

FATOR MASCULINO: ESTADO DA ARTE



Edson Borges Jr.

Declaro:

Ausência de Conflito de Interesse

Resolução do Conselho Federal de Medicina nº 1.595/2.000



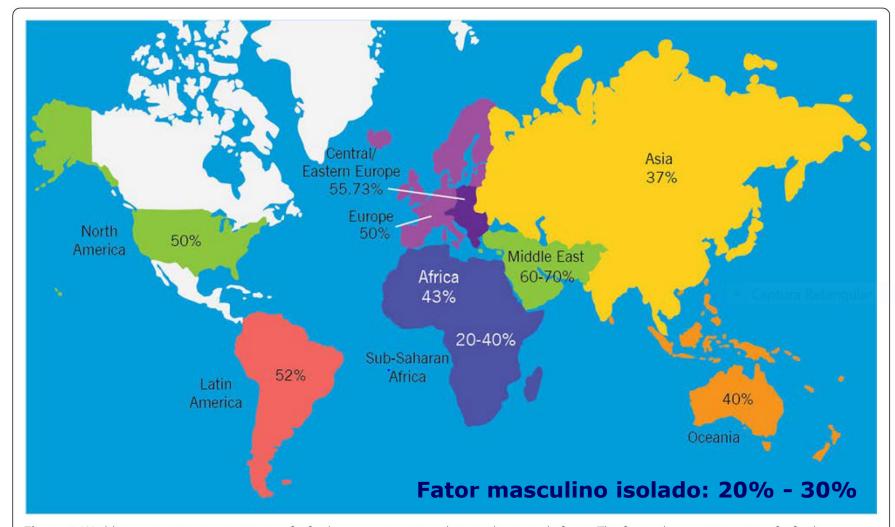
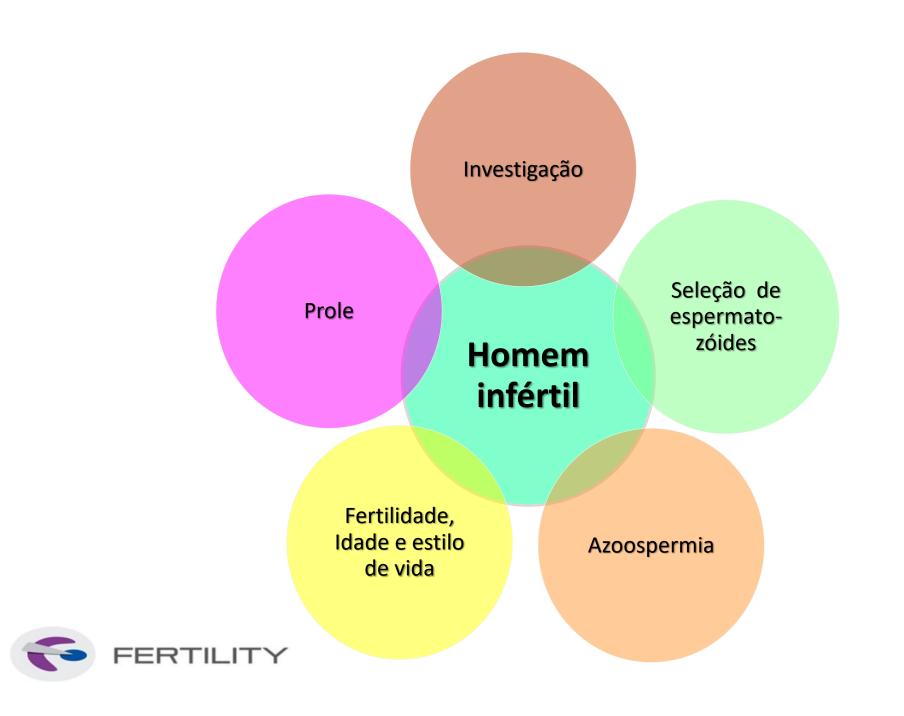
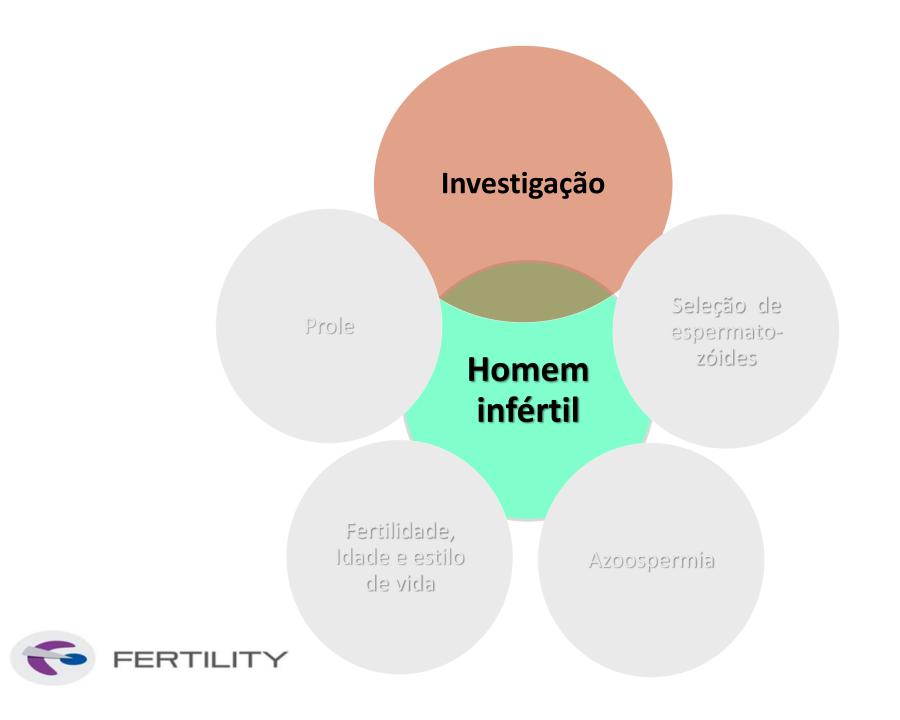


Figure 2 World map containing percentages of infertility cases per region that are due to male factor. This figure demonstrates rates of infertility cases in each region studied (North America, Latin America, Africa, Europe, Central/Eastern Europe, Middle East, Asia, and Oceania) due to male factor involvement.









Análise Seminal

VAN LEEUWENHOEK 1677

SIMS 1866

WEISMAN 1940

AMERICAN FERTILITY ASS 1951

FREUND 1966

ELIASSON 1971

O.M.S. 1980/87/92/99/2010



O.M.S. 1980/87/92/99/2010

Table 1. Cut-off values for semen variables as published in consecutive WHO manuals [6–9] and as proposed in the fifth World Health Organization (WHO) manual [1].

Semen variable	1980	1987	1992	1999	2010 ¹
Volume (mL)	_	≥ 2.0	≥ 2.0	≥ 2.0	1.5
Concentration (10 ⁶ mL ⁻¹)	20-200	\geq 20	\geq 20	\geq 20	15
Total sperm number (10 ⁶ /ejaculate)	_	≥ 40	≥ 40	≥ 40	39
Motility (% motile)	≥ 60	$\geq 50 (a+b)^2$	\geq 50 (a + b)	\geq 50 (a + b)	40 (a + b + c)
Forward progression (for 1980 only)	$\geq 2^3$	≥ 25 (a)	≥ 25 (a)	≥ 25 (a)	32 (a + b)
Morphology (% normal)	80.5 ⁴	≥ 50	$\geq 30^{5}$	$(14)^6$	4
Viability/vitality (% live)	_	≥ 50	≥ 75	≥ 75	58
White blood cells (10 ⁶ mL ⁻¹)	< 4.7	< 1.0	< 1.0	< 1.0	< 1.0



human reproduction update

World Health Organization reference values for human semen characteristics*

Trevor G. Cooper^{1,10}, Elizabeth Noonan², Sigrid von Eckardstein³, Jacques Auger⁴, H.W. Gordon Baker⁵, Hermann M. Behre⁶, Trine B. Haugen⁷, Thinus Kruger⁸, Christina Wang⁹, Michael T. Mbizvo^{3,†}, and Kirsten M. Vogelsong^{3,†}

- 4.500 amostras seminais
- 14 países
- 4 continentes



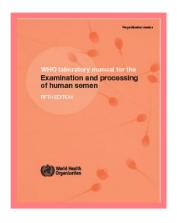


Table II Distribution of values, lower reference limits and their 95% CI for semen parameters from fertile men whose partners had a time-to-pregnancy of I2 months or less (n= 1953)

	N	Centi	Centiles											
		2.5	(95% CI)	5	(95% CI)	10	25	50	75	90	95	97.5		
Semen volume (ml)	1941	1.2	(1.0-1.3)	1.5	(1.4–1.7)	2	2.7	3.7	4.8	6	6.8	7.6		
Sperm concentration (10 ⁶ /ml)	1859	9	(8-11)	15	(12–16)	22	41	73	116	169	213	259		
Total number (10 ⁶ /Ejaculate)	1859	23	(18-29)	39	(33-46)	69	142	255	422	647	802	928		
Total motility (PR + NP, %)*	1781	34	(33-37)	40	(38-42)	45	53	61	69	75	78	81		
Progressive motility (PR, %)*	1780	28	(25-29)	32	(3 I – 3 4)	39	47	55	62	69	72	75		
Normal forms (%)	1851	3	(2.0-3.0)	4	(3.0-4.0)	5.5	9	15	24.5	36	44	48		
Vitality (%)	428	53	(48–56)	58	(55-63)	64	72	79	84	88	91	92		

^{*}PR, progressive motility (WHO, 1999 grades a + b); NP, non-progressive motility (WHO, 1999 grade c).

The values are from unweighted raw data. For a two-sided distribution the 2.5th and 97.5th centiles provide the reference limits; for a one-sided distribution the fifth centile provides the lower reference limit.



Manual O.M.S. 2010 - Limitações

Coleta seminal única

- População de TTP < 12 meses; correto seria população geral??
- Um único país A.L. (Chile); variações populacionais??
- Discordância com outras publicações criteriosas!!





- > Definição: TMSC = volume x conc/ml x % A+B / 100%
- ✓ TMSC: pré-processamento seminal
- ✓ WHO e TMSC em gestação espontânea
- ✓ Seguimento de 3 anos
- \checkmark TMSC > 20 \times 10⁶ normal
- √ 1.177 casais



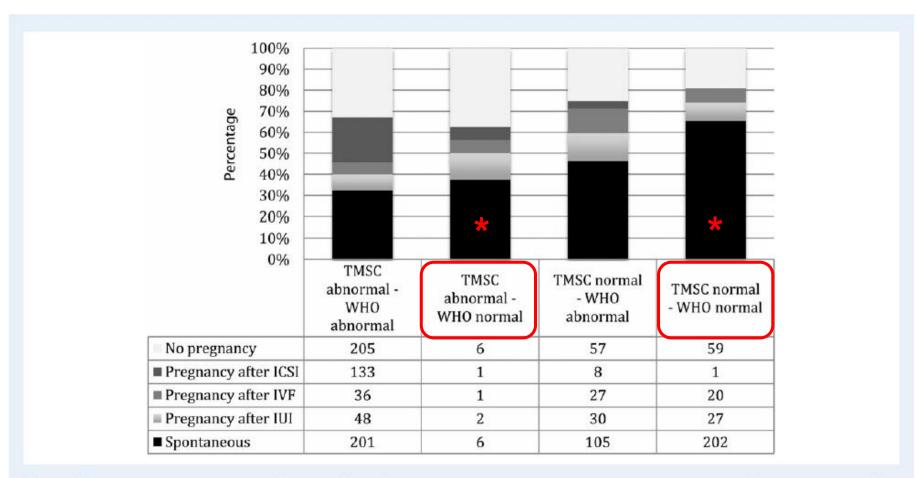


Figure 4 Results showing where the TMSC and WHO classification systems overlap or disagree. The bars on the right and left show the outcome if the two systems are in agreement. The middle bars show the outcome if both systems give contradictory results. TMSC normal – WHO normal = 'real unexplained' infertility.



