

CONVEGNO  
ECM

evento in  
modalità  
mista:  
in presenza e  
da remoto

11 maggio 2023  
ore 9.30-13.00

La Toscana delle *donne*  
LA RAGIONE DEL VALORE

# LA SALUTE DI GENERE IN TOSCANA

Presentazione del nuovo Documento ARS



**siamS**  
Società Italiana di Andrologia  
e Medicina della Sessualità



## TEMATICHE AL MASCHILE

**Linda Vignozzi**

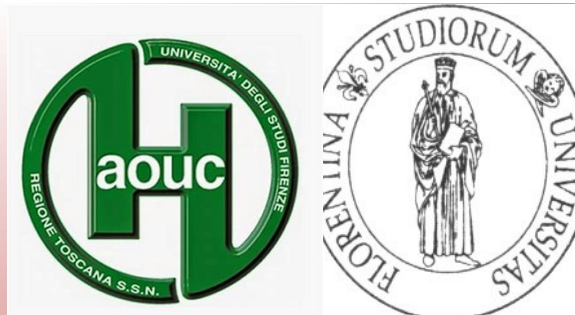
**Associate Professor**

**Head, Andrology, Women's endocrinology and  
gender incongruence**

**AOU Careggi University of Florence,  
Training Center of the European Academy of  
Andrology**



**European Academy of Andrology**



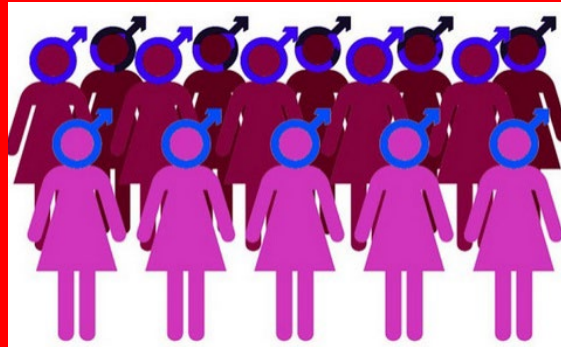
# DISCLOSURES

Dichiaro di aver avuto NEGLI ULTIMI 2 ANNI i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario, quali  
Bayer, Lipocine, Teva, Galecto, Therascience



**WARNING!**

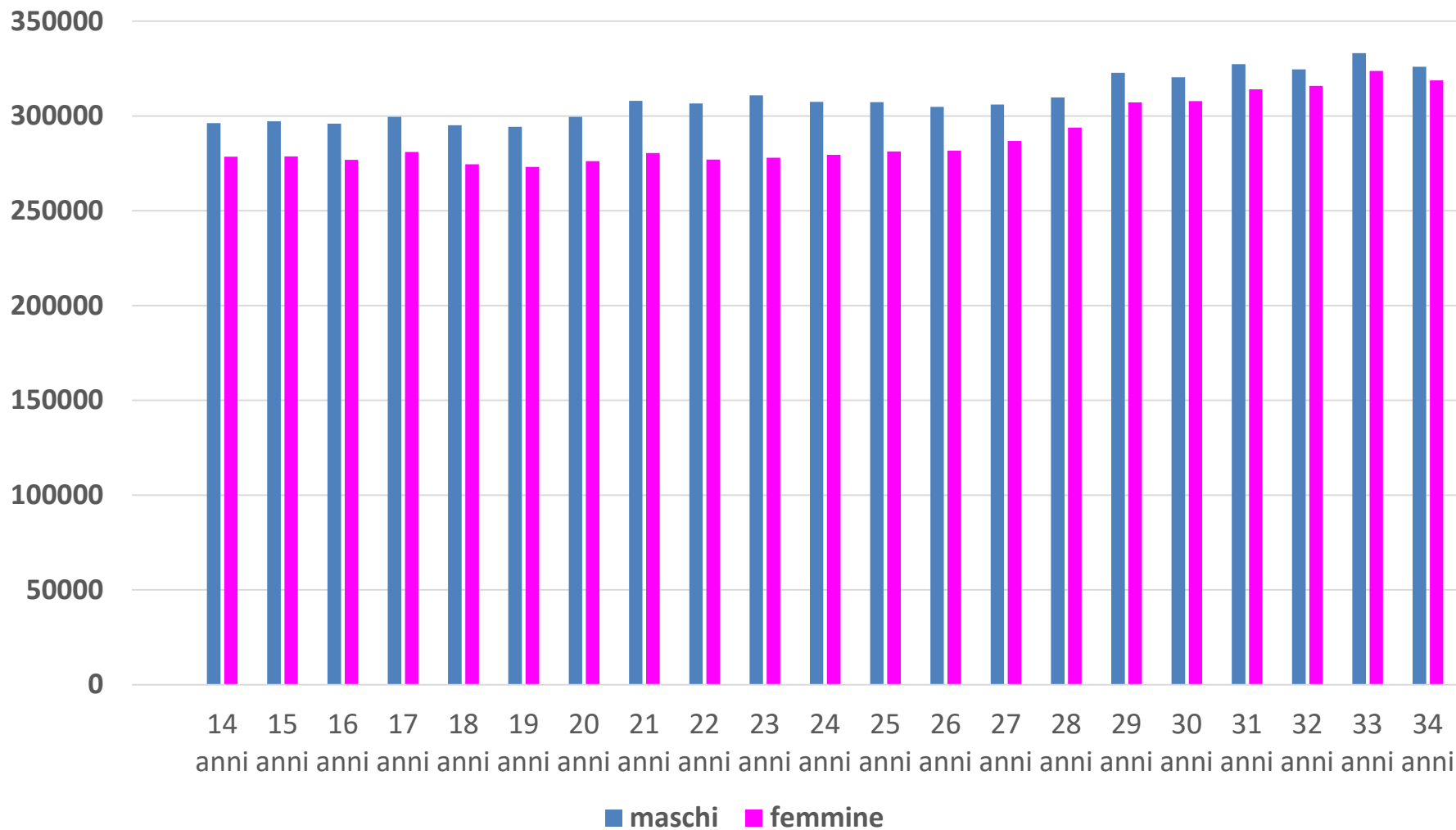
**GENDER  
MEDICINE  
ISSUE**



**Young male subjects**



### Popolazione 14-34 anni per genere

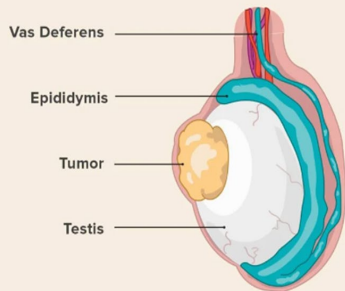


# #1. ...Tumore più frequente nei maschi tra i 15 e i 40 anni...



Associazione italiana registri tumori

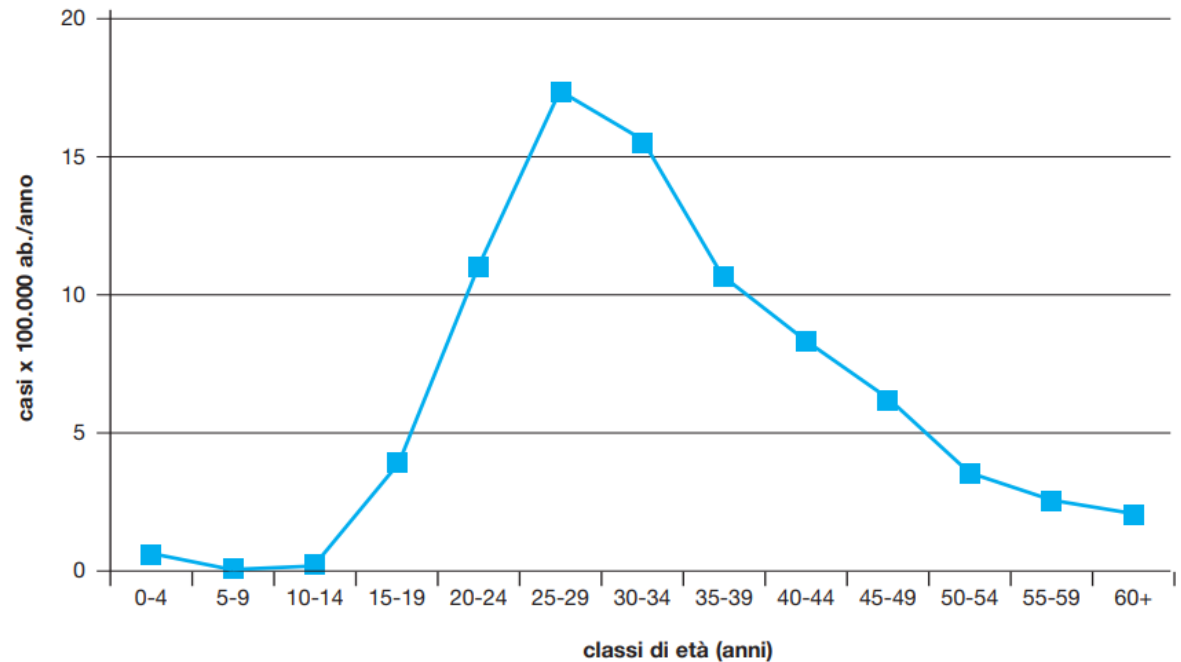
Testicular Cancer



healthline

## Il tumore del testicolo è la neoplasia più comune tra i giovani

Tassi di incidenza specifici per età, 2003-2005

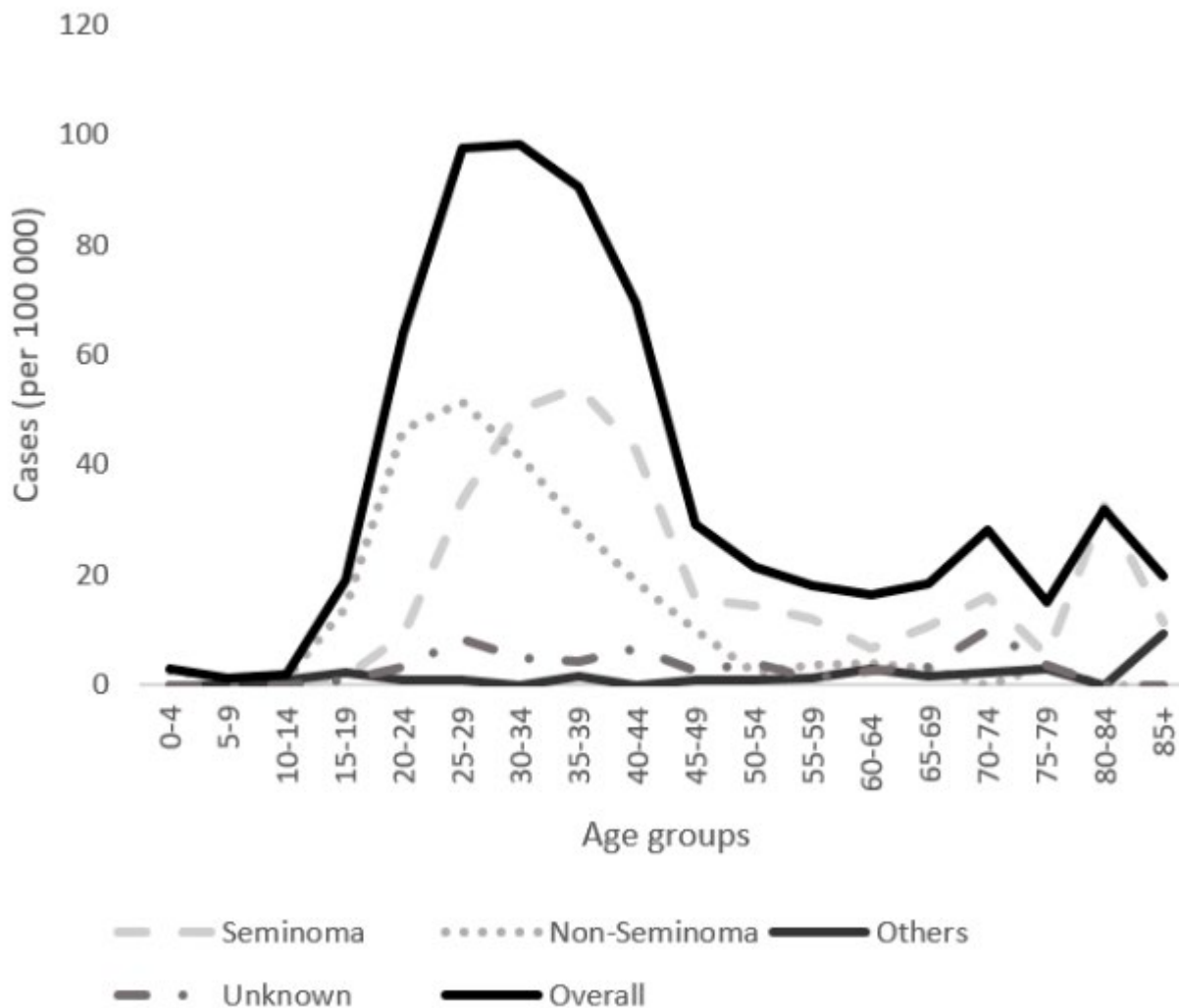


# #1. ...ulteriore picco di incidenza dopo i 70 anni

Article

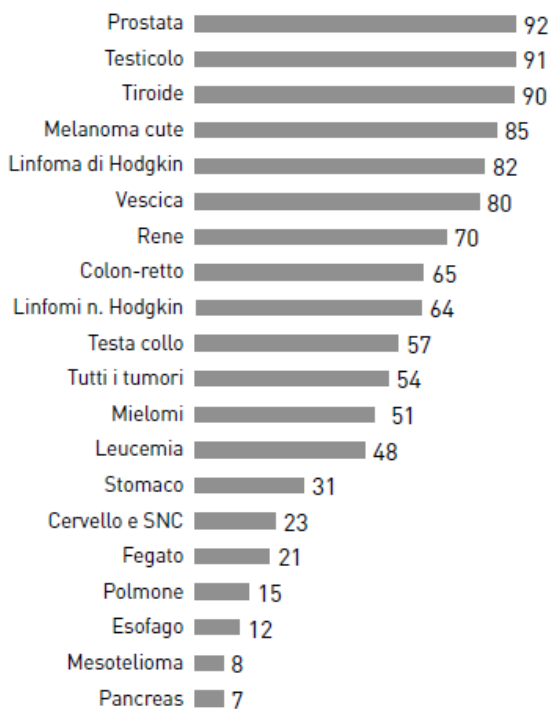
## A Population-Based Analysis of Incidence, Mortality, and Survival in Testicular Cancer Patients in Lithuania

Mingaile Drevinskaite <sup>1,2,\*</sup>, Ausvydas Patasius <sup>2,3</sup>, Marius Kincius <sup>4</sup>, Mindaugas Jievaltas <sup>5</sup> and Giedre Smailyte <sup>2,3</sup>



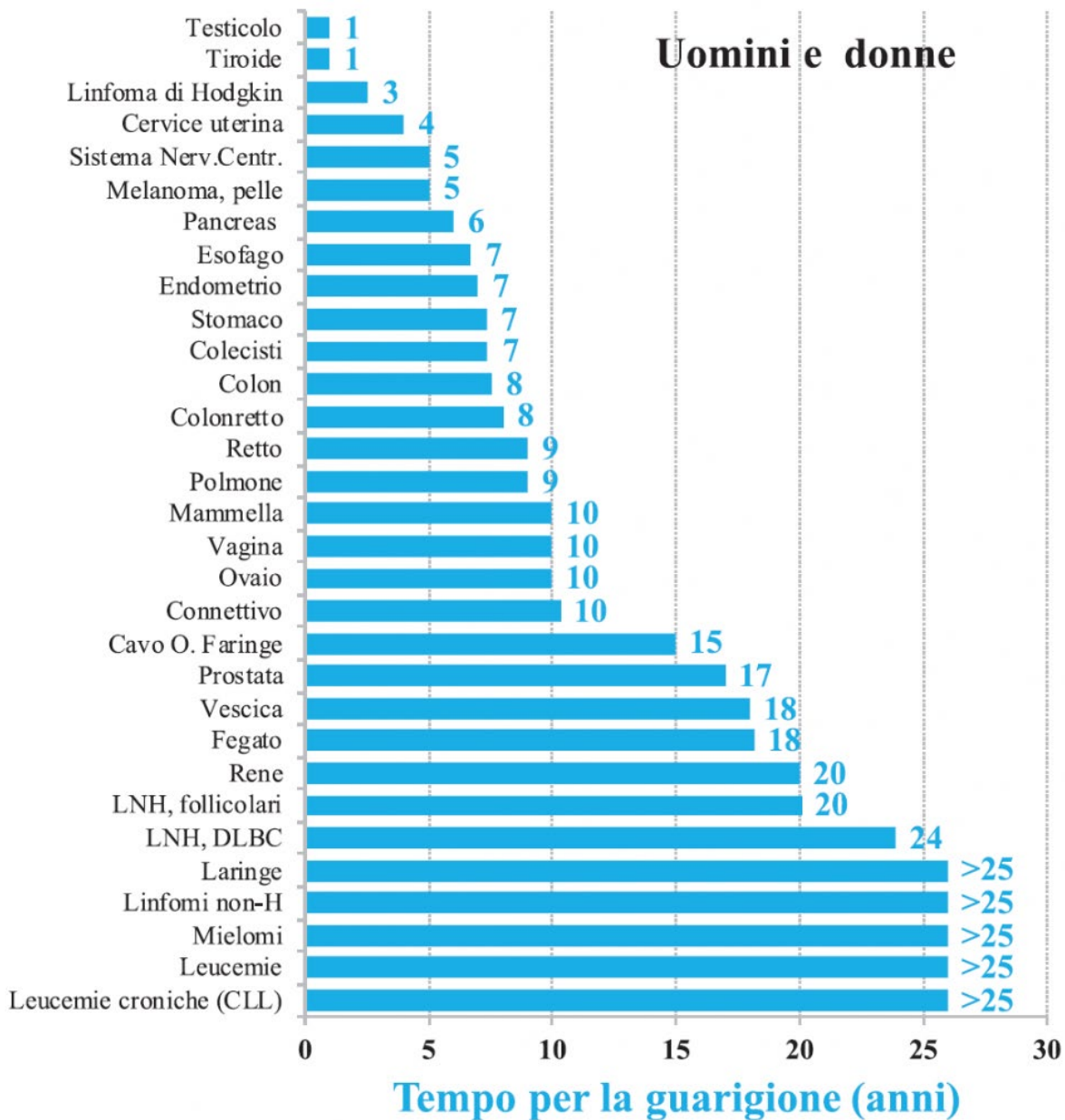
# #1. ... se diagnosi precoce: rapida guarigione e alta sopravvivenza

