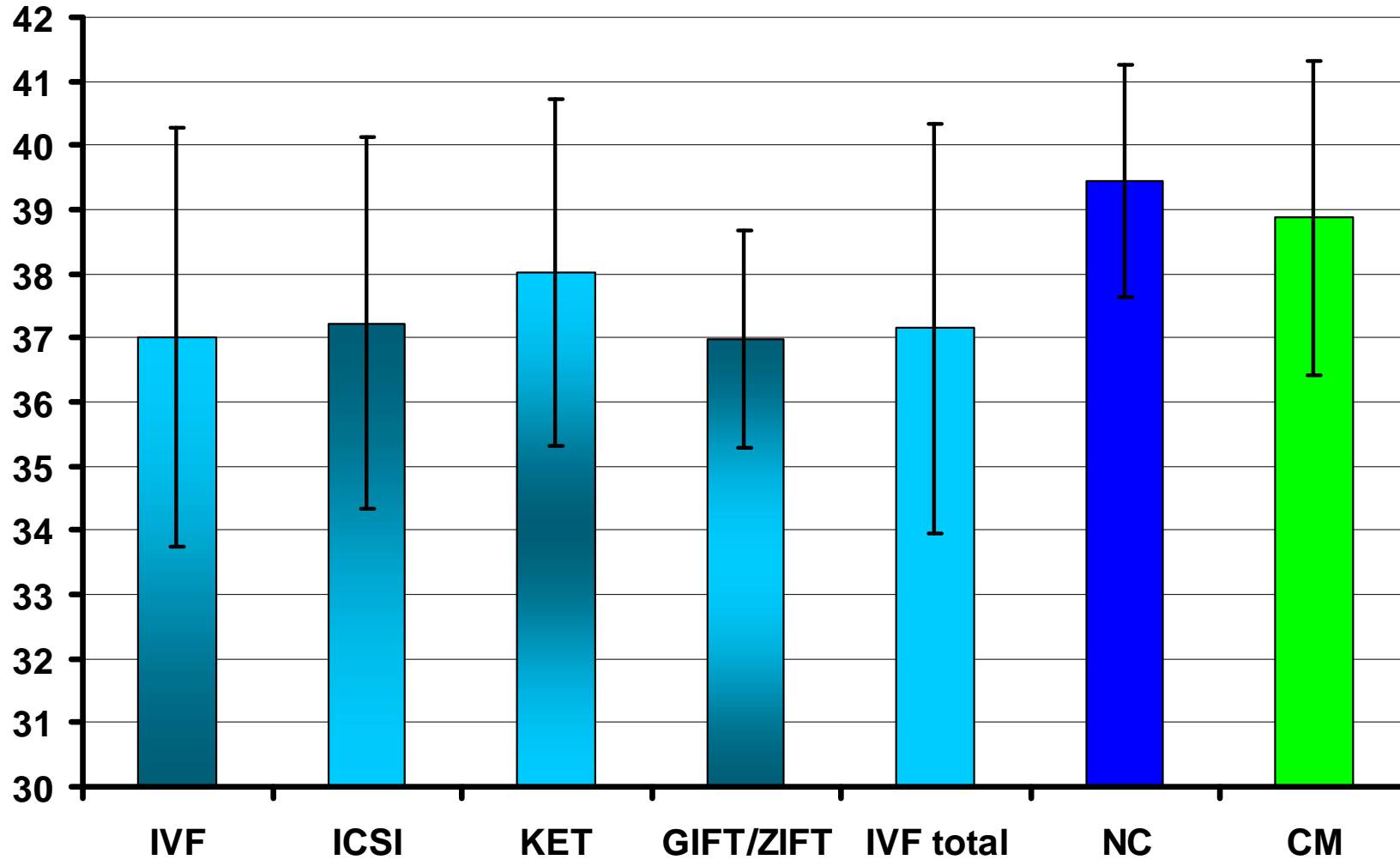
GIFT / ZIFT - **Gamete IntraFallopian Transfer**

