Η ΑΝΑΠΑΡΑΓΩΓΙΚΗ ΛΕΙΤΟΥΡΓΙΑ ΤΟΥ ΑΝΔΡΑ ΩΣ ΔΕΙΚΤΗΣ ΤΗΣ ΓΕΝΙΚΗΣ ΥΓΕΙΑΣ ΤΟΥ

Βασιλική Συρίου, Ενδοκρινολόγος, Διευθύντρια ΕΣΥ, ΓΝΑ << Η ΕΛΠΙΣ >>

ΔΗΛΩΝΩ

- ΤΗΝ ΜΗ ΥΠΑΡΞΗ ΣΥΜΦΕΡΟΝΤΟΣ
- ΑΠΟ ΤΙΣ ΕΤΑΙΡΕΙΕΣ ΧΟΡΗΓΟΥΣ ΤΟΥ ΣΥΝΕΔΡΙΟΥ

- 11-05-2019

2017: American Medical Association

Αναγνώρισε την υπογονιμότητα σαν ξεχωριστή νόσο με δυνητικά μακροπρόθεσμες επιπτώσεις στην υγεία γυναικών & ανδρών

Infertility : “canary in the coal mine.” ??

Fertility : rejuvenating factor ??

Fertility as a window to health Kurt T. Barnhart Fertil Steril 2018;110: 781–2

ΜΕ ΟΦΕΛΟΣ ??

Ενα μεγαλο ποσοστό πληθυσμού (του υπογόνιμου),
από την αναπαραγωγική ηλικία ακόμα,
θα πρέπει να αντιμετωπίζεται προληπτικά για συγκεκριμμένα μελλοντικά νοσήματα ?

ΣΤΑ **3** ΚΑΤΩΘΙ ΠΕΔΙΑ ΑΝΑΖΗΤΟΥΝ ΟΙ ΕΡΕΥΝΗΤΕΣ ΤΗΝ ΑΠΑΝΤΗΣΗ ΣΧΕΤΙΚΑ ΜΕ ΤΟ ΑΝ Η ΑΝΔΡΙΚΗ ΑΝΑΠΑΡΑΓΩΓΙΚΗ ΙΚΑΝΟΤΗΤΑ ΑΠΟΤΕΛΕΙ ΔΕΙΚΤΗ ΤΗΣ ΥΓΕΙΑΣ ΤΟΥ ΑΝΔΡΑ ΣΥΝΟΛΙΚΑ

ΓΕΝΕΤΙΚΟΙ ΛΟΓΟΙ (10% ΤΟΥ ΑΝΘΡΩΠΙΝΟΥ ΓΟΝΙΔΙΩΜΑΤΟΣ ΕΜΠΛΕΚΕΤΑΙ

ΣΤΗΝ ΑΝΑΠΑΡΑΓΩΓΗ ΚΑΙ ΟΧΙ ΜΟΝΟ)

ΑΝΑΠΤΥΞΙΑΚΗ ΔΙΑΔΙΚΑΣΙΑ : ΕΝΔΟΜΗΤΡΙΑ – ΕΜΒΡΥΙΚΗ & ΝΕΟΓΝΙΚΗ ΖΩΗ

(ΠΕΡΙΒΑΛΛΟΝ, ΓΕΝΕΤΙΚΗ)

ΣΥΝΗΘΕΙΕΣ & ΤΡΟΠΟΣ ΖΩΗΣ

Male infertility as a window to health Jeremy T. Choy et al Fertil Steril 2018;110:810–4.

ΕΛΑΧΙΣΤΕΣ ΟΙ ΠΡΟΟΠΤΙΚΕΣ ΤΥΧΑΙΟΠΟΙΗΜΕΝΕΣ ΜΕΛΕΤΕΣ ΜΕ ΟΜΑΔΑ ΕΛΕΓΧΟΥ ΚΑΙ ΜΑΚΡΟΧΡΟΝΙΑ ΠΑΡΑΚΟΛΟΥΘΗΣΗ

ΠΟΥ ΤΕΚΜΗΡΙΩΝΟΥΝ ΤΗΝ ΣΧΕΣΗ ΥΠΟΓΟΝΙΜΟΤΗΤΑΣ ΜΕ ΤΗΝ ΜΕΛΛΟΝΤΙΚΗ ΝΟΣΗΡΟΤΗΤΑ & ΘΝΗΤΟΤΗΤΑ

ΠΡΟΟΠΤΙΚΗ ΜΕΛΕΤΗ 5177 ♂ υπογόνιμων ζευγαριών, με πλήρη έλεγχο, έδειξαν ↑ νοσηρότητα & θνησιμότητα σε σχέση με την ομάδα ελέγχου

Οι υπογόνιμοι ♂ είχαν κυρίως

- υπογοναδισμό
- μεταβολικές διαταραχές
- οστεοπόρωση

Low sperm :

1. υπογοναδισμό (↓ BMD → 51% με οστεοπενία & οστεοπόρωση)
2. υψηλότερο BMI
3. ↑ W/H ratio
4. ↑ συστολική πίεση
5. ↑ LDL, Tg, HOMA index
6. ↓ HDL…….δηλ. ↑ MS

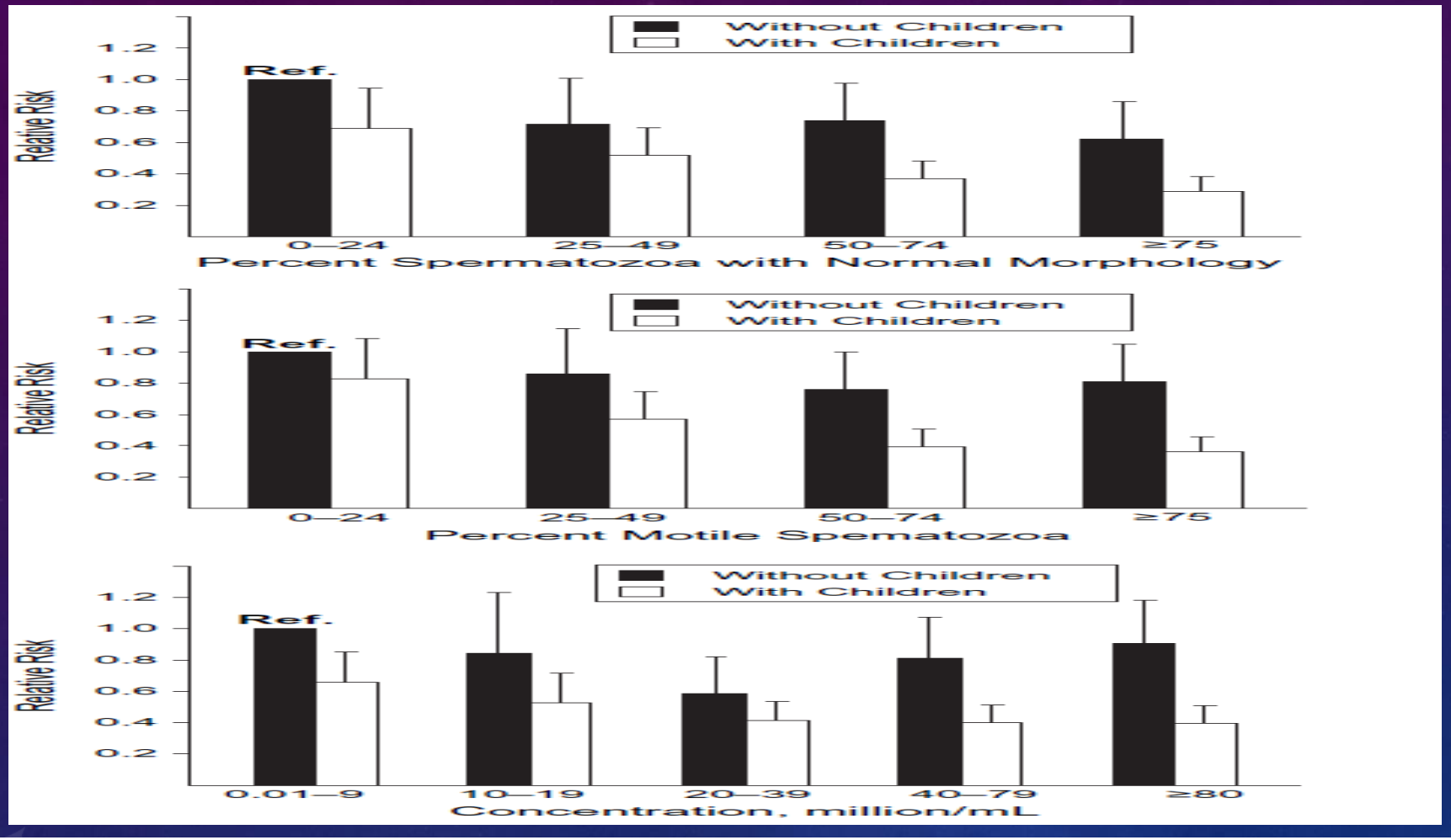
Lipid Concentrations and Couple Fecundity: The LIFE Study Enrique F. Schisterman et al. JCEM 99: 2786–2794, 2014

Alberto Ferlin, 10th European Congress of Andrology, 11-13 October 2018, Budapest

ΔΗΜΟΣΙΕΥΣΕΙΣ ΜΕΧΡΙ ΤΟ 2012

GOOD SEMEN QUALITY AND LIFE EXPECTANCY: A COHORT STUDY OF 43,277 MEN

Am J Epidemiology, 2009



$(P_{trend} < 0.05)$

threshold of 40 million/mL

Figure 1. Relative risk of death according to fertility status and percent of sperm with normal morphology, percent motile spermatozoa, and sperm concentration among 43,277 Danish infertile men without azospermia referred to the Copenhagen Sperm Analysis Laboratory for infertility between 1963 and 2001. "Ref." indicates the reference group and includes men aged 50 years in 1980. Error bars represent 95% confidence intervals.

Table 3. Age- and Period-adjusted Standardized Mortality Ratio and 95% Confidence Intervals by Cause of Death Among 43,277 Danish Men Without Azospermia Referred to the Copenhagen Sperm Analysis Laboratory for Infertility Between 1963 and 2001 According to Sperm Concentration[a]

Cause of Death	No. of Deaths	Standardized Mortality Ratio	95% Confidence Interval
Infectious diseases including tuberculosis	32	0.44	0.22, 0.90
Cancer	233	0.95	0.71, 1.26
Vascular diseases	55	0.60	0.33, 1.09
Cardiac disease	162	1.15	0.80, 1.65
All diseases of the respiratory organs (including bronchitis, emphysema, and asthma)	24	1.29	0.49, 3.41
All diseases of the digestive organs (including cirrhosis of the liver, gall bladder diseases)	120	1.04	0.72, 1.50
Diseases of the urogenital organs	6	1.10	0.07, 18.5
Suicide and accidents	211	0.81	0.59, 1.10
Other causes of death	260	0.80	0.61, 1.04

[a] Reference group, <20 million/mL.