Maschi



Sopravvivenza a 5 anni (AIRTUM)

Uomini e donne







Ministero della Salute

RELAZIO  
STATO D  
MATERIA  
(LEGGE I

WARNING!

presenta

16.2% ca  
(fattore r



Figura 8. Indicazioni di in  
tra

PMA di II e III livello con

# GENDER MEDICINE ISSUE



**Undertreated**

**Underdiagnosed**

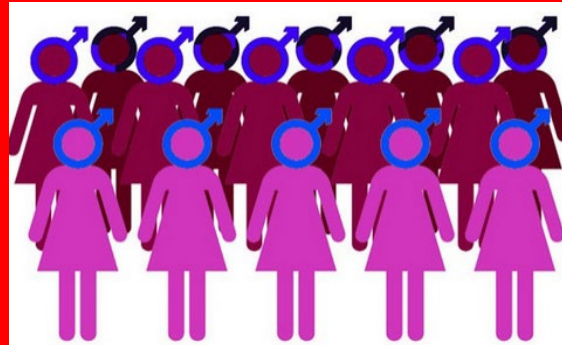
**Understudied**

**Underinvestigated**



**WARNING!**

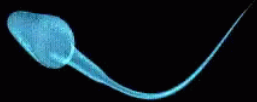
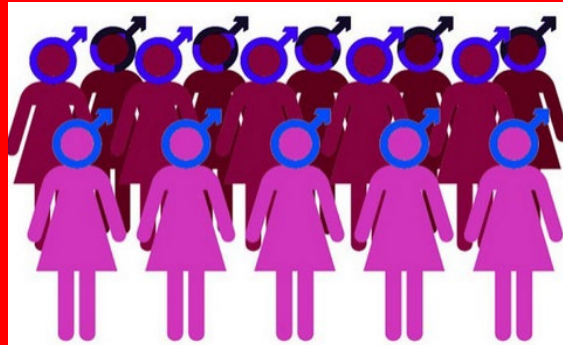
# GENDER MEDICINE ISSUE





**WARNING!**

**GENDER  
MEDICINE  
ISSUE**



# WHO laboratory manual for the examination and processing of human semen

Sixth Edition



## Chapter 1: Introduction

|     |  |   |
|-----|--|---|
| 1.1 | Scope of the manual.....   | 1 |
| 1.2 | Introduction .....   | 1 |
| 1.3 | The sixth edition.....   | 2 |
| 1.4 | Methodology for the preparation of the sixth edition of the <i>WHO laboratory manual for the examination and processing of human semen</i> ..... | 4 |

**“-semen analysis is never prognostic for couple fertility**

**-alterations in semen parameters may be associated with an individual’s general health”**

# How to assess male partner of an infertile couple?

Journal of Endocrinological Investigation (2022) 45:1085–1113  
https://doi.org/10.1007/s40618-022-01741-6

CONSENSUS STATEMENT



## Management of male factor infertility: position statement from the Italian Society of Andrology and Sexual Medicine (SIAMS)

Endorsing Organization: Italian Society of Embryology, Reproduction, and Research (SIERR)

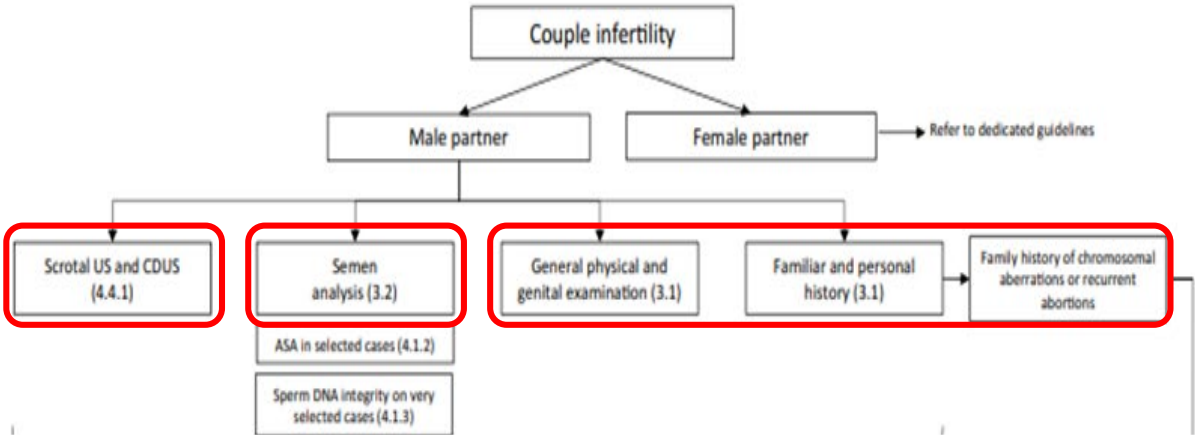
A. Ferlin<sup>1</sup> · A. E. Calogero<sup>2</sup> · C. Krausz<sup>3</sup> · F. Lombardo<sup>4</sup> · D. Paoli<sup>4</sup> · R. Rago<sup>5</sup> · C. Scarica<sup>6</sup> · M. Simoni<sup>7</sup> · C. Foresta<sup>1</sup> · V. Rochira<sup>7</sup> · E. Sbardella<sup>8</sup> · S. Francavilla<sup>9</sup> · G. Corona<sup>10</sup>

Received: 16 December 2021 / Accepted: 5 January 2022 / Published online: 24 January 2022  
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**Not only a semen analysis assessment!!!!!!**



**1° step**







- Attività anno 2019 centri procreazione medicalmente assistita

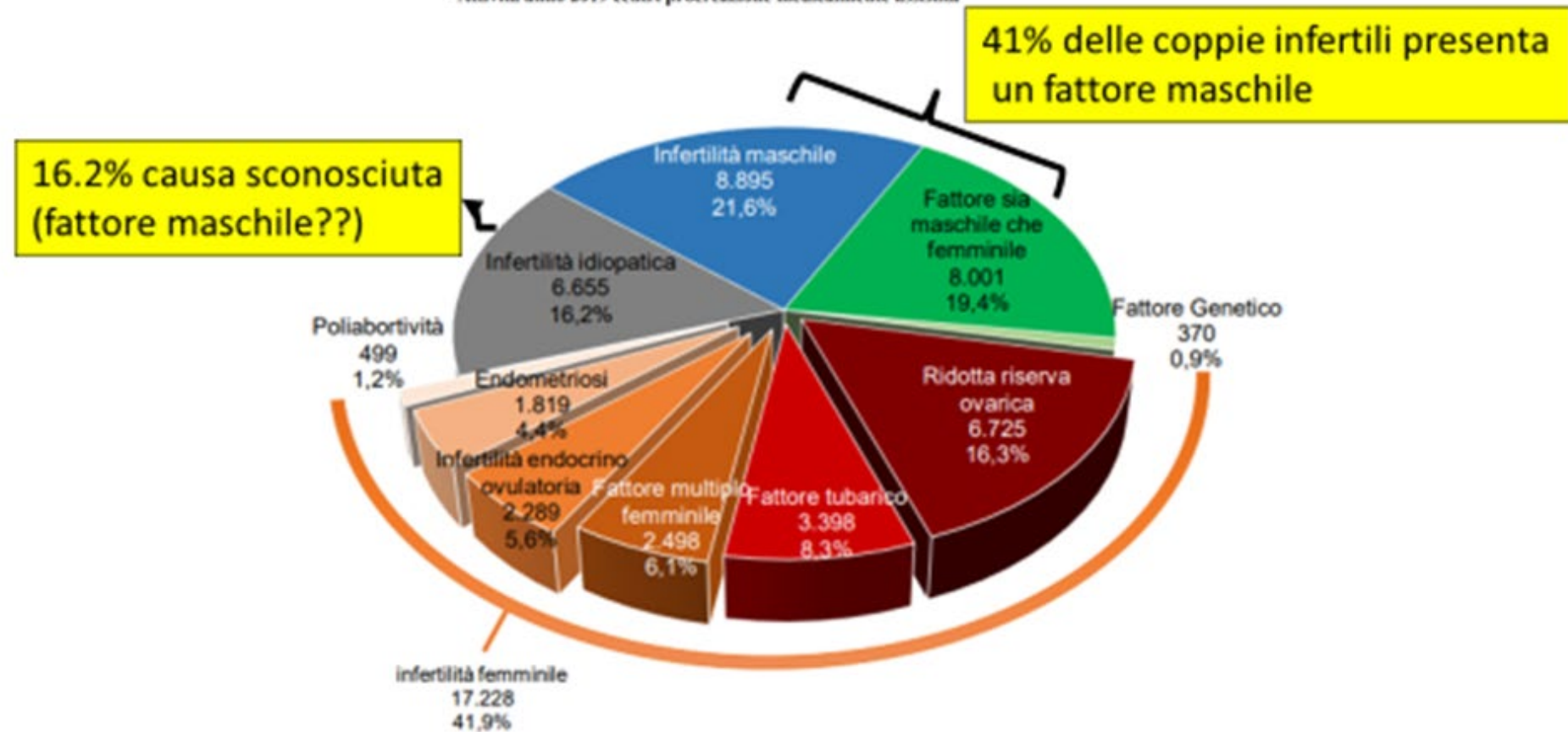
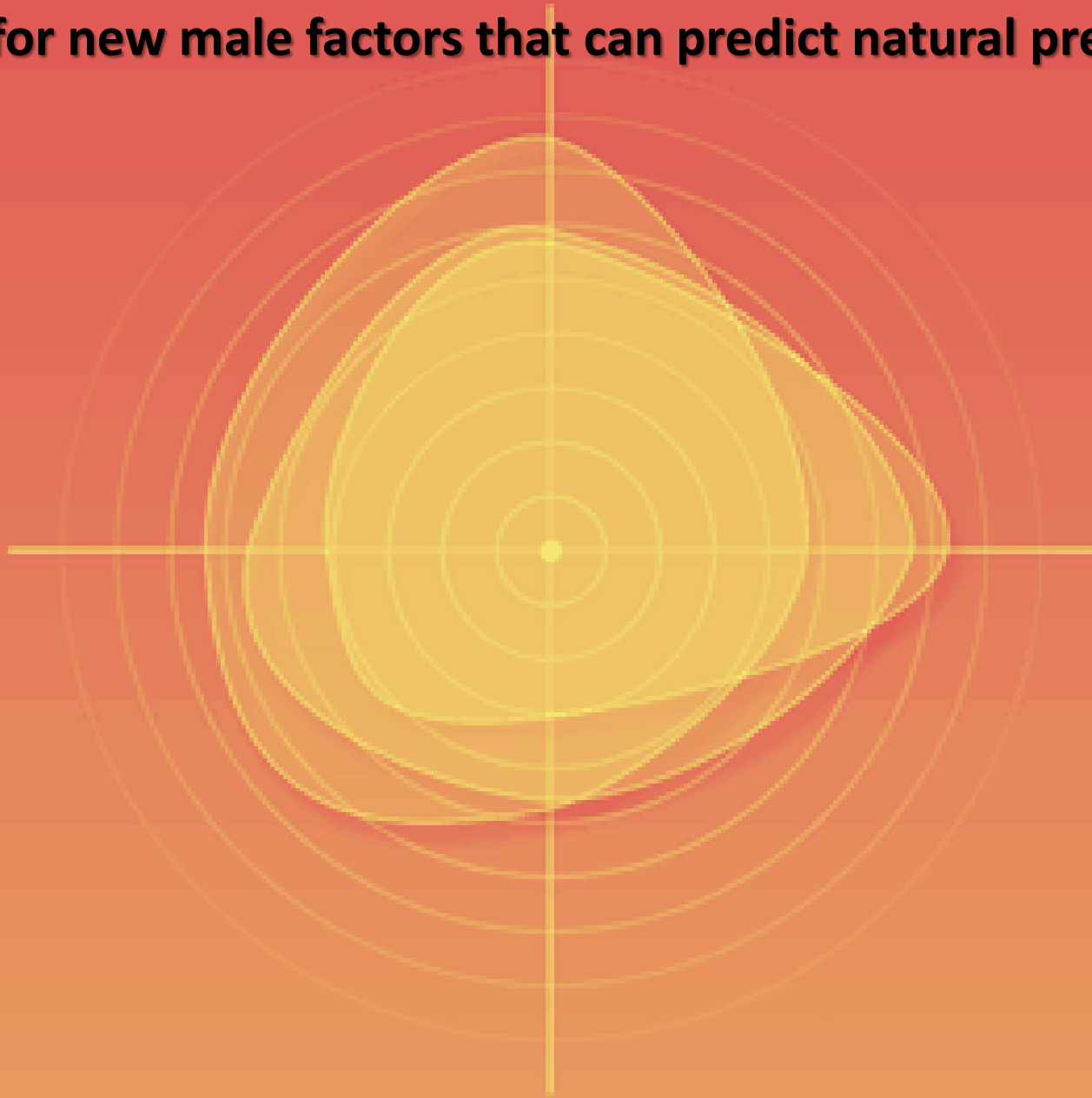


Figura 8. Indicazioni di infertilità per le 41.149 coppie trattate con tecniche di PMA di II e III livello con trasferimento di embrioni a fresco (FIVET/ICSI) nel 2019

# Searching for new male factors that can predict natural pregnancy

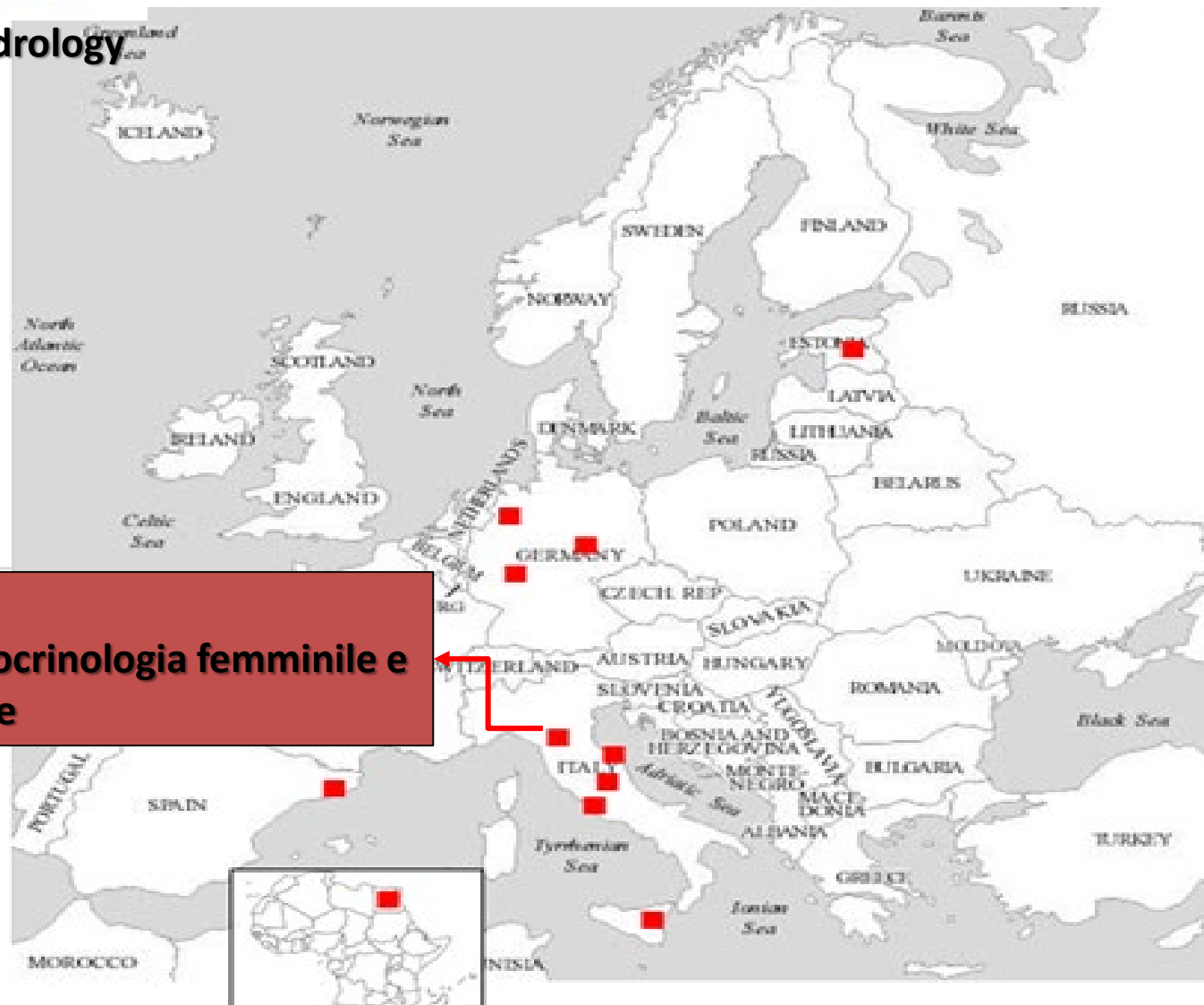




**European Academy of Andrology**



**Florence-AOU Careggi  
SODc Andrologia, Endocrinologia femminile e  
Incongruenza di genere**







European Academy of Andrology



Azienda  
Ospedaliero  
Universitaria  
Careggi

Received: 20 March 2020 | Revised: 16 April 2020 | Accepted: 27 April 2020  
DOI: 10.1111/andr.12808

ORIGINAL ARTICLE

ANDROLOGY WILEY

The European Academy of Andrology (EAA) ultrasound study on healthy, fertile men: clinical, seminal and biochemical characteristics

Francesco Lotti<sup>1</sup> | Francesca Frizza<sup>1</sup> | Giancarlo Balercia<sup>2</sup> | Arcangelo Barbonetti<sup>3</sup> | Hermann M. Behre<sup>4</sup> | Aldo E. Calogero<sup>5</sup> | Jann-Frederik Cremers<sup>6</sup> | Felice Francavilla<sup>3</sup> | Andrea M. Isidori<sup>7</sup> | Sabine Kliesch<sup>6</sup> | Sandro La Vignera<sup>5</sup> | Andrea Lenzi<sup>7</sup> | Marios Marcou<sup>4</sup> | Adrian Pilatz<sup>6</sup> | Olev Poolamets<sup>9</sup> | Margus Punab<sup>9</sup> | Maria Fernanda Peraza Godoy<sup>10</sup> | Osvaldo Rajmil<sup>10</sup> | Gianmaria Salvio<sup>2</sup> | Osama Shaeer<sup>11</sup> | Wolfgang Weidner<sup>8</sup> | Elisa Maseroli<sup>1</sup> | Sarah Cipriani<sup>1</sup> | Elisabetta Baldi<sup>1</sup> | Selene Degl'Innocenti<sup>1</sup> | Giovanna Danza<sup>12</sup> | Anna Lucia Caldini<sup>13</sup> | Alessandro Terreni<sup>13</sup> | Luca Boni<sup>14</sup> | Csilla Krausz<sup>1</sup> | Mario Maggi<sup>12</sup>

Fertile men  
n = 248  
(EAA US study)

vs.