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ORIGINAL ARTICLE

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Total motile sperm count has a superior predictive value over the WHO 2010 cut-off values for the outcomes of intracytoplasmic sperm injection cycles

^{1,2}*E. Borges Jr, ^{1,2}*A. S. Setti, ^{1,2}D. P. A. F. Braga, ¹R. C. S. Figueira and ^{1,2}A. laconelli Ir

- 518 ciclos de ICSI
- OMS / TMSC
- TMSC normal: > 20 milhões



ANDROLOGY ISSN: 2047-2919 Total motile sperm count has a Edson Borges Jr., MD, PhD, Av. Brigadeiro Luis superior predictive value over the E-mail: edson@fertility.com.hr. WHO 2010 cut-off values for the *These authors contributed equally to this

outcomes of intracytoplasmic sperm injection cycles

^{1,2}*E. Borges Jr, ^{1,2}*A. S. Setti, ^{1,2}D. P. A. F. Braga, ¹R. C. S. Figueira

- OMS: 518 (100%) fator masculino
- Oligozoospermia: 148
- Astenozoospermia: 106
- Teratozoospermia: 361

• TMSC

count, sperm motility, spermatozoa

Accepted: 21-Mar-2016

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- normal: 190 (36,7%): ausência de fator masculino
- anormal: 328 (63,3%): fator masculino +



Table 4 Comparison of ICSI outcomes between normal and abnormal TMSC groups

Variables	Normal TMSC group ($n = 328$)	Abnormal TMSC group ($n = 190$)	<i>p</i> -value
Paternal age (year-old)	37.4 ± 4.8	38.1 ± 6.1	0.187
Maternal age (year-old)	35.4 ± 3.9	33.5 ± 4.0	< 0.001
Number of aspirated follicles	17.8 ± 9.7	20.8 ± 11.2	0.002
Number of obtained oocytes	12.7 ± 7.2	15.1 ± 8.1	0.001
Number of mature oocytes	9.7 ± 5.5	11.2 ± 6.2	0.003
Number of injected oocytes	9.4 ± 4.3	10.2 ± 4.9	0.067
Fertilization rate (%)	84.9 ± 14.4	81.1 ± 15.8	0.016
Number of obtained embryos	8.2 ± 3.8	8.7 ± 4.4	0.204
Number of transferred embryos	2.2 ± 0.6	2.2 ± 0.5	0.469
Implantation rate (%)	25.1 ± 36.0	25.8 ± 35.2	0.832
Pregnancy rate (%)	134/328 (40.9)	94/190 (49.5)	0.060
Miscarriage rate (%)	29/162 (17.9)	23/78 (29.5)	0.041

SD, standard deviation; TMSC: total motile sperm count.



Table 5 Linear and binary regression analysis results for the influences of TMSC and WHO cut-off values on ICSI outcome

Variables	Method	OR or RC	CI or R ²	<i>p</i> -value
Fertilization rate	Concentration	3.994	1.4%	0.015
	Motility	0.097	0.0%	0.957
	Progressive motility	2.299	0.5%	0.163
	Morphology	8.735	0.9%	0.047
	TMSC	3.784	1.5%	0.013
	Normal TMSC	-0.253	0.1%	0.592
Formation of	Concentration	1.64	1.09 - 2.46	0.018
high-quality	Motility	1.34	0.85 - 2.12	0.208
zygotes on D1	Progressive motility	1.22	0.80 - 1.85	0.355
	Morphology	0.89	0.65 - 1.22	0.461
	TMSC	1.13	1.01-1.28	0.049
	Normal TMSC	0.99	0.97–1.02	0.629
Formation of	Concentration	0.93	0.76 - 1.09	0.101
high-quality	Motility	0.91	0.79 - 1.06	0.222
embryos on D2	Progressive motility	1.06	0.92 - 1.22	0.420
	Morphology	0.84	0.60 - 1.18	0.314
	TMSC	1.18	1.03-1.35	0.013
	Normal TMSC	0.97	0.94–1.01	0.098
Formation of	Concentration	0.91	0.79 - 1.06	0.229
high-quality	Motility	0.93	0.79 - 1.09	0.379
embryos on D3	Progressive motility	1.00	0.85 - 1.17	0.969
	Morphology	1.18	0.83 - 1.67	0.354
	TMSC	1.12	1.07 - 1.29	0.037
	Normal TMSC	0.98	0.95-1.02	0.319
Formation of	Concentration	1.11	0.97 - 1.27	0.116
blastocyst	Motility	1.03	0.90 - 1.19	0.660
on D5	Progressive motility	0.91	0.70 - 1.23	0.303
	Morphology	1.13	0.83 - 1.55	0.427
	TMSC	1.16	1.04-1.26	0.011
	Normal TMSC	1.00	0.97–1.04	0.802
Blastocyst	Concentration	0.83	0.66 - 1.05	0.120
expansion	Motility	1.01	0.79 - 1.29	0.948
grade on D5	Progressive motility	1.08	0.85 - 1.38	0.533
	Morphology	0.99	0.57 - 1.71	0.962
	TMSC	1.27	1.01-1.60	0.042
	Normal TMSC	1.03	0.98-1.07	0.287



Guideline

Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios

Ashok Agarwal¹, Ahmad Majzoub², Sandro C. Esteves³, Edmund Ko⁴, Ranjith Ramasamy⁵, Armand Zini⁶

Transl Androl Urol 2016;5(6):935-950



Translational Andrology and Urology, Vol 5, No 6 December 2016

Table 1 Sperm DNA fragmentation (SDF) testing methods

Table 1 Sperm DN	A fragmentation (SDF	r) testing methods		
	Test	Principle	Advantage	Disadvantage
[1]	AO test	Metachromatic shift in fluorescence of AO when bound to single strand (ss)DNA. Uses fluorescent microscopy	Rapid, simple and inexpensive	Inter-laboratory variations and lack of reproducibility
[2]	AB staining	Increased affinity of AB dye to loose chromatin of sperm nucleus. Uses optical microscopy	Rapid, simple and inexpensive	Inter-laboratory variations and lack of reproducibility
[3]	CMA3 staining	CMA3 competitively binds to DNA indirectly visualizing protamine deficient DNA. Uses fluorescent microscopy	Yields reliable results as it is strongly correlated with other assays	Inter-observer variability
[4]	TB staining	Increased affinity of TB to sperm DNA phosphate residues. Uses optical microscopy	Rapid, simple and inexpensive	Inter-observer variability
[5]	TUNEL	Quantifies the enzymatic incorporation of dUTP into DNA breaks. Can be done using both optical microscopy and fluorescent microscopy. Uses optical microscopy, fluorescent microscopy and flow cytometry	Sensitive, reliable with minimal inter- observer variability. Can be performed on few sperm	Requires standardization between laboratories
[6]	SCSA	Measures the susceptibility of sperm DNA to denaturation. The cytometric version of AO test. Uses flow cytometry	Reliable estimate of the percentage of DNA-damaged sperm	Requires the presence of expensive instrumentation (flow cytometer) and highly skilled technicians
[7]	SCD or Halo test	Assess dispersion of DNA fragments after denaturation. Uses optical or fluorescent microscopy	Simple test	Inter-observer variability
[8]	SCGE or comet assay	Electrophoretic assessment of DNA fragments of lysed DNA. Uses fluorescent microscopy	Can be done in very low sperm count. It is sensitive and reproducible	Requires an experienced observer. Inter-observer variability

^[1] Acridine orange (AO) stains normal DNA fluoresces green; whereas denatured DNA fluoresces orange-red. [2] Aniline blue (AB) staining showing sperm with fragmented DNA and normal sperm. [3] Chromomycin A3 (CMA3) staining: protamine deficient spermatozoa appear bright yellow; spermatozoa with normal protamine appear yellowish green. [4] Toulidine blue (TB) staining: normal sperm appear light blue and sperm with DNA fragmentation appear violet. [5] Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay fluorescent activated cell sorting histogram showing percentage of SDF. [6] Sperm chromatin structure assay (SCSA): flow cytometric version of AO staining. [7] Sperm chromatin dispersion (SCD) test: spermatozoa with different patterns of DNA dispersion; large-sized halo; medium-sized halo [2]; very small- sized halo. [8] Comet images showing various levels of DNA damage.

937

- 16 estudos 2.969 casais
- Aumento significativo de abortamento em homens com aumento da fragDNA espermática: RR =2,16 (1,54 3,03)
- \bullet TUNEL: RR = 3,94 (2,45 6,32)



Sperm DNA fragmentation in miscarriage – a promising diagnostic, or a test too far?

Um número de revisões sistemáticas tem avaliado o efeito da *fragDNA espermático* nos resultados de IIU/FIV/ICSI (Osman et al., 2015; Zini et al., 2011, Simon et al., 2016), <u>com resultados não totalmente conclusivos e dependentes da técnica de avaliação</u>.

Perda gestacional:

- Sem evidências (Coughlan et al.,2015)
- Confirmam resultados de 2012 (Carlini et al.,2017; Bareh et al., 2016; Zidi-Jrah et al., 2016).



Antioxidants for male subfertility

Showell MG, Brown J, Yazdani A, Stankiewicz MT, Hart RJ

Oxidative stress may cause sperm cell damage. This damage can be reduced by the body's own natural antioxidant defences.

Antioxidants can be part of our diet and taken as a supplement. It is believed that in many cases of unexplained subfertility, and also in instances where there may be a sperm-related problem, taking an oral antioxidant supplement may increase a couple's chance of conceiving when undergoing fertility treatment. This review identified 34 randomised controlled trials involving 2876 couples. Pooled

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findings from three small trials suggest an increase in live birth rates for the partners of subfertile men taking an antioxidant supplement as part of an assisted reproductive program. However, further well-designed large randomised placebo-controlled trials are needed to

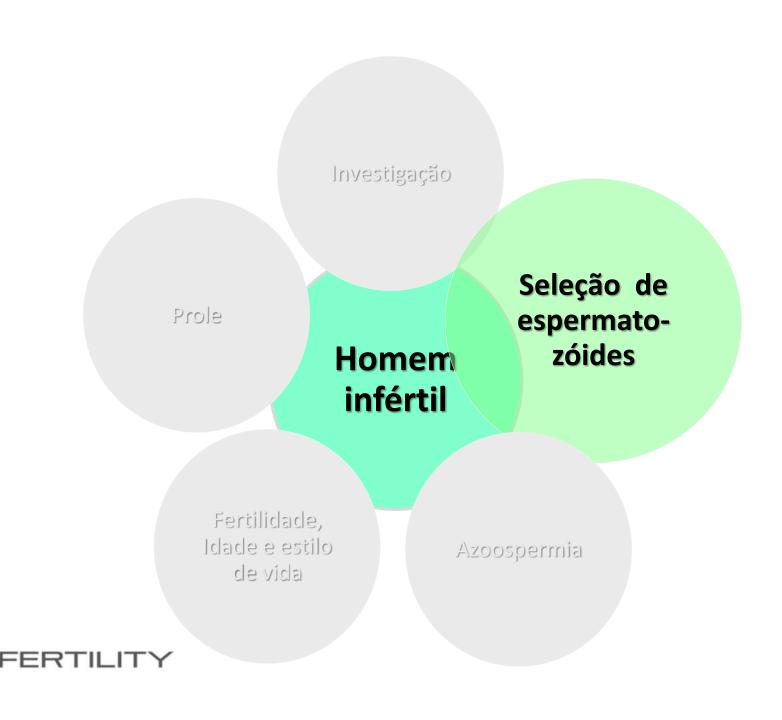
confirm these findings.