- **Zygote IntraFallopian Transfer**

DESCRIPTIVE STATISTICS

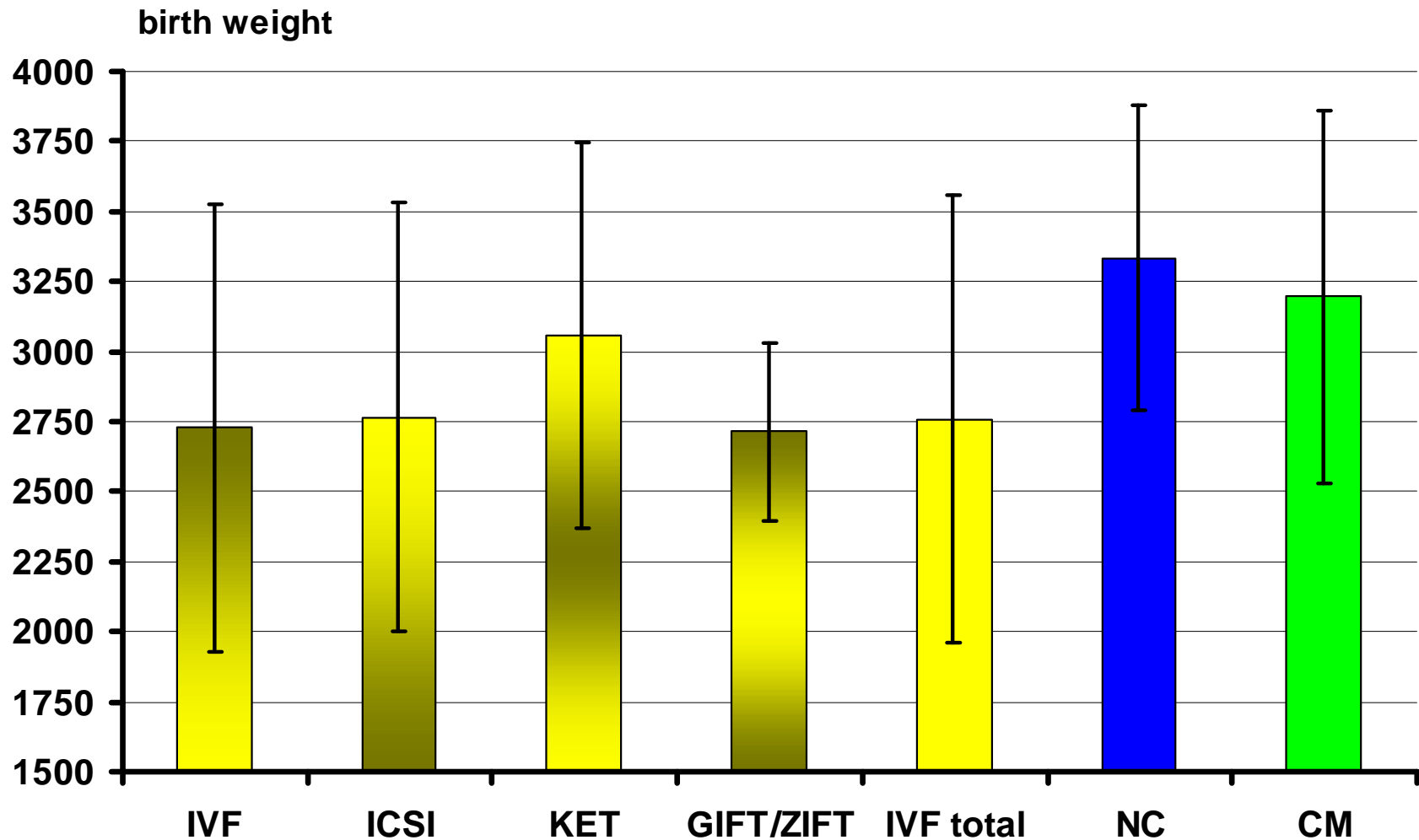
gestation

DISTRIBUTION DIFFERENCES between IVF methods



DESCRIPTIVE STATISTICS birth weight

DISTRIBUTION DIFFERENCES between IVF methods



DESCRIPTIVE STATISTICS

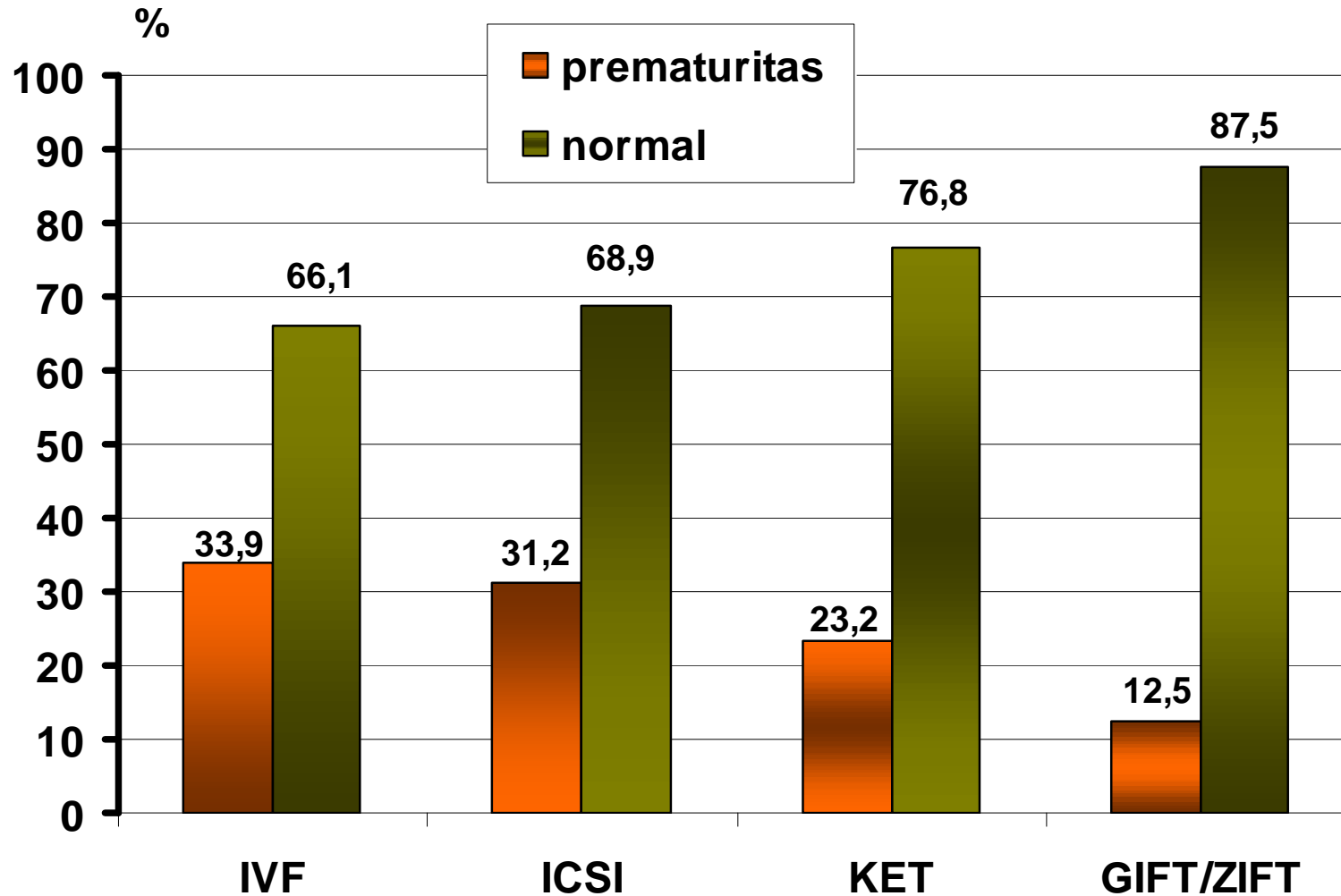
DISTRIBUTION DIFFERENCES between IVF methods

		<i>gestation</i>	<i>Birth weight</i>
IVF	Mean	37.01	2727
	Std. Deviation	3.27	796
	N	3191	3191
ICSI	Mean	37.23	2765
	Std. Deviation	3.15	807
	N	1695	1695
KET	Mean	38.01	3058
	Std. Deviation	2.70	691
	N	284	284
GIFT/ZIFT	Mean	39.63	3114
	Std. Deviation	1.69	317
	N	8	8

DESCRIPTIVE STATISTICS

IVF methods

prematuritas (< 37 week of gestation)