Elevated LH predicts IHD events in older men: the Health in Men Study

Eur.J. Endocrinology,2011

Η ↑ LH ΣΧΕΤΙΖΕΤΑΙ ΘΕΤΙΚΑ ΜΕ ↓ ΕΠΙΒΙΩΣΗ

Low testosterone is associated with an increased risk of MACE lethality in subjects with erectile dysfunction

J. Sex. Med,2010

προοπτική μελέτη παρατήρησης

Male factor infertility associated with comorbidities

Are Infertile Men Less Healthy than Fertile Men?

Results of a Prospective Case-Control Survey' by Dr. Andrea Salonia et al.

The study provides novel evidence that male factor infertility (MFI) accounts for a higher Charlson Comorbidity Index (CCI), which may be considered a reliable proxy of a lower general health status, regardless of the etiology of pure MFI.

"Since the current sample size is limited, we cannot derive general conclusions; therefore, additional studies in larger population-based samples are needed to confirm these results"

European Urology, Volume 56, issue 6, pages 891-1104, December 2009

Body composition, metabolic syndrome and type 2 diabetes in Klinefelter syndrome

Gravholt et al. Acta Pædiatrica 2011 **100**, pp. 871–877

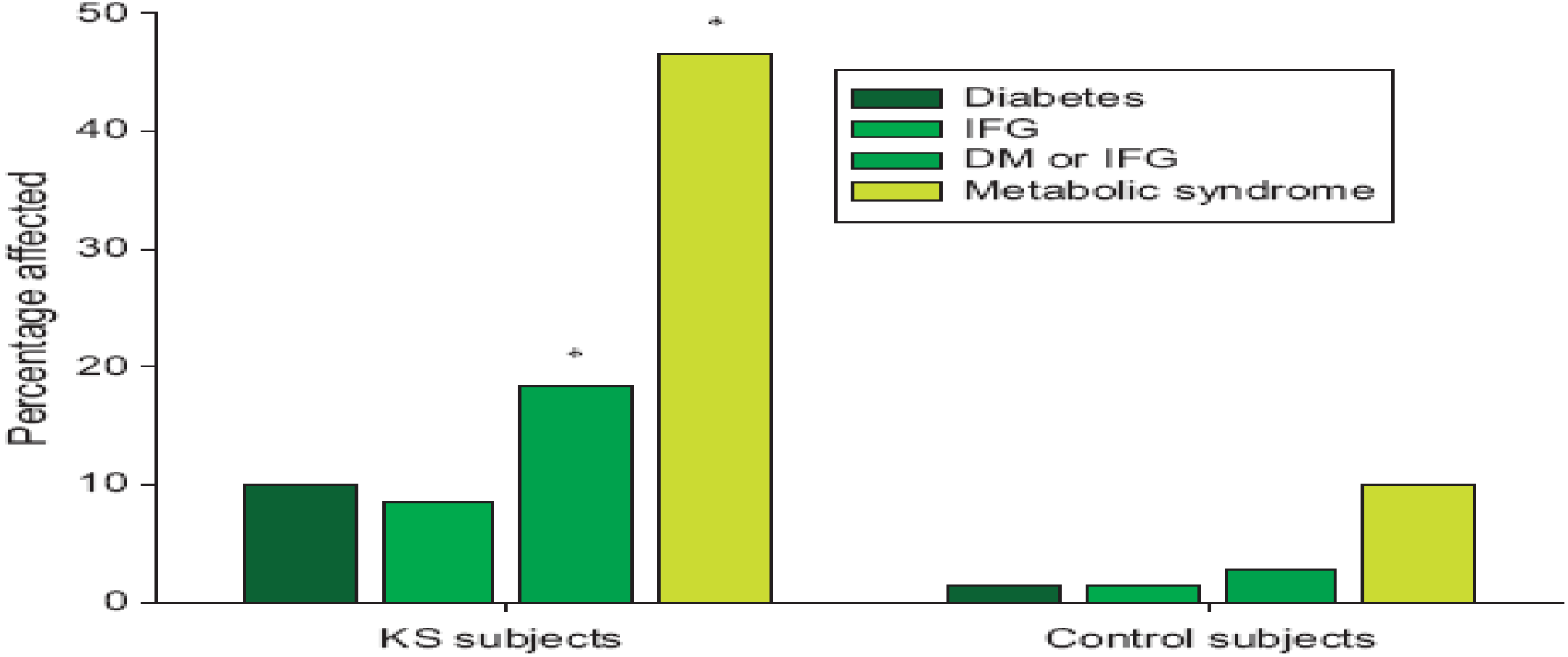


Figure 1 Distribution of 70 Klinefelter syndrome (KS) and 70 age-matched controls with regard to frequency of diabetes (DM), impaired fasting glucose (IFG) or the metabolic syndrome. * indicates $p < 0.05$ (16).

ΔΗΜΟΣΙΕΥΣΕΙΣ
2013-2019

Το σύνδρομο KLINEFELTER

- Γνωστό > 70 χρόνια, υποδιαγιγνώσκεται & υποθεραπεύεται με καθυστέρηση στην ενήλικο ζωή
- Μελετάται ευρύτατα, σε σχέση με την παθοφυσιολογία και τον φαινότυπο
- Αποτελεί την συχνότερη γενετική αιτία υπογονιμότητας, που συσχετίζεται με

Αυξημένη νοσηρότητα & θνησιμότητα
Χαμηλότερο κοινωνικό & οικονομικό status

metabolic syndrome, type 2 diabetes, cardiovascular disease, breast cancer, and extragonadal germ cell tumors.

Claus H. Gravholt et al. Klinefelter Syndrome: Integrating Genetics, Neuropsychology, and Endocrinology Endocrine Reviews 39: 389 – 423, 2018

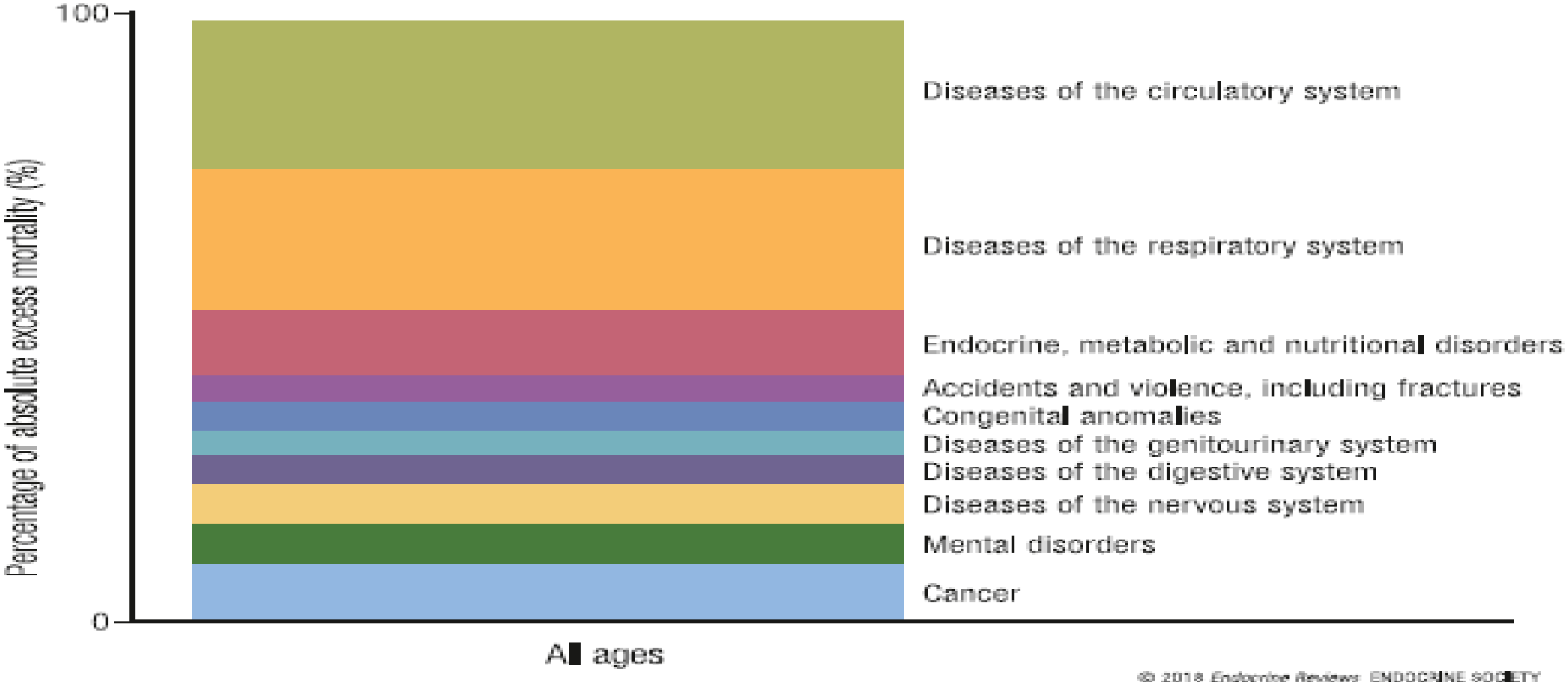


Figure 3. Differentiated excess mortality in KS for all age groups. Categories were defined according to ICD-9. Numbers are adapted to express the percentage of total absolute excess risk caused by the group of disorders in question. Includes data from Swerdlow *et al.* (4).

