Metabolik Reprodüktif Durum
«İnsülin direnci ve reprodüktif bozukluk»

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Hacettepe Üniversitesi Tıp Fakültesi
Endokrinoloji ve Metabolizma Hastalıkları BD

53. Ulusal Diyabet Kongresi
19-23 Nisan 2017, K.K.T.C.

Metabolik reprodüktif durum

Sunum planı

- **Metabolik reprodüktif durum ve PKOS**
- **PKOS, insülin direnci ve diyabet**
- **PKOS ve obezite**
- **PKOS mu yeni bir isim mi?**

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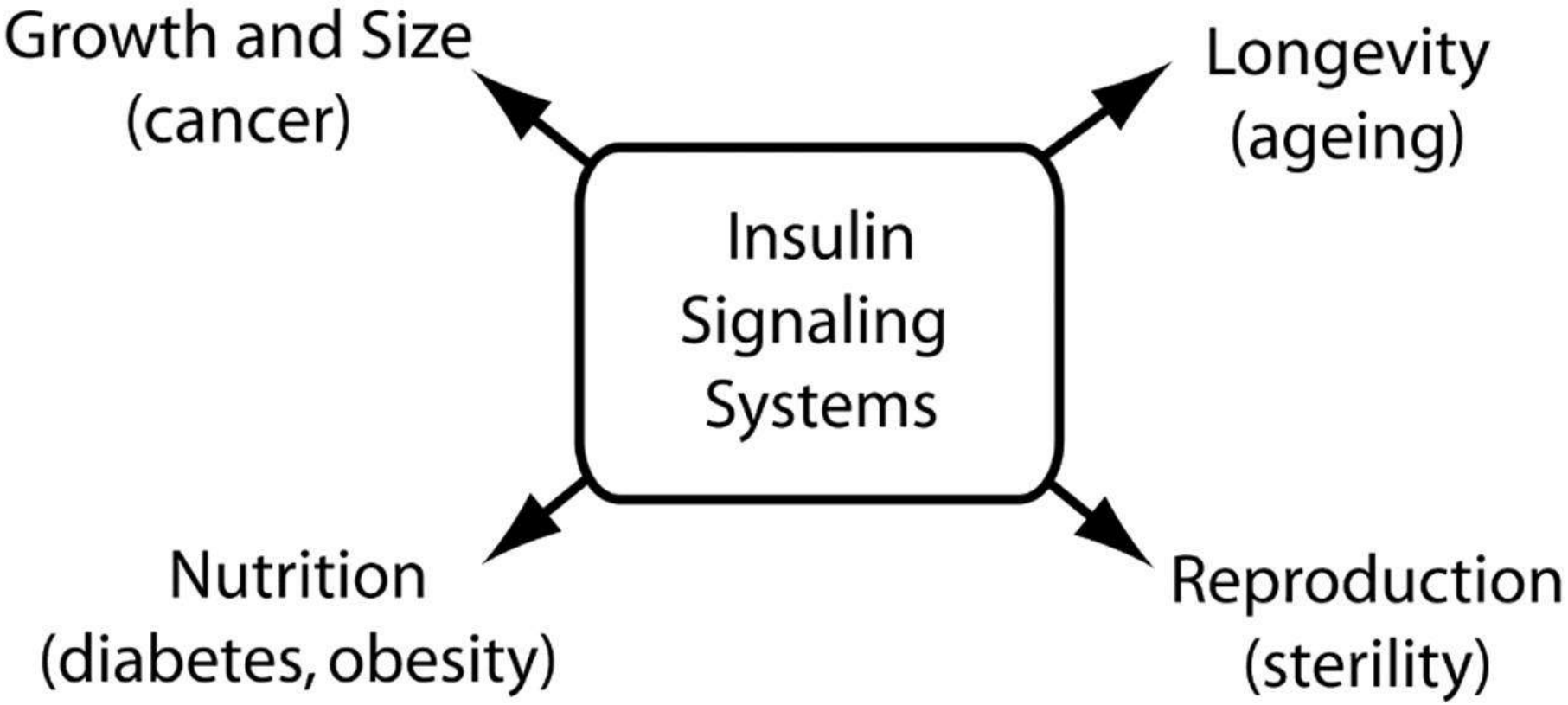
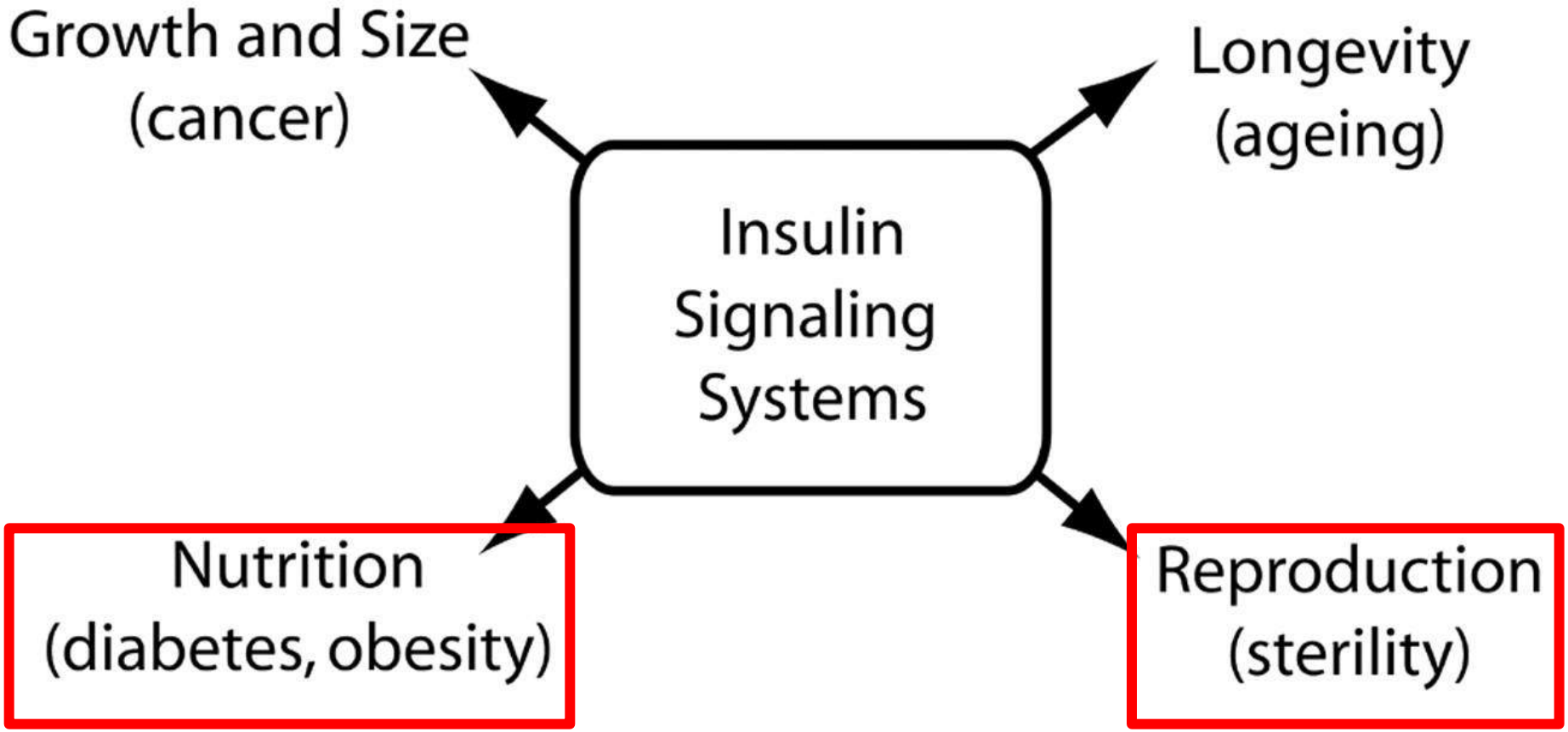