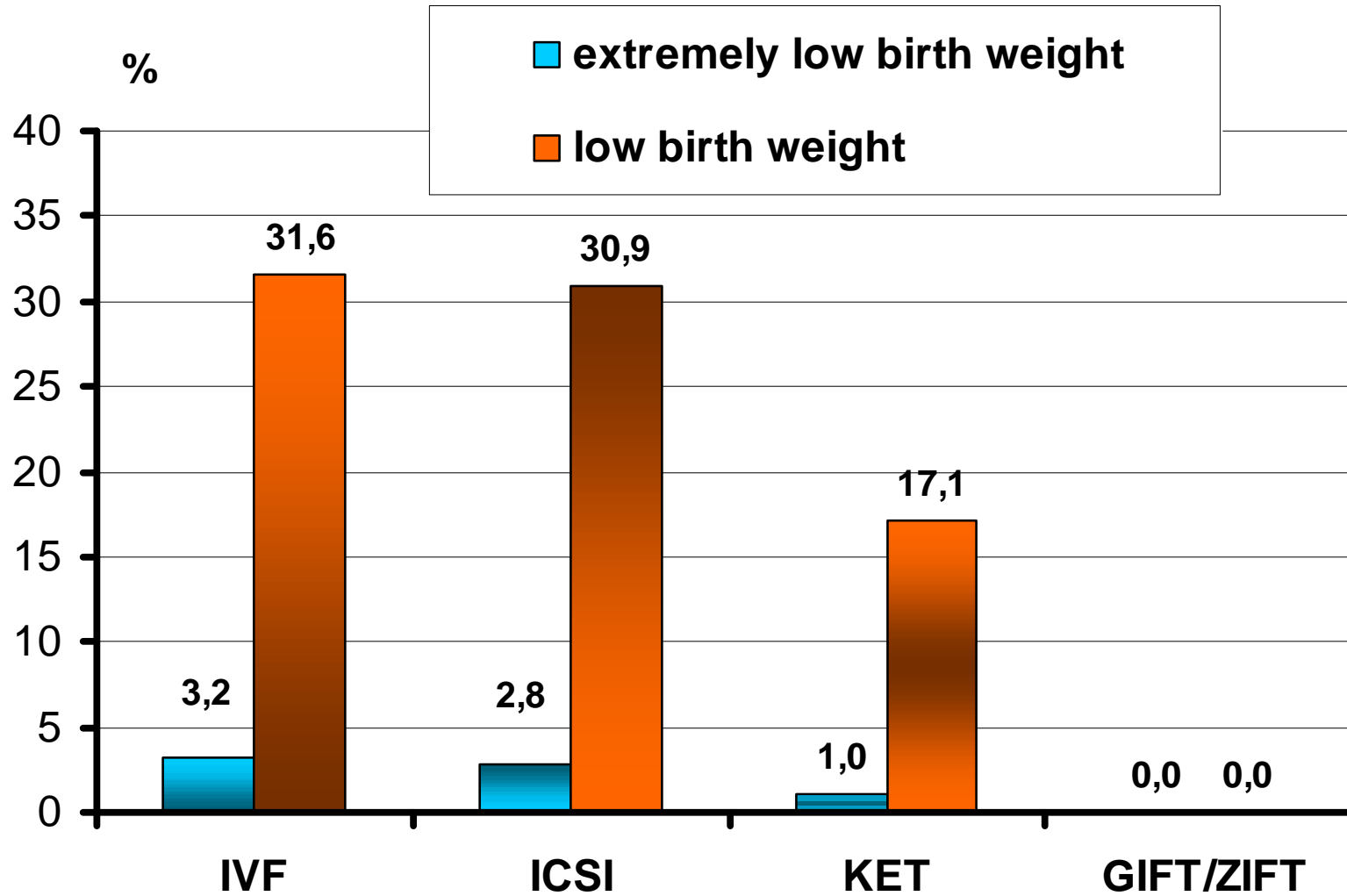


DESCRIPTIVE STATISTICS

IVF methods

ELBW(< 1 000 g)