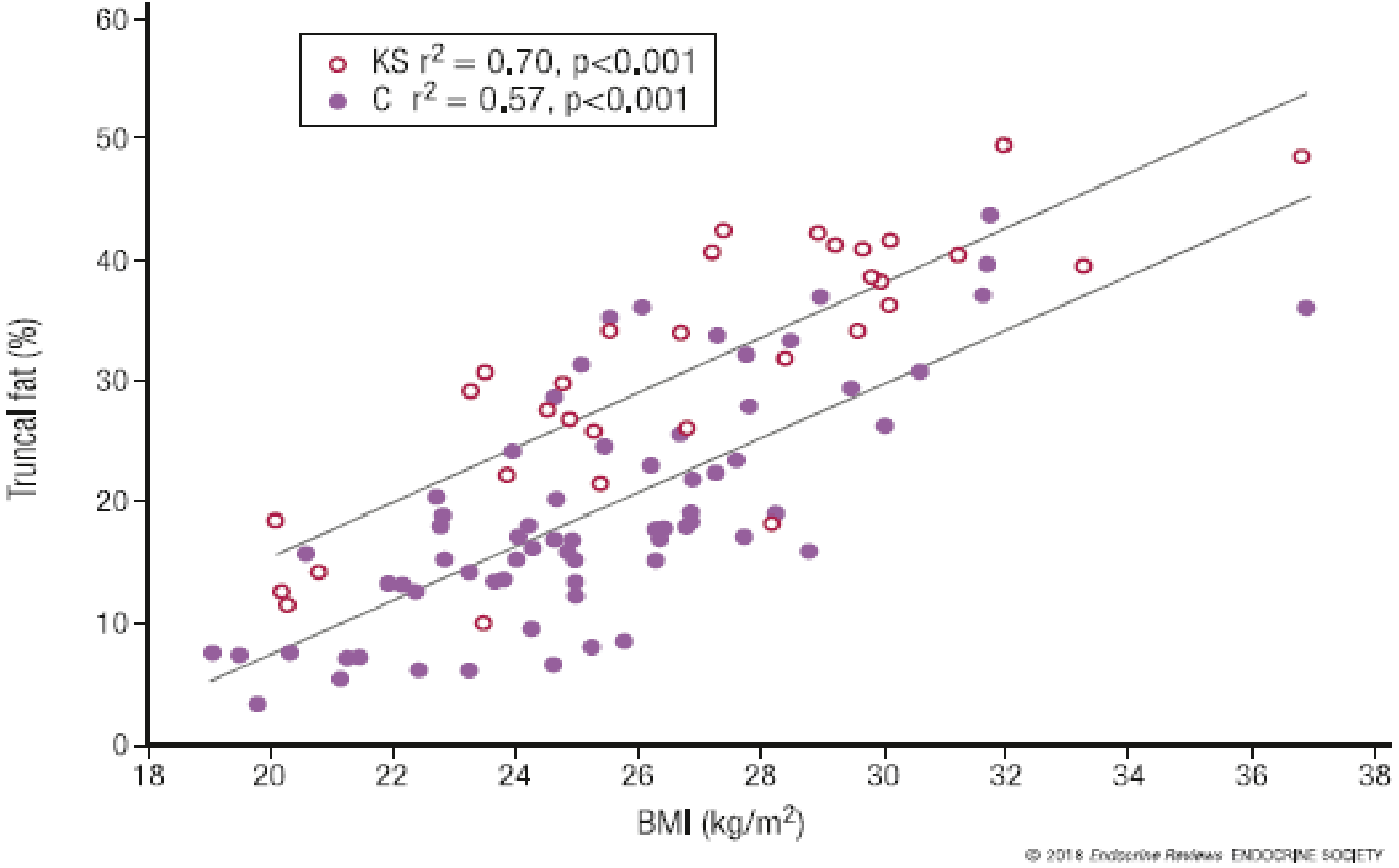


Figure 5. Truncal body fat in correlation with BMI. KS patients (red circles) have more truncal body fat (~8% more) for any given value of BMI than control subjects (C; purple circles). Reproduced with permission from Bojesen *et al.* (32).

CVD:(standardized mortality ratio, SMR, 2.2, but it is not clear whether the cause of the death is of thrombotic or hemorrhagic nature

Cardiovascular congenital anomalies :SMR, 7.3

32% : anxiety and 24% depressive disorders

.....

Η ΘΕΡΑΠΕΙΑ ΥΠΟΚΑΤΑΣΤΑΣΗΣ ΤΟΥ ΥΠΟΓΟΝΑΔΙΣΜΟΥ ΜΕ ΤΕΣΤΟΣΤΕΡΟΝΗ

ΕΝ ΜΕΡΕΙ ΠΡΟΣΤΑΤΕΥΕΙ ΑΠΟ ΤΗΝ ΚΔΑ ΝΟΣΟ ΕΝΩ ΓΙΑ ΤΙΣ ΜΕΤΑΒΟΛΙΚΕΣ

ΔΙΑΤΑΡΑΧΕΣ ΔΕΝ ΕΙΝΑΙ ΑΠΟΔΕΔΕΙΓΜΕΝΗ Η ΘΕΤΙΚΗ ΕΠΙΔΡΑΣΗ

Endocrinol Invest. 2017 Jul;40(7):705-712. Klinefelter syndrome: cardiovascular abnormalities and metabolic disorders. Calogero AE et al

Comorbidities in KS and related mortality, followed by evidence for the possible etiopathogenesis (attributed to supernumerary X chromosome or hypogonadism or both) and the effect of testosterone replacement therapy (TRT) on each specific manifestation/comorbidity (modified from ref. [6]).

	Incidence (%)	Mortality (SMR)	Etiopathogenesis	Effects of TRT
Verbal disorders	70–80	–	Extra X chromosome associated with:	• Improvement of developmental and behavioral issues
Mental retardation	4.2	–	• Abnormal structure of brain areas [53] • Executive and social dysfunction [117]	• Partial amelioration [130,132]
Metabolic syndrome	44	–	• Prevalence of T2 diabetes and MetS is higher in KS than in other forms of hypogonadism [69]	• Improvement of body composition and measures of cardiometabolic risk [131]
Type 2 diabetes	10	6	• Obesity precedes puberty [25]	
Osteoporosis	10	–	• No significant relationship has been demonstrated between testosterone levels and bone mass [106]	• Does not seem to normalize BMD in KS adults
Osteopenia	40	–		• Prevents bone loss in patients <20 years [107]
Hip fracture	?	39		
Gynecomastia	38	–	• Not present before puberty – associated with hypogonadism	• Improved if gynecomastia is of recent onset
Maldescended testes	27	–	• Increased 2D:4D suggests a relative androgen deficiency in the intrauterine milieu [114]	• No effect
Thrombosis	4.7	8	• Combination of imbalance between thrombosis and hemostasis with increased platelet aggregation rate [85,86]	• Not assessed in KS
Pulmonary embolism	2.3	6		
Mediastinal tumors	0.4	–	• Gynecomastia does not present a risk factor [94]	• Long-term TRT has been associated with an increased risk for male breast cancer [95]
Breast cancer	0.3	29		

Klinefelter syndrome: more than hypogonadism George A. Kanakis, Eberhard Nieschlag

Metabolism Clinical and Experimental 86 (2018) 135–144

ΚΑΡΚΙΝΟΣ & ΥΠΟΓΟΝΙΜΟΤΗΤΑ

ΚΑΡΚΙΝΟΣ ΟΡΧΕΩΝ
ΟΥΡΟΔΟΧΟΥ ΚΥΣΤΕΟΣ
ΘΥΡΕΟΕΙΔΟΥΣ
ΜΕΛΑΝΩΜΑ
ΑΙΜΑΤΟΛΟΓΙΚΕΣ ΚΑΚΟΗΘΕΙΕΣ

ΑΝΤΙΦΑΤΙΚΑ ΑΠΟΤΕΛΕΣΜΑΤΑ ΓΙΑ ΤΟΝ ΚΑΡΚΙΝΟ ΤΟΥ ΠΡΟΣΤΑΤΗ

Male infertility as a proxy of the overall male health status P. Capogrosso et al. Minerva Urologica e Nefrologica, 2018 June;70(3):286-99

ΤΑ ΠΟΣΟΣΤΑ ΚΑΡΚΙΝΟΥ (ΟΡΧΕΩΝ & ΘΥΡΕΟΕΙΔΟΥΣ)

ΕΙΝΑΙ ΑΥΞΗΜΕΝΑ ΚΑΙ ΜΕΤΑΞΥ ΣΥΓΓΕΝΩΝ ΠΡΩΤΟΥ &

ΔΕΥΤΕΡΟΥ ΒΑΘΜΟΥ ΑΝΔΡΩΝ ΜΕ ΧΑΜΗΛΗ ΠΟΙΟΤΗΤΑ

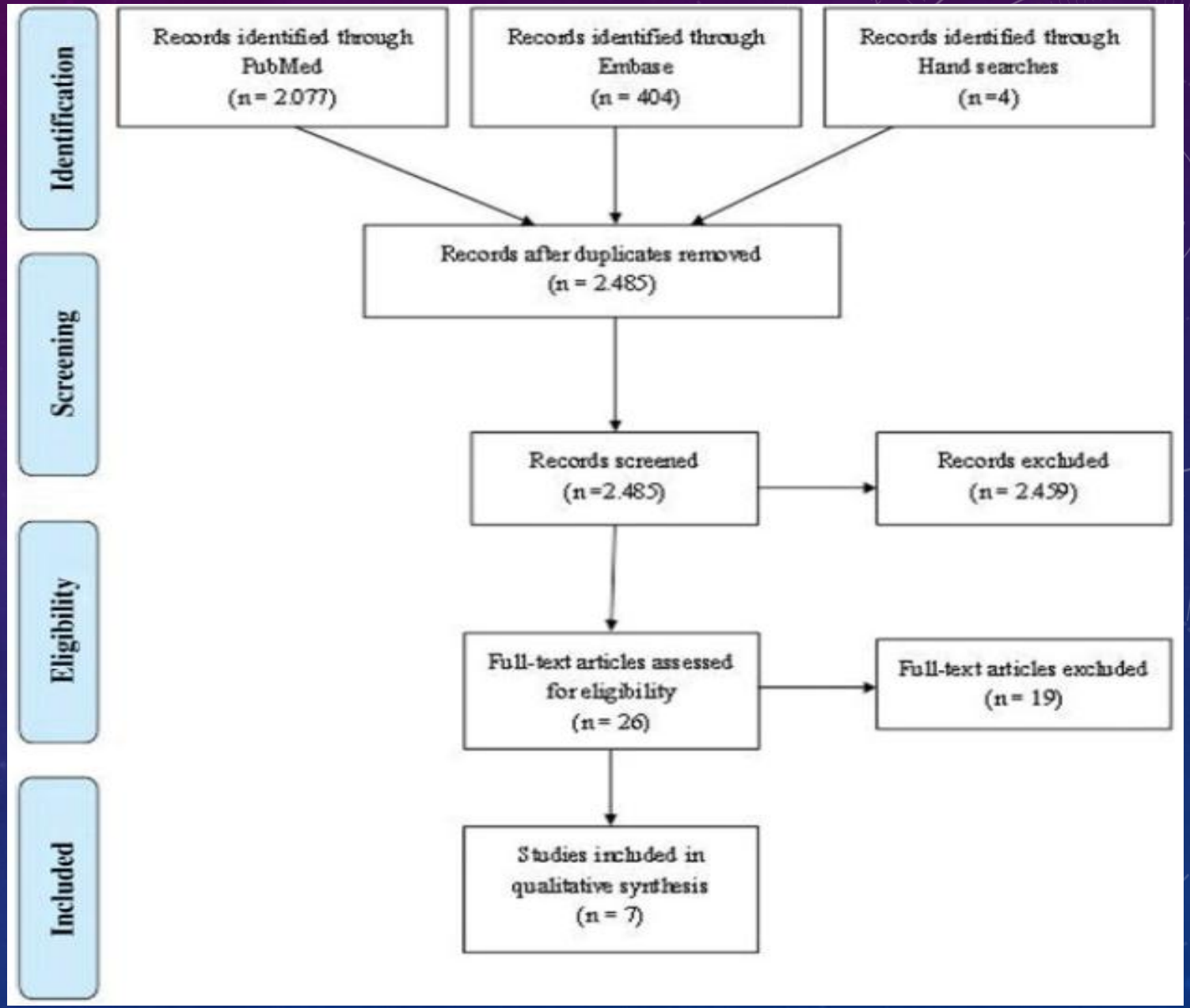
ΣΠΕΡΜΑΤΟΣ (ΜΕΓΑΛΗ ΑΝΑΔΡΟΜΙΚΗ ΜΕΛΕΤΗ)

Anderson RE, Hanson HA, Patel DP, Johnstone E, Aston KI, Carrell DT, et al . Cancer risk in first- and second-degree relatives of men with poor semen quality. Fertil Steril 2016;106:731–8.