34 estudos randomizados - 2.876 casais

Aumento da taxa gestação (OR=4,18)



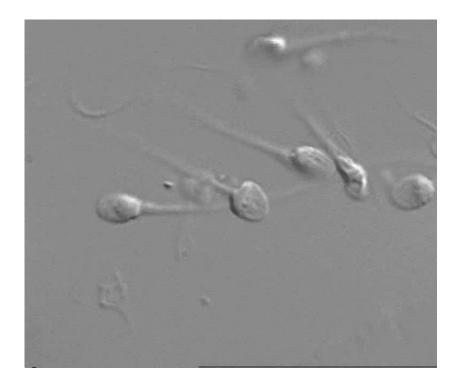
Aumento na taxa de nascidos vivos (OR=4,85)



<u>MSOME</u> Motile Sperm Organellar Morphology Examination

IMSI Intracytoplasmic Morphologically Select Sperm Injection









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Obstetrics & Gynecology

journal homepage: www.elsevier.com/locate/ejogrb

Review

Intracytoplasmic morphologically selected sperm injection results in improved clinical outcomes in couples with previous ICSI failures or male factor infertility: a meta-analysis



Amanda S. Setti ^{a,b,c}, Daniela P.A.F. Braga ^{a,b}, Rita C.S. Figueira ^{b,c}, Assumpto Iaconelli Jr. ^{a,b}, Dr.Edson Borges ^{a,b,*}

2.1 Previous ICSI failures

a) Implantation

	IMS	ı	ICS	ı		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI Ye	ar M-H, Fixed, 95% CI
Bartoov et al.	53	190	17	175	24.0%	3.60 [1.99, 6.50] 20	03
Berkovitz et al.	69	248	23	248	31.2%	3.77 [2.26, 6.29] 20	06
Gonzalez-Ortega et al.	35	78	25	84	25.0%	1.92 [1.01, 3.67] 20	10
Oliveira et al.	24	164	11	128	19.8%	1.82 [0.86, 3.88] 20	11 +
Total (95% CI)		680		635	100.0%	2.88 [2.13, 3.89]	•
Total events	181		76				
Heterogeneity: Chi ² = 4.5	52, df = 3 (P = 0.2	(1); I ² = 34	1%			1 1 10
Test for overall effect: Z	= 6.88 (P	< 0.000	01)				0.01 0.1 1 10 100 Favours ICSI Favours IMSI

b) Pregnancy

	IMS	I	ICS	ı		Odds Ratio		Odds	Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl Ye	ear	M-H, Rand	om, 95% CI
Bartoov et al.	33	50	15	50	15.3%	4.53 [1.95, 10.51] 20	03		
Berkovitz et al.	48	80	20	80	17.8%	4.50 [2.29, 8.84] 20	06		
Gonzalez-Ortega et al.	19	30	15	30	12.8%	1.73 [0.62, 4.84] 20	10	\dashv	
Oliveira et al.	14	63	8	55	13.8%	1.68 [0.65, 4.37] 20	11	-	
Klement et al.	52	127	97	322	21.6%	1.61 [1.05, 2.46] 20	13		-
El Khattabi et al.	22	90	34	130	18.7%	0.91 [0.49, 1.70] 20	13	_	_
Total (95% CI)		440		667	100.0%	2.07 [1.22, 3.50]			•
Total events	188		189						
Heterogeneity: Tau ² = 0.	29; Chi² =	16.40,	df = 5 (P	= 0.006	s); I ² = 709	6	0.01	0.1	10 100
Test for overall effect: Z	= 2.71 (P =	0.007)				0.01	0.1 1 Favours ICSI	l 10 100 Favours IMSI

c) Miscarriage

	IMS	ı	ICSI			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI Yea	r M-H, Fixed, 95% CI
Bartoov et al.	3	33	5	15	28.6%	0.20 [0.04, 0.99] 2003	3 -
Berkovitz et al.	7	48	8	20	44.2%	0.26 [0.08, 0.85] 2006	s
Gonzalez-Ortega et al.	3	19	4	15	17.2%	0.52 [0.10, 2.77] 2010)
Oliveira et al.	2	14	2	8	10.0%	0.50 [0.06, 4.47] 2011	·
Total (95% CI)		114		58	100.0%	0.31 [0.14, 0.67]	•
Total events	15		19				
Heterogeneity: Chi ² = 0.9	2, df = 3 (P = 0.8	2); I ² = 0%	6			0.01 0.1 1 10 100
Test for overall effect: Z	= 2.96 (P	= 0.003)				0.01 0.1 1 10 100 Favours IMSI Favours ICSI



2.2 Male factor

a) Implantation rate

	IMS	ı	ICS	1		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI Y	ear M-H, Random, 95% CI
Antinori et al.	97	560	59	521	19.9%	1.64 [1.16, 2.32] 2	008
Oliveira et al.	11	93	13	116	9.6%	1.06 [0.45, 2.50] 2	011 —
Setti et al.	158	664	156	613	22.0%	0.91 [0.71, 1.18] 2	011
Knez et al.	6	35	3	44	4.4%	2.83 [0.65, 12.24] 2	011
Balaban et al.	32	108	16	105	12.6%	2.34 [1.19, 4.59] 2	011
Wilding et al.	86	355	48	324	18.8%	1.84 [1.24, 2.72] 2	011
Knez et al.	27	93	19	115	12.7%	2.07 [1.06, 4.02] 2	012
Total (95% CI)		1908		1838	100.0%	1.56 [1.11, 2.18]	◆
Total events	417		314				
Heterogeneity: Tau ² = 0	0.12; Chi ²	= 17.9	8, df = 6 (P = 0.0	06); 2 = 67	7%	0.01 0.1 1 10 100
Test for overall effect: 2	Z = 2.58 (P = 0.0	10)				Favours ICSI Favours IMSI

b) Pregnancy rate

	IMS	ı	ICS			Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Antinori et al.	89	227	58	219	14.0%	1.79 [1.20, 2.67]	2008	-
Wilding et al.	80	122	44	110	12.0%	2.86 [1.68, 4.87]	2011	
Knez et al.	5	20	3	37	3.5%	3.78 [0.80, 17.89]	2011	
Setti et al.	93	250	92	250	14.5%	1.02 [0.71, 1.46]	2011	+
Oliveira et al.	12	37	11	45	6.9%	1.48 [0.56, 3.90]	2011	+-
Knez et al.	25	52	17	70	8.8%	2.89 [1.34, 6.24]	2012	
De Vos et al.	43	125	51	139	12.4%	0.90 [0.55, 1.50]	2013	+
Klement et al.	126	269	473	1033	15.8%	1.04 [0.80, 1.37]	2013	*
El Khattabi et al.	61	132	33	126	12.1%	2.42 [1.43, 4.09]	2013	
Total (95% CI)		1234		2029	100.0%	1.61 [1.17, 2.23]		
Total events	534		782					ı
Heterogeneity: Tau ² = 6	0.15; Chi ²	= 27.87	7, df = 8 (P = 0.0	005); $I^2 = 1$	71%		0.000 0.4 4 40 500
Test for overall effect: 2	Z = 2.90 (i	P = 0.00	04)					0.002 0.1 1 10 500 Favours ICSI Favours IMSI



c) Miscarriage rate

	IMS	I	ICSI			Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M-H, Fixed, 95% CI
Antinori et al.	15	89	14	58	31.2%	0.64 [0.28, 1.44]	2008	
Wilding et al.	1	80	0	44	1.4%	1.68 [0.07, 42.09]	2011	
Knez et al.	1	5	2	3	4.4%	0.13 [0.00, 3.22]	2011	
Setti et al.	29	158	28	156	51.0%	1.03 [0.58, 1.82]	2011	
Oliveira et al.	2	12	4	11	7.7%	0.35 [0.05, 2.47]	2011	
Knez et al.	5	25	2	17	4.2%	1.88 [0.32, 11.02]	2012	
Total (95% CI)		369		289	100.0%	0.86 [0.56, 1.32]		♦
Total events	53		50					
Heterogeneity: Chi ² = 3	3.96, df = 5	5(P = 0)).55); l ² =	0%				0.04 0.4 1 10 100
Test for overall effect: 2	Z = 0.70 (I	P = 0.48	3)					0.01 0.1 1 10 100 Favours IMSI Favours ICSI Favours





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ORIGINAL ARTICLE

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Keywords:

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Sperm morphological normality under high magnification is correlated to male infertility and predicts embryo development

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MSOME I+II



Grade I:

- Normal form
- No vacuoles



Grade II:

- Normal form
- ≤ 2 small vacuoles



Grade III:

- · Normal form
- > 2 small vacuoles or at least one large vacuole



Grade IV:

- Abnormal head shapes or other abnormalities
- Large vacuole

Linear regression analysis of the association between sperm parameters and MSOME

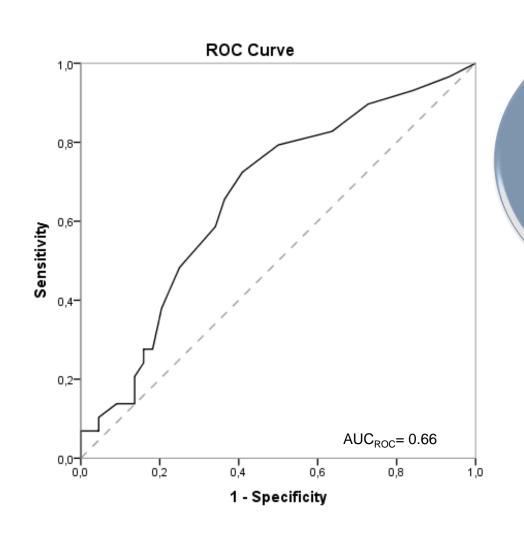
SEMEN PARAMETER	MSOI	ME I+II	MSO	ME III	MSO	ME IV
	β	р	β	р	β	р
Volume	-0.031	0.508	-0.029	0.539	0.025	0.592
Concentration	0.281	<0.001	0.022	0.630	-0.252	<0.001
Total sperm count	0.224	<0.001	-0.013	0.782	-0.193	<0.001
Total motility	0.178	<0.001	-0.012	0.791	-0.175	<0.001
Progressive motility	0.192	<0.001	0.008	0.856	-0.188	<0.001
Morphology	0.341	<0.001	0.136	0.003	-0.350	<0.001
TMSC	0.210	<0.001	-0.017	0.716	-0.180	<0.001

Logistic regression analyses of MSOME grades correlation with ICSI outcomes

	MSOME	I+II	MSOME	E III	MSOM	E IV
	β	р	β	р	β	р
Fertilization rate	0.197	0.044	0.150	0.134	-0.192	0.052
High-quality embryos rate	0.306	0.013	0.379	0.002	-0.378	0.002
Blastocyst rate	0.248	0.047	0.008	0.954	-0.195	0.130
Implantation rate	-0.098	0.405	-0.137	0.252	0.138	0.244
	95% CI	p	95% CI	p	95% CI	p
Cancelation rate	0.95; 1.07	0.817	0.94; 1.12	0.557	0.95; 1.03	0.716
Pregnancy rate	0.90; 1.05	0.493	0.84;1.09	0.528	0.96; 1.09	0.396



ROC Curve of MSOME grades I+II and blastocyst formation rate (below or equal and above 50%)



AUC: 0,66
MSOME I+II
cut-off: 5,5%
sensitivity of 0.72
specificity of 0.41



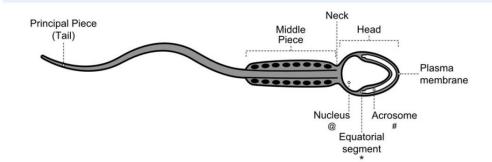
Descriptive statistic of ICSI outcomes per MSOME I+II normality classification