Infertile men  
n = 689  
(Andrology Unit, University of Florence)

## IL FATTORE MASCHILE PREDICE L'OUTCOME NELLA RIPRODUZIONE NATURALE

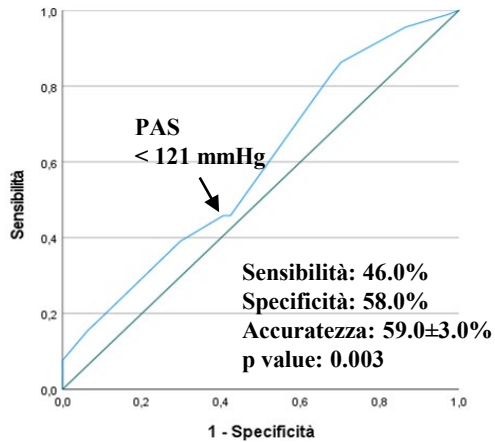
Predittori seminali, clinici e biochimici  
di gravidanza con figlio nato vivo

valutando un ampio numero di parametri

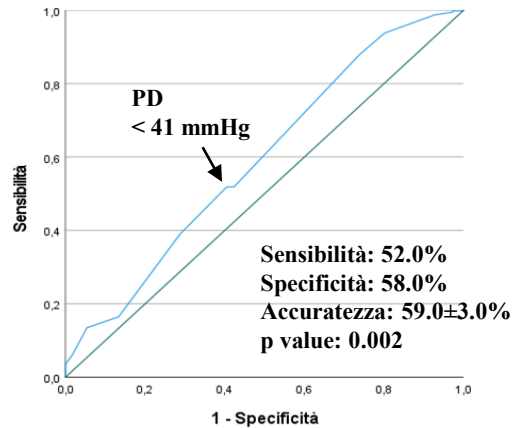
in maschi di coppie infertili e fertili con nato vivo

# Nuovi PARAMETRI in grado di PREDIRE LA FERTILITA' NATURALE CON «NEONATI IN BRACCIO»

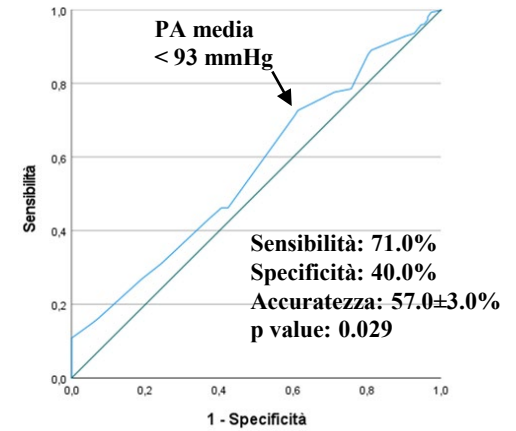
**A** Curva ROC per **PA sistolica (PAS)** predittiva di gravidanza con nato vivo



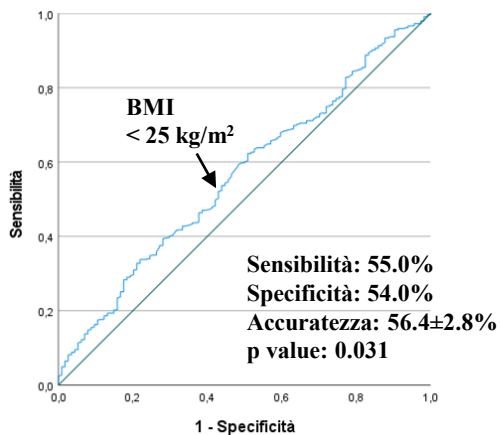
**B** Curva ROC per **Pressione Differenziale (PD)** predittiva di gravidanza con nato vivo



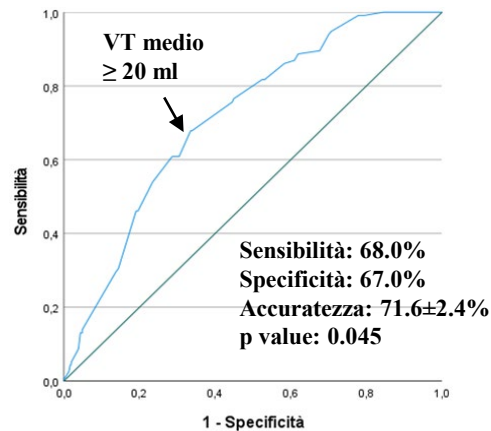
**C** Curva ROC per **PA media** predittiva di gravidanza con nato vivo



**D** Curva ROC per **BMI** predittiva di gravidanza con nato vivo



**E** Curva ROC per **volume testicolare (VT)** predittiva di gravidanza con nato vivo



**LA VISITA  
ANDROLOGICA**



# Soglie relative ai PARAMETRI CLINICI della visita Andrologica e probabilità di gravidanza naturale con «neonato in braccio»

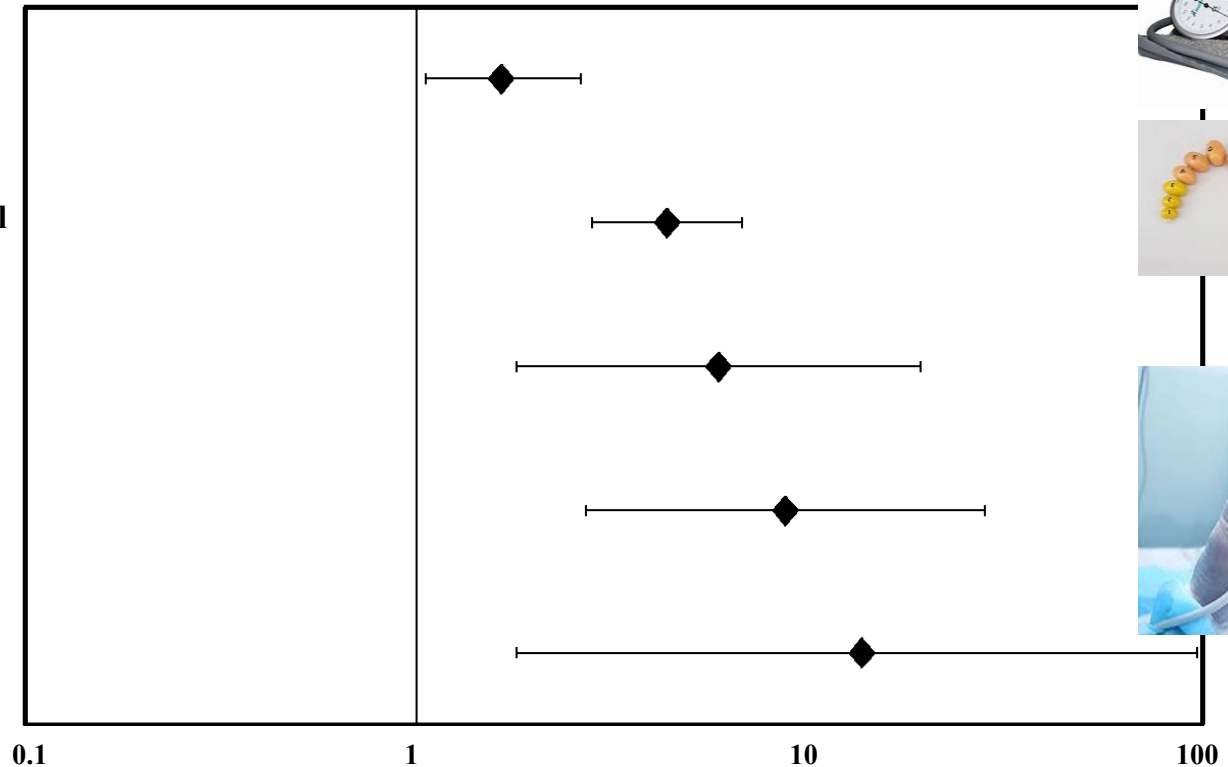
PA media < 93 mmHg

Volume testicolare medio  $\geq 20$  ml

Caput epididimo non dilatato

Cauda epididimo non dilatata

Assenza di  
agenesia bilaterale deferenti

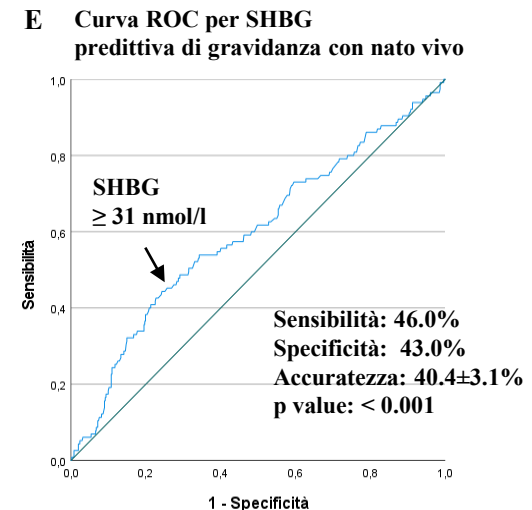
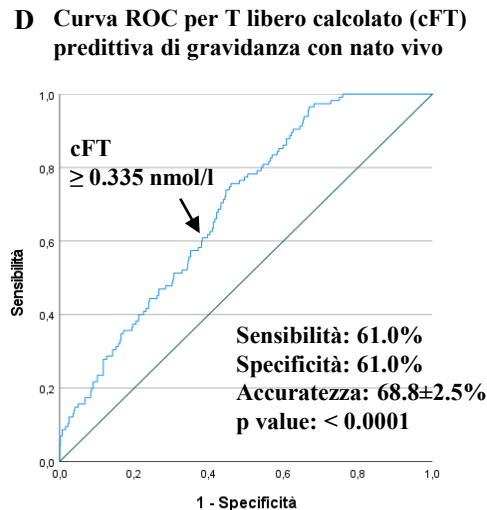
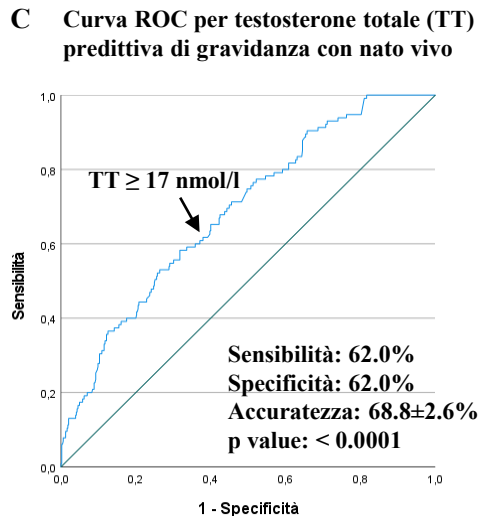
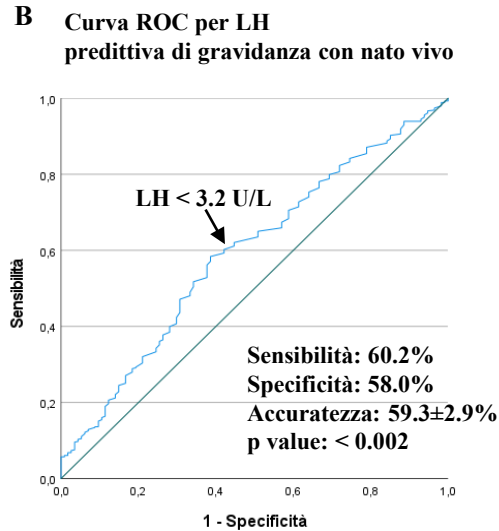
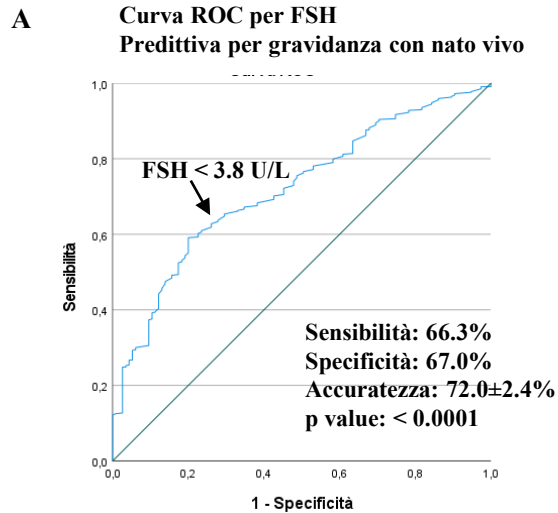