January 1, 1980, to September 1, 2016
epidemiological studies
4 prospective (three on risk of mortality, one on risk of chronic diseases)
3 cross-sectional relating male infertility

⇧ ΚΔΑ
ΣΔ2
ΘΝΗΣΙΜΟΤΗΤΑ

ΜΙΚΡΟΣ ΑΡΙΘΜΟΣ ΠΡΟΟΠΤΙΚΩΝ ΜΕΛΕΤΩΝ



Semin Reprod Med. 2017 May;35(3):282-29 Male Infertility and Risk of Nonmalignant Chronic Diseases: A Systematic Review of the Epidemiological Evidence. Glazer CH et al

1. C-reactive protein

2. Interleukin-6

3.Tumour necrosis factor-alpha

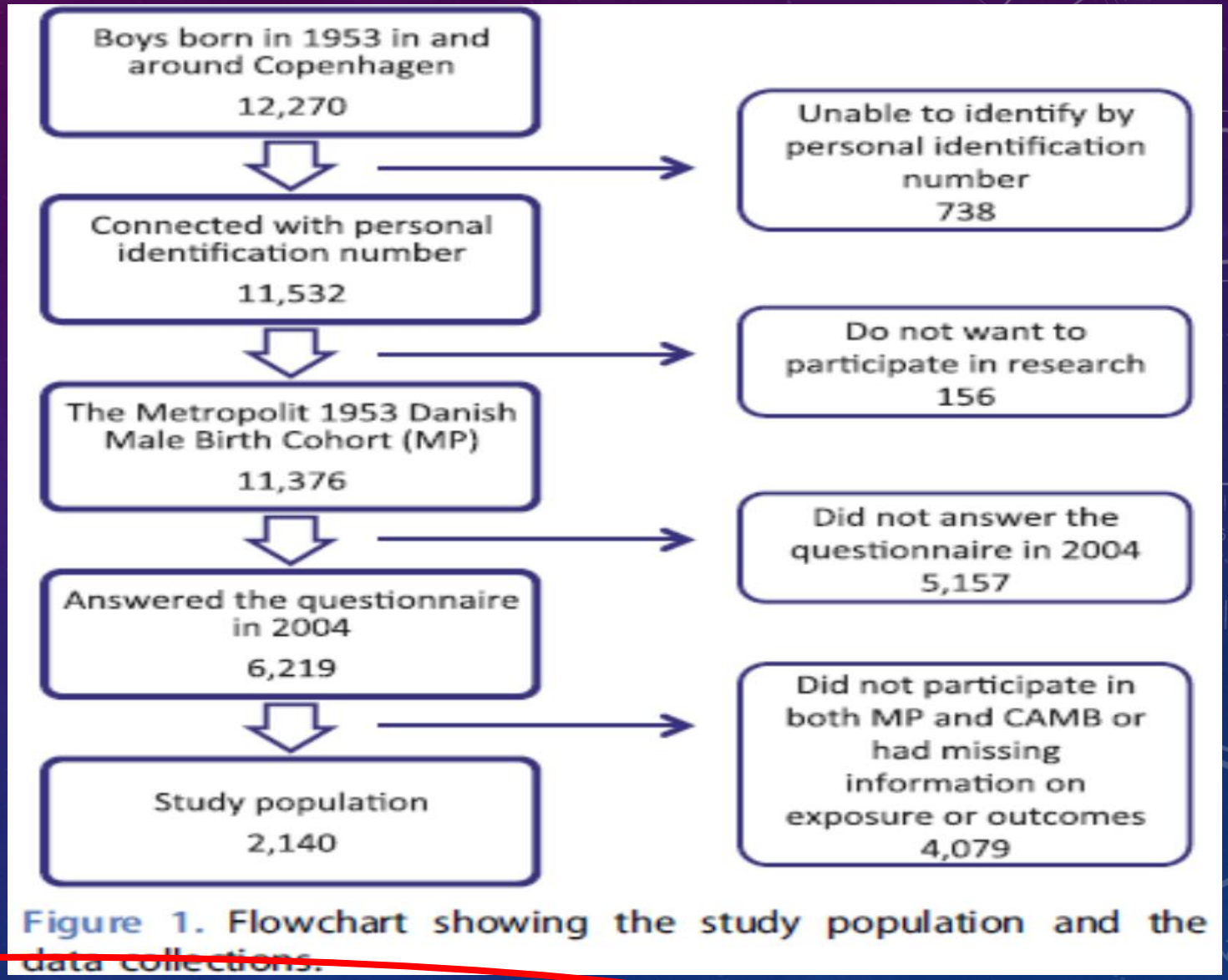


Figure 1. Flowchart showing the study population and the data collections.

Is male factor infertility associated with midlife low-grade inflammation? A population based study. Hærvig KK et al.

Hum Fertil (Camb). 2018 Jun;21(2):146-154.

The findings suggest that male factor infertility might be associated with an increased level of interleukin-6.

Table 2. Linear regressions of the association between male factor infertility and high sensitive C-reactive protein (hsCRP), interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α) in 1821 middle-aged Danish men born in 1953[a].

Variable	Model	No male factor infertility exp(β)	Male factor infertility exp(β)[b]	Confidence interval (CI) 95% CI	p Value
hsCRP					
	1	Reference	1.01	0.85–1.20	0.889
	2	Reference	1.01	0.86–1.20	0.868
	3	Reference	1.01	0.86–1.19	0.903
	4	Reference	1.01	0.86–1.19	0.906
	5	Reference	1.01	0.86–1.19	0.908
IL-6					
	1	Reference	1.18	1.04–1.33	0.010
	2	Reference	1.18	1.04–1.33	0.009
	3	Reference	1.17	1.04–1.32	0.010
	4	Reference	1.17	1.04–1.32	0.010
	5	Reference	1.17	1.04–1.32	0.010
TNF-α					
	1	Reference	1.03	0.95–1.11	0.472
	2	Reference	1.03	0.95–1.11	0.476
	3	Reference	1.03	0.96–1.11	0.426
	4	Reference	1.03	0.96–1.11	0.396
	5	Reference	1.03	0.96–1.11	0.387

Model 1: unadjusted.
Model 2: adjusted for father's occupation during study population's childhood.
Model 3: adjusted for father's occupation during study population's childhood, smoking, alcohol consumption and BMI.
Model 4: adjusted for father's occupation during study population's childhood, smoking, alcohol consumption, BMI, diagnosed depression and other diagnosed mental disorders.
Model 5: adjusted for father's occupation during study population's childhood, smoking, alcohol consumption, BMI, diagnosed depression and other diagnosed mental disorders, diagnosed cancer and diagnosed hypertension.
[a]In all analysis 1821 men were included, of whom 177 men had male factor infertility.
[b]In these analyses, the natural logarithm has been used.

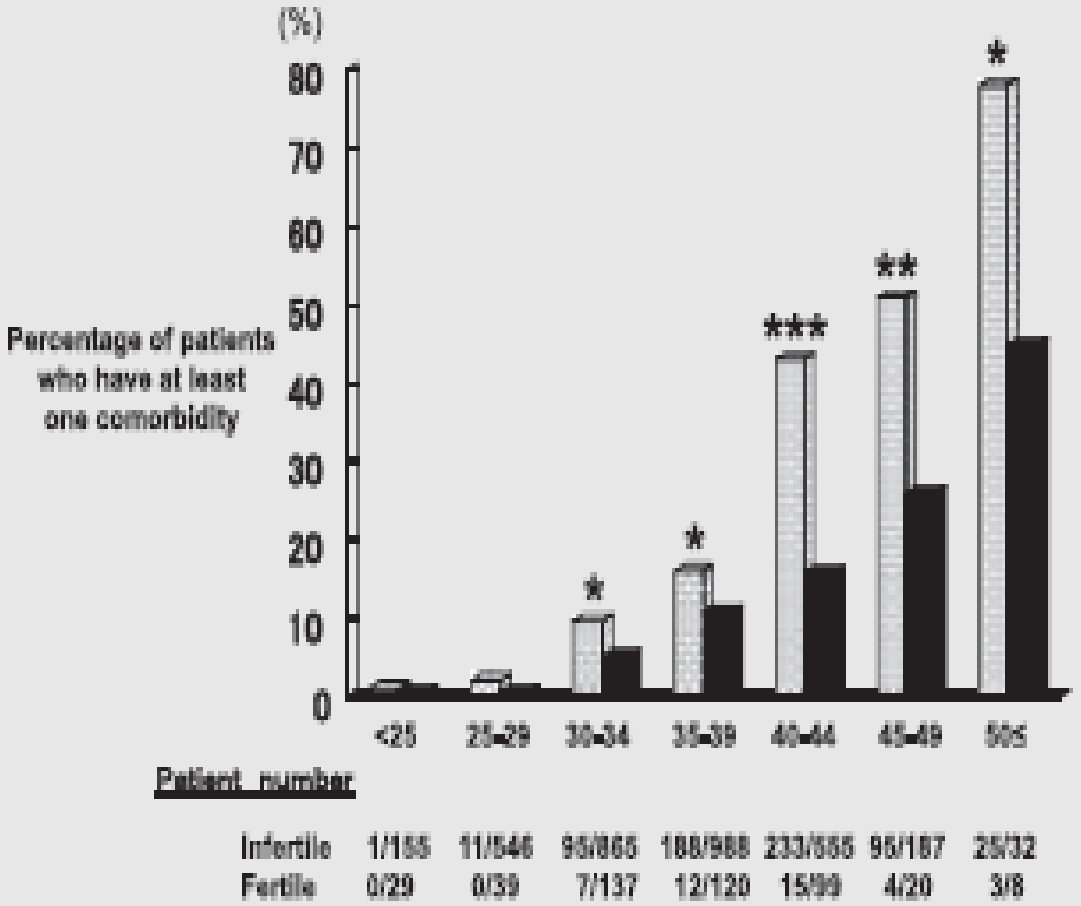
Single-center case–control study.

1η ΜΕΛΕΤΗ ΣΕ ΑΣΙΑΤΙΚΟ ΠΛΗΘΥΣΜΟ (ΙΑΠΩΝΕΣ)

Patients' background and prevalence of comorbidities of fertile and infertile men.

Variable	Infertile (n = 3,328)	Fertile (n = 452)	*P* value
Patient characteristic			
Age (y)	35.5 ± 6.7	34.9 ± 9.1	n.s.
Body mass index (kg/m^2)	23.7 ± 2.4	23.4 ± 1.9	n.s.
Semen volume (mL)	2.2 ± 1.3	3.1 ± 1.2	< .0001
Sperm concentration (×10^6/mL)	7.3 ± 3.8	49.7 ± 32.6	< .0001
Sperm motility (%)	27.1 ± 23.2	61.8 ± 13.5	< .0001
LH (IU/L)	4.8 ± 2.6	3.3 ± 1.7	< .0001
FSH (IU/L)	6.9 ± 3.1	3.6 ± 2.5	< .0001
T (ng/dL)	387.4 ± 159.1	425.3 ± 184.1	< .0001
Varicocele	965 (29.0)	85 (18.8)	< .0001
Comorbidity			
Hypertension/cardiovascular disease	592 (17.8)	32 (7.1)	< .0001
Hyperlipidemia	198 (5.9)	12 (2.7)	< .01
Hyperuricemia	172 (5.2)	9 (2.0)	< .01
Mental disorders	102 (3.1)	12 (2.5)	n.s.
Skin disease	99 (3.0)	5 (1.1)	< .05
Diabetes, IGT, IFG	67 (2.0)	4 (0.9)	n.s.
Cancer survivor	60 (1.8)	2 (0.4)	n.s.
Gastro-intestinal disease	33 (1)	4 (0.9)	n.s.
Pulmonary disease	32 (1)	4 (0.9)	n.s.
Kidney and genitourinary disease	32 (1)	5 (1.1)	n.s.
Immune disease	13 (0.4)	2 (0.4)	n.s.
Endocrine disease	10 (0.3)	2 (0.4)	n.s.
Total (at least one comorbidity)	723 (21.7)	41 (9.1)	< .0001
Total (at least one comorbidity excluding hypertension)	352 (10.6)	29 (6.4)	< .05

Notes: Value are mean ± SD or number (percentage). IFG = impaired fasting glycemia; IGT = impaired glucose tolerance; n.s. = nonsignificant.