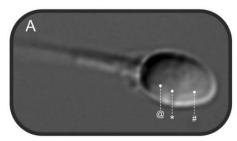
	Normal (MSOME I+II ≥5.5%)	Abnormal (MSOME I+II <5.5%)	р
Female age (years)	36.18 ± 4.29	36.66 ± 3.58	0.527
Total dose of FSH administered (IU)	2346.38 ± 680.43	2422.61 ± 704.55	0.560
Number of follicles	14.28 ± 12.49	14.06 ± 10.97	0.925
Number of retrieved oocytes	9.92 ± 9.95	10.81 ± 7.74	0.608
Fertilization rate	86.94 ± 19.04	84.59 ± 14.79	0.708
High-quality embryos rate	41.78 ± 16.04	38.40 ± 21.73	0.463
Blastocyst rate	50.14 ± 5.05	28.53 ± 5.69	0.005
Implantation rate (%)	20.10 ± 35.59	24.24 ± 37.05	0.618
Pregnancy rate (%)	28.26	36.36	0.472

ORIGINAL ARTICLE Andrology

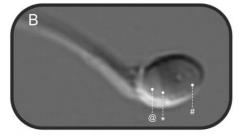
The significance of human spermatozoa vacuoles can be elucidated by a novel procedure of array comparative genomic hybridization

Arie Berkovitz^{1,*}, Yaron Dekel^{2,3,4,5}, Revital Goldstein^{3,4}, Shhadeh Bsoul³, Yossy Machluf⁶, and Dani Bercovich^{3,4}

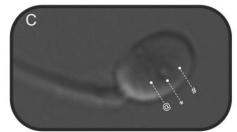




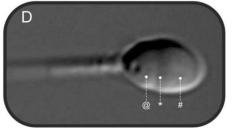
No vacuoles No Suspicion of nuclear damage Total CNVs: 234



A small acrosomal vacuole No Suspicion of nuclear damage Total CNVs: 245

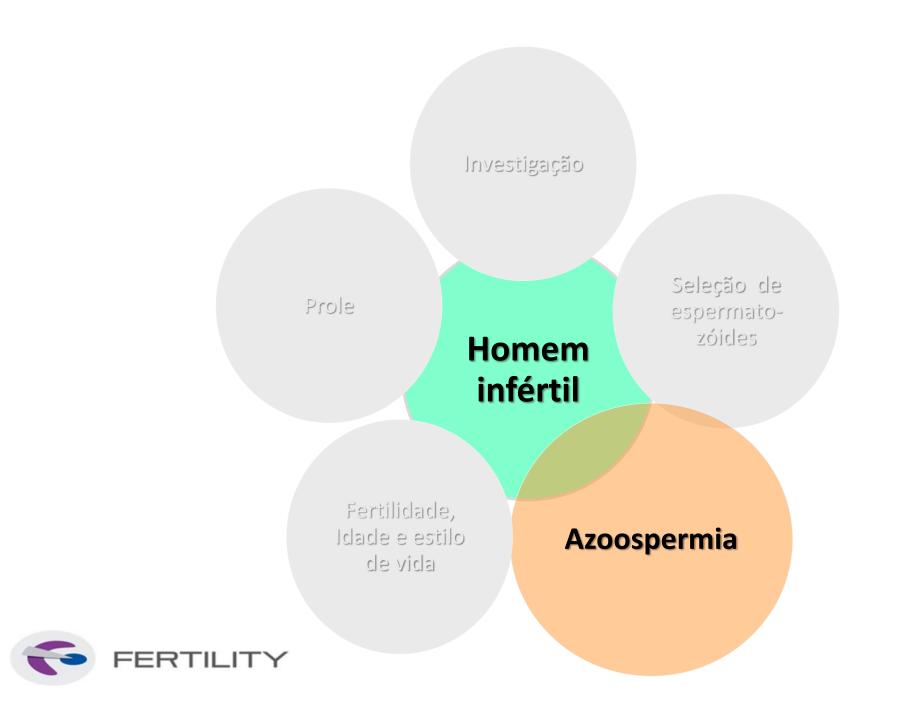


Two small equatorial vacuoles
Suspected of nuclear damage: Vacuole location
Total CNVs: 285



Small and deep nuclear vacuole
Suspected of nuclear damage: Vacuole location & depth
Total CNVs: 744





PERCUTANEOUS
EPIDYDIMAL
SPERM
ASPIRATION

ESPERMATOZÓIDES
ESPIDIDIMÁRIOS

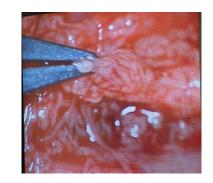
TESTICULAR
SPERM
ASPIRATION
ESPERMA
ASPIRATION
EXTRACTION

ESPERMATOZÓIDES

TESTICULARES



Micro
TESTICULAR
SPERM
EXTRACTION





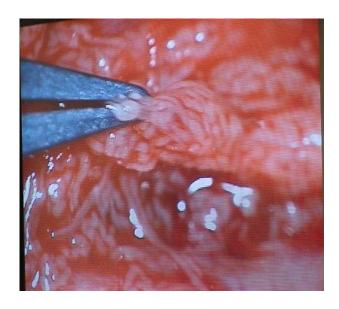


TESE MICROCIRURGICA MicroTESE

PETER SCHLEGEL. HUMAN REPROD, 14: 131-135, 1999

SHERMAN J. SILBER. *HUMAN REPROD*, 15: 2278-2284, 2000









Schlegel 1999 10 22 Amer 2000 30 100 Okada 2002 4 24 Tsujimura 2002 13 37 Colpi 2009 29 69 Ghalayini 2011 26 68 Friedler 1997 4 37 Okada 2002 4 203 Okada 2002 2035 Okada 2002 204 56 Okada 2002 33 74 Okada 2002 33 74 Okada 2002 33 74 Okada 2002 33 74 Okada 2002 34 24 56 Okada 2002 34 24 56 Okada 2002 34 24 56 Okada 2002 34 56 Okada 2002 34 24 56 Okada 2002 34 56 Okada 2002 35 Okada 2002 34 56 Okada 2002 36 Friedler 1997 16 37 Okada 2002 34 56 Okada 2002 35 Okada 2002 36 Okada 2002 36 Okada 2002 37 Okada 2002 37 Okada 2002 38 Okada 2002 38 Okada 2002 38 Okada 2002 39 Okada 2002 30 Okada 2002 39 Okada 2002 30 Oka	0.11 [0.03; 0.25] 0.14 [0.05; 0.30] 0.41 [0.21; 0.64]						•		Fotal		Study
Schlegel 1999 17 27	0.07 [0.00; 0.34] 0.26 [0.19; 0.35] 0.41 [0.31; 0.52] 0.42 [0.37; 0.47] 0.28 [0.19; 0.39]	0.41 0.07 0.26 0.41 0.42	35 22 14 - 125 87 385	9 1 33 36 161	Friedler 1997 Ezeh 1998 Rosenlund 1998 Tournaye 1999 Bettella 2005 Hauser 2006 Nowroozi 2012 RE model	[0.21; 0.40] [0.05; 0.37] [0.20; 0.53] [0.23; 0.44] [0.30; 0.55] [0.27; 0.51]	0.30 0.17 0.35 0.33 0.42 0.38	***	100 24 37 83 69 68	30 4 13 27 29 26	cTESE Schlegel 1999 Amer 2000 Okada 2002 Tsujimura 2002 Ramasamy 2005 Colpi 2009 Ghalayini 2011 RE model 1² = 19.2% tau² = 0.0194, p =
Colpi 2009 36 69 0.52 [0.40; 0.64] Hauser 2006 54 87 Ghalayini 2011 37 65 0.57 [0.44; 0.69] Nowroozi 2012 196 385 RE model 851 0.52 [0.47; 0.58] RE model 705 P ² = 47.9%, tau ² = 0.0394, p = 0.0739	0.43 [0.27; 0.61] 0.63 [0.45; 0.79] 0.59 [0.36; 0.79] 0.64 [0.35; 0.87] 0.59 [0.50; 0.68] 0.62 [0.51; 0.72] 0.51 [0.46; 0.56] 0.56 [0.50; 0.61]	0.63 0.59 0.64 0.59 0.62 0.51	35 22 14 125 87 385	22 13 9 74 54 196	Friedler 1997 Ezeh 1998 Rosenlund 1998 Tournaye 1999 Bettella 2005 Hauser 2006 Nowroozi 2012 RE model	[0.37; 0.57] [0.33; 0.57] [0.30; 0.57] [0.53; 0.63] [0.40; 0.64] [0.44; 0.69]	0.47 0.45 0.43 0.58 0.52 0.57	——————————————————————————————————————	100 74 56 460 69 65	47 33 24 267 36 37	Ghalayini 2011 RE model

(A) Meta-analysis of the association of cTESE vs. micro-TESE with SR outcome for men with nonobstructive azoospermia. (B) Meta-analysis of the association of TESA vs. cTESE with SR outcome for men with nonobstructive azoospermia.

Bernie. Comparison of micro-TESE, cTESE, and TESA. Fertil Steril 2015.



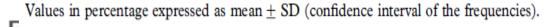


ORIGINAL ARTICLE

Assisted reproductive technology outcomes in azoospermic men: 10 years of experience with surgical sperm retrieval

Table II. ICSI outcomes from patients with obstructive azoospermia when the injected spem were retrieved from the testicle (TESA) or epididymis (PESA).

		Study group				
Variable	OA-TESA(n=103)	OA-PESA (n=171)	p value			
Normal fertilization rate (%)	57.9 ± 9.5 (48.5–67.5)	$65.2 \pm 4.1 \ (54.7 - 69.3)$	0.0017			
Abnormal fertilization rate (%)	13.2 ± 6.3 (6.5–19.5)	$12.7 \pm 5.3 \ (7.9 - 18.0)$	0.9437			
Fertilization failure rate (%)	$28.9 \pm 8.9 \ (20.2 – 37.8)$	$22.1 \pm 6.0 \ (15.8 - 28.1)$	0.1081			
Non-cleaved rate (%)	$9.87 \pm 5.9 \ (4.2 - 15.8)$	$7.46 \pm 3.9 \ (3.5-11.4)$	0.4406			
Pregnancy rate (%)	$31.9 \pm 9.0 (23.0 - 41.0)$	$32.5 \pm 7.5 (25.9 - 40.0)$	0.8803			
Abortion rate (%)	$38.8 \pm 9.6 \ (29.6 - 48.4)$	$18.0 \pm 5.8 \ (12.2 - 23.8)$	0.0387			
Implantation rate (%)	9.4 ± 5.6 (3.8–15.0)	10.5 ± 4.0 (5.5–14.5)	0.6054			





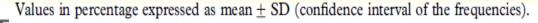


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Pregnancy rate (%)	$31.9 \pm 9.0 \ (23.0 - 41.0)$	$32.5 \pm 7.5 (25.9 - 40.0)$	0.8803			
Abortion rate (%)	38.8 ± 9.6 (29.6–48.4)	18.0 ± 5.8 (12.2–23.8)	0.0387			
Implantation rate (%)	9.4 ± 5.6 (3.8–15.0)	$10.5 \pm 4.0 \ (5.5 - 14.5)$	0.6054			







ORIGINAL ARTICLE

Assisted reproductive technology outcomes in azoospermic men: 10 years of experience with surgical sperm retrieval

Table IV. ICSI outcomes when the injected sperm were retrieved from the testicle (TESA) of patients with obstructive (OA) or non-obstructive (NOA) azoospermia.