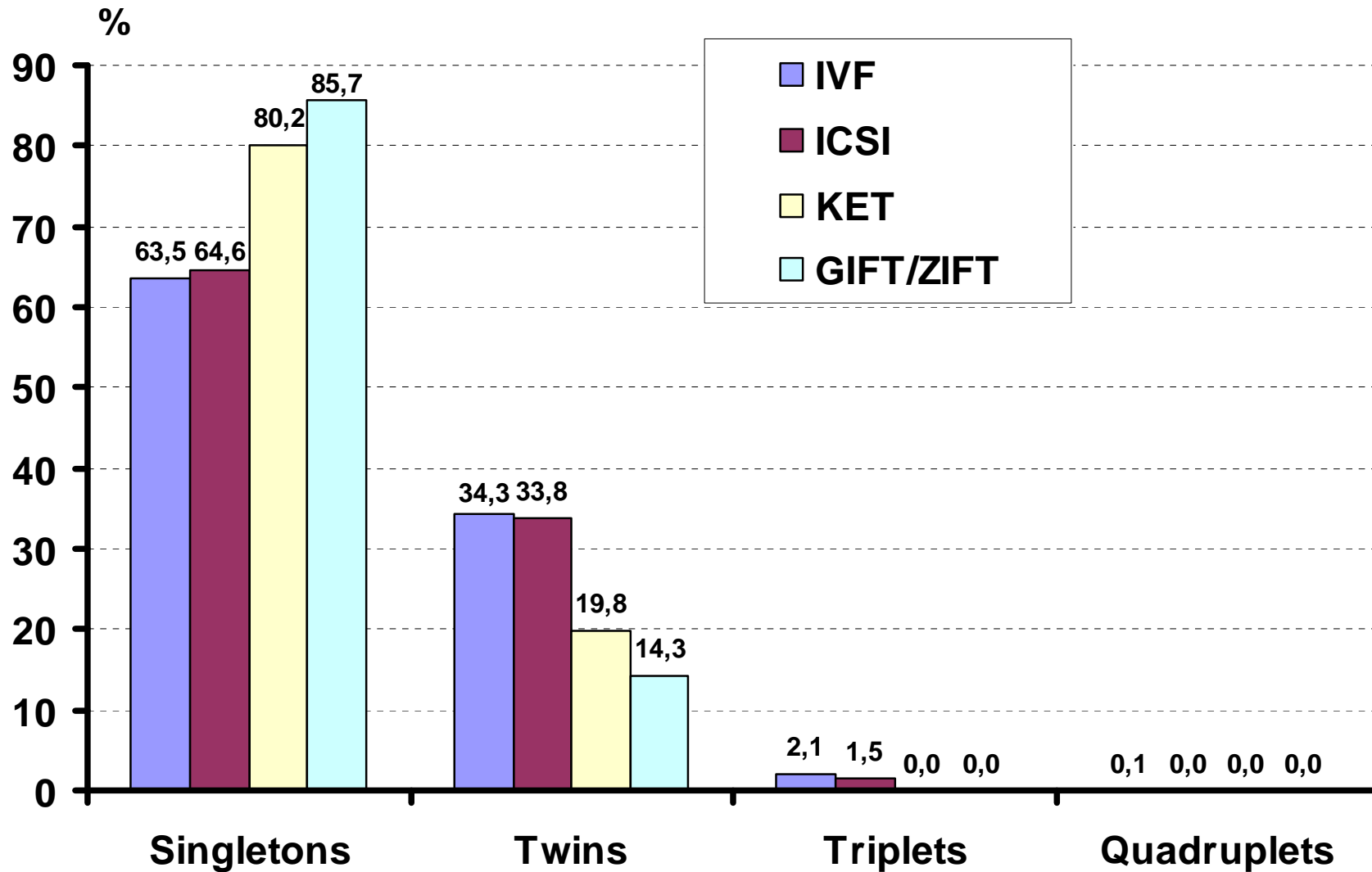
LBW(1 000 - 2 499 g)