Percentage of patients who had at least one comorbidity, subdivided by age. The dotted and solid bars indicate the infertile and fertile groups, respectively. *$P<.05$, **$P<.01$, and ***$P<.0001$ between groups.

Reproductive functions of men with or without comorbidities.

Variable	Comorbidity (n = 723)	Healthy (n = 2,605)	*P* value
Total testicular volume (mL)	26.6 ± 10.1	28.8 ± 11.6	<.0001
Semen volume (mL)	2.0 ± 1.1	2.3 ± 1.1	<.0001
Concentration ($\times 10^6$/mL)	5.1 ± 2.9	7.9 ± 4.2	<.0001
Motility (%)	17.8 ± 11.1	29.7 ± 21.2	<.0001
LH (IU/L)	5.2 ± 2.5	4.7 ± 2.6	<.0001
FSH (IU/L)	7.8 ± 3.1	6.6 ± 2.5	<.0001
T (ng/dL)	351 ± 111.7	397 ± 129.3	<.0001
Varicocele	200 (27.7%)	765 (29.4%)	n.s.
Azoospermia	83 (11.4%)	230 (8.8%)	<.05

Notes: Value are mean ± SD or number (percentage). n.s. = nonsignificant.

Effects of medical comorbidity on male infertility and comorbidity treatment on spermatogenesis

Koji Shiraishi et al. Fertil Steril 2018;110:1006–11.

After treatment for comorbidities

1. significant increase in the total motile sperm count compared with both :
the baseline values
and with the poorly controlled men.

2. A multivariate analysis showed that varicocele and comorbidity treatments were independent predictors of an improved total motile sperm count, with odds ratios of 2.895 and 2.057, respectively.

1η αναδρομική μελέτη κοόρτης απο 2004-2014, που εκτίμησε την υγεία του άνδρα σε σχέση με το αποτέλεσμα της IVF & ICSI

2,690 men 5,037 fresh ART cycles.
27% : at least one medical diagnosis.
15% : two or more
nervous system diseases : lower pregnancy rates (23% vs. 30%) and live-birth rates (15% vs. 23%) than men without nsd
respiratory diseases: lower fertilization rates (61% vs. 64%)
musculoskeletal diseases : (61% vs. 64%) .
endocrine system diseases : smaller children (2,970 vs. 3,210 g)
mental disorders: children born at an earlier gestational age (36.5 vs. 38.0 weeks).

Of the cycles, 7.2% : male factor.

no
significant association between the diagnosis of male factor
infertility and medical comorbidity.

Eisenberg ML, et al. Relationship between paternal somatic health and assisted reproductive technology outcomes. Fertil Steril 2016;106:559–65.

ΣΑΚΧΑΡΩΔΗΣ ΔΙΑΒΗΤΗΣ

prospective cohort study

39 516 men who had since 1994 undergone fertility treatment with their female partner were identified from the Danish national IVF Register

follow-up time of 5.6 years

separate analyses : first (1994–2005) and second (2006–2012) IVF registration period

18 499 : infertility and 21 017 : reference group.

651 (1.6%) diabetes cases, during the follow-up period

HR = 1.08 for the first
HR = 1.45 and second IVF registration period
HR's for men with oligospermia : 1.44
azoospermia : 2.10
aspermia : 3.20

Eisenberg ML, Li S, Cullen MR, Baker LC. Increased risk of incident chronic medical conditions in infertile men: analysis of United States claims data. Fertil Steril 2015b;105:629–636. 30% increased risk of diabetes among infertile men

Risk of diabetes according to male factor infertility: a register-based cohort study Clara Helene Glazer

Human Reproduction, Vol.32, No.7 pp. 1474–1481, 2017

ΚΟΙΛΙΟΚΑΚΗ

Cross-sectional screening for coeliac disease in men and women referred to fertility treatment using IgA tissue transglutaminase antibodies as a marker of coeliac disease and small-bowel biopsies questionnaire on gluten intake, gastrointestinal symptoms and reproductive history.

893 participants (51% women)
eight : coeliac disease antibody positive.
seven :Small-bowel biopsies from antibody positive participants
unrecognised coeliac disease was confirmed in one woman and three men,
prevalence of 0.45% (95% confidence interval 0.12–1.14).
total prevalence, combining already diagnosed and unrecognised CD : 0.63%

Unrecognised coeliac disease among men and women undergoing fertility treatment: A screening study

Louise B Grode United European Gastroenterology Journal 2018, Vol. 6(10) 1477–1484

ΗΔΗ ΓΝΩΣΤΑ

Coeliac disease has been associated with infertility and adverse reproductive outcomes.
. It has been estimated that only 10–20% of coeliac disease affected patients have been diagnosed.
. Active case finding and screening of risk-groups is recommended

ΝΕΟ ΕΥΡΗΜΑ

This is the first cross-sectional study on coeliac disease in infertile men and women in Denmark.
. We find a low prevalence of unrecognised coeliac disease among infertile patients.
. This finding does not support routine screening for coeliac disease among patients referred to fertility treatment.
. More men than women had coeliac disease and male infertility and coeliac disease could be an important issue for future research.

Η ΚΑΚΗ ΠΟΙΟΤΗΤΑ ΤΟΥ ΣΠΕΡΜΑΤΟΣ ΕΙΝΑΙ ΒΙΟΛΟΓΙΚΟΣ ΔΕΙΚΤΗΣ ΓΙΑ ΜΕΛΛΟΝΤΙΚΗ ΝΟΣΗΡΟΤΗΤΑ & ΘΝΗΤΟΤΗΤΑ ??

5370 men infertile at Frederiksberg Hospital, Denmark, during 1977–2010

4712 were followed in the Danish National Patient Registry until first

hospitalization, death, or the end of the study.

hospitalizations

cardiovascular disease, diabetes, testicular cancer, or prostate cancer.

RESULTS

clear association between sperm concentration < 15million/mL and all-cause hospitalizations hazard ratio = 1.5

cardiovascular disease hazard ratio = 1.4,, compared with men with a concentration > 40million/mL.

Probabilities for hospitalizations : higher with a low total sperm count and motility.

Sperm concentration : 195–200million/mL average, hospitalizations for the first time 7 years later, than of 0–5million/mL.

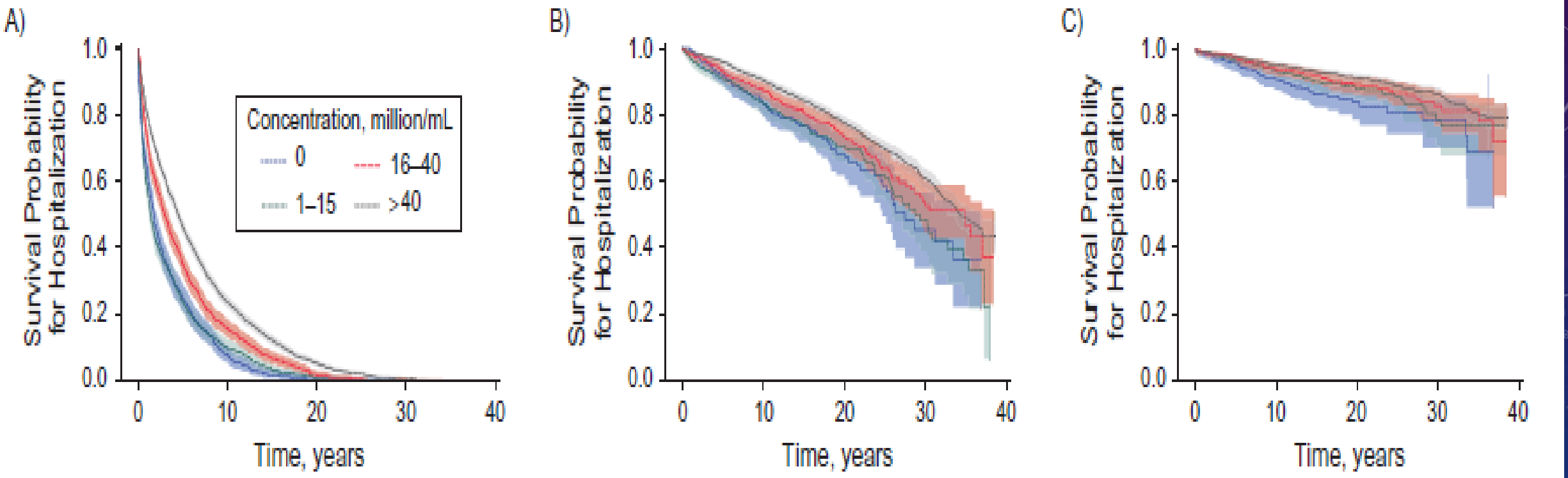


Figure 1. Annual survival probabilities among 4,712 men seen for infertility, Frederiksberg Hospital, Denmark, 1977–2010. Annual survival probabilities for first hospitalization following first semen analysis for all causes (A), cardiovascular diseases (B), and diabetes (C), according to sperm concentration. Shaded areas are 95% confidence intervals.

Semen Quality as a Predictor of Subsequent Morbidity: A Danish Cohort Study of 4,712 Men With Long-Term Follow-up Tabassam Latif et al American Journal of Epidemiology, 2017.