Dati corretti per età del  
maschio e della partner

OR per gravidanza con nato vivo



# Nuovi PARAMETRI in grado di PREDIRE LA FERTILITA' NATURALE CON «NEONATI IN BRACCIO»



# VALORI ORMONALI

# Soglie relative ai VALORI ORMONALI e probabilità di gravidanza naturale con «neonato in braccio»

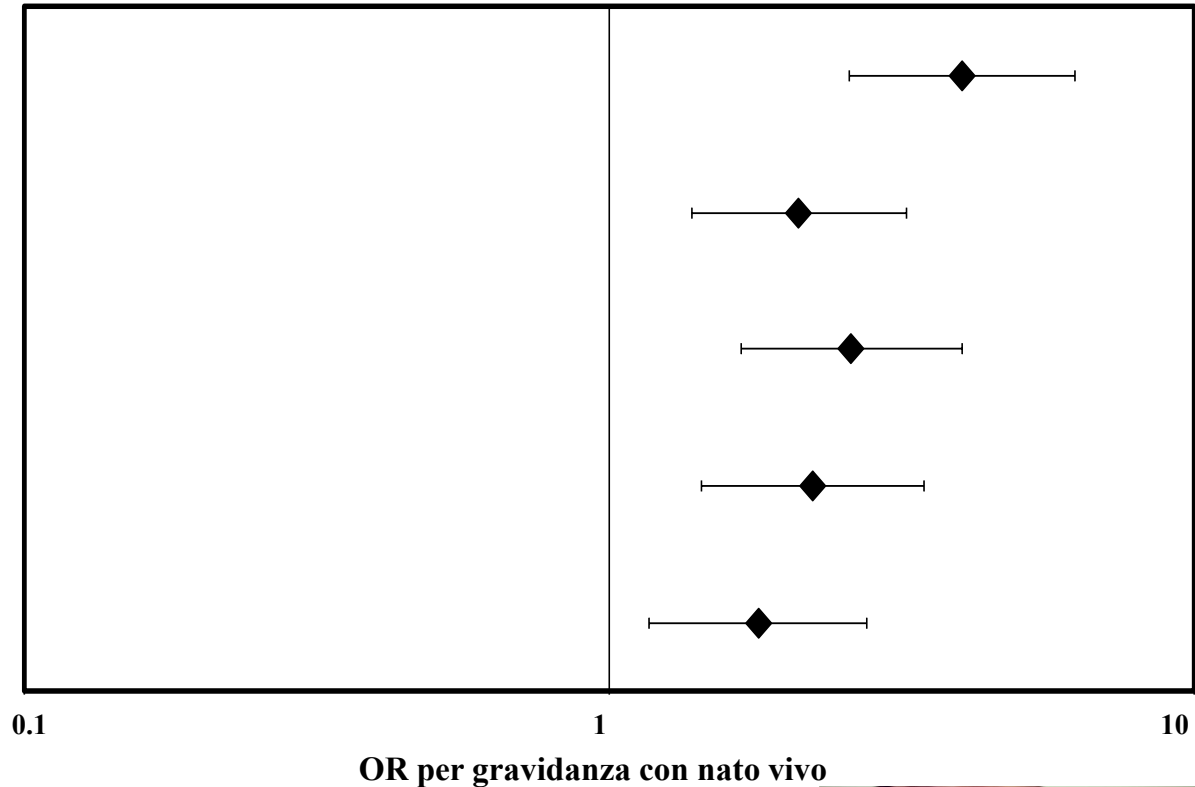
FSH < 3.8 U/L

LH < 3.2 U/L

TT ≥ 17 nmol /l

cFT ≥ 0.335 nmol /l

SHBG ≥ 31 nmol /l



Dati corretti per età del  
maschio e della partner



# Soglie relative ai parametri clinici e Probabilità' di gravidanza naturale con neonato in braccio

età partner, anamnesi, questionari psicologici e andrologici

Età partner < 34.5 anni

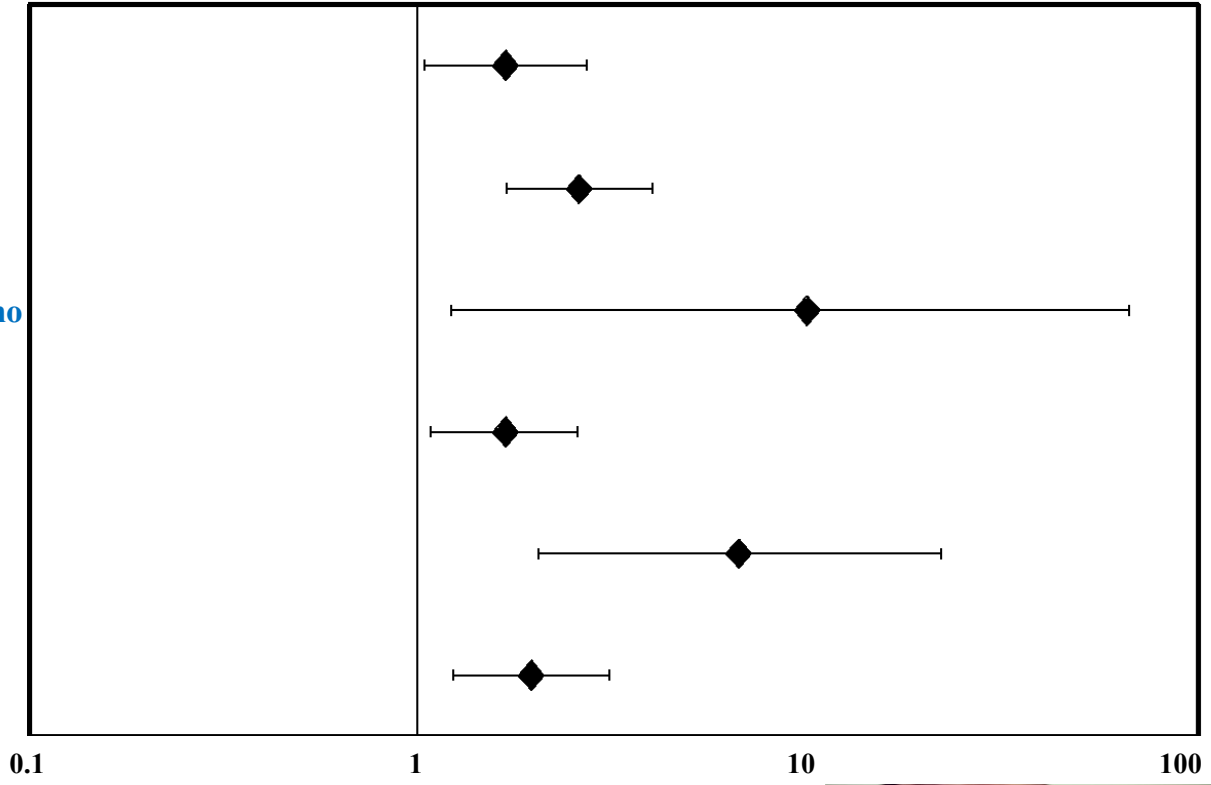
Consumo di alcol lieve

Assenza di storia di criptorchidismo

Assenza di storia di parotite

Assenza di disfunzione erettile

Punteggio totale MHQ ≤ 20



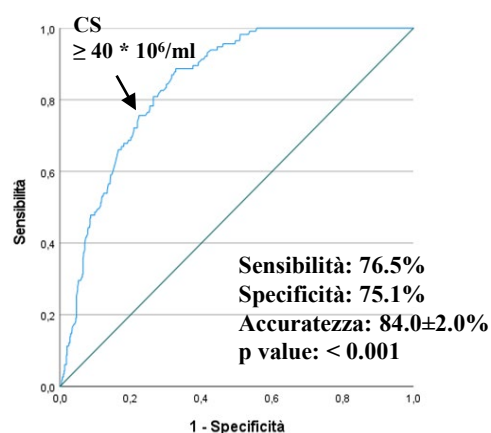
OR per gravidanza con nato vivo

Dati corretti per età del maschio e della partner

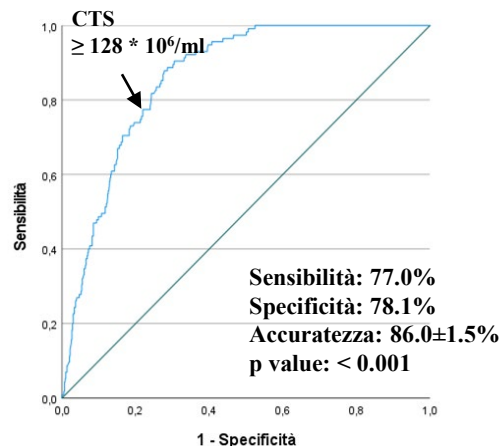


# Alterazione dei parametri del liquido seminale e degli spermatozoi predice la gravidanza con «neonato in braccio»

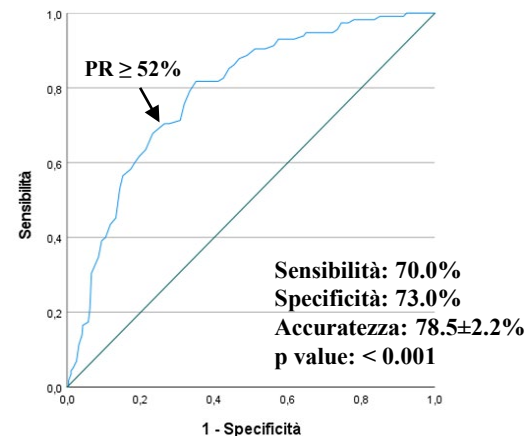
**A** Curva ROC per **concentrazione spermatica (CS)** predittiva di gravidanza con nato vivo



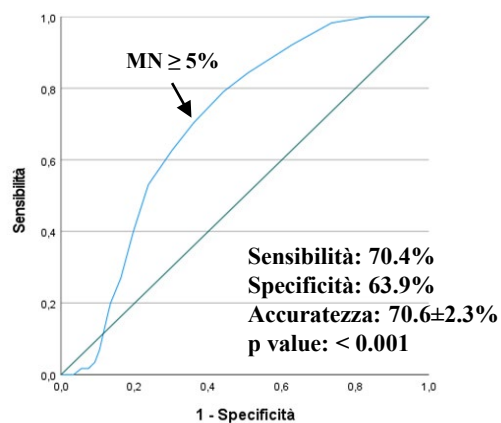
**B** Curva ROC per **conta totale spermatica (CTS)** predittiva di gravidanza con nato vivo



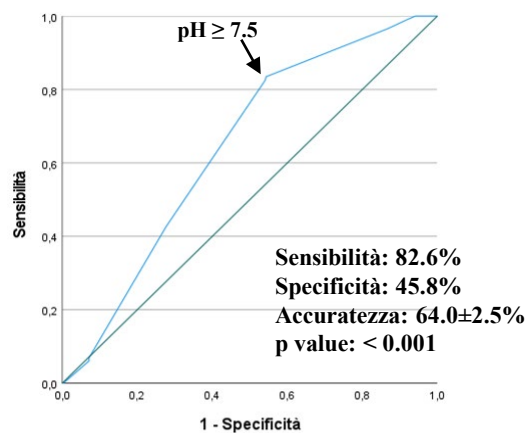
**C** Curva ROC per **motilità progressiva (PR)** predittiva di gravidanza con nato vivo



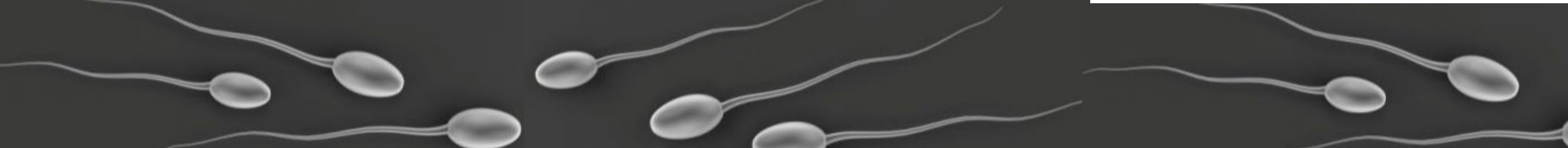
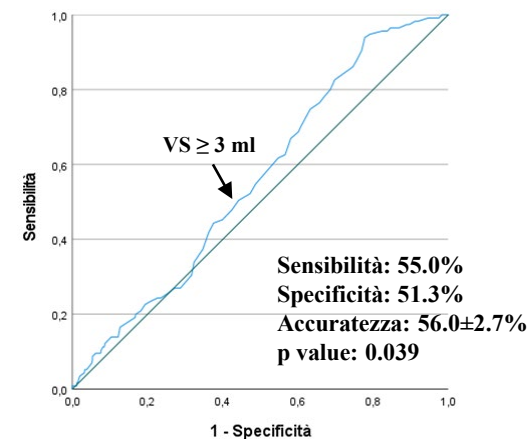
**D** Curva ROC per **morfologia normale (MN)** predittiva di gravidanza con nato vivo



**E** Curva ROC per **pH seminale** predittiva di gravidanza con nato vivo



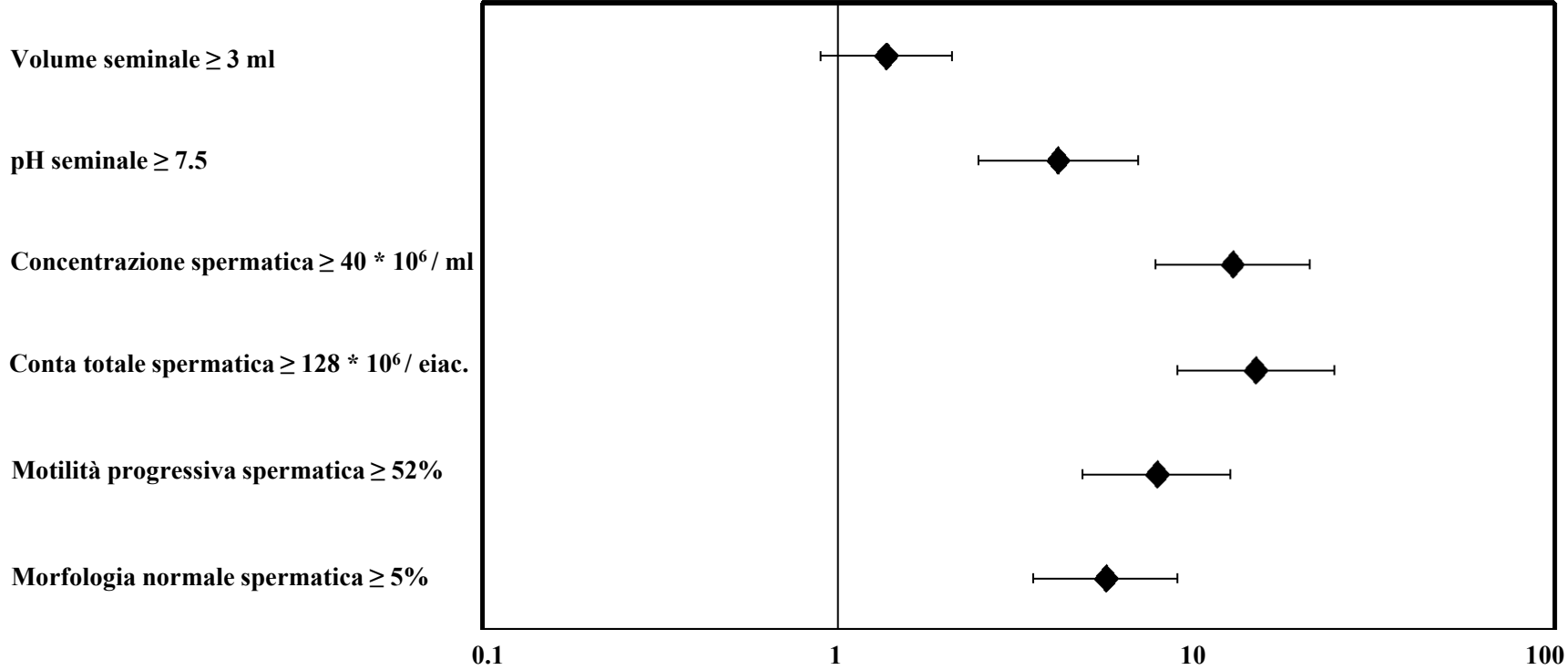
**F** Curva ROC per **volume seminale** predittiva di gravidanza con nato vivo





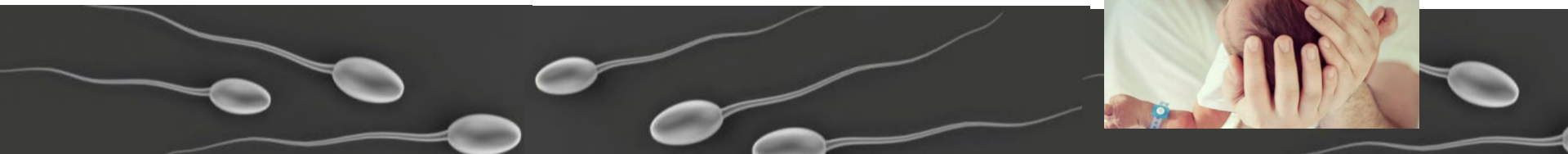
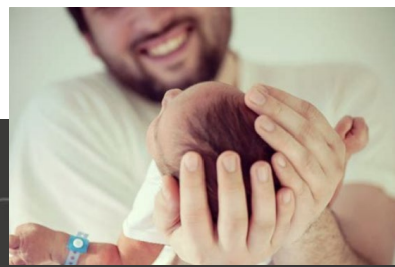


# Soglie relative ai parametri seminali e probabilità di gravidanza con «neonato in braccio»



Dati corretti per età del  
maschio e della partner

Odds Ratio (OR) per gravidanza con nato vivo





## Management of male factor infertility: position statement from the Italian Society of Andrology and Sexual Medicine (SIAMS)

Endorsing Organization: Italian Society of Embryology, Reproduction, and Research (SIERR)

A. Ferlin<sup>1</sup> · A. E. Calogero<sup>2</sup> · C. Krausz<sup>3</sup> · F. Lombardo<sup>4</sup> · D. Paoli<sup>4</sup> · R. Rago<sup>5</sup> · C. Scarica<sup>6</sup> · M. Simoni<sup>7</sup> · C. Foresta<sup>1</sup> · V. Rochira<sup>7</sup> · E. Sbardella<sup>8</sup> · S. Francavilla<sup>9</sup> · G. Corona<sup>10</sup>

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**Varicocele**

- Suggest treating varicocele in infertile couple in which male partner has abnormal semen parameters and the female partner has normal fertility or a potentially treatable cause of infertility and time to conception is not a concern
- Suggest only monitoring in cases with subclinical varicocele
- It's still debatable whether treatment of varicocele might increase the pregnancy rates in IVF

# Comparison between males of fertile and infertile couples for varicocele prevalence

## Infertile men

n = 689 consecutive men with couple infertility  
Andrology, Female Endocrinology  
and Gender Incongruence Unit, University of Florence

## Fertile men

n = 248 (EAA US study)

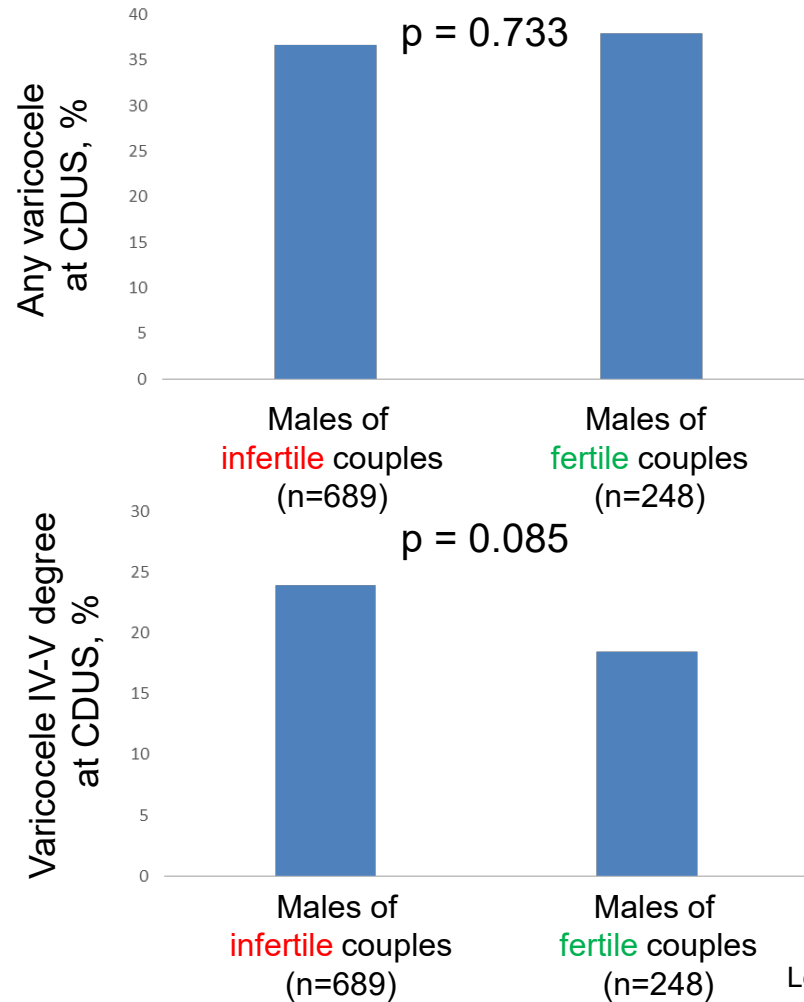
Received: 19 October 2020 | Revised: 19 November 2020 | Accepted: 23 November 2020  
DOI: 10.1111/andr.12951