	Study group				
Variable	OA-TESA (n=103)	NOA-TESA (n=102)	p value		
Normal fertilization rate (%)	57.9 ± 9.5 (48.5–67.5)	50.4 ± 9.3 (40.3–59.7)	0.0050		
Abnormal fertilization rate (%)	$13.2 \pm 6.3 \ (6.5 - 19.5)$	$13.98 \pm 6.8 (7.3-20.7)$	0.4421		
Fertilization failure rate (%)	$28.9 \pm 8.9 \ (20.2-37.8)$	$35.65 \pm 11.8 (27.6 - 47.4)$	0.0023		
Non cleaved rate (%)	$9.87 \pm 5.9 \ (4.2 - 15.8)$	$16.1 \pm 17 \ (8.9-23.1)$	0.0034		
Pregnancy rate (%)	$31.9 \pm 9.0 \ (23.0 - 41.0)$	$29.7 \pm 9.2 \ (21.1 - 38.9)$	0.4166		
Abortion rate (%)	$38.8 \pm 9.6 \ (29.6 - 48.4)$	$37.0 \pm 9.4 \ (27.6 - 46.4)$	0.9992		
Implantation rate (%)	$9.4 \pm 5.6 \ (3.8 - 15.0)$	$9.65 \pm 6.1 \ (4.2 - 15.8)$	0.8519		

Values in percentage expressed as mean \pm SD (confidence interval of the frequencies).





ORIGINAL ARTICLE

Assisted reproductive technology outcomes in azoospermic men: 10 years of experience with surgical sperm retrieval

Table IV. ICSI outcomes when the injected sperm were retrieved from the testicle (TESA) of patients with obstructive (OA) or non-obstructive (NOA) azoospermia.

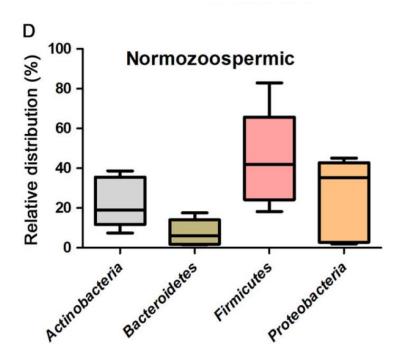
		Study group				
Variable	OA-TESA (n=103)	NOA-TESA (n=102)	p value			
Normal fertilization rate (%)	57.9 ± 9.5 (48.5–67.5)	50.4 ± 9.3 (40.3–59.7)	0.0050			
Abnormal fertilization rate (%)	$13.2 \pm 6.3 \ (6.5 - 19.5)$	$13.98 \pm 6.8 \ (7.3-20.7)$	0.4421			
Fertilization failure rate (%)	$28.9 \pm 8.9 \ (20.2-37.8)$	$35.65 \pm 11.8 \ (27.6 - 47.4)$	0.0023			
Non cleaved rate (%)	9.87 + 5.9 (4.2 - 15.8)	16.1 + 17 (8.9 - 23.1)	0.0034			
Pregnancy rate (%)	$31.9 \pm 9.0 \ (23.0 - 41.0)$	$29.7 \pm 9.2 \ (21.1 - 38.9)$	0.4166			
Abortion rate (%)	$38.8 \pm 9.6 \ (29.6 - 48.4)$	$37.0 \pm 9.4 \ (27.6 - 46.4)$	0.9992			
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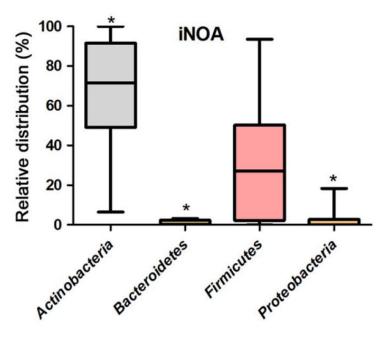
Values in percentage expressed as mean \pm SD (confidence interval of the frequencies).



Testicular microbiome in azoospermic men—first evidence of the impact of an altered microenvironment

Massimo Alfano^{1,*}, Roberto Ferrarese², Irene Locatelli¹, Eugenio Ventimiglia^{1,2}, Silvia Ippolito¹, Pierangela Gallina³, Daniela Cesana³, Filippo Canducci⁴, Luca Pagliardini⁵, Paola Viganò⁵, Massimo Clementi², Manuela Nebuloni⁶, Francesco Montorsi^{1,2}, and Andrea Salonia^{1,2}

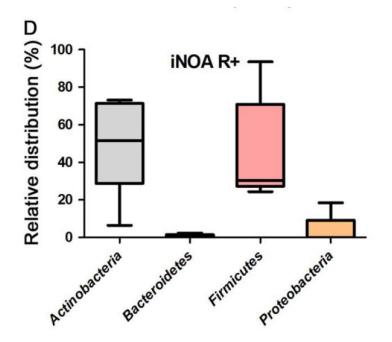


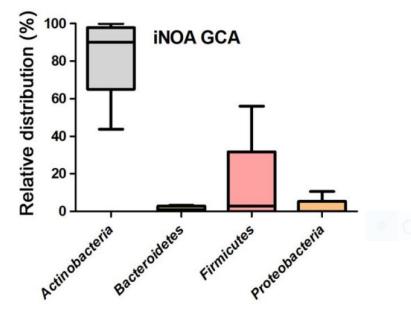




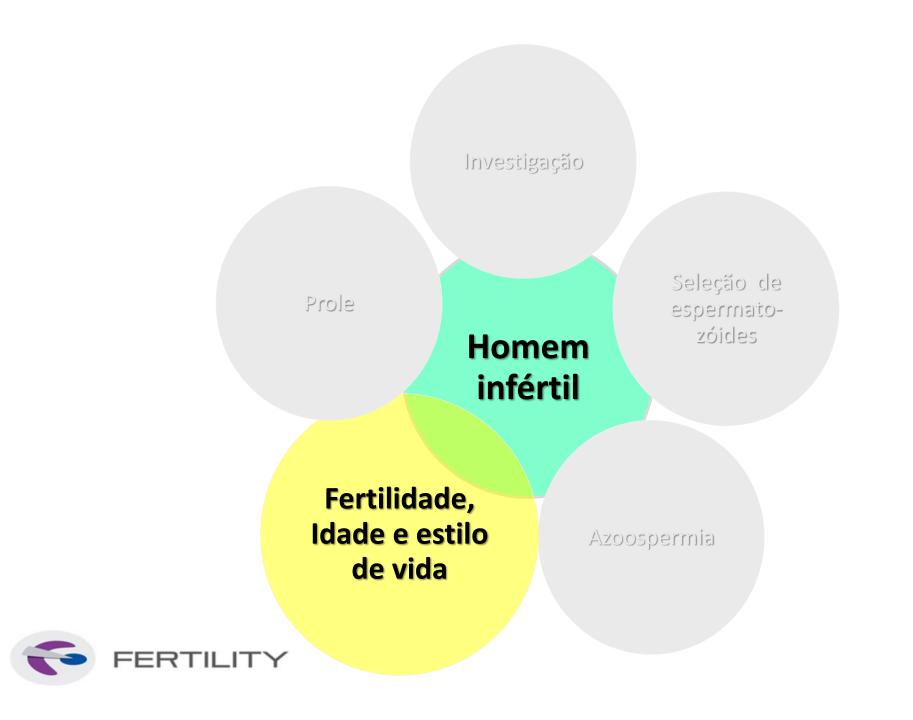
Testicular microbiome in azoospermic men—first evidence of the impact of an altered microenvironment

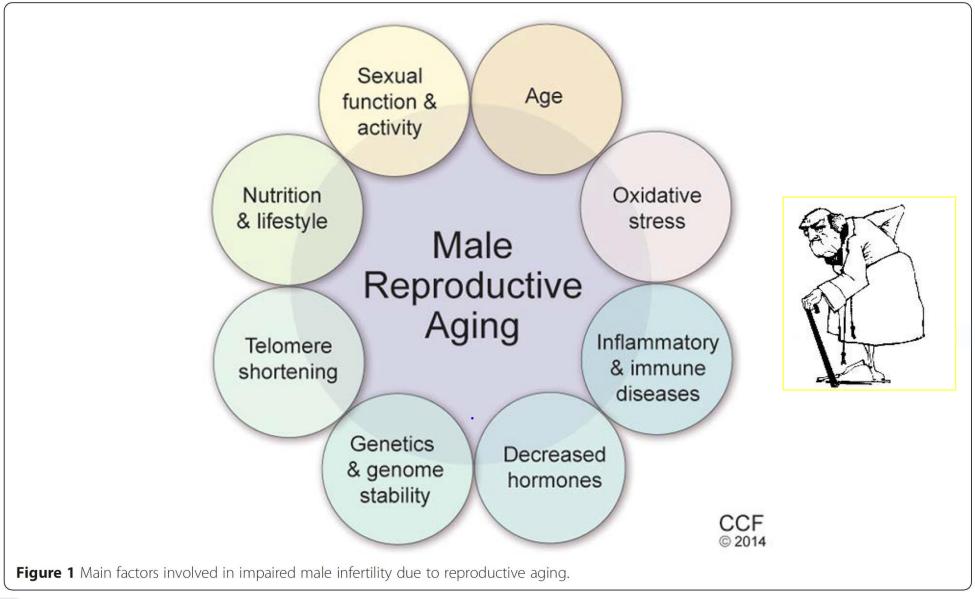
Massimo Alfano^{1,*}, Roberto Ferrarese², Irene Locatelli¹, Eugenio Ventimiglia^{1,2}, Silvia Ippolito¹, Pierangela Gallina³, Daniela Cesana³, Filippo Canducci⁴, Luca Pagliardini⁵, Paola Viganò⁵, Massimo Clementi², Manuela Nebuloni⁶, Francesco Montorsi^{1,2}, and Andrea Salonia^{1,2}















Paternal age and reproduction

Gideon A. Sartorius^{1,2} and Eberhard Nieschlag^{1,3}

¹Centre of Reproductive Medicine and Andrology of the University, Domagkstrasse 11, D-48149 Muenster, Germany ²Present address:

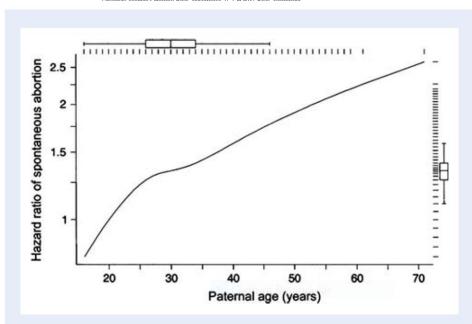


Figure 3 Hazard ratios of spontaneous miscarriages between 6 and 20 weeks according to paternal age adjusted for different confounders including maternal age (using prospective data from 5121 Californian women, men aged 20 years as referent).

Boxplots along the top and right side indicate data distribution according to each axis (with permission from Slama et al., 2005).

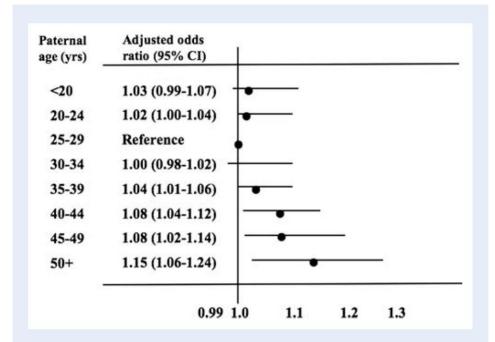


Figure 4 Relative risk of birth defects depending on paternal age. Retrospective analysis of 5 213 248 subjects in the USA. Increased risk for heart defects, circulatory/respiratory defects, diaphragmatic hernia, tracheo-oesophageal fistulas, musculo-sceletal anomalies (data extracted from Yang et al., 2007).



Is advanced paternal age a health risk for the offspring?

Anne-Marie Nybo Andersen, M.D., Ph.D. and Stine Kjaer Urhoj, M.Sc. Department of Public Health, University of Copenhagen, Copenhagen, Denmark

Adverse health outcomes in offspring probably affected by advanced paternal age, their occurrence, and assessed evidence for the paternal age effect (strong/medium/weak).