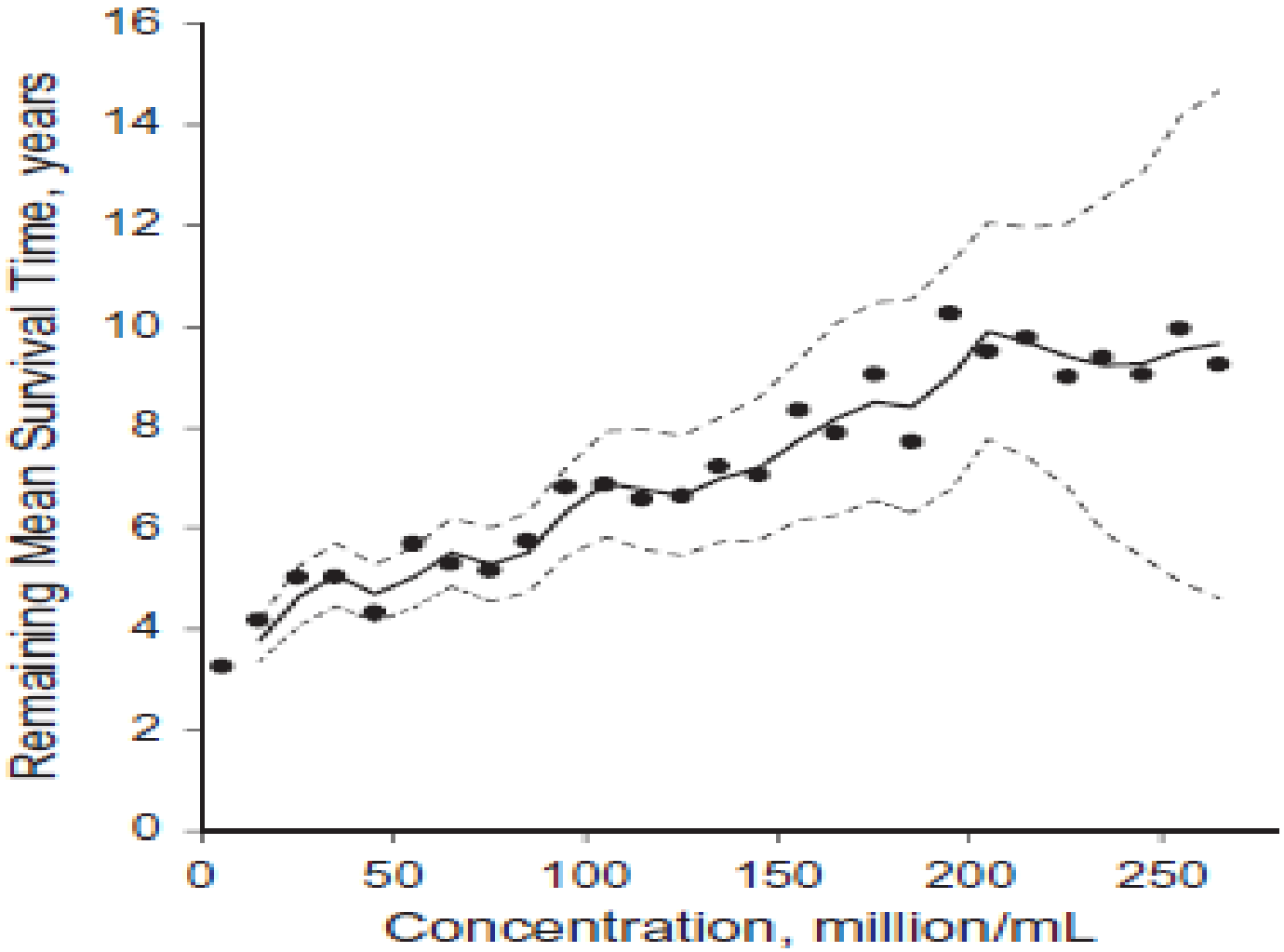


Figure 2. Remaining mean survival time among 4,712 men seen for infertility, Frederiksberg Hospital, Denmark, 1977–2010. Remaining mean survival time and 95% confidence intervals for first-time hospitalizations according to sperm concentrations. For concentrations from 0–200 million/mL, there seems to be a linear association.

ΗΓΕΡΘΗ ΤΟ ΕΡΩΤΗΜΑ ΑΝ Η ΚΟΙΝΩΝΙΚΗ-ΟΙΚΟΝΟΜΙΚΗ ΚΑΤΑΣΤΑΣΗ ΕΞΗΓΟΥΣΑΝ ΕΝ ΜΕΡΕΙ ΤΑ ΑΠΟΤΕΛΕΣΜΑΤΑ

ΔΕΝ ΥΠΗΡΞΕ ΣΤΑΤΙΣΤΙΚΑ ΣΗΜΑΝΤΙΚΗ ΔΙΑΦΟΡΑ ΣΤΙΣ

ΝΟΣΗΛΕΙΕΣ ΣΕ ΣΧΕΣΗ ΜΕ ΣΥΝΗΘΕΙΕΣ ΚΑΘΗΜΕΡΙΝΟΤΗΤΑΣ

& ΚΟΙΝΩΝΙΚΟ-ΟΙΚΟΝΟΜΙΚΟ ΕΠΙΠΕΔΟ

Latif T, Lindahl-Jacobsen R, Mehlsen J, Eisenberg ML, Holmboe SA, Pors K, et al. Semen quality associated with subsequent hospitalizations—can the effect be explained by socio-economic status and lifestyle factors? Andrology 2018;6:428–35.

ΠΟΛΛΑΠΛΗ ΣΚΛΗΡΥΝΣΗ

The Danish Multiple Sclerosis Registry is
the oldest
population-based MS register in the world.

It was
established in 1956 and consists of all
incident persons
with onset of MS after 1947.

Male factor infertility and risk of multiple sclerosis: A register-based cohort study Clara Helene Glazer et al. Multiple Sclerosis Journal 1–8,2017

51,063 men whose partners had undergone fertility treatment in all public and private fertility clinics in Denmark between 1994 and 2015

RESULTS: With a median age of 34 years at baseline

24,011 : male factor infertility

27,052 did not have male factor infertility and made up the reference group.

Men diagnosed with male factor infertility had a higher risk of prevalent (odds ratio (OR) = 1.61, 95% confidence interval (95% CI) 1.04-2.51) and incident MS (hazard ratio (HR) = 1.28, 95% CI 0.76-2.17) when compared to the reference group.

This nationwide cohort study has shown, for the first time, an association between male infertility and MS which may be due to underlying common etiologies such as hypogonadism, shared genetics, or a joint autoimmune component.

ΨΥΧΙΑΤΡΙΚΕΣ ΔΙΑΤΑΡΑΧΕΣ

255 ♂ 22–51 yrs

General Health Questionnaire-28 (GHQ-28)

(a) at the baseline, before their initial fertility evaluation (T1)

(b) before their second andrological appointment 2–3 months after diagnostic disclosure (T2)

(c) before subsequent treatment-related/follow-up appointments (T3, T4)

αποτελέσματα

Ενώ στην αρχική εκτίμηση το ποσοστό ήταν εντός των τιμών αναφοράς, αυξάνεται μετά την διάγνωση & παραμένει υψηλό σε σχέση με το αρχικό, στην διάρκεια της θεραπείας , κυρίως σε όσους έχουν μόνο ανδρικό παράγοντα υπογονιμότητας η μικτό (ανδρικό & γυναικείο)

The Risk of Psychiatric Morbidity and Course of Distress in Males Undergoing Infertility Evaluation Is Affected by Their Factor of Infertility Katarzyna Warchol-Biedermann American Journal of Men's Health Volume 13(1): 1– 10, 2019

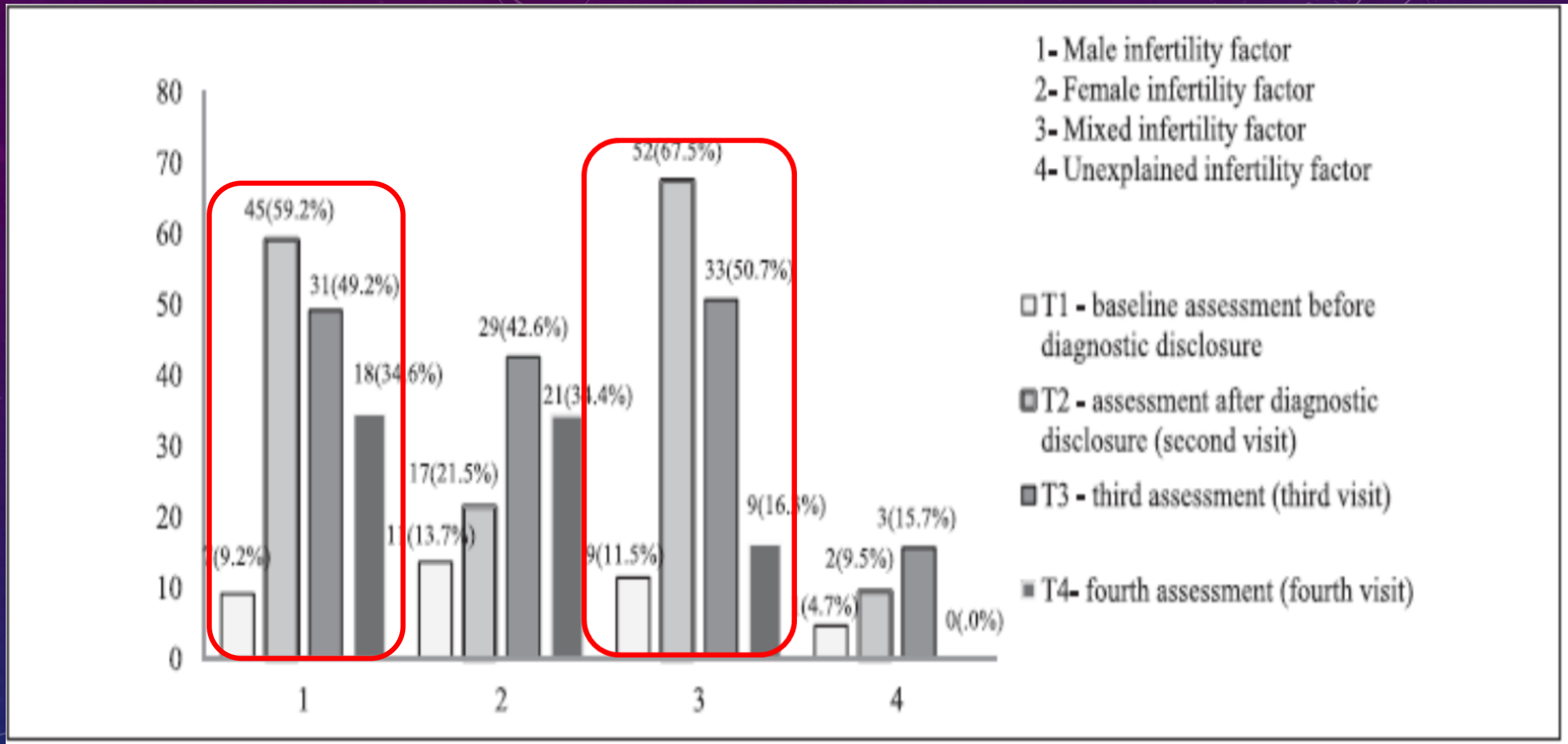


Figure 1. The numbers and percentages of respondents at risk for psychiatric morbidity at various stages of the procedure.