ORIGINAL ARTICLE

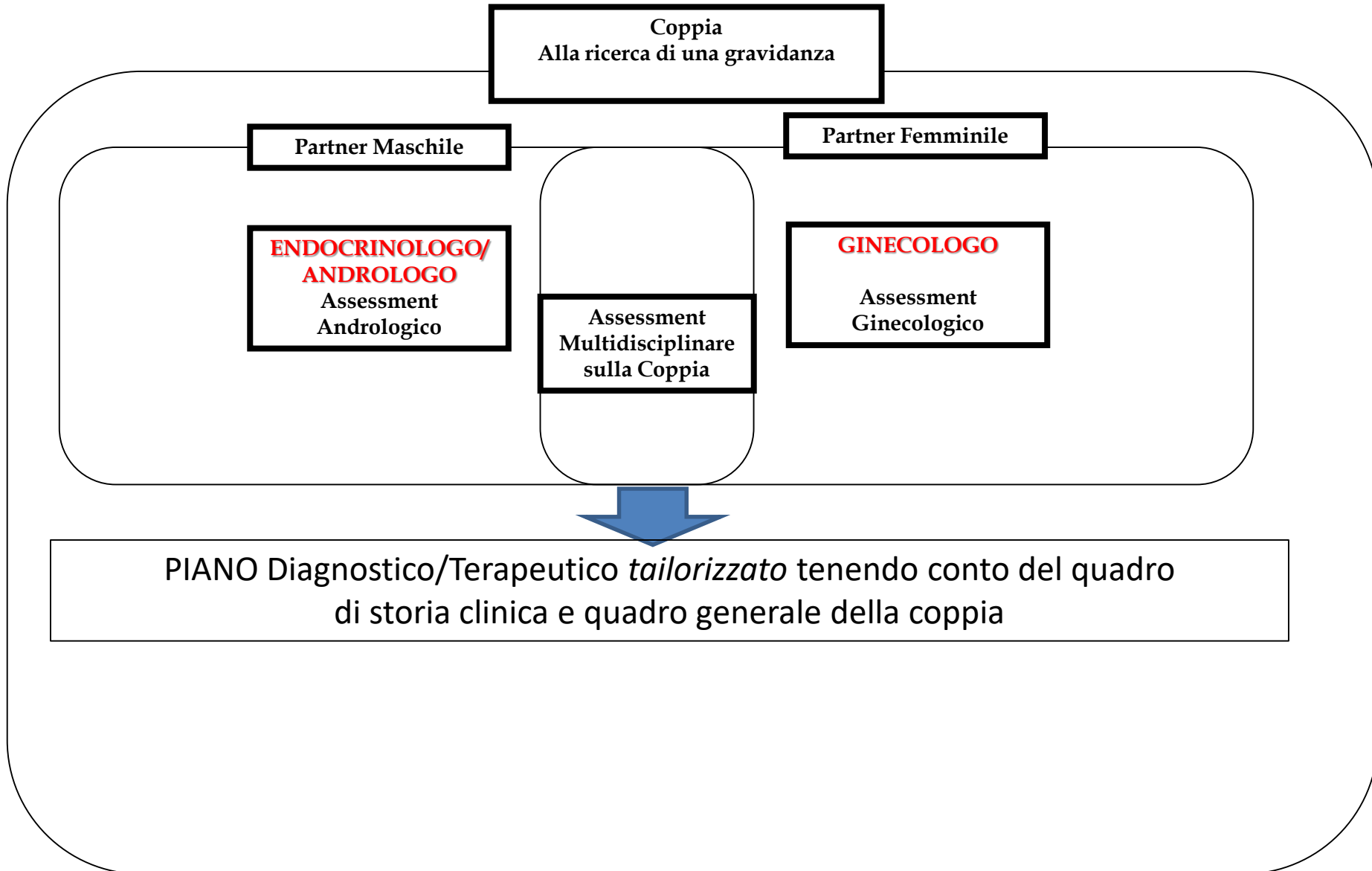


The European Academy of Andrology (EAA) ultrasound study on healthy, fertile men: Scrotal ultrasound reference ranges and associations with clinical, seminal, and biochemical characteristics

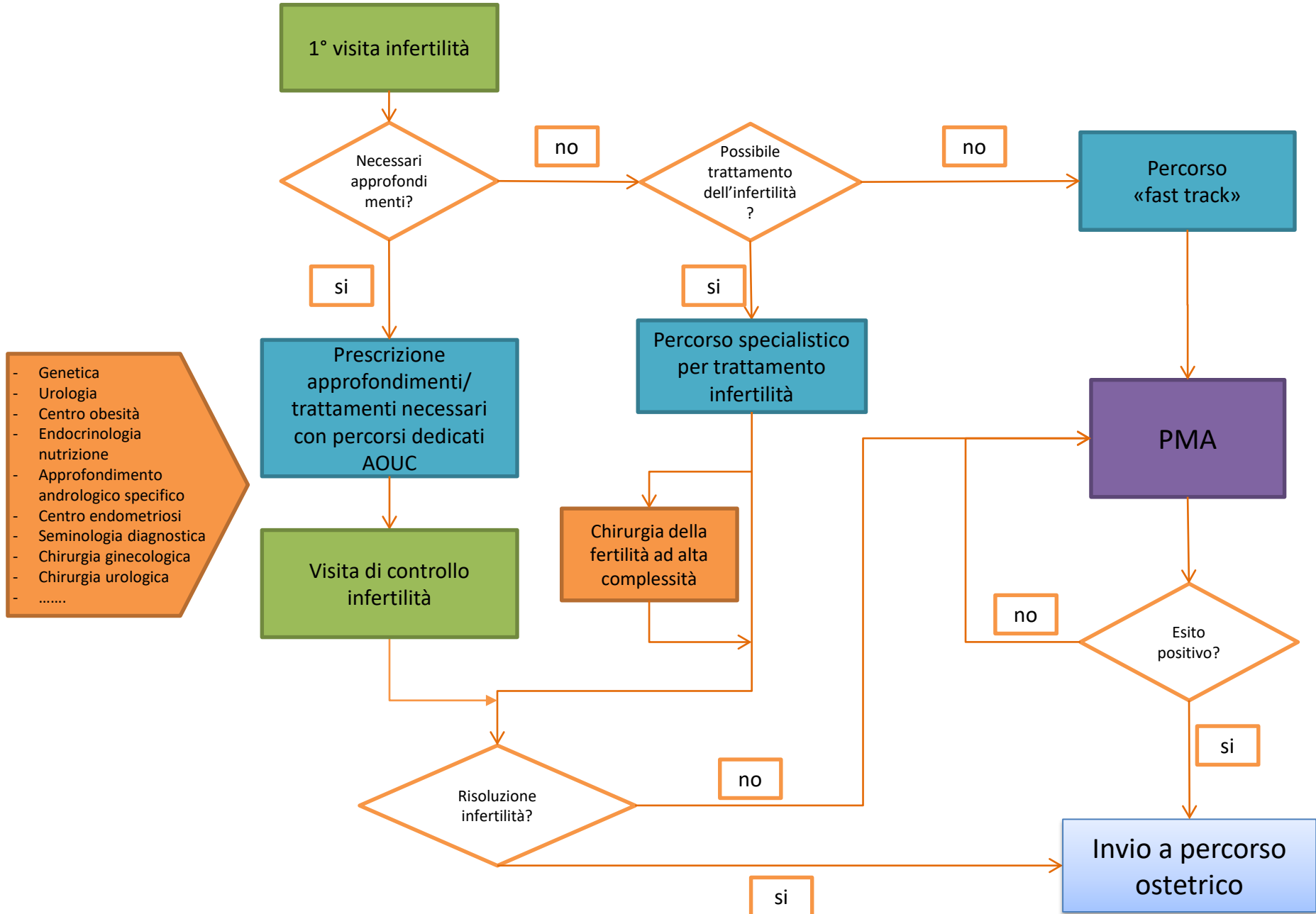
Lotti F<sup>1</sup> | Frizza F<sup>1</sup> | Balercia G<sup>2</sup> | Barbonetti A<sup>3</sup> | Behre HM<sup>4</sup> | Calogero AE<sup>5</sup> | Cremers JF<sup>6</sup> | Francavilla F<sup>3</sup> | Isidori AM<sup>7</sup> | Kliesch S<sup>6</sup> | La Vignera S<sup>5</sup> | Lenzi A<sup>7</sup> | Marcou M<sup>4</sup> | Pilatz A<sup>8</sup> | Poolamets O<sup>9</sup> | Punab M<sup>9</sup> | Peraza Godoy MF<sup>10</sup> | Rajmil O<sup>10</sup> | Salvio G<sup>2</sup> | Shaer O<sup>11</sup> | Weidner W<sup>8</sup> | Maseroli E<sup>1</sup> | Cipriani S<sup>1</sup> | Baldi E<sup>1</sup> | Degl'Innocenti S<sup>1</sup> | Danza G<sup>12</sup> | Caldini AL<sup>13</sup> | Terreni A<sup>13</sup> | Boni L<sup>14</sup> | Krausz C<sup>1</sup> | Maggi M<sup>12</sup>



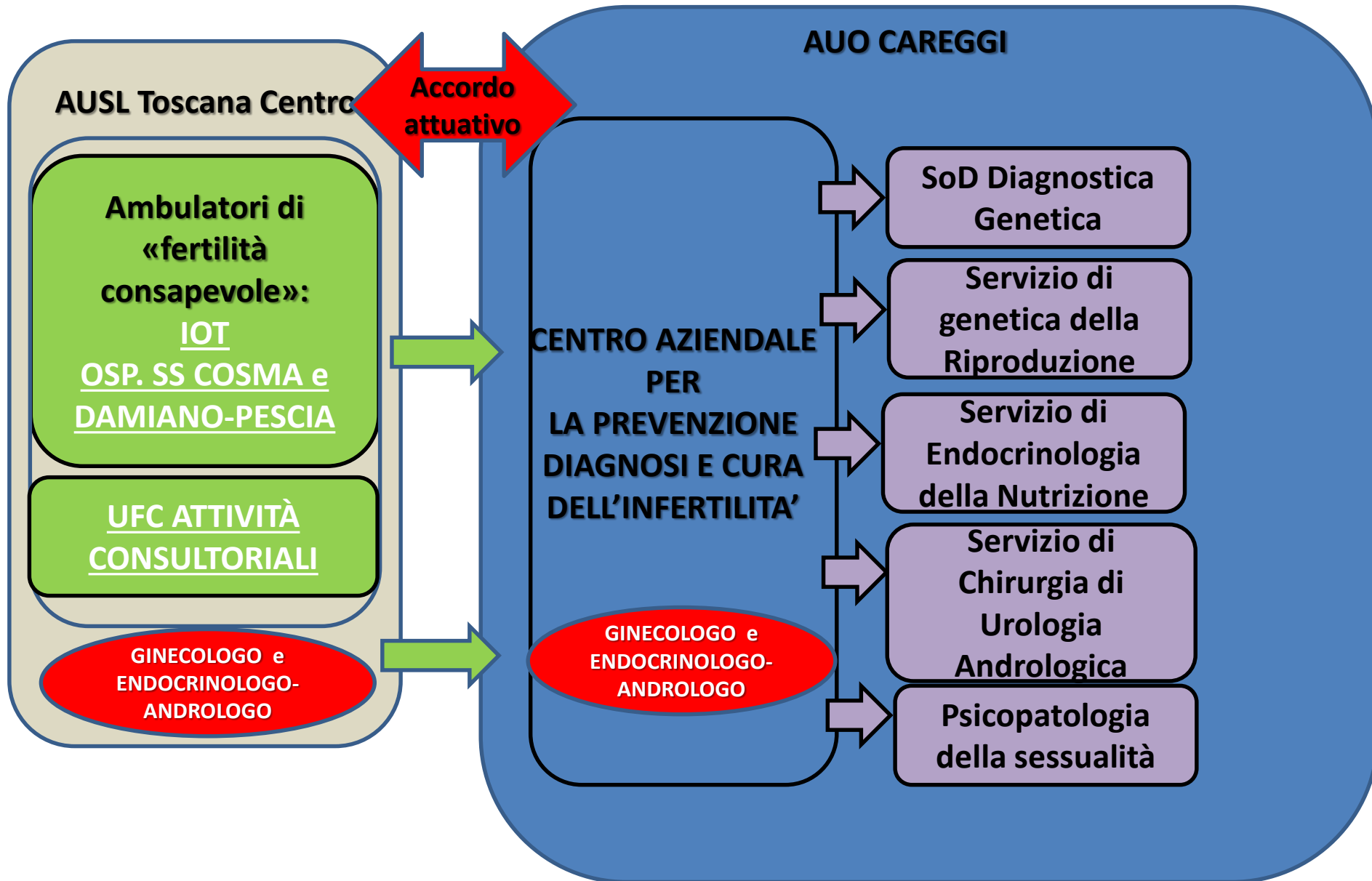
Lotti et al., unpublished



# PERCORSO DELLA COPPIA NEL CENTRO



# RAPPORTI DEL CENTRO CON ALTRE STRUTTURE

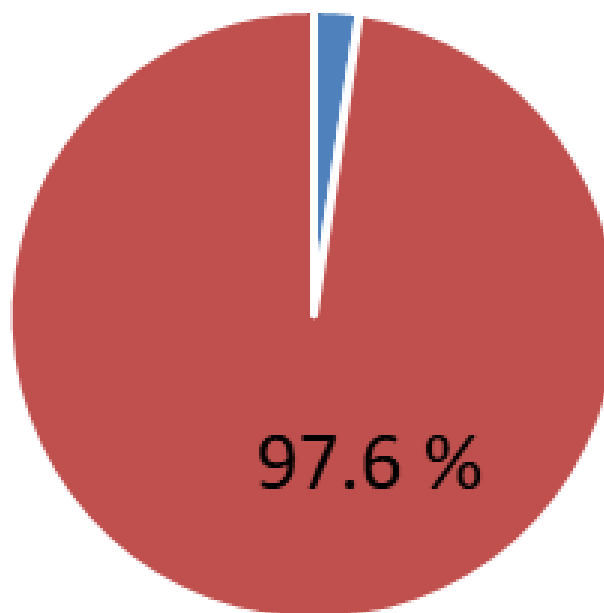


## Coppie già inviate per PMA e visitate al centro

Età media  $37 \pm 2$

Età media della partner :  $34 \pm 3.5$

PREGRESSA VALUTAZIONE ANDROLOGICA  
2.4 %



■ SI ■ NO

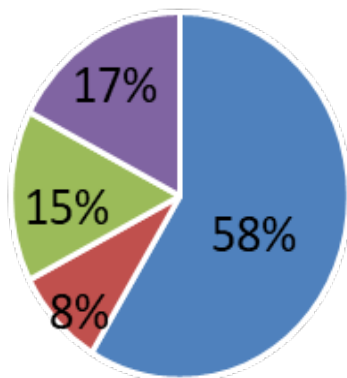


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**Età media  $37 \pm 2$**

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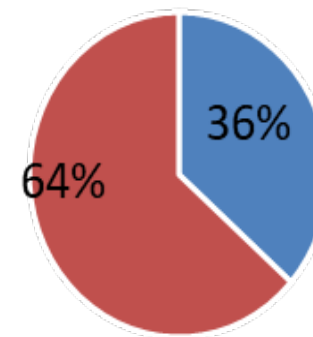
## ALTERAZIONE LIQUIDO SEMINALE



QUANDO PATOLOGICO



## RICHIESTA CONFERMA CON SECONDO SPERMIOGRAMMA



■ NORMOZOO ■ AZOO ■ OAT SEVERA ■ OAT MODERATA-LIEVE

■ CONFERMATO CON SECONDO SPERMIOGRAMMA ■ SINGOLO

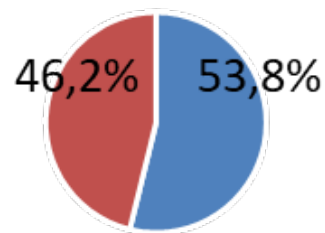
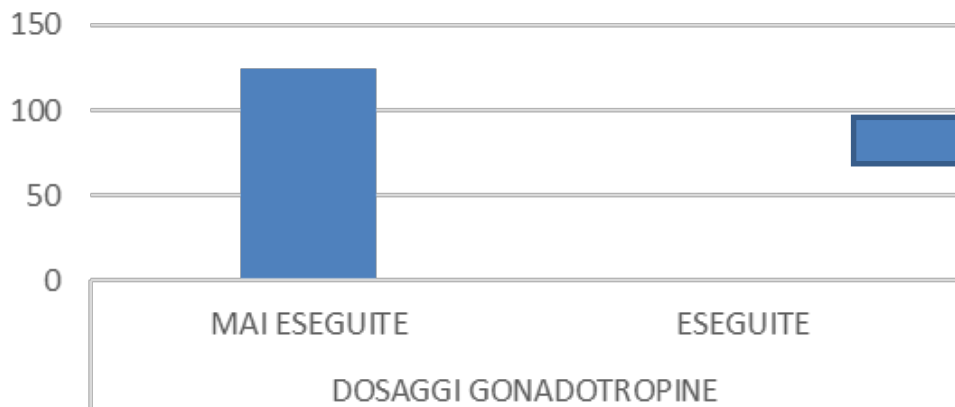
# Coppie già inviate per PMA e visitate al centro

**Età media  $37 \pm 2$**

**Età media della partner :  $34 \pm 3.5$**

DOSAGGI ORMONALI  
GONDATROPINE MASCHIO

Dosaggi ormonali richiesti durante la  
visita

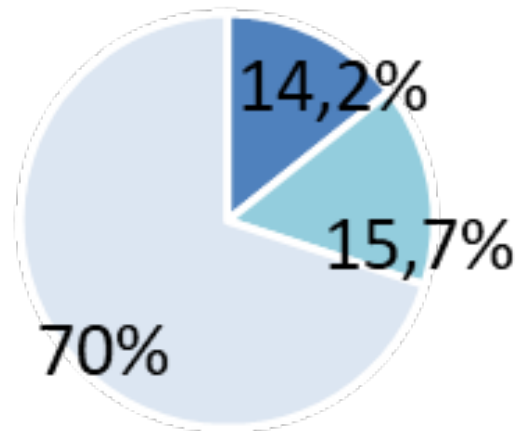


- RISULTATI DELL'ESECUZIONE DOSAGGIO PRESENTI
- RISULTATI DELL'ESECUZIONE DOSAGGIO ANCORA IN CORSO

DOSAGGI GONADOTROPINE

# Coppie già inviate per PMA e visitate al centro

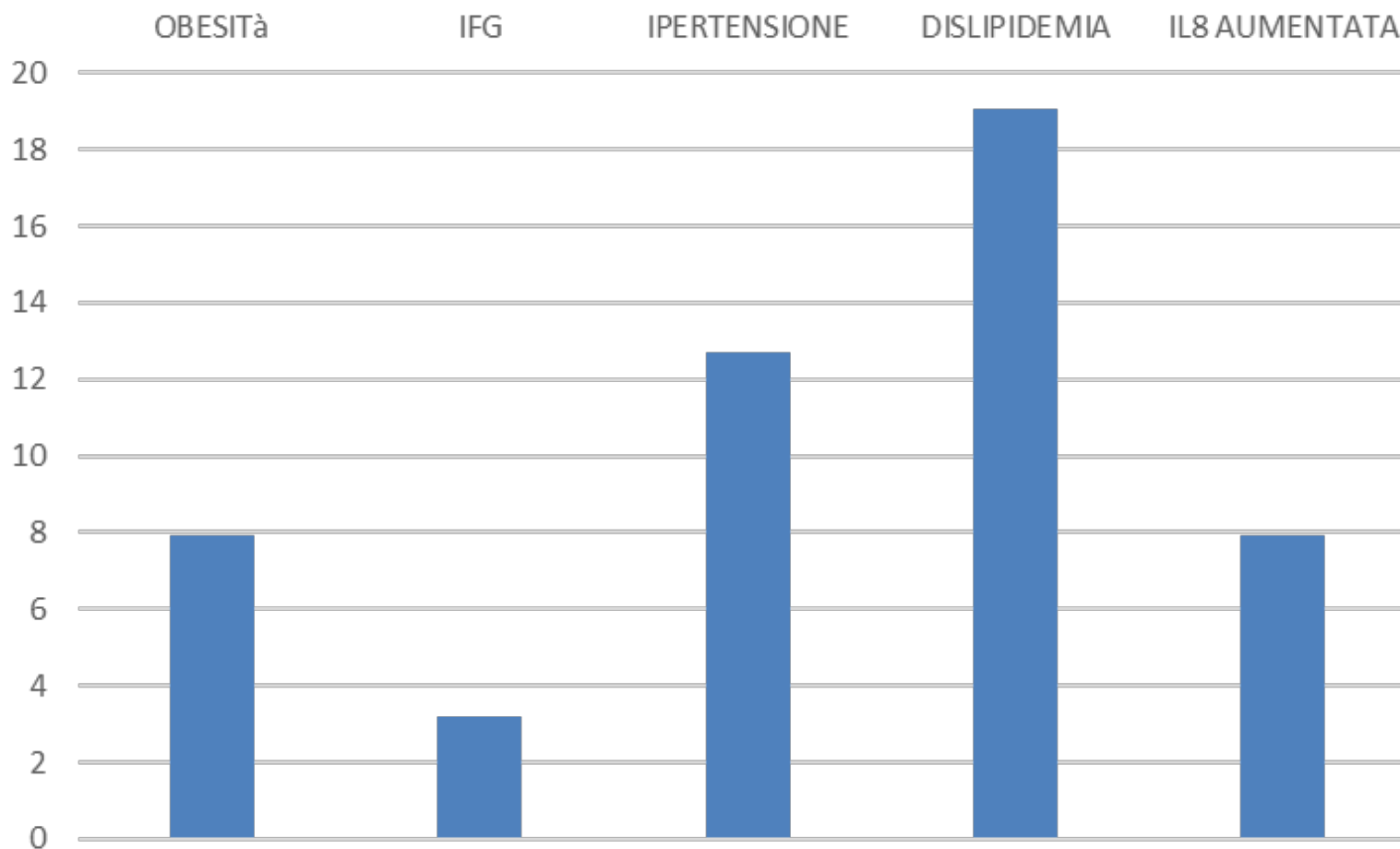
## DIAGNOSI DI IPOGONADISMO



- DOPO RICHIESTA DOSAGGI ORMONALI VALORI PATOLOGICI MERITEVOLI TRATTAMENTO ORMONALE SOSTITUTIVO
- DOPO RICHIESTA DOSAGGI ORMONALI VALORI PATOLOGICI FSH >8
- DOPO RICHIESTA DOSAGGI ORMONALI NORMALI