Adverse health condition	Population-based prevalence/lifetime risk	Evidence for a paternal age effect
Fetal death ^a		
Miscarriage (early fetal death)	1,500/10,000 clinically recognized pregnancies	Weak
Stillbirth (late fetal death)	0.4/10,000 births	Medium
Congenital syndromes and anomalies ^b		
Achondroplasia	<1/10,000 births	Strong
Thanatophoric dysplasia	<1/10,000 births	Strong
Osteogenesis imperfecta	<1/10,000 births	Strong
Apert syndrome	<1/10,000 births	Strong
Pfeiffer's syndrome	<1/10,000 births	Strong
Crouzon's syndrome	<1/10,000 births	Strong
Marfan syndrome	2/10,000 births	Strong
Neurofibromatosis (NF-1)	3/10,000 births	Strong
Syndactyly	5/10,000 births	Medium
Cleft palate	15/10,000 births	Strong
Patent ductus arteriosus	5/10,000 births (term babies)	Medium-weak
Down syndrome	5/10.000 births ^c	Weak
Club foot	15/10.000 births	Weak
Other perinatal conditions ^a		
Preterm birth	700/10,000 births	Medium
Preeclampsia	300/10,000 births	Weak
Childhood cancers ^a		
Retinoblastoma	0.6/10,000 individuals	Medium
Acute lymphatic leukemia	12/10.000 individuals	Strong
Neurodevelopmental outcomes ^d		ā.
Autism spectrum disorders	93/10,000 individuals	Strong
Schizophrenia/psychosis	367/10,000 individuals	Strong
Attention deficit-hyperactivity disorder	192/10,000 individuals	Weak
Bipolar disorder	184/10,000 individuals	Weak

^a If the occurrences vary substantially between countries, we have given population-based occurrence measures from Denmark, 2000–2010.

d Lifetime prevalence according to Pedersen et al. (68).



Fertility and Sterility® Vol. 107, No. 2, February 2017

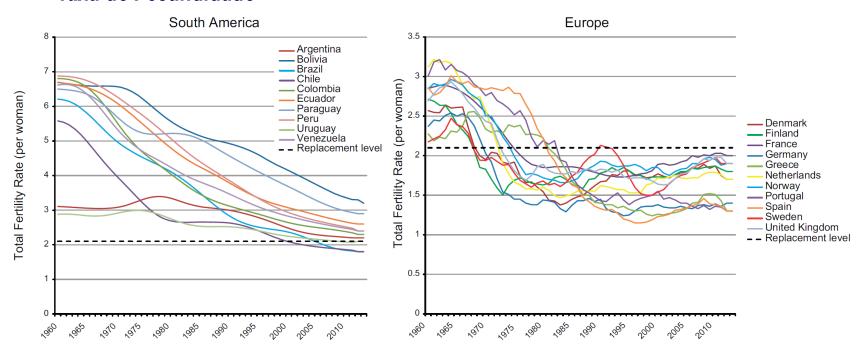
^b Prevalence according to www.orpha.net.

^c Prevalence among births in a population with prenatal screening and termination of pregnancy on demand. The prevalence is approximately 130/10,000 in an unscreened population, depending on parental age distribution.

MALE REPRODUCTIVE DISORDERS AND FERTILITY TRENDS: INFLUENCES OF ENVIRONMENT AND GENETIC SUSCEPTIBILITY

Niels E. Skakkebaek, Ewa Rajpert-De Meyts, Germaine M. Buck Louis, Jorma Toppari, Anna-Maria Andersson, Michael L. Eisenberg, Tina Kold Jensen, Niels Jørgensen, Shanna H. Swan, Katherine J. Sapra, Søren Ziebe, Lærke Priskorn, and Anders Juul

Taxa de Fecundidade





MALE REPRODUCTIVE DISORDERS AND FERTILITY TRENDS: INFLUENCES OF ENVIRONMENT AND GENETIC SUSCEPTIBILITY

Niels E. Skakkebaek, Ewa Rajpert-De Meyts, Germaine M. Buck Louis, Jorma Toppari, Anna-Maria Andersson, Michael L. Eisenberg, Tina Kold Jensen, Niels Jørgensen, Shanna H. Swam, Katherine J. Sapra, Søren Ziebe, Lerke Priskorn, and Anders Juul

Incidência de Criptorquidia

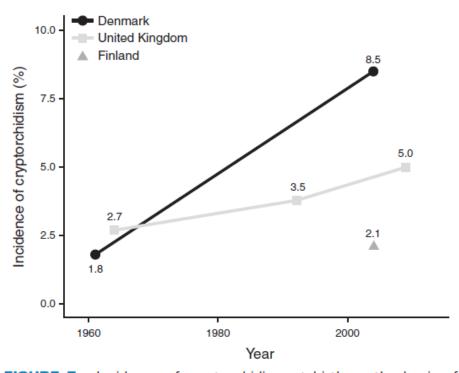


FIGURE 7. Incidence of cryptorchidism at birth on the basis of prospective clinical studies from the 1950s to the 2000s in Denmark, Finland, and United Kingdom. The data points are marked on the year of the publication of the study which represents the preceding incidence rate (3, 47, 61, 184, 377).



MALE REPRODUCTIVE DISORDERS AND FERTILITY TRENDS: INFLUENCES OF ENVIRONMENT AND GENETIC SUSCEPTIBILITY

Niels E. Skakkebaek, Ewa Rajpert-De Meyts, Germaine M. Buck Louis, Jorma Toppari, Anna-Maria Andersson, Michael L. Eisenberg, Tina Kold Jensen, Niels Jergensen, Shanna H. Swan, Katherine J. Sapra, Seron Ziebe, Lesrke Priskorn, and Anders Juul

Incidência de Câncer de Testículo

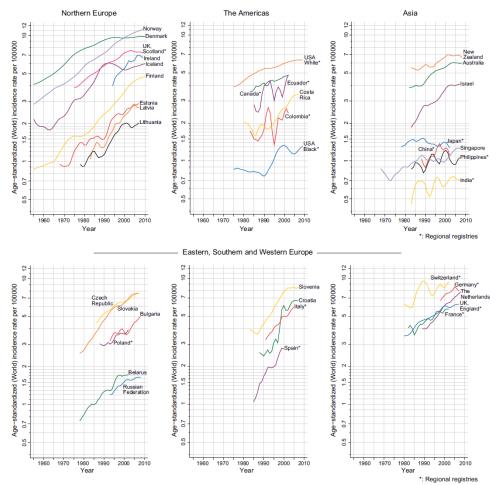




FIGURE 4. Trends in testicular cancer; age-standardized (world) incidence (regional or national), all ages. [Modified from Znaor et al. (481). Courtesy of Dr. Arinana Znaor and statistician Mathieu Laversanne, M.Sc., WHO, International Agency for Research in Cancer (IARC), Lyon, France.]

MALE REPRODUCTIVE DISORDERS AND FERTILITY TRENDS: INFLUENCES OF ENVIRONMENT AND

Niels E. Skakkebaek, Ewa Rajpert-De Meyts, Germaine M. Buck Louis, Jorma Toppari, Anna-Maria Andersson, Michael L. Eisenberg, Tina Kold Jensen, Niels Jørgensen, Shanna H. Swan, Katherine J. Sapra, Søren Ziebe, Lærke Priskorn, and Anders Juul

GENETIC SUSCEPTIBILITY

Idade da Puberdade

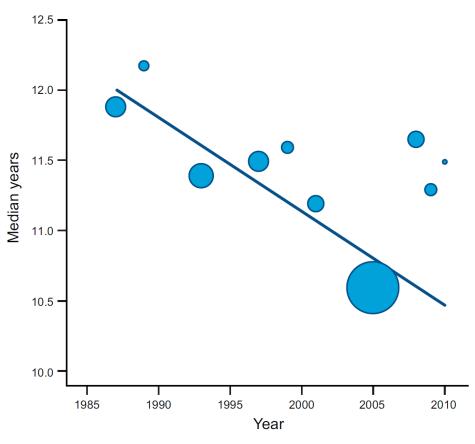


FIGURE 8. Recent changes in male pubertal timing. Testicular volume was >3 ml. [From Mouritsen et al. (293).]





Decline in sperm count in European men during the past 50 years

Human and Experimental Toxicology

1-9

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DOI: 10.1177/0960327117703690
journals.sagepub.com/home/het



P Sengupta^{1,2}, E Borges Jr³, S Dutta⁴ and E Krajewska-Kulak²

Purpose: To investigate whether the sperm concentration of European men is deteriorating over the past 50 years of time.

Materials and Methods: We analysed the data published in English language articles in the past 50 years in altering sperm concentration in European men.



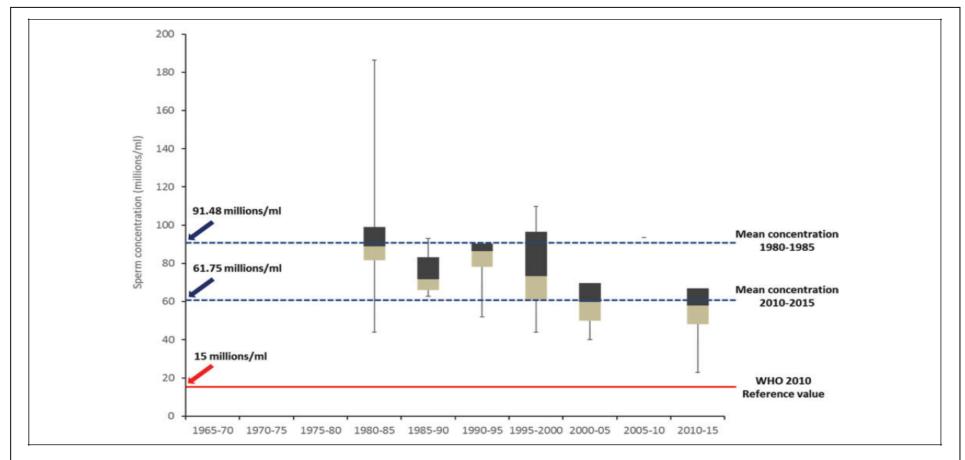


Figure 2. Box and whisker plot of sperm concentration data of European men of the past 50 years.

Declínio tempo-dependente na concentração esopermática observada de 1965 to 2015 (r= -0.307, p<0.02; diminuição de 32.5%)





Vol. 41 (4): 757-763, July - August, 2015 doi:10.1690/S1677-5538.IBJU.2014.0186

Decline in semen quality among infertile men in Brazil during the past 10 years

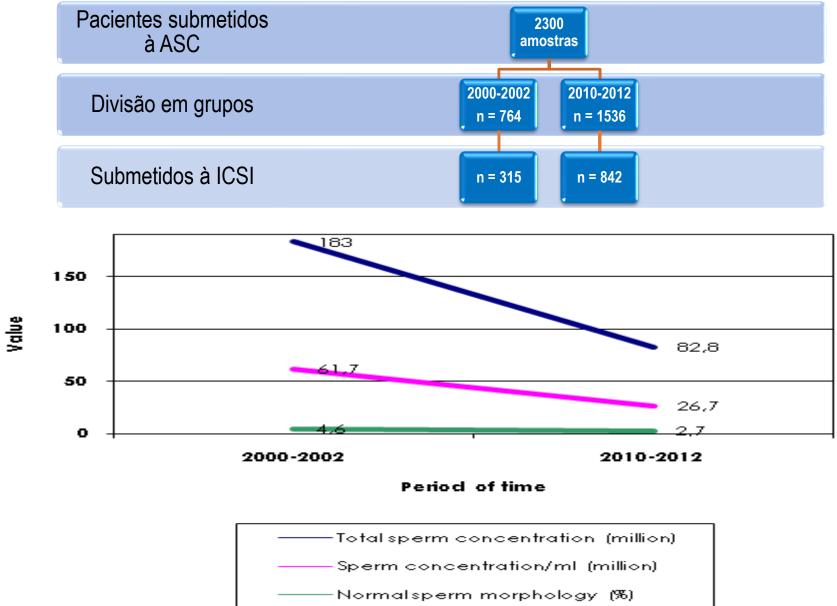
Edson Borges Jr. 12, Amanda Souza Setti 12, Daniela Paes de Almeida Ferreira Braga 12, Rita de Cassia Savio Figueira 1, Assumpto Iaconelli Jr. 12

Table 1 - General characteristics of analyzed semen samples (n=2300).