1146 infertile patients in a referral fertility center in Tehran, between May and October 2017

Generalized Anxiety Disorder-7 (GAD-7) scale

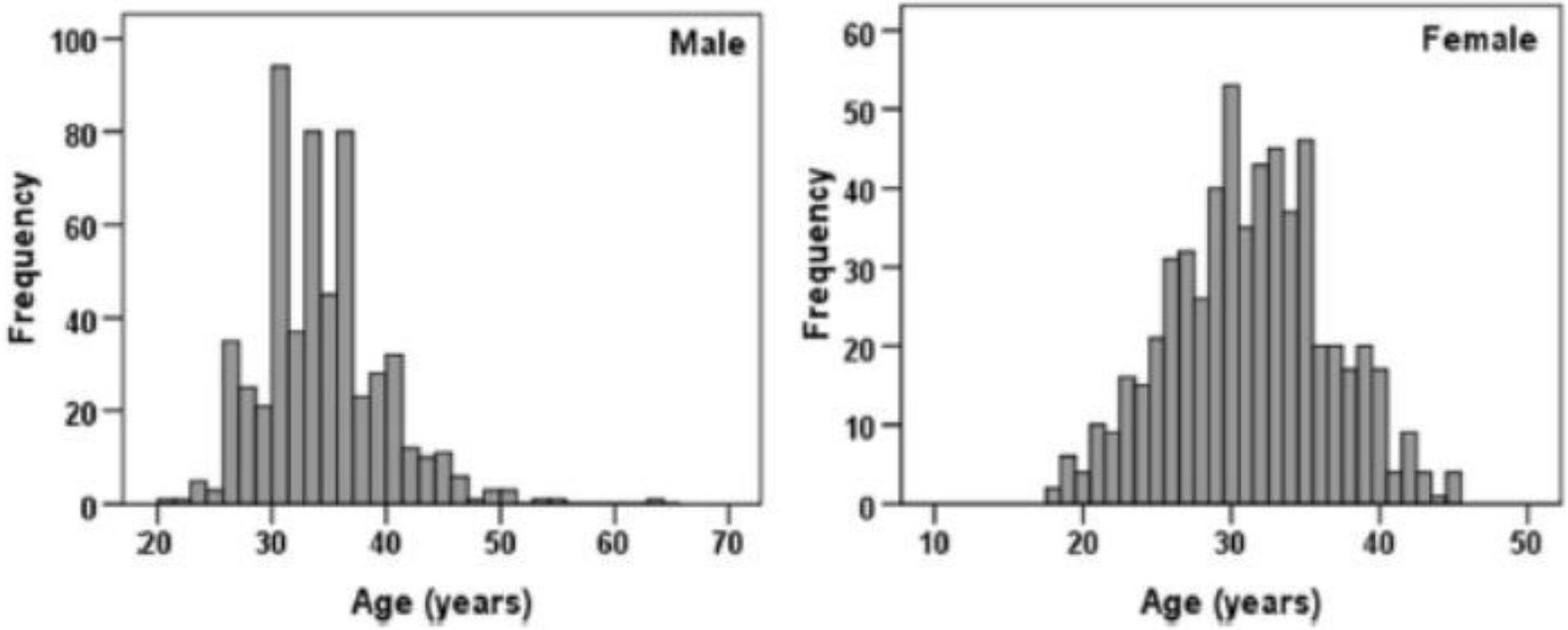


Fig. 1 The distribution of age in both men and women

Prevalence of generalized anxiety disorder and its related factors among infertile patients in Iran: a cross-sectional study
Reza Omani-Samani et al. Health and Quality of Life Outcomes (2018) 16:129

Results: mean total GAD-7 score:6.61

cut-off value:10

prevalence of GAD: 28.3%.

In adjusted analysis:

female sex (OR = 2.54, 95% CI = 1.88–3.42, P < 0.001)
low educational level (OR = 1.45,95% CI = 1.08–1.94, P = 0.012)
high infertility duration (OR = 1.05, 95% CI = 1.01–1.09, P = 0.013)
treatment failure (OR = 1.52, 95% CI = 1.13–2.04, P = 0.006)

2016 , ΜΕΛΕΤΗ ΣΤΗΝ ΑΥΣΤΡΑΛΙΑ ΕΔΕΙΞΕ ΑΥΞΗΣΗ ΤΩΝ ΔΙΑΤΑΡΑΧΩΝ ΥΠΝΟΥ ΣΕ ΣΧΕΣΗ ΜΕ ΤΟ 2010

ΠΟΙΑ ΕΙΝΑΙ Η ΣΧΕΣΗ ΑΙΤΙΑΣ –ΑΙΤΙΑΤΟΥ ΑΝ ΥΠΑΡΧΕΙ ΜΕ ΤΗΝ ΠΑΡΑΛΛΗΛΗ ΑΥΞΗΣΗ ΤΗΣ ΥΠΟΓΟΝΙΜΟΤΗΤΑΣ?

ΟΙ ΠΕΡΙΣΣΟΤΕΡΕΣ ΜΕΛΕΤΕΣ ΑΦΟΡΟΥΝ ΓΥΝΑΙΚΕΣ ΜΕ ΣΠΩ

ΠΑΧΥΣΑΡΚΙΑ?

ΑΠΝΟΙΑ ΥΠΝΟΥ ΑΝΕΞΑΡΤΗΤΗ ΠΑΧΥΣΑΡΚΙΑΣ, ΛΟΓΩ ΜΕΙΩΜΕΝΗΣ ΤΕΣΤΟΣΤΕΡΟΝΗΣ ?

ΚΥΚΛΙΚΗ ΕΡΓΑΣΙΑ ? ΑΓΧΟΣ ?

ΚΙΡΚΑΔΙΟΣ ΡΥΘΜΟΣ ?

ΧΡΗΣΗ & ΚΑΤΑΧΡΗΣΗ ΥΠΟΛΟΓΙΣΤΩΝ ? ΕΚΘΕΣΗ ΣΕ ΜΠΛΕ ΑΚΤΙΝΟΒΟΛΙΑ ?

ΟΞΕΙΔΩΤΙΚΟ STRESS ? ΚΥΤΟΚΙΝΕΣ ?

ΑΝΤΙΣΤΑΣΗ ΣΤΗΝ ΙΝΣΟΥΛΙΝΗ ?

Sleep Med Rev. 2018 Dec;42:149-159. doi: Linking sleep disturbance to idiopathic male infertility. Palnitkar G et al.

ΚΑΙ Η ΕΠΟΜΕΝΗ ΓΕΝΙΑ ??? ΤΩΝ ΥΠΟΓΟΝΙΜΩΝ ΑΝΔΡΩΝ

1. Σε αναδρομική μελέτη κοόρτης το 4,9% από 2224 παιδιά (ζώντα & θνησιγενή) είχαν συγγενείς ανωμαλίες , οι οποίες δεν συσχετίσθηκαν με το είδος της υποβοηθούμενης αναπαραγωγής, ούτε με τις ποιοτικές παραμέτρους του ΣΠΔ

2. Επίσης σε αναδρομική, η θνησιμότητα μεγάλου αριθμού συγγενών, 1ου & 2ου βαθμού, δεν ήταν στατιστικά διαφορετική από των γόνιμων .....περιορισμοί

Heidi A. Hanson et al. Risk of childhood mortality in family members of men with poor semen quality Human Reproduction, Vol.32, No.1 pp. 239–247, 2017

Hum Reprod. 2019 Feb 12. The risk of birth defects is not associated with semen parameters or mode of conception in offspring of men visiting a reproductive health clinic. Pastuszak AW et al.

erectile dysfunction (ED), cardiovascular disease (CVD), diabetes, and metabolic syndrome.

Η ΣΥΧΝΟΤΕΡΗ ΑΙΤΙΑ ΟΡΓΑΝΙΚΗΣ ΣΤΥΤΙΚΗΣ ΔΙΑΤΑΡΑΧΗΣ ΕΙΝΑΙ Η ΑΓΓΕΙΑΚΗΣ ΑΙΤΙΟΛΟΓΙΑΣ,
Η ΟΠΟΙΑ ΔΙΑΓΙΓΝΩΣΚΕΤΑΙ ΣΕ ΑΝΔΡΕΣ ΚΥΡΙΩΣ < 60 ΕΤΩΝ ΜΕ dynamic penile color Doppler US,(ενδοθηλιακή δυσλειτουργία, αθηροσκλήρυνση)

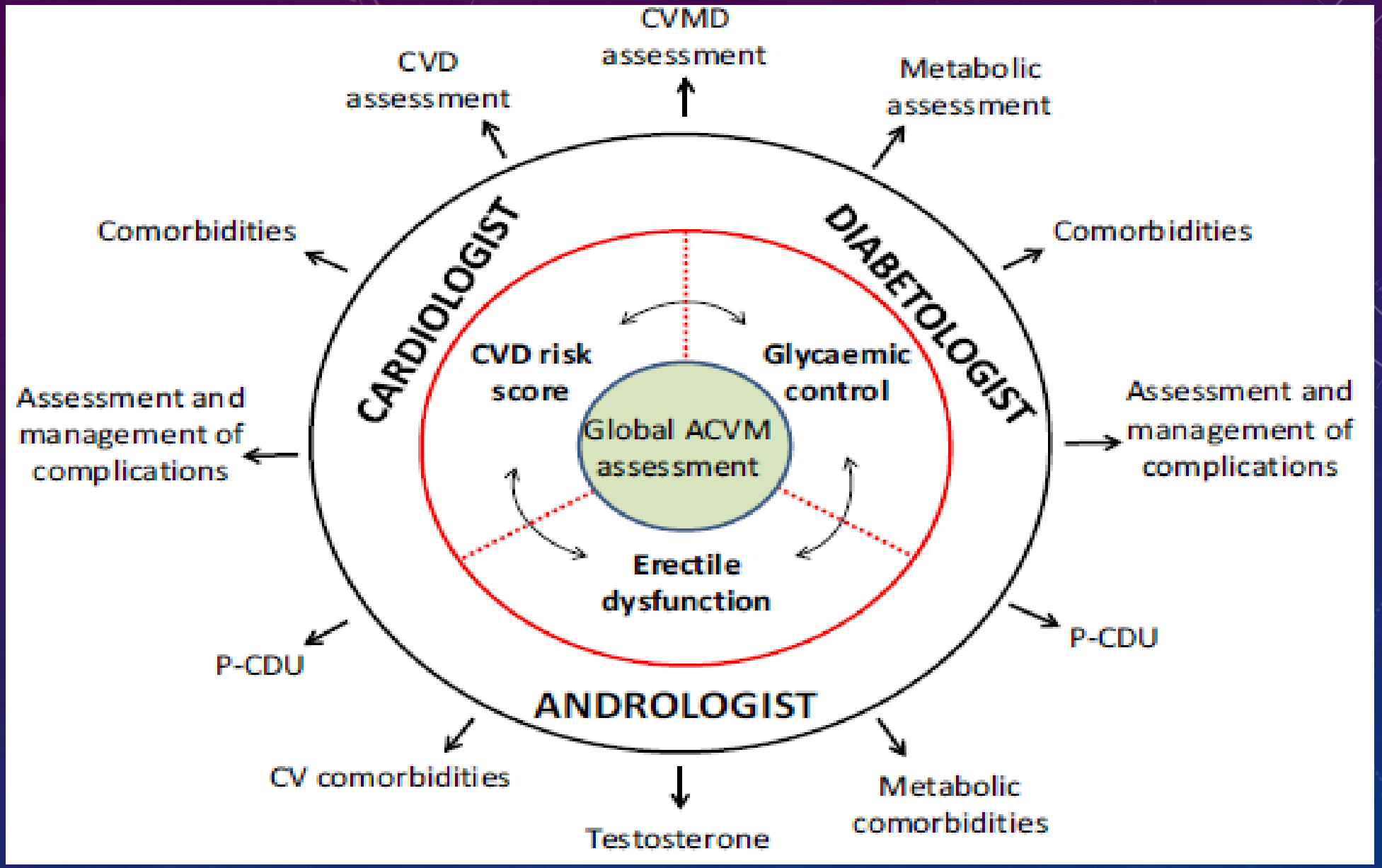
Αποτελεί ανεξάρτητο παράγοντα CVD & CV mortality

Ακολούθως πλήρης καρδιολογικός έλεγχος

Απαραίτητος έλεγχος λιπιδίων κα σακχάρου

Επίσης μέτρηση τεστοστερόνης

Italian Study Group on Cardiometabolic Andrology



opportunity of the andrological patient: cardiovascular and metabolic risk assessment and prevention C. Foresta et al.