DESCRIPTIVE STATISTICS

IVF methods

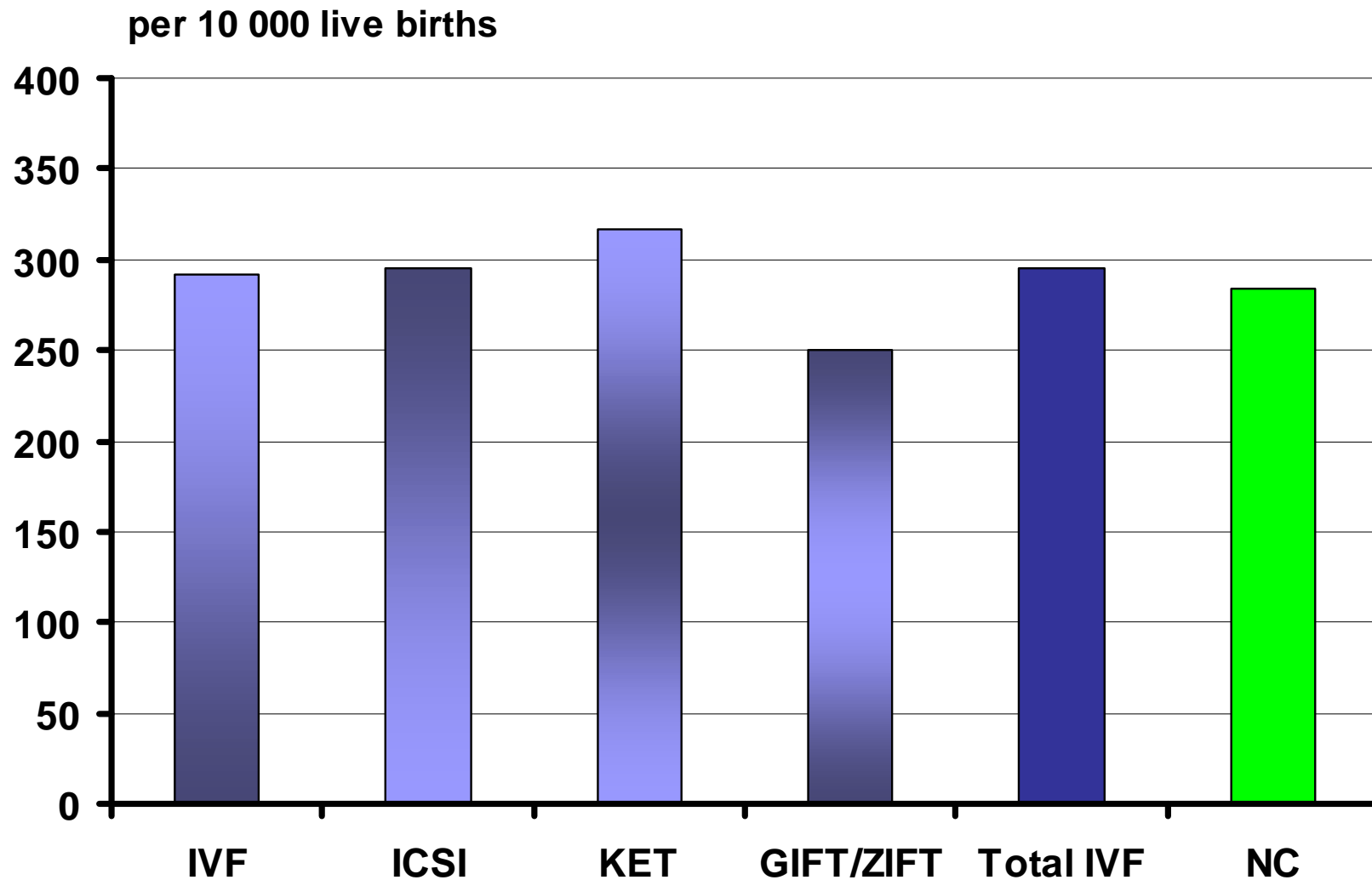
Singletons, Twins, Triplets, Quadruplets