Variable	Mean	SD	Min	Max
Male age (y-old)	35.7	7.8	15.0	71.0
Days of abstinence	4.2	2.8	0.0	30.0
Semen sample volume (ml)	3.3	1.7	0.1	11.3
Sperm concentration/ml (million)	38.3	46.7	0.0	540.0
Total sperm concentration (million)	116.0	143.0	0.0	984.0
Progressive sperm motility (%)	36.9	18.9	0.0	84.0
Sperm morphology	3.4	2.9	0.0	16.0

values are mean ± SD, unless otherwise noticed. SD= standard deviation; Min= minimum; Max = maximum.







Variável	2000-2002 (n=764)	2010-2012 (n=1536)	p
Idade masculina (anos)	35.0 ± 8.6	35.3 ± 8.1	0.318
Dias de abstinência	4.2 ± 3.1	4.2 ± 2.7	0.777
Volume da amostra (ml)	3.4 ± 1.8	3.3 ± 1.6	0.473
Concentração/ml (milhão)	61.7 ± 69.4	26.7 ± 27.3	<0.001
Concentração total (milhão)	183.0 ± 197.0	82.8 ± 89.5	<0.001
Motilidade progressiva (%)	36.4 ± 18.3	36.5 ± 19.2	0.812
Morfologia normal (%)	4.6	2.7	<0.001
Azoospermia (%)	38/764 (4.9)	131/1536 (8.5)	<0.001
Oligozoospermia grave (%)	114/726 (15.7)	426/1405 (30.3)	<0.001



Food intake and social habits in male patients and its relationship to intracytoplasmic sperm injection outcomes

Daniela Paes de Almeida Ferreira Braga, D.V.M., M.Sc., ^{a,b} Gabriela Halpern, M.Sc., ^a Rita de Cássia S. Figueira, M.Sc., ^a Amanda S. Setti, B.Sc., ^b Assumpto laconelli Jr., M.D., ^a and Edson Borges Jr., M.D., Ph.D. ^{a,b}

Fertility and Sterility® Vol. 97, No. 1, January 2012

- ❖ Influência dos hábitos sociais e alimentares no sêmen e nos resultados de ICSI
- Estudo coorte observacional com 250 homens tratados com ICSI



Concentração:

- negativamente influenciada pelo IMC e álcool;
- positivamente influenciada pelo consumo de cereal e nº refeições/dia

Motilidade:

- negativamente influenciada pelo IMC, álcool e cigarro;
- positivamente influenciada pelo consumo de cereal e frutas



TABLE 2

Linear regression analysis of eating and social habits that may affect the sperm concentration, sperm motility, and sperm morphology.

Alcoholic drinks	15.293 5.380 7.983 5.541 -7.776 2.764 2.834 -4.046 -5.003 -0.233 2.749 7.888 9.487 -0.238 5.836	<.01 .104 .035 .129 .310 .441 .440 .089 <.01 .897 .138 .074 .045 .945
Weight loss diet Smoking Meals/d	-2.3331	<.01
Sperm motility Cereals Vegetables Legumes Fruits Meat Fish Dairy products Sweet foods Alcoholic drinks Soft drinks Coffee Exercising Weight loss diet Smoking Meals/d	-2.3331 10.974 9.602 2.861 7.453 -0.078 4.091 2.579 2.568 -8.5592 0.595 -0.109 2.861 -3.848 -8.003 4.295 -2.7780	<.01 <.01 .436 .444 .028 .991 .217 .445 .239 <.01 .721 .949 .444 .374 .013 .110 <.01
Sperm morphology Cereals Vegetables Legumes Fruits Meat Fish Dairy products Sweet foods Alcoholic drinks Soft drinks Coffee Exercising Weight loss diet	-2.7760 0.749 6.029 6.823 5.760 -5.829 6.456 3.765 1.963 -8.865 0.934 -0.312 3.164 -2.484 -2.484 -8.003 3.457 -0.876	.01 .327 .643 .326 .609 .878 .564 .604 .421 .974 .612 .906 .231 .984 .567 .476

Note: BMI = body mass index; RC = regression coefficient.

Braga. Lifestyle and assisted reproduction. Fertil Steril 2012.

- **Alcool**:
- impacto negativo na fertilização
- Carne vermelha e dieta (perda peso):
- impacto negativo na implantação
- diminui as chances de gestação

TABLE 3

Linear regression analysis of eating and social habits that may affect the fertilization and implantation rates.

Response variable	Predictor variable	RC	P valu
Fertilization rate Implantation rate Note: BMI = body mass inde	Cereals Vegetables Legumes Fruits Meat Fish Dairy products Sweet foods Alcoholic drinks Coffee Exercising Weight loss diet Smoking Meals/d BMI Female smoking Female BMI Cereals Vegetables Legumes Fruits Meat Fish Dairy products Sweet foods Alcoholic drinks Soft drinks Coffee Exercising Weight loss diet Smoking Meals/d BMI Female smoking Female BMI Cereals Vegetables Legumes Fruits Meat Fish Dairy products Sweet foods Alcoholic drinks Soft drinks Coffee Exercising Weight loss diet Smoking Meals/d BMI Female smoking Female BMI Female smoking Female BMI	1.151 3.539 1.483 1.201 -8.096 5.028 0.715 -1.727 -3.958 -1.471 -3.963 0.681 -18.046 -3.540 0.313 0.2620 -4.352 0.575 6.555 11.081 5.733 7.234 -36.2 4.507 3.061 3.031 -3.100 -0.541 -1.269 3.833 -17.43 -0.713 4.513 0.8011 -2.984 -12.43 t.	.646 .246 .601 .657 .152 .164 .792 .339 .007 .115 .007 .801 .018 .887 .542 .043 .398 .292 .072 .320 .213 .003 .446 .602 .428 .314 .602 .568 .028 .896 .347 .380 .543 .035

Braga. Lifestyle and assisted reproduction. Fertil Steril 2012.

TABLE 4

Binary regression analysis of eating and social habits that may affect the pregnancy and miscarriage outcome.

Response variable	Predictor variable	OR	95% CI	P value
Pregnancy Miscarriage	Cereals Vegetables Legumes Fruits Meat Fish Dairy products Sweet foods Alcoholic drinks Coffee Exercising Weight loss diet Smoking Meals/d BMI Female smoking Female BMI Cereals Vegetables Legumes Fruits Meat Fish Dairy products Sweet foods Alcoholic drinks Coffee Exercising Weight loss diet Smoking Meals/d BMI Female smoking Female BMI Cereals Fruits Meat Fish Dairy products Sweet foods Alcoholic drinks Coffee Exercising Weight loss diet Smoking Meals/d BMI Female smoking Female BMI	1.59 1.67 1.93 0.62 0.06 0.81 0.71 1.06 1.02 0.93 0.21 0.86 1.23 1.04 1.02 0.43 1.02 1.43 0.89 1.23 1.04 1.02 1.03 0.85 1.21 1.09 0.86 1.23 1.04 1.02 0.83 1.02 1.03 0.83 1.04 1.02 1.03 0.83 1.04 1.02 1.03 1.04 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03	0.73–2.48 0.87–4.32 0.33–2.47 0.28–1.35 0.06–0.7 0.36–1.81 0.33–1.55 0.63–1.77 0.69–1.50 0.62–1.39 0.54–1.26 0.86–2.70 0.01–1.19 0.38–1.93 0.64–2.35 0.92–1.17 0.88–2.02 0.25–1.13 0.91–1.12 0.83–1.84 0.63–1.16 0.87–2.24 0.43–1.16 0.65–1.18 0.97–1.21 0.78–1.32 0.65–1.74 0.56–1.92 0.55–1.74 0.56–1.93	.259 .398 .107 .230 .042 .605 .393 .838 .936 .737 .380 .341 .011 .706 .540 .579 .484 .027 .674 .763 .549 .976 .267 .293 .653 .784 .736 .540 .182 .943 .432 .273 .187 .298 .476 .354
Note: BMI = body mass in	ndex: CI = confidence inter	val: OR =	odds ratio.	

Braga. Lifestyle and assisted reproduction. Fertil Steril 2012.





DOI: 10.1111/and.13090

ORIGINAL ARTICLE



WILEY andrologia

Paternal lifestyle factors in relation to semen quality and in vitro reproductive outcomes

Edson Borges Jr^{1,2} Daniela Paes de Almeida Ferreira Braga^{1,2} Rodrigo R. Provenza¹ | Rita de Cassia Savio Figueira¹ | Assumpto Iaconelli Jr^{1,2} | Amanda Souza Setti^{1,2}

- Fator masculino isolado
- ❖ 1º. ciclo de tratamento
- ❖ Idade mulher < 36 anos</p>
- ❖ 233 ciclos ICSI
- 1. Quantos cigarros/dia?
- 2. Consumo semanal de álcool?
- **3.** Frequência de exercícios ?
- 4. Medicações nos últimos 3 meses? Qual?
- 5. Exposição a agentes tóxicos, pesticidas, radiação etc...



Linear regression analyses' results for the influence of paternal lifestyle factors on semen quality (n=965)

	Cigarette smoking A		Alcohol co	Alcohol consumption	
	В	Р	В	р	
Semen volume	-0.417	0.047	-0.1363	0.592	
Sperm count/mL	-7.363	0.014	-12.527	0.040	
Total sperm count	-4.43	0.023	-34.91	0.156	
Total sperm motility	2.316	0.347	0.342	0.895	
Progressive sperm motility	-0.369	0.887	2.547	0.240	
TMSC	- 1.38	0.045	-16.33	0.278	
Sperm morphology	-0.0563	0.779	0.3751	0.180	
SDF	0.014	0.033	5.833	0.002	



Linear regression analyses' results for the association between paternal lifestyle factors and ICSI outcomes (n=233)

	Cigarette smoking		Alcohol consumption	
	В	р	В	р
Fertilisation rate	-1.349	0.039	-3.617	0.041
High-quality embryos (day 3)	4.383	0.450	9.559	0.166
Blastocyst formation rate	-14.244	0.025	-34.801	0.042
Implantation rate	5.384	0.451	-0.770	0.190



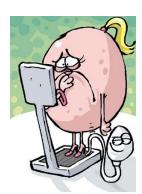
Human Reproduction Update, Vol.0, No.0 pp. 1-11, 2012



BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis

N. Sermondade^{1,2}, C. Faure^{1,2}, L. Fezeu², A.G. Shayeb³, J.P. Bonde⁴, T.K. Jensen⁵, M. Van Wely⁶, J. Cao⁷, A.C. Martini⁸, M. Eskandar⁹, J.E. Chavarro^{10,11}, S. Koloszar¹², J.M. Twigt¹³, C.H. Ramlau-Hansen¹⁴, E. Borges Jr¹⁵, F. Lotti¹⁶, R.P.M. Steegers-Theunissen¹³, B. Zorn¹⁷, A.J. Polotsky¹⁸, S. La Vignera¹⁹, B. Eskenazi²⁰, K. Tremellen²¹, E.V. Magnusdottir²², I. Fejes²³, S. Hercberg^{2,24}, R. Lévy^{1,2†}, and S. Czernichow^{25,26,*†}