Andrology, 2017, 5, 408–413

ΣΥΜΠΕΡΑΣΜΑΤΙΚΑ ?

Η ΥΠΟΓΟΝΙΜΟΤΗΤΑ ΦΑΙΝΕΤΑΙ ΟΤΙ ΕΙΝΑΙ ΔΕΙΚΤΗΣ & ΠΡΟΑΓΓΕΛΟΣ ΚΑΚΗΣ ΥΓΕΙΑΣ ΣΤΟΝ ΑΝΔΡΑ

ΜΕ ΠΟΛΛΑ ΑΝΑΠΑΝΤΗΤΑ ΕΡΩΤΗΜΑΤΑ ΝΑ ΕΝΑΠΟΚΕΙΝΤΑΙ ΣΤΗΝ ΠΕΡΑΙΤΕΡΩ ΕΡΕΥΝΑ

ΤΟ ΕΡΩΤΗΜΑ

Η ΒΕΛΤΙΩΣΗ ΤΗΣ ΓΕΝΙΚΗΣ ΥΓΕΙΑΣ ΤΟΥ ΝΕΟΥ ΥΠΟΓΟΝΙΜΟΥ ΑΝΔΡΑ ΜΕΤΑ ΑΠΟ ΘΕΡΑΠΕΙΑ ΤΩΝ ΣΥΝΟΣΗΡΟΤΗΤΩΝ:

1. ΕΙΝΑΙ ΕΝΑ ΒΗΜΑ ΠΡΟΣ ΤΗΝ ΒΕΛΤΙΩΣΗ ΤΟΥ ΣΠΕΡΜΑΤΟΣ ?
2. ΑΠΑΛΛΑΣΣΕΙ ΑΠΟ ΑΚΡΙΒΕΣ ΠΕΡΑΙΤΕΡΩ ΘΕΡΑΠΕΙΕΣ ΥΠΟΓΟΝΙΜΟΤΗΤΑΣ ΤΟ ΖΕΥΓΟΣ ?
3. ΜΕΙΩΝΕΙ ΤΗΝ ΤΑΛΑΙΠΩΡΙΑ ΤΗΣ ΓΥΝΑΙΚΑΣ ? (ΣΩΜΑΤΙΚΗ & ΨΥΧΟΛΟΓΙΚΗ)

Clara Helene Glazer Fertility Sterility, 110, 6 / NOVEMBER 2018

Guo D, Li S, Behr B, Eisenberg ML. Hypertension and male fertility. World J Mens Health 2017;35:59–64.

ΣΑΣ ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ
ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ

Andrology. 2019 Jan 20. doi: 10.1111/andr.12587.Mediterranean diet and the risk of poor semen quality: cross-sectional analysis of men referring to an Italian Fertility Clinic. Ricci E et al

BACKGROUND: Several diet patterns have been suggested as involved in processes of spermatogenesis and thus in male subfertility. To study the relation between Mediterranean diet and abnormal sperm parameters in men of subfertile couples, we performed a cross-sectional analysis of baseline data from a prospective cohort study. METHODS: Patients were enrolled in an Italian Fertility Clinic. Couples undergoing assisted reproduction techniques (ART) were interviewed to obtain information on personal and health history, lifestyle habits, and diet, on the day of oocyte retrieval. On the same day, a semen sample was also collected and analyzed to proceed with ART. Adherence to Mediterranean diet was evaluated using a Mediterranean Diet Score (MDS). Odds ratios (OR) and 95% confidence intervals (CI) were calculated for semen volume <1.5 mL, sperm concentration <15 mil/mL, and total count <39 mil. RESULTS: Three hundred nine men, age range 27-60, were enrolled: 19.3% had semen volume < 1.5 mL, 30.5% sperm concentration <15 mil/mL, and 32.1% total count <39 mil. MDS was low (0-3) in 86 men (27.8%), intermediate (4-5) in 131 (42.4%), and high (6-9) in 92 (29.8%). Semen volume was not associated with MDS. Compared to the highest MDS category (6-9), the ORs for low sperm concentration were 1.34 (95% CI 0.69-2.50) for MDS 4-5 and 2.42 (95% CI 1.21-4.83) for MDS 0-3, with significant trend (p = 0.011). The corresponding estimates for total count were 1.26 (95% CI 0.66-2.42) and 2.08 (95% CI 1.05-4.12), with significant trend (p = 0.034). These findings were consistent in strata of history of reproductive organ diseases. CONCLUSIONS: Mediterranean Diet Score was positively associated with normal sperm concentration and total count, but not with semen volume.

Endocrine. 2016 Sep;53(3):831-8. doi: 10.1007/s12020-015-0851-z. Epub 2016 Jan 12. Hypovitaminosis D is associated with erectile dysfunction in type 2 diabetes. Caretta N et al. Diabetes is an established risk factor for erectile dysfunction (ED). The pathophysiology of ED in diabetic men is multifactorial, but it mainly involves a vascular disorder related to a reduction of endothelial function. Recently, several studies have correlated ED risk factors with vitamin D deficiency. In this study, we evaluate the relationship between 25-hydroxyvitamin D [25(OH)D] levels, erectile dysfunction, and vascular disease, in type 2 diabetes mellitus men (T2DM). In this observational study, 92 T2DM males (58.83 ± 9.73 years) underwent medical history collection, International Index of Erectile Function (IIEF-5) questionnaire, that allows the identification and grading of DE, physical examination, biochemical/hormonal blood tests, and penile echo-color Doppler ultrasonography. T2DM patients with lower 25(OH)D levels (<25 nmol/l) showed higher penile IMT ($p < 0.05$), waist circonference ($p < 0.05$), glucose concentrations ($p < 0.05$), and lower IIEF-5 score ($p < 0.005$), testosterone concentrations ($p < 0.05$), and cavernous peak systolic velocity (PSV) ($p < 0.05$), compared to patients with 25(OH)D >50 nmol/l. 25(OH)D levels were directly correlated with IIEF-5 ($R = 0.39$; $p = 0.0001$), testosterone ($R = 0.24$; $p = 0.02$), and PSV ($R = 0.24$; $p = 0.04$) and inversely with waist ($R = -0.33$; $p = 0.002$), HbA1c ($R = -0.22$; $p = 0.03$), triglyceride ($R = -0.21$; $p = 0.06$), and penile IMT ($R = -0.30$; $p = 0.009$). At multivariate analysis, 25(OH)D deficiency remained an independent predictor of DE. We demonstrate a significant association between 25(OH)D deficiency and erectile dysfunction in T2DM men. This association may be due to the influence of 25(OH)D deficiency on cardiovascular risk factor (glycaemia, HDL cholesterol, and triglycerides), testosterone plasma levels and endothelial dysfunction.

,. Klinefelter syndrome (KS) is one of the most common genetic causes of male infertility. This condition is associated with much comorbidity and with a lower life expectancy. The aim of this review is to explore more in depth cardiovascular and metabolic disorders associated to KS. KS patients have an increased risk of cerebrovascular disease (standardized mortality ratio, SMR, 2.2; 95% confidence interval, CI, 1.6-3.0), but it is not clear whether the cause of the death is of thrombotic or hemorrhagic nature. Cardiovascular congenital anomalies (SMR, 7.3; 95% CI, 2.4-17.1) and the development of thrombosis or leg ulcers (SMR, 7.9; 95% CI, 2.9-17.2) are also more frequent in these subjects. Moreover, cardiovascular abnormalities may be at least partially reversed by testosterone replacement therapy (TRT). KS patients have also an increased probability of endocrine and/or metabolic disease, especially obesity, metabolic syndrome and type 2 diabetes mellitus. The effects of TRT on these abnormalities are not entirely clear.

Endocrinol Invest. 2017 Jul;40(7):705-712. doi: 10.1007/s40618-017-0619-9. Klinefelter syndrome: cardiovascular abnormalities and metabolic disorders. Calogero AE et al

STUDY QUESTION: What is the relationship between semen parameters and birth defect (BD) rates in offspring of men evaluated for infertility?
SUMMARY ANSWER: Among men undergoing infertility evaluation, there is no significant relationship between semen parameters and defect rates in live or still births, even when considering mode of conception.
WHAT IS KNOWN ALREADY: Approximately 15% of couples have fertility difficulties, with up to a 50% male factor contribution. An increased risk of BDs exists in couples using ART, particularly IVF and ICSI, but it is unknown if this related to the ART procedures or an underlying male factor.
STUDY DESIGN, SIZE, DURATION: To determine if the severity of male factor infertilty, as assessed via sperm quality and mode of conception, is associated with BD rates, we performed a retrospective cohort study. Fathers with semen analysis data in the Baylor College of Medicine Semen Database (BCMSD) were linked with their offspring using Texas Birth Defects Registry (TBDFR) data between 1999 and 2009. In this 10-year period, a total of 1382 men were identified in linkage between the BCMSD and TBDFR. A total of 109 infants with and 2115 infants without BDs were identified.
PARTICIPANTS/MATERIALS, SETTING, METHODS: To determine the association between BDs and semen parameters, we used hierarchical linear modeling to determine odds ratios between BD rates, semen parameters, and mode of conception before and after adjustment for paternal, maternal and birth covariates. Semen parameters were stratified based on thresholds defined by the WHO fifth edition laboratory manual for the examination and processing of human semen.
MAIN RESULTS AND THE ROLE OF CHANCE: In total 4.9% of 2224 infants were identified with a BD. No statistically significant association was observed between BD rates and semen parameters, before or after adjustment for covariates. The association between sperm concentration and BDs demonstrated an odds ratio (OR) of 1.07 (95% confidence interval: 0.63-1.83); motility: OR 0.91 (0.52-2.22); and total motile count: OR 1.21 (0.70-2.08). Likewise, mode of conception, including infertility treatment and ART, did not affect BD rates ($P > 0.05$).
LIMITATIONS, REASONS FOR CAUTION: BDs recorded in the TBDFR only include live born infants or still births after 20 weeks, our study did not evaluate the effect of impaired semen parameters on developmental defects prior to 20 weeks of gestation. With 109 BDs, our statistical analysis was powered to detect moderate differences associated with particular semen parameters. Additionally, data about mode of conception was not available for 1053 of 2224 births.
WIDER IMPLICATIONS OF THE FINDINGS: BD rates are not associated with semen quality or mode of conception. The current study suggests that the severity of male factor infertility does not impact the rate of congenital anomalies. This information is important when counseling couples concerned about the relationship between impaired semen quality and BDs.