# Coppie già inviate per PMA e visitate al centro

## Diagnosi di fattori di rischio non convenzionali





**WARNING!**

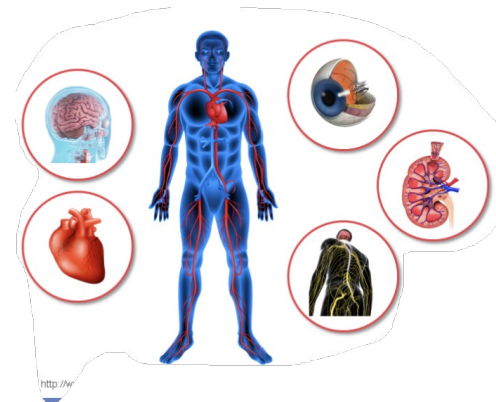
**GENDER  
MEDICINE  
ISSUE**

# Lack of Andrological evaluation leads to

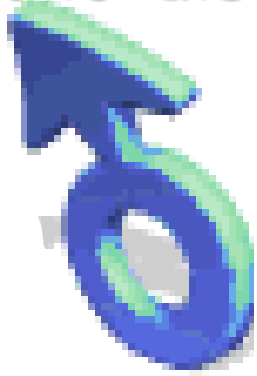
- Infertility as Female centered problem (and not a couple-centered one)



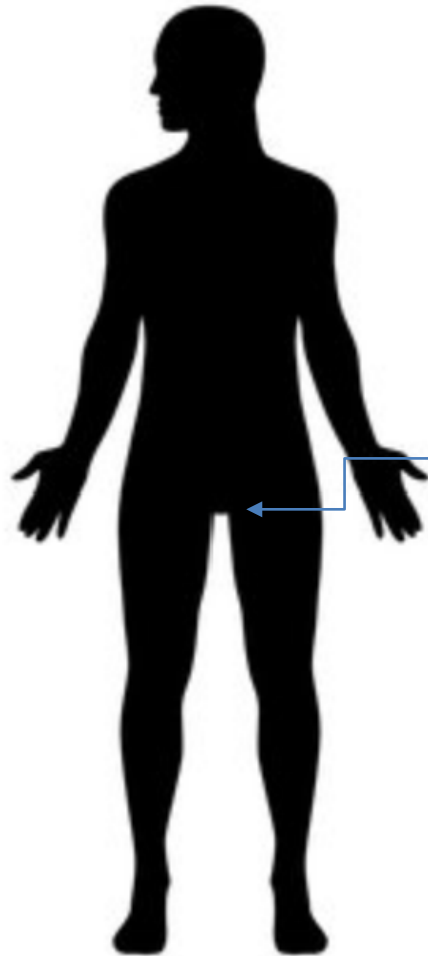
- Young male adults are not screened and diagnosed for high prevalent diseases that are associated to male infertility, such as the metabolic ones



# Metabolic diseases, obesity .....



Reproductive alterations



Sperm Alterations



# Clinical data

Human Reproduction Update, Vol.19, No.3 pp. 221–231, 2013

Advanced Access publication on December 12, 2012 doi:10.1093/humupd/dms050

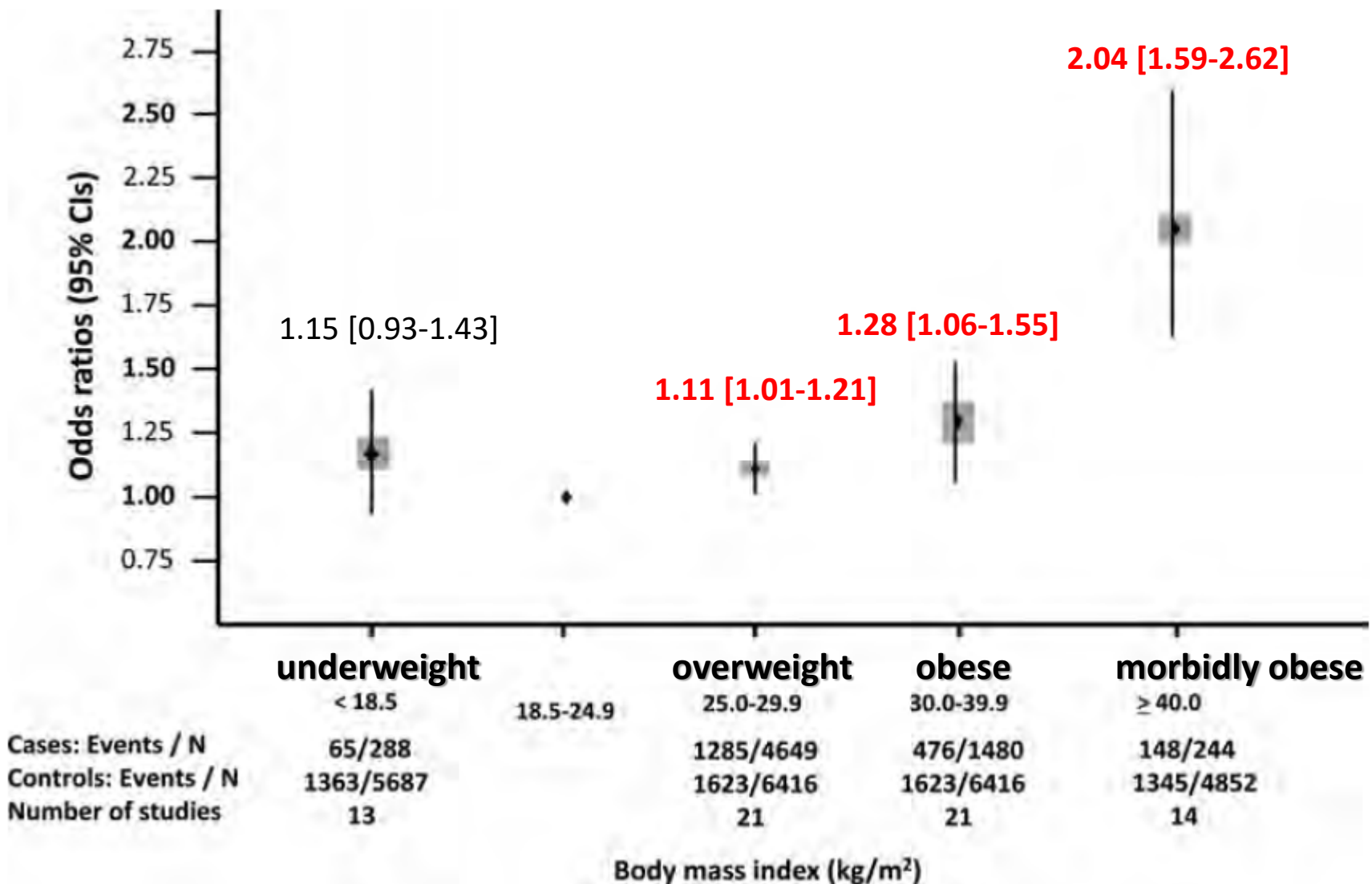
human  
reproduction  
update

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

N. Sermondade<sup>1,2</sup>, C. Faure<sup>1,2</sup>, L. Fezeu<sup>2</sup>, A.G. Shayeb<sup>3</sup>, J.P. Bonde<sup>4</sup>,  
T.K. Jensen<sup>5</sup>, M. Van Wely<sup>6</sup>, J. Cao<sup>7</sup>, A.C. Martini<sup>8</sup>, M. Eskandar<sup>9</sup>,  
J.E. Chavarro<sup>10,11</sup>, S. Koloszar<sup>12</sup>, J.M. Twigt<sup>13</sup>, C.H. Ramlau-Hansen<sup>14</sup>,  
E. Borges Jr<sup>15</sup>, F. Lotti<sup>16</sup>, R.P.M. Steegers-Theunissen<sup>13</sup>, B. Zorn<sup>17</sup>,  
A.J. Polotsky<sup>18</sup>, S. La Vignera<sup>19</sup>, B. Eskenazi<sup>20</sup>, K. Tremellen<sup>21</sup>,  
E.V. Magnusdottir<sup>22</sup>, I. Fejes<sup>23</sup>, S. Hercberg<sup>2,24</sup>, R. Lévy<sup>1,2†</sup>,  
and S. Czernichow<sup>25,26,\*†</sup>

**A total of 21 studies were included in the meta-analysis, resulting in a sample of 13 077 men from the general population and attending fertility clinics.**

# Association between BMI and abnormal TCS (oligozoospermia or azoospermia) according to categories of BMI.





# The relationship between male BMI and waist circumference on semen quality: data from the LIFE study

Michael L. Eisenberg<sup>1,\*</sup>, Sungduk Kim<sup>2</sup>, Zhen Chen<sup>2</sup>,  
Rajeshwari Sundaram<sup>2</sup>, Enrique F. Schisterman<sup>2</sup>, and  
Germaine M. Buck Louis<sup>2</sup>

<sup>1</sup>Departments of Urology, Obstetrics and Gynecology, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305-5118, USA <sup>2</sup>Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, 6100 Executive Blvd., Room 7B03, Rockville, MD 20852, USA

The LIFE study is a population-based prospective cohort of 501 couples attempting to conceive in two geographic areas (Texas and Michigan, USA) recruited in 2005–2009

**Table III** Association of abnormal semen quality end-points with anthropometric measurements and physical activity.

| Characteristic                           | Category    | Volume<br><1.5 ml, n (%) | Concentration<br><15 M/ml, n (%) | Sperm count<br><39 M, n (%) | Vitality<br><58% n (%) | WHO normal<br>morphology <30%, n (%) | Strict morphology<br>< 4%, n (%) | DFI > 30%,<br>n (%) |
|--|-------------|--------------------------|----------------------------------|-----------------------------|------------------------|--------------------------------------|----------------------------------|---------------------|
| <b>BMI</b><br>BMI (kg/m <sup>2</sup> )   | <25.0       | 8 (5.03)                 | 9 (5.66)                         | 9 (5.66)                    | 25 (15.72)             | 36 (45.00)                           | 2 (2.50)                         | 6 (7.32)            |
|  | 25.0–29.99  | 33 (9.59)                | 27 (7.85)                        | 24 (6.98)                   | 67 (19.48)             | 88 (49.44)                           | 8 (4.49)                         | 20 (10.47)          |
|  | 30.0–34.99  | 19 (8.92)                | 17 (7.98)                        | 17 (7.98)                   | 40 (18.78)             | 51 (43.59)                           | 4 (3.42)                         | 7 (5.88)            |
|  | ≥35.0       | 19 (15.20)               | 21 (16.80)                       | 24 (19.20)                  | 16 (13.11)             | 33 (54.10)                           | 4 (6.56)                         | 1 (1.49)            |
|  | P-trend*    | 0.033                    | 0.028                            | 0.005                       | 0.791                  | 0.549                                | 0.252                            | 0.035               |
| <b>WC</b><br>Waist circumference<br>(cm) | <93.99      | 19 (6.62)                | 17 (5.92)                        | 16 (5.57)                   | 53 (18.47)             | 65 (44.52)                           | 5 (3.42)                         | 9 (5.88)            |
|  | 94.0–101.59 | 26 (11.35)               | 17 (7.42)                        | 15 (6.55)                   | 42 (18.34)             | 62 (50.82)                           | 5 (4.10)                         | 16 (12.70)          |
|  | ≥101.6      | 34 (10.73)               | 38 (11.99)                       | 41 (12.93)                  | 48 (15.29)             | 79 (47.88)                           | 8 (4.85)                         | 9 (5.08)            |
|  | P-trend*    | 0.099                    | 0.025                            | 0.008                       | 0.459                  | 0.479                                | 0.377                            | 0.882               |
| Vigorous weekly<br>activity              | <1          | 56 (11.64)               | 44 (9.15)                        | 51 (10.60)                  | 87 (18.16)             | 116 (46.03)                          | 10 (3.97)                        | 19 (7.17)           |
|  | ≥1          | 23 (6.39)                | 30 (8.33)                        | 23 (6.39)                   | 61 (16.99)             | 92 (50.00)                           | 8 (4.35)                         | 15 (7.73)           |
|  | P-trend*    | 0.053                    | 0.64                             | 0.422                       | 0.8                    | 0.287                                | 0.972                            | 0.532               |

Each semen end-point was dichotomized as normal/abnormal according to WHO standard.

Semen parameters dichotomized per WHO 5th edition.

\*P-values of trend test based on linear models. In particular, linear mixed effects models were used for end-points measured in two semen samples, including volume, concentration, motility, total sperm count and vitality, while linear regression models were used for % WHO normal and the DFI. All models adjusted for age (<24, 25–29, 30–34, ≥35 years), college education (yes/no) and serum cotinine (non-smoker/active smoker).

## Men's body mass index in relation to embryo quality and clinical outcomes in couples undergoing in vitro fertilization

Daniela S. Colaci, M.D., M.Sc.,<sup>a</sup> Myriam Afeiche, Ph.D., M.P.H.,<sup>a</sup> Audrey J. Gaskins, B.S.E.,<sup>a</sup> Diane L. Wright, Ph.D.,<sup>b</sup> Thomas L. Toth, M.D.,<sup>b</sup> Cigdem Tanrikut, M.D.,<sup>c</sup> Russ Hauser, M.D., M.P.H., Sc.D.,<sup>b,d,e</sup> and Jorge E. Chavarro, M.D., Sc.D.<sup>a,d,f</sup>

<sup>a</sup> Department of Nutrition, Harvard School of Public Health, Harvard University; <sup>b</sup> Vincent Obstetrics and Gynecology, Massachusetts General Hospital and Harvard Medical School; <sup>c</sup> Department of Urology, Massachusetts General Hospital and Harvard Medical School; <sup>d</sup> Department of Epidemiology, Harvard School of Public Health; <sup>e</sup> Department of Environmental Health, Harvard School of Public Health; and <sup>f</sup> Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Harvard University, Boston, Massachusetts

## Possible deleterious effect of male obesity among couples undergoing ICSI

114 couples who underwent 172 assisted reproduction cycles

Odds ratios (95% CI) for clinical outcomes in couples undergoing assisted reproduction according to fertilization method (conventional in vitro fertilization and intracytoplasmic sperm injection).

| Clinical outcome                                      | No. of cycles | Male BMI                     |                            |                               | P trend          |
|---|---------------|------------------------------|----------------------------|-------------------------------|------------------|
|   |               | 18.5–24.99 kg/m <sup>2</sup> | 25–29.99 kg/m <sup>2</sup> | ≥ 30 kg/m <sup>2</sup>        |                  |
| <b>IVF cycles</b>                                     |               |                              |                            |                               |                  |
| Clinical pregnancy per initiated cycle <sup>a,b</sup> | 74            | Ref                          | 0.83 (0.34–2.06)           | 1.69 (0.52–5.46)              | .38              |
| Live birth per initiated cycle <sup>a,b</sup>         | 74            | Ref                          | 1.80 (0.58–5.65)           | 1.84 (0.48–7.06)              | .35              |
| Clinical pregnancy per embryo transfer <sup>c,b</sup> | 72            | Ref                          | 0.92 (0.38–2.22)           | 1.54 (0.47–5.06)              | .51              |
| Live birth per embryo transfer <sup>c,b</sup>         | 72            | Ref                          | 1.81 (0.59–1.71)           | 1.63 (0.43–6.16)              | .44              |
| <b>ICSI cycles</b>                                    |               |                              |                            |                               |                  |
| Clinical pregnancy per initiated cycle <sup>b,d</sup> | 91            | Ref                          | 0.57 (0.20–1.63)           | 0.62 (0.14–2.67)              | .35              |
| ● Live birth per initiated cycle <sup>b,d</sup>       | 91            | Ref                          | 0.40 (0.14–1.17)           | 0.20 (0.04–1.00)              | .03 <sup>f</sup> |
| Clinical pregnancy per embryo transfer <sup>b,e</sup> | 86            | Ref                          | 0.53 (0.16–1.68)           | 0.53 (0.11–2.55)              | .29              |
| ● Live birth per embryo transfer <sup>b,e</sup>       | 86            | Ref                          | 0.40 (0.12–1.37)           | 0.16 (0.03–0.90) <sup>f</sup> | .04 <sup>f</sup> |

Note: BMI = body mass index; ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization; Ref = reference value.