DESCRIPTIVE STATISTICS

IVF methods

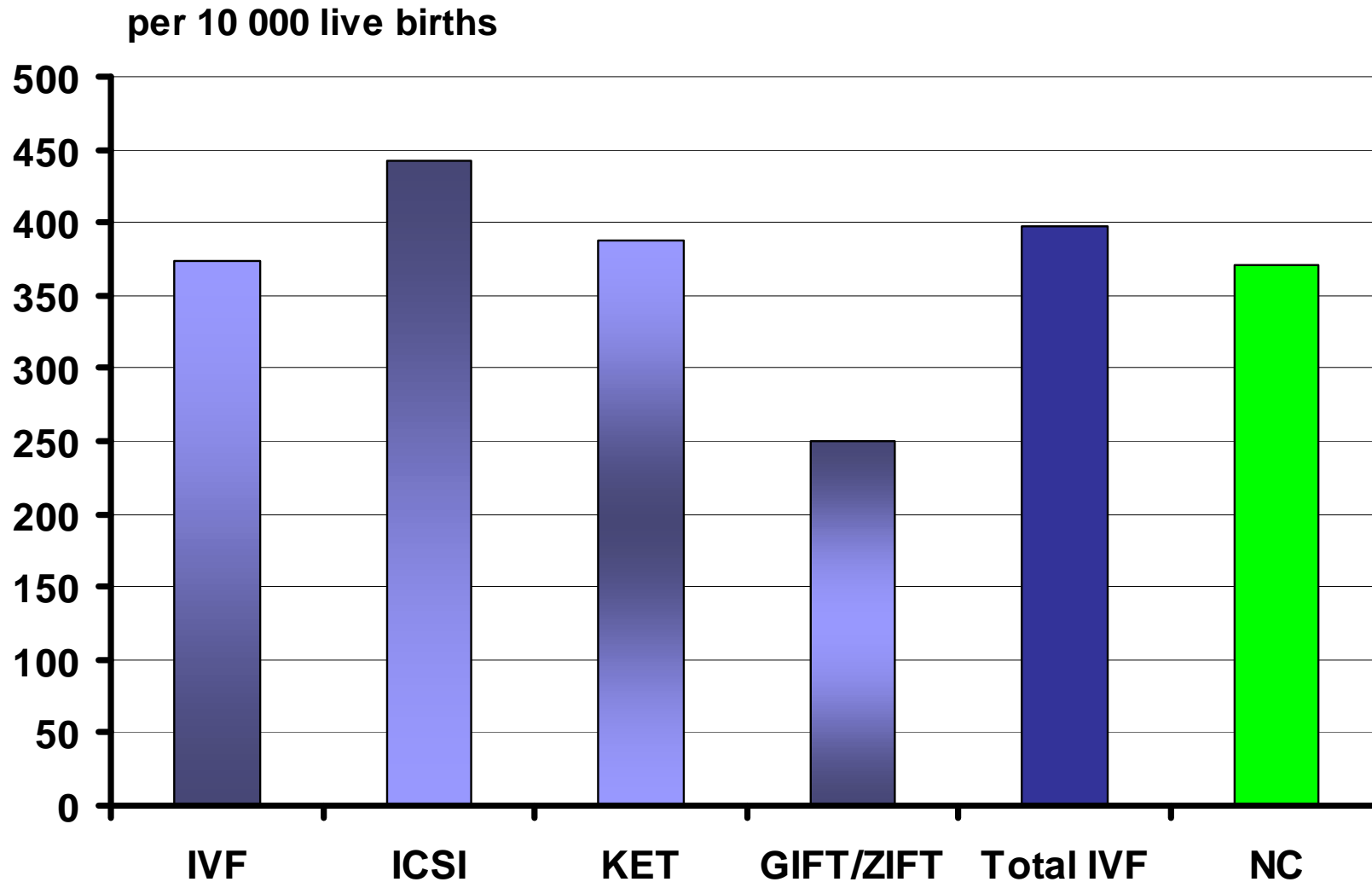
Congenital malformations - newborns



DESCRIPTIVE STATISTICS

IVF methods

Congenital malformations - total



DESCRIPTIVE STATISTICS

IVF methods

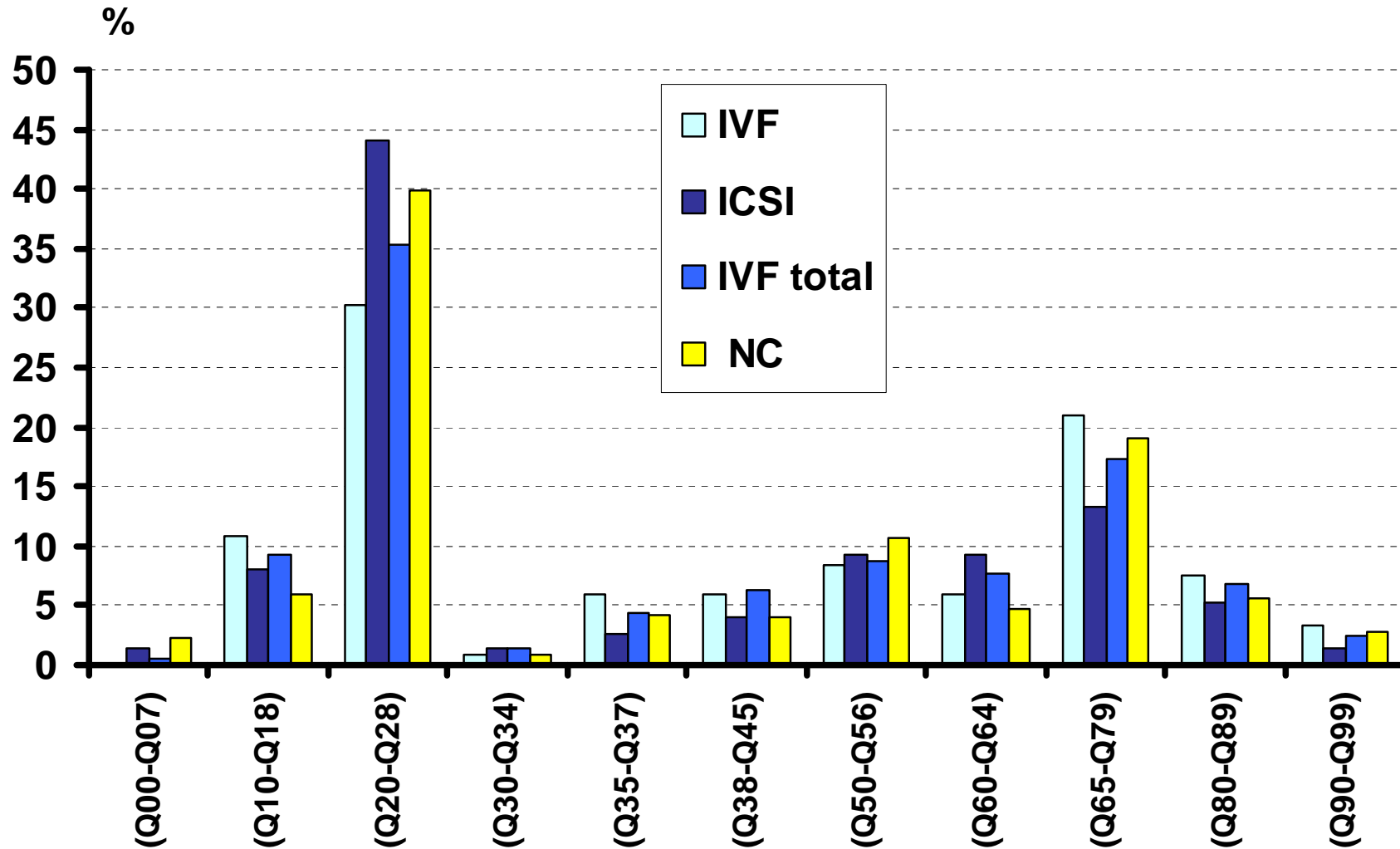
Congenital malformations - groups

Congenital malformations of the nervous system	(Q00-Q07)
Congenital malformations of eye, ear, face and neck	(Q10-Q18)
Congenital malformations of the circulatory system	(Q20-Q28)
Congenital malformations of the respiratory system	(Q30-Q34)
Cleft lip and cleft palate	(Q35-Q37)
Other congenital malformations of the digestive system	(Q38-Q45)
Congenital malformations of genital organs	(Q50-Q56)
Congenital malformations of the urinary system	(Q60-Q64)
Congenital malformations of the musculoskeletal system	(Q65-Q79)
Other congenital malformations	(Q80-Q89)
Chromosomal abnormalities	(Q90-Q99)

DESCRIPTIVE STATISTICS

IVF methods

Congenital malformations - groups



DESCRIPTIVE STATISTICS

IVF methods

Congenital malformations

	IVF	ICSI	IVF total
Anencephaly		1	1
Spina bifida			0
Encephalocele			0
Hydrocephaly			0
Transposition of great vessels	1		1
Tetralogy of Fallot			0
Hypoplastic left heart syndrome	2		2
Cleft palate	4	1	5
Total cleft lip	3	1	4
Oesophageal atresia	2	3	5
Anorectal atresia	2		2
Hypospadias	9	6	15
Renal agenesis	2	2	4
Cystic kidney disease		1	1
Limb reduction deformity	3	2	5
Omphalocele	1		1
Gastroschisis			0
Down syndrome	2		2
Edward's syndrome			0
Patau's syndrome			0
Klinefelter's syndrome	1		1
Turner syndrome			0

Conclusion:

This study shows pregnancy outcome after in vitro fertilisation and after naturally conceived pregnancy.

Among the ICSI children, we did not observe any increase in the general major malformations rates in newborns, or in the total malformations rates.

No differences in major malformations rates were observed in the different organ systems in ICSI compared to IVF.