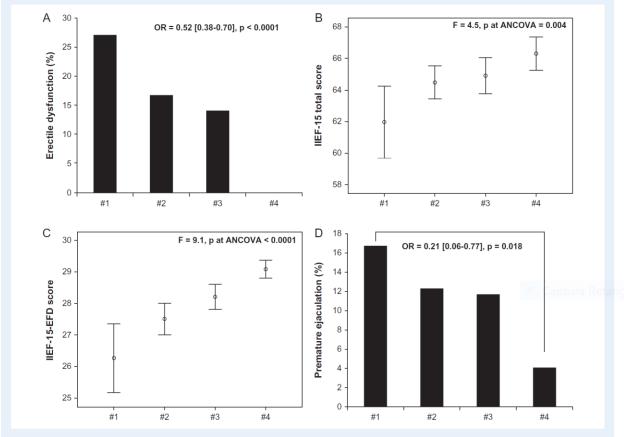
- 21 estudos, 13.077 homens da população geral e em investigação de infertilidade
- Estudo da relação entre BMI e incidência de oligozoospermia / azoospermia
- Comparados com homens com peso normal:
- Sobpeso: OR= 1,15 (0,93-1,43)
- ❖ Sobrepeso: OR= 1,11 (1,01-1,21)
- Obeso: OR= 1,28 (1,06-1,55)
- Obeso mórbido: OR= 2,04 (1,59-2,62)

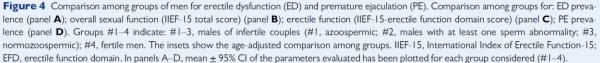




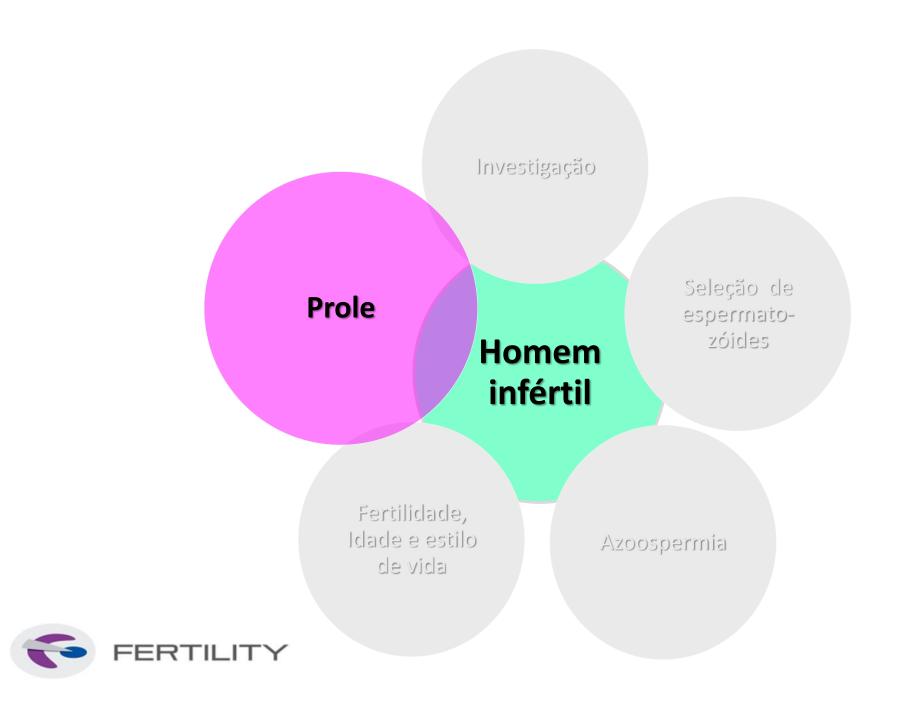
Semen quality impairment is associated with sexual dysfunction according to its severity

F. Lotti^{1,†}, G. Corona^{1,2,†}, G. Castellini¹, E. Maseroli¹, M.G. Fino¹, M. Cozzolino³, and M. Maggi^{1,4,*}









Birth defects in children conceived by in vitro fertilization and intracytoplasmic sperm injection: a meta-analysis Fertility and Sterility® Vol. 97, No. 6, June 2012

Juan Wen, B.S.,^{a,b} Jie Jiang, B.S.,^{a,b} Chenyue Ding, B.S.,^d Juncheng Dai, M.D.,^b Yao Liu, B.S.,^b Yankai Xia, M.D., Ph.D.,^{a,c} Jiayin Liu, M.D., Ph.D.,^{a,d} and Zhibin Hu, M.D., Ph.D.,^{a,b}

- > 124.468 crianças: FIV/ICSI comparadas com Concepção natural (CN)
- RR Anormalidades Congênitas: 1,37 (95%; CI: 1,26-1,48)
- FIV (46.890) x ICSI (27.754): sem diferença
 (RR: 1,05, 95%; CI: 0,91-1,02)



human reproduction

ORIGINAL ARTICLE Reproductive epidemiology

Risk of childhood mortality in family members of men with poor semen quality

Heidi A. Hanson^{1,2,*}, Erik N. Mayer³, Ross E. Anderson³, Kenneth I. Aston^{3,4,5}, Douglas T. Carrell^{3,5}, Justin Berger², William T. Lowrance³, Ken R. Smith^{2,6}, and James M. Hotaling^{3,4}

- Relação entre Fertilidade e Malformações Congênitas
- O risco de defeitos congênitos ao nascimento pode não ser devido as TRA, mas a fatores genéticos e ambientais
- Risco aumentado de morte devido a Malformações Congênitas em descendentes de 1º. grau de homens com <u>alterações dos parâmetros seminais</u>



human reproduction update

The effect of paternal factors on perinatal and paediatric outcomes: a systematic review and meta-analysis

Nan B. Oldereid ^{1,*}, Ulla-Britt Wennerholm², Anja Pinborg³, Anne Loft⁴, Hannele Laivuori^{5,6,7,8}, Max Petzold⁹, Liv Bente Romundstad ^{10,11}, Viveca Söderström-Anttila ¹², and Christina Bergh ¹³

¹Livio IVF-klinikken Oslo, Sørkedalsveien 10A, 0369 Oslo, Norway ²Department of Obstetrics and Gynaecology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Sahlgrenska University Hospital East, SE 416 85 Gothenburg, Sweden ³Department of Obstetrics and Gynecology, Hvidovre Hospital, Institute of Clinical Medicine, Copenhagen University Hospital, Copenhagen, Denmark ⁴Fertility Clinic, Section 4071, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK–2100 Copenhagen, Denmark ⁵Department of Obstetrics and Gynecology, Tampere University Hospital, Teiskontie 35, Fl-33521 Tampere, Finland ⁶Faculty of Medicine and Life Sciences, University of Tampere, Arvo Ylpön katu 34, Fl-33520 Tampere, Finland ⁷Medical and Clinical Genetics, University of Helsinki university Hospital, Haartmaninkatu 8, Fl-00290 Helsinki, Finland ⁸Institute for Molecular Medicine Finland, Helsinki Institute of Life Science, University of Helsinki, Tukhomankatu 8, Fl-00290 Helsinki, Finland ⁹Swedish National Data Service and Health Metrics Unit, University of Gothenburg, 405 30 Gothenburg, Sweden ¹⁰Spiren Fertility Clinic, Norwegian University of Science and Technology, Trondheim NO-7010, Norway ¹¹Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway ¹²Mehiläinen Felicitas, Mannerheimintie 20A, 00100 Helsinki, Finland ¹³Department of Obstetrics and Gynaecology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Reproductive Medicine, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden

- 14.371 artigos, 238 incluídos, 81 para a meta-análise
- Idade, estilo de vida, peso, altura, gordura corporal, cigarro



Table XI Summary results of the meta-analyses of the association between paternal factors and perinatal and paediatric outcomes.

Exposure	Outcome	Pooled estimate (with 95% CI)	Certainty of evidence GRADE
Paternal age	РТВ	1.02 (1.00–1.05)	00 00
	Low BW	1.00 (0.97–1.03)	$\oplus \oplus \bigcirc \bigcirc$
	Stillbirth	1.19 (1.10–1.30)	$\oplus \oplus \bigcirc \bigcirc$
	Children with any birth defects	1.05 (1.02–1.07)	$\oplus \oplus \oplus \bigcirc$
	CHDs	1.03 (0.99-1.06)	$\oplus\oplus\oplus\ominus$
	Orofacial clefts	0.99 (0.95–1.04) 1.14 (1.02–1.29)*	⊕⊕○○
	Gastroschisis	0.88 (0.78–1.00)	$\oplus\oplus\oplus\ominus$
	Spina bifida	0.97 (0.90–1.04)	$\oplus\oplus\oplus\ominus$
	Trisomy 21	1.13 (1.05–1.23)	$\oplus \oplus \oplus \bigcirc$
	Acute lymphoblastic leukaemia	1.08 (0.96–1.21)	000
	Autism and ASDs	1.25 (1.20–1.30)	$\oplus\oplus\oplus\ominus$
	Schizophrenia	1.31 (1.23–1.38)	$\oplus\oplus\oplus\ominus$
Paternal BMI	No meta-analysis		
Paternal	PTB	1.16 (1.00–1.35)	⊕⊕○○
smoking	Low BW	1.10 (1.00–1.21)	0000
	SGA	1.22 (1.03–1.44)	$\oplus \oplus \bigcirc \bigcirc$
	CHDs	1.75 (1.25–2.44)	$\oplus \oplus \bigcirc \bigcirc$
	Orofacial clefts	1.51 (1.16–1.97)	$\oplus \oplus \bigcirc \bigcirc$
	Brain tumours	1.12 (1.03–1.22)	$\oplus \oplus \bigcirc \bigcirc$



^{*}Exposure: Paternal age >45 years.

INVITED SESSION

SESSION 01: KEYNOTE SESSION

Monday 2 July 2018

Forum (Auditorium)

08:30-09:30

O-001 Human Reproduction Keynote Lecture - Semen quality of young adult ICSI offspring: The first results

F. Belva¹, M. Bonduelle¹, M. Roelants², D. Michielsen³, A. Van Steirteghem⁴, G. Verheyen⁴, H. Tournaye⁴

- ❖ UZ Brussel, entre 03/2013 04/2016, 54 jovens
- ❖ Saúde reprodutiva e metabólica de jovens 18-22 anos, nascidos de ICSI com espermatozóide ejaculado x concepção natural (CN)



O-001 Human Reproduction Keynote Lecture - Semen quality of young adult ICSI offspring: The first results

<u>F. Belva</u>¹, M. Bonduelle¹, M. Roelants², D. Michielsen³, A. Van Steirteghem⁴, G. Verheyen⁴, H. Tournaye⁴



ICSI: menor concentração espermática/mL, total, TMSC (17,7 mil/ml, 31,9 mil e 12,7 mil) que os nascidos por CN (37 mil/ml; 86.8 mil; 38.6 mil)

- **CN:** dobro na concentração espermática/mL (*ratio 1.9*, 95% CI 1.1-3.2)
- ❖ ICSI: duas vezes menor concentração espermática total (ratio 2.3, 95% CI 1.3-4.1) e TMSC (ratio 2.1, 95% CI 1.2-3.6)

ICSI:

- 3X menor chance de ter concentração espermática/mL (15 mil/mL) abaixo OMS (AOR 2.7; 95% CI 1.1–6.7)
- 4X menor chance de ter concentração espermática total (39 mil) (AOR 4.3; 95% CI 1.7-11.3)



Considerações

- TMSC na avaliação do espermatozoide, principalmente no prognóstico do ICSI
- fragDNA espermático como nova ferramenta diagnóstica; antioxidantes como forma de tratamento
- ❖ MSOME IMSI eficazes no selecionamento espermático e resultados do ICSI
- Espermatozóide epididimário melhor que o testicular nas AO
- Espermatozóide testicular da AO melhor que o ANO
- Idade do homem como prognóstico da função espermática e DNA
- Estilo de vida muito relacionado com o comportamento do espermatozoide (também no ICSI)
- Idade paterna e cigarro: influência na prole
- Filhos de homens tratados com ICSI: maior probabilidade alteração seminal



http://fertility.com.br/producao-cientifica-2018/





Obrigado!



Edson Borges Jr.

edson@fertility.com.br