<sup>a</sup> 53 Couples initiate an IVF cycle and underwent 74 IVF cycles.

<sup>b</sup> Odds ratio (95% CI) adjusted for men's age, women's age, day-3 FSH level, infertility diagnosis, stimulation protocol, and women's BMI.

<sup>c</sup> 52 couples underwent 72 embryo transfers among IVF cycles.

<sup>d</sup> 55 couples initiated an ICSI cycle and underwent 91 ICSI cycles.

<sup>e</sup> 52 couples underwent 86 embryo transfers among ICSI cycles.

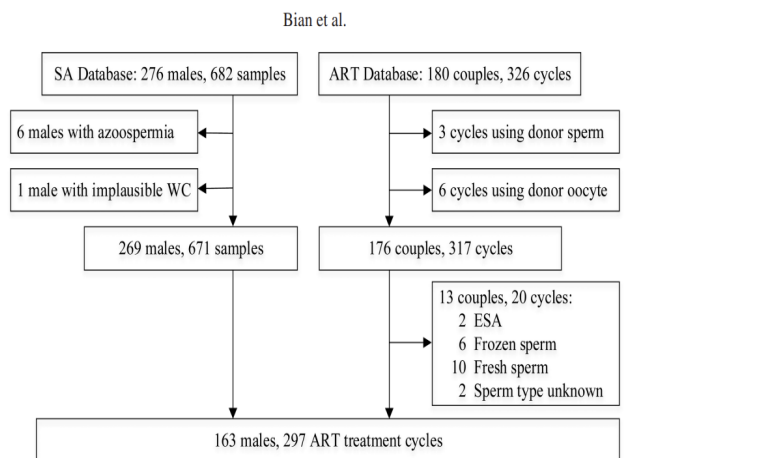
<sup>f</sup>  $P < .05$  compared with the reference group (men's BMI 19–24.99 kg/m<sup>2</sup>).

Colaci. Men's BMI and IVF outcomes. *Fertil Steril* 2012.

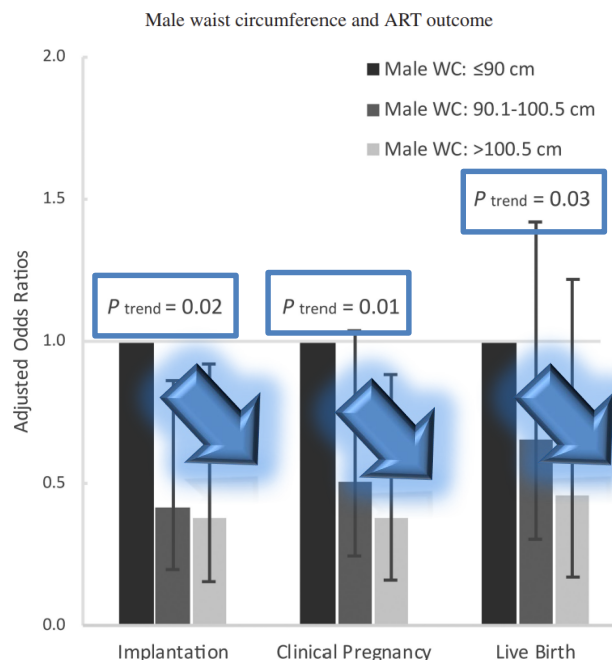
## Male waist circumference in relation to semen quality and partner infertility treatment outcomes among couples undergoing infertility treatment with assisted reproductive technologies

Haiyang Bian,<sup>1,2</sup> Lidia Mínguez-Alarcón,<sup>3</sup> Albert Salas-Huetos,<sup>1</sup> David Bauer,<sup>4</sup> Paige L Williams,<sup>5,6</sup> Irene Souter,<sup>7</sup> Jill Attaman,<sup>7</sup> and Jorge E Chavarro,<sup>1,5,8</sup> for the EARTH Study Team

834



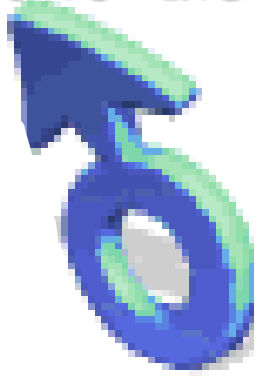
**FIGURE 1** Flowchart of the study participants. ART, assisted reproductive technology; ESA, epididymal sperm aspiration; SA, semen quality analysis; WC, waist circumference.



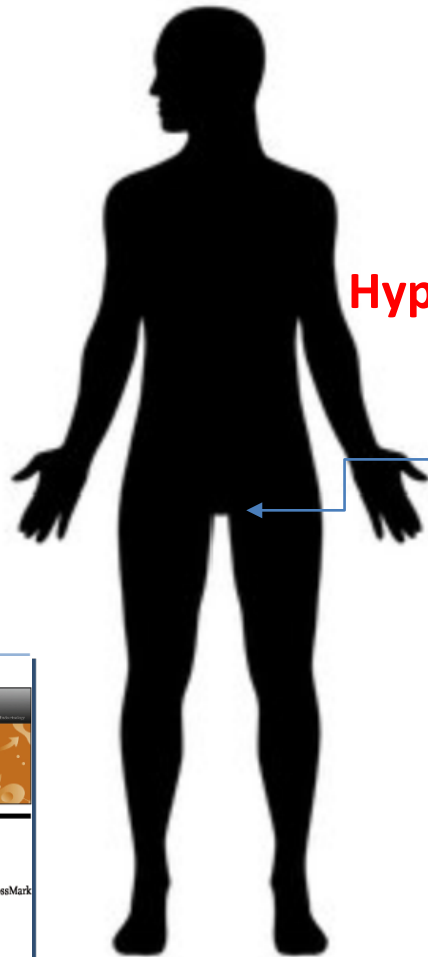
**After Adjustment for:**  
male age, BMI, height, race, education, smoking status, and history of varicocele, and their partner's age and BMI, height, education and primary infertility diagnosis (male factor, female factor, unexplained).

**FIGURE 2** Associations between male WC and infertility treatment outcomes in 176 couples (317 initiated cycles) from the Environment and Reproductive Health Study (2009–2019). The analyses were conducted using cluster-weighted generalized estimating equations with a binomial distribution and log link function with adjustment for male age (continuous) and BMI (continuous), height (continuous), race (White, non-White), education (high school or some college, college, graduate), smoking status (ever, never), and history of varicocele (yes, no), and their partner's age (continuous) and BMI (continuous), height (continuous), education (high school or some college, college, graduate), and primary infertility diagnosis (male factor, female factor, unexplained). WC, waist circumference.

# Metabolic diseases, obesity .....



Reproductive alterations



Hyperestrogenism      Inflammation

Sperm Alterations

Molecular and Cellular Endocrinology 401 (2015) 12–24

Contents lists available at ScienceDirect

Molecular and Cellular Endocrinology

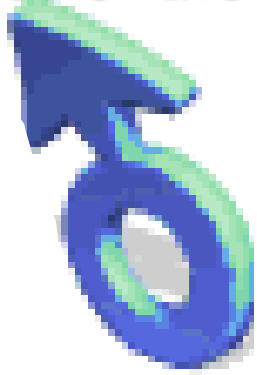
journal homepage: [www.elsevier.com/locate/mce](http://www.elsevier.com/locate/mce)

Metabolic syndrome-associated sperm alterations in an experimental rabbit model: Relation with metabolic profile, testis and epididymis gene expression and effect of tamoxifen treatment

Sara Marchiani <sup>a</sup>, Linda Vignozzi <sup>a</sup>, Sandra Filippi <sup>b</sup>, Bruna Gurrieri <sup>a</sup>, Paolo Comeglio <sup>a</sup>, Annamaria Morelli <sup>c</sup>, Giovanna Danza <sup>d</sup>, Gianluca Bartolucci <sup>e</sup>, Mario Maggi <sup>a</sup>, Elisabetta Baldi <sup>a\*</sup>

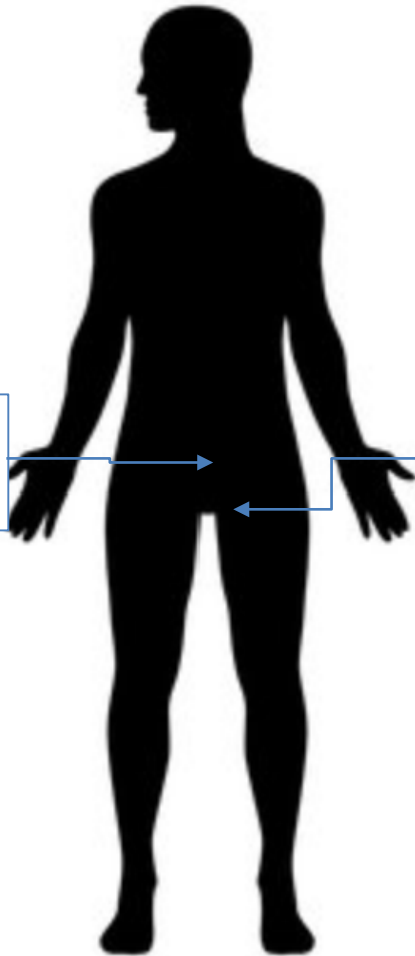


# Metabolic diseases, obesity .....



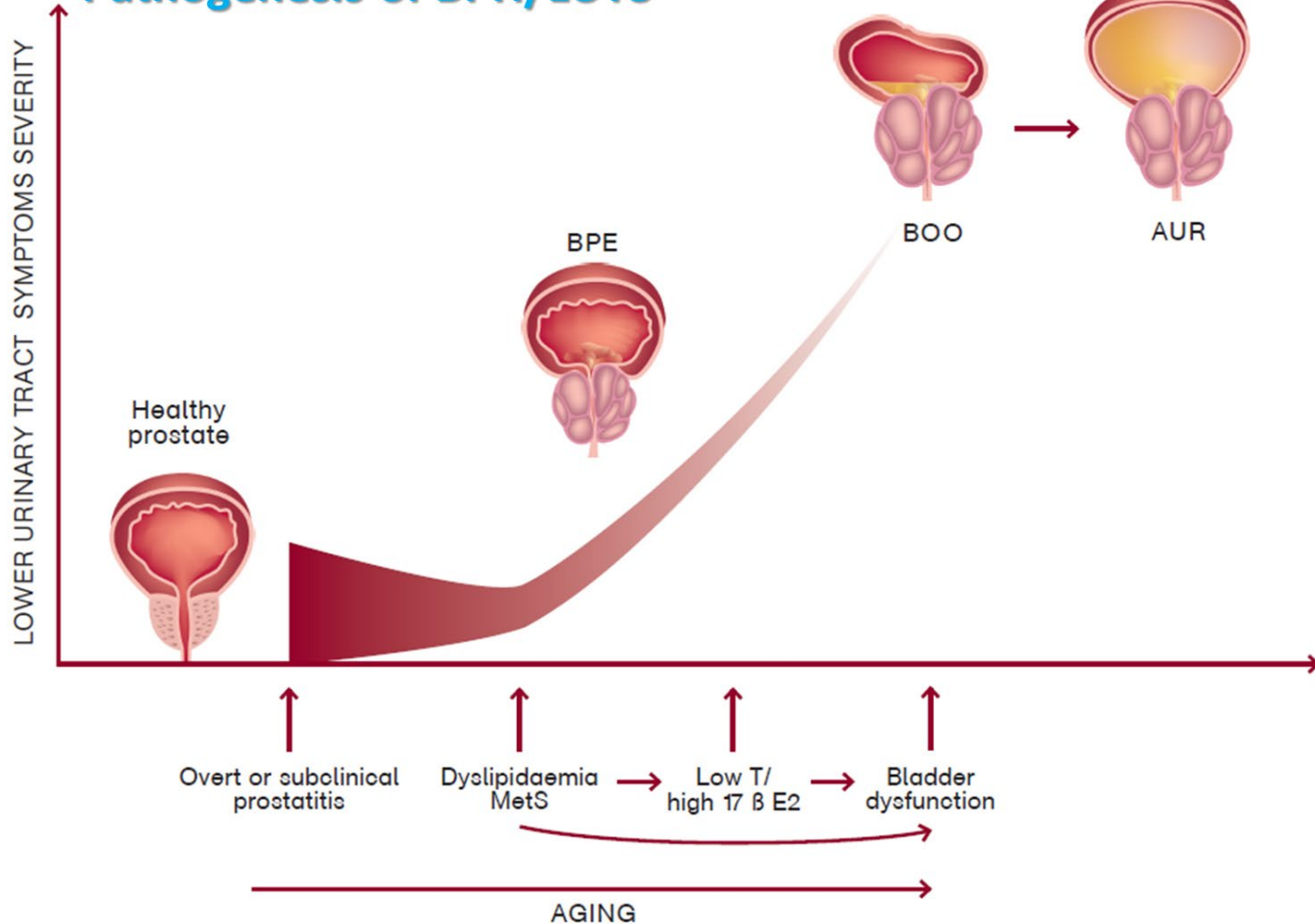
Reproductive alterations

Male accessory  
Gland inflammation



Sperm Alterations

# Pathogenesis of BPH/LUTS



**Lotti et al.,** J Endocrinol Invest. 2011;34:e336

**Vignozzi et al.,** J Endocrinol Invest. 2014 Apr;37(4):313-22.

doi: 10.1007/s40618-014-0051-3. Epub 2014 Jan 24. PubMed PMID: 24458832.

**Vignozzi L et al** Prostate. 2013 Sep;73(13):1391-402. doi:

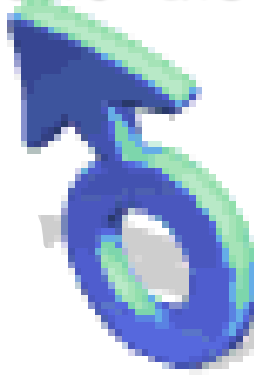
10.1002/pros.22686.

Epub 2013 Jun 13. PubMed PMID: 23765639.

**Vignozzi L et al.,** Prostate. 2013 Jun;73(8):789-800. doi:

10.1002/pros.22623. Epub 2012 Nov 28. PubMed PMID: 236202

# Metabolic diseases, obesity .....

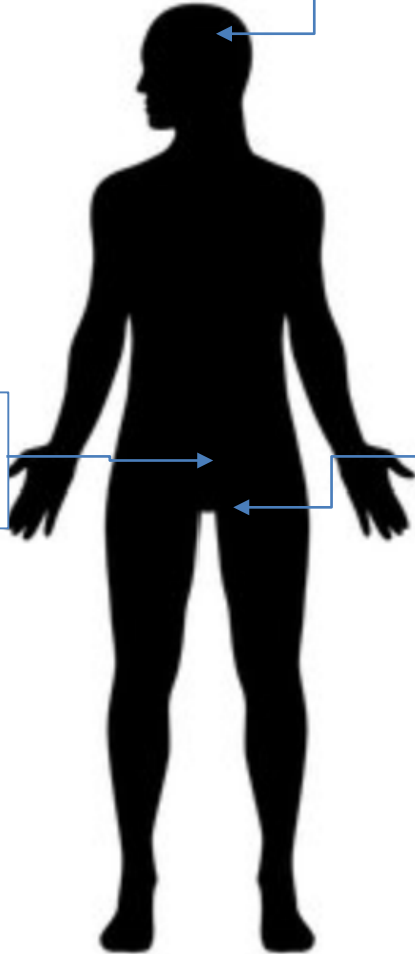


## Reproductive alterations

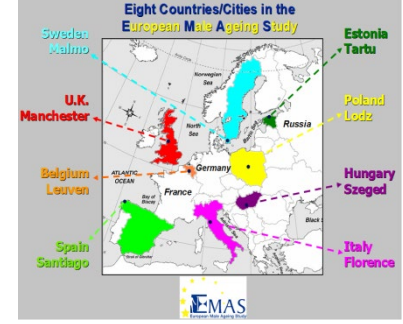
Hypogonadotropic  
Hypogonadism

Male accessory  
Gland inflammation

Sperm Alterations





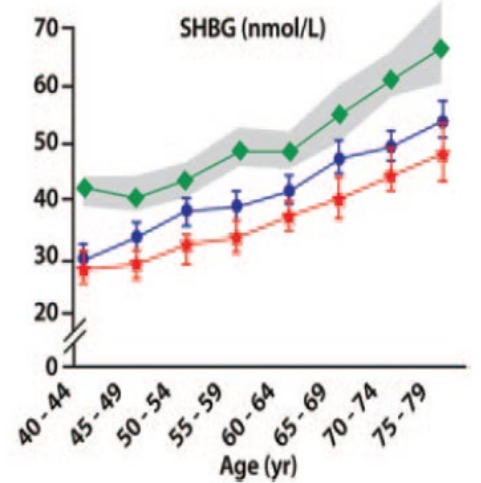
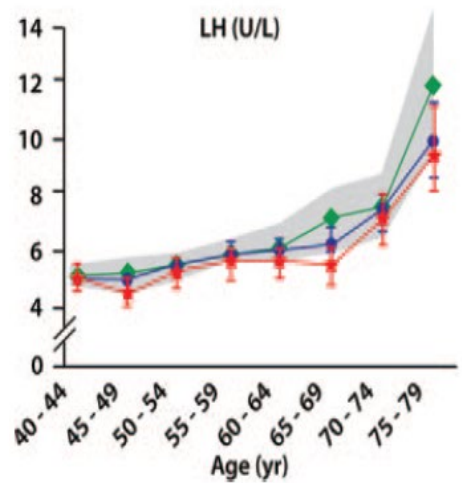
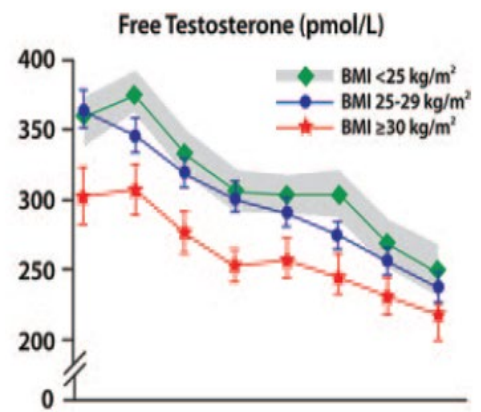
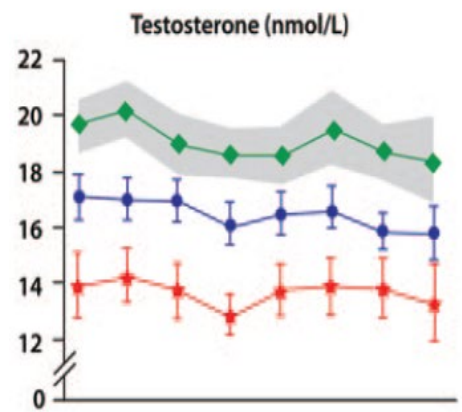
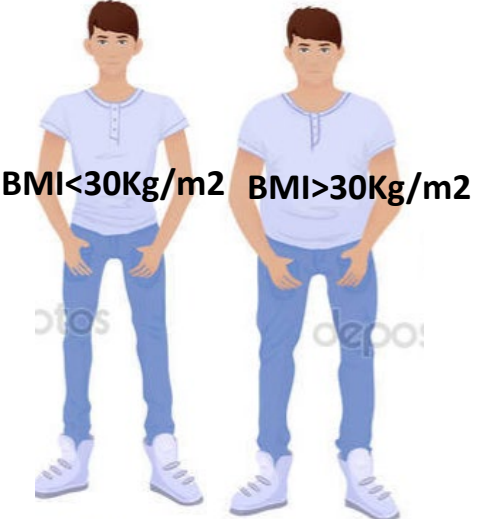


# Hypothalamic-Pituitary-Testicular Axis Disruptions in Older Men Are Differentially Linked to Age and Modifiable Risk Factors: The European Male Aging Study

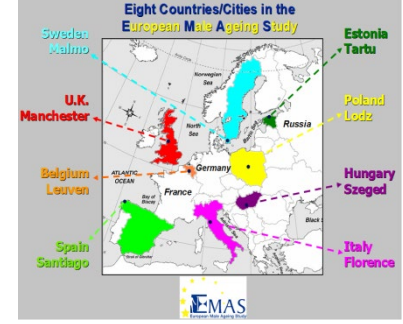
Frederick C. W. Wu, Abdelouahid Tajar, Stephen R. Pye, Alan J. Silman, Joseph D. Finn, Terence W. O'Neill, Gyorgy Bartfai, Felipe Casanueva, Gianni Forti, Aleksander Giwercman, Ilpo T. Huhtaniemi, Krzysztof Kula, Margus Punab, Steven Boonen, Dirk Vanderschueren, and The European Male Ageing Study Group

J Clin Endocrinol Metab, July 2008, 93(7):2737-2745

dojournals.org). Thus, a change in BMI from nonobese to obese may be equivalent to a 15 yr fall in T. Similar findings have recently been reported in longitudinal U.S. population studies (26). It is noteworthy that the effects of obesity on the HPT axis





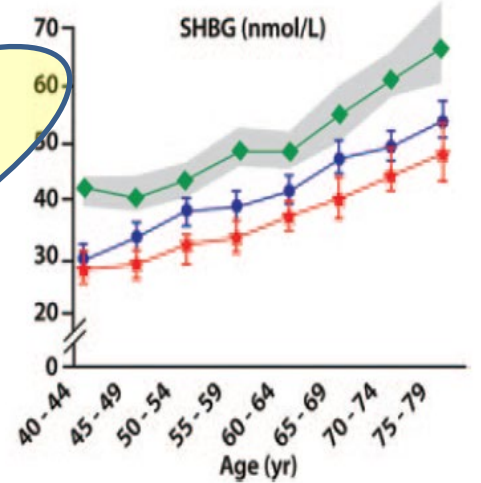
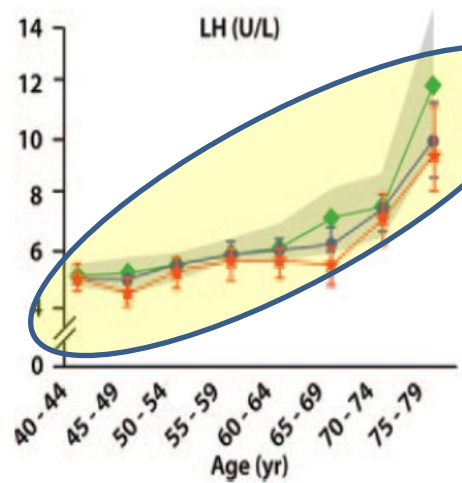
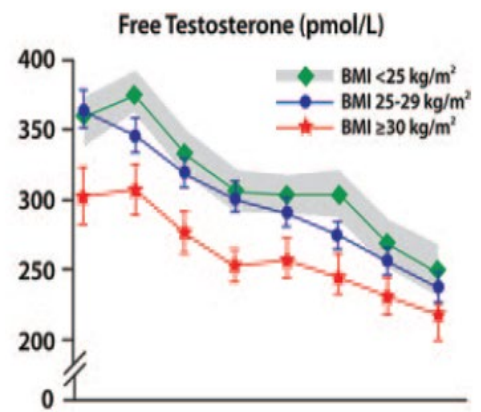
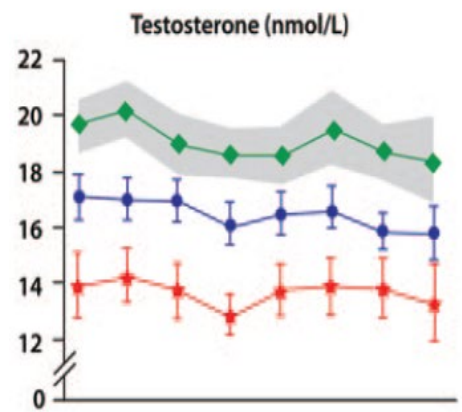
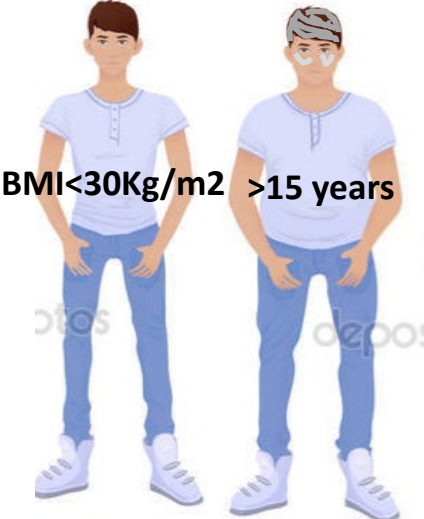


# Hypothalamic-Pituitary-Testicular Axis Disruptions in Older Men Are Differentially Linked to Age and Modifiable Risk Factors: The European Male Aging Study

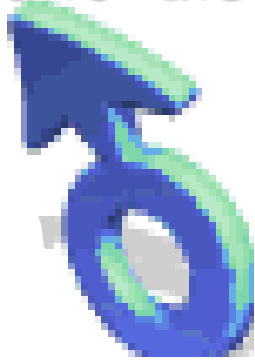
Frederick C. W. Wu, Abdelouahid Tajar, Stephen R. Pye, Alan J. Silman, Joseph D. Finn, Terence W. O'Neill, Gyorgy Bartfai, Felipe Casanueva, Gianni Forti, Aleksander Giwercman, Ilpo T. Huhtaniemi, Krzysztof Kula, Margus Punab, Steven Boonen, Dirk Vanderschueren, and The European Male Ageing Study Group

J Clin Endocrinol Metab, July 2008, 93(7):2737-2745

dojournals.org). Thus, a change in BMI from nonobese to obese may be equivalent to a 15 yr fall in T. Similar findings have recently been reported in longitudinal U.S. population studies (26). It is noteworthy that the effects of obesity on the HPT axis



# Metabolic diseases, obesity .....



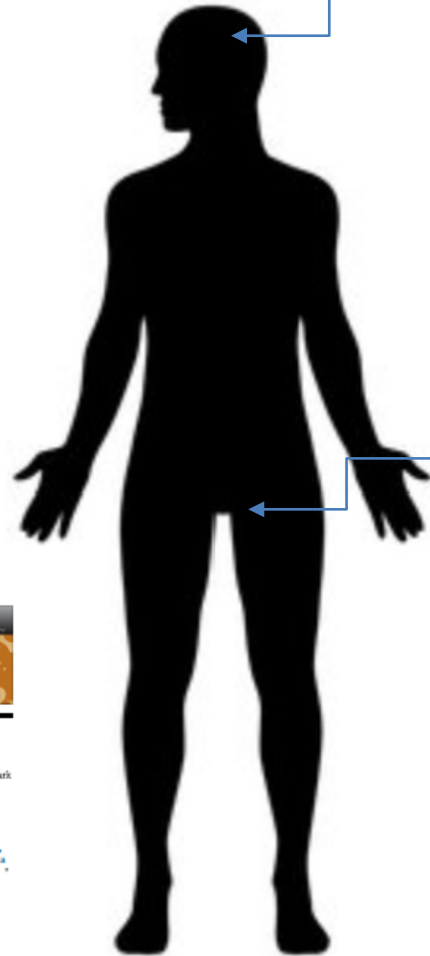
Reproductive alterations

Hyperestrogenism

Inflammation



Hypogonadotropic  
Hypogonadism



Sperm Alterations

CLINICAL RESEARCH ARTICLE

## Tumor Necrosis Factor- $\alpha$ Impairs Kisspeptin Signaling in Human Gonadotropin-Releasing Hormone Primary Neurons

Erica Sarchielli,<sup>1</sup> Paolo Comeglio,<sup>4</sup> Roberta Squecco,<sup>2</sup> Lara Ballerini,<sup>3</sup> Tommaso Mello,<sup>3</sup> Giulia Guarnieri,<sup>1</sup> Eglantina Idrizaj,<sup>2</sup> Benedetta Mazzanti,<sup>3</sup> Linda Vignozzi,<sup>4</sup> Pasquale Gallina,<sup>6</sup> Mario Maggi,<sup>4,7</sup> Gabriella B. Vannelli,<sup>1</sup> and Annamaria Morelli<sup>1</sup>

<sup>1</sup>Section of Human Anatomy and Histology, <sup>2</sup>Section of Physiological Sciences, and <sup>3</sup>Cell Therapy and Transfusion Medicine Unit, Department of Experimental and Clinical Medicine, University of Florence, 50134 Florence, Italy; <sup>4</sup>Sexual Medicine and Andrology Unit and <sup>5</sup>Gastroenterology Unit, Department of Experimental and Clinical Biomedical Sciences "Mario Serio," University of Florence, 50134 Florence, Italy; <sup>6</sup>Neurosurgery School of Tuscany, Department of Surgery and Translational Medicine, University of Florence, 50139 Florence, Italy; and <sup>7</sup>Istituto Nazionale Biostrutture e Biosistemi, 00136 Rome, Italy

Molecular and Cellular Endocrinology 382 (2014) 107–119

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journal homepage: [www.elsevier.com/locate/mce](http://www.elsevier.com/locate/mce)



Metabolic syndrome induces inflammation and impairs gonadotropin-releasing hormone neurons in the preoptic area of the hypothalamus in rabbits



Annamaria Morelli<sup>a</sup>, Erica Sarchielli<sup>a</sup>, Paolo Comeglio<sup>b</sup>, Sandra Filippi<sup>c</sup>, Linda Vignozzi<sup>b</sup>, Mirca Marini<sup>a</sup>, Giulia Rastrelli<sup>b</sup>, Elena Maneschi<sup>b</sup>, Ilaria Cellai<sup>b</sup>, Luca Persani<sup>d,f</sup>, Luciano Adorini<sup>e</sup>, Gabriella B. Vannelli<sup>a</sup>, Mario Maggi<sup>b,g,\*</sup>

# TREATMENT of HYPOGONADOTROPIC HYPOGONADISM

**Goal:** IMPROVEMENT OF SEMEN  
QUALITY



## *Gonadotropins*

- HCG
- HCG + FSH
- HCG & FSH

## Nota 74

Farmaco in nota: Urofollitropina, Menotropina, Lutropina alfa, Follitropina delta, Follitropina beta, Follitropina alfa/Lutropina alfa, Follitropina alfa, Coriogonadotropina alfa, Corifollitropina alfa

Farmaci per l'infertilità  
femminile e maschile:

- Corifollitropina alfa
- Coriogonadotropina alfa
- Follitropina alfa
- Follitropina alfa/Lutropina alfa
- Follitropina beta
- Follitropina delta
- Lutropina alfa
- Menotropina
- Urofollitropina

*La prescrizione a carico del SSN, su diagnosi e piano terapeutico di strutture specialistiche, secondo modalità adottate dalle Regioni e dalle Province Autonome di Trento e Bolzano, è limitata alle seguenti condizioni:*

- trattamento dell'infertilità femminile: in donne di età non superiore ai 45 anni con valori di FSH, al 3° giorno del ciclo, non superiori a 30 mUI/ml
- trattamento dell'infertilità maschile: in maschi con ipogonadismo-  
ipogonadotropo con livelli di gonadotropine bassi o normali e comunque con FSH non superiore a 8 mUI/ml
- preservazione della fertilità femminile: in donne di età non superiore ai 45 anni affette da patologie neoplastiche che debbano sottoporsi a terapie oncologiche in grado di causare sterilità transitoria o permanente.
- Corifollitropina alfa
- Coriogonadotropina alfa
- Follitropina alfa
- Follitropina beta
- Follitropina delta
- Menotropina
- Urofollitropina



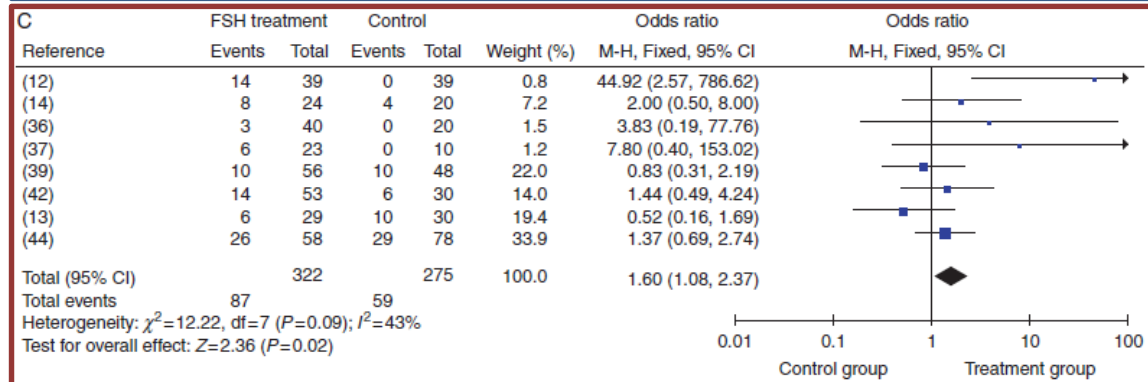
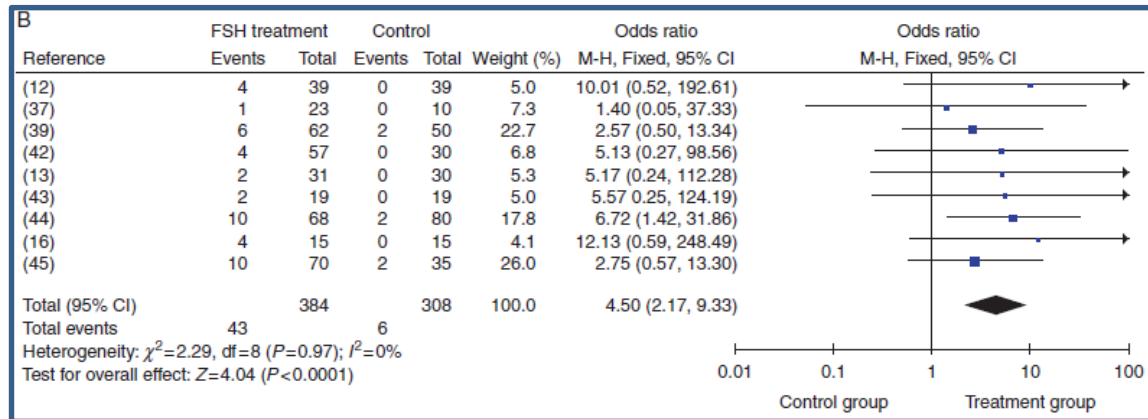
All controlled clinical trials;  
Randomization not  
considered as an inclusion criterion

# FSH treatment of male idiopathic infertility improves pregnancy rate: a meta-analysis

spontaneous pregnancy rate  
after FSH administration

pregnancy rate during ART  
after FSH administration

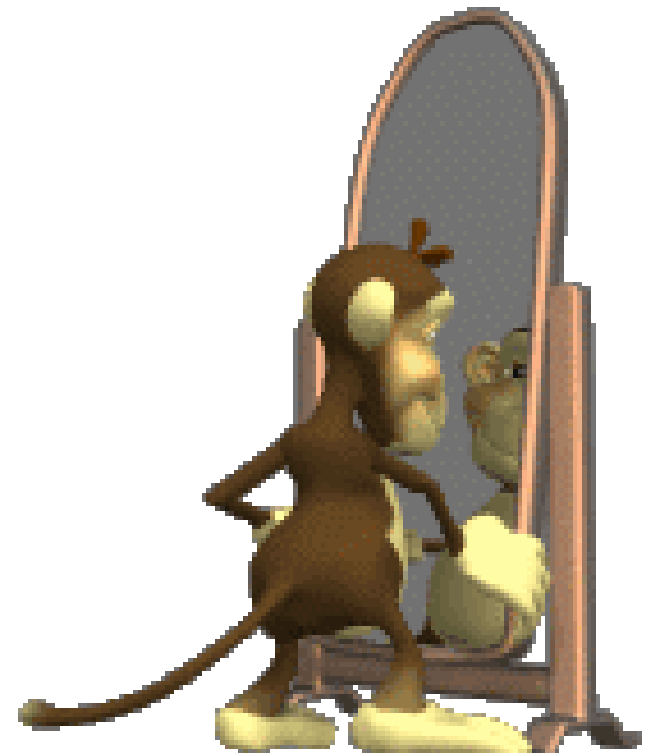
Santi et al. Endocrine Connections 2015



The number needed to treat (NNT) is high:  
from 10 to 18 men should be treated to achieve one pregnancy

# Final Remarks:

- **Male partner of an infertile couple should be carefully assessed (NOT ONLY A SEMEN ANALYSIS!!!!)**





**THANK YOU FOR  
YOUR ATTENTION!**