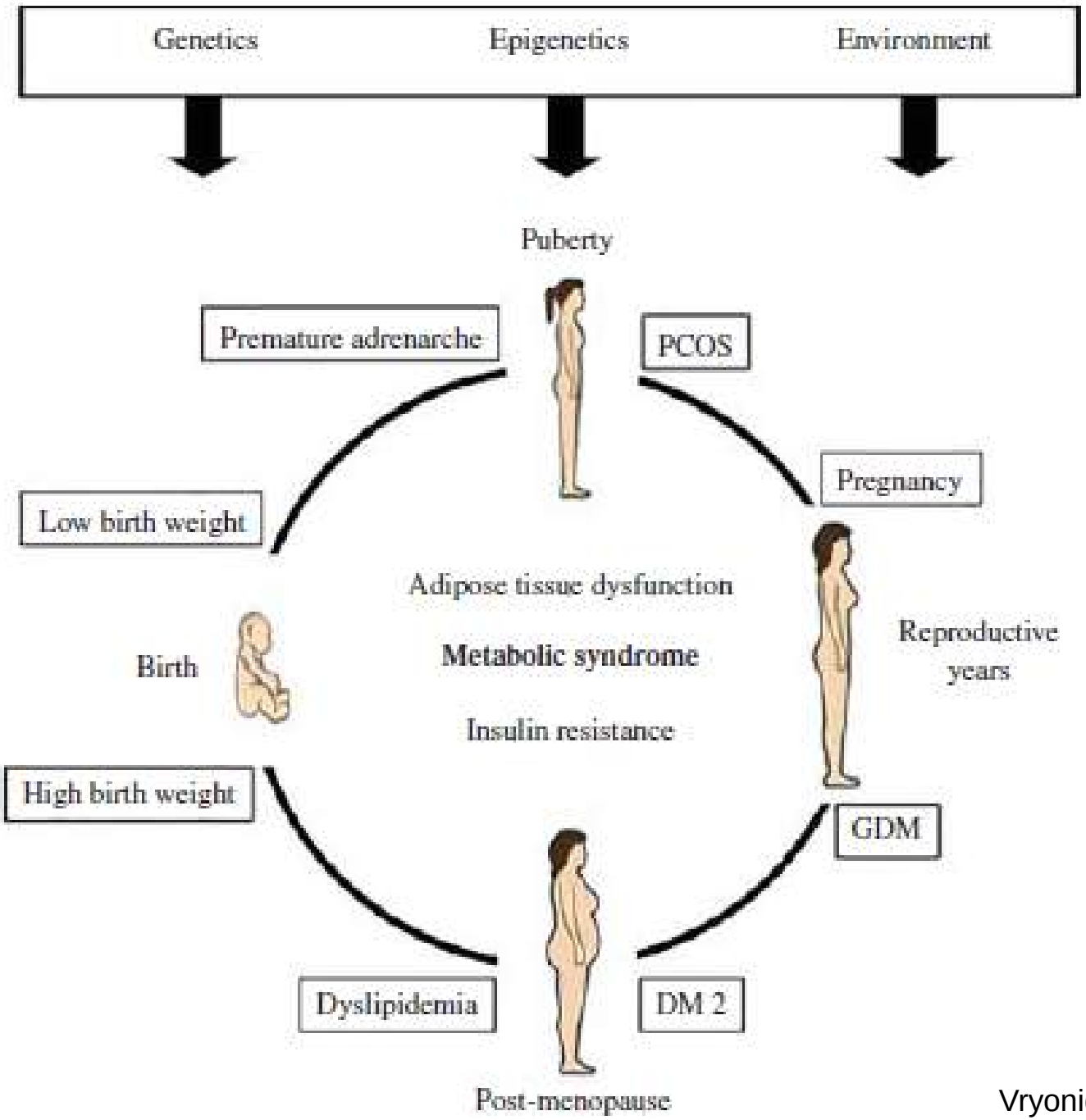
Metabolik reprodüktif durum

«İnsülin direnci ve reprodüktif bozukluk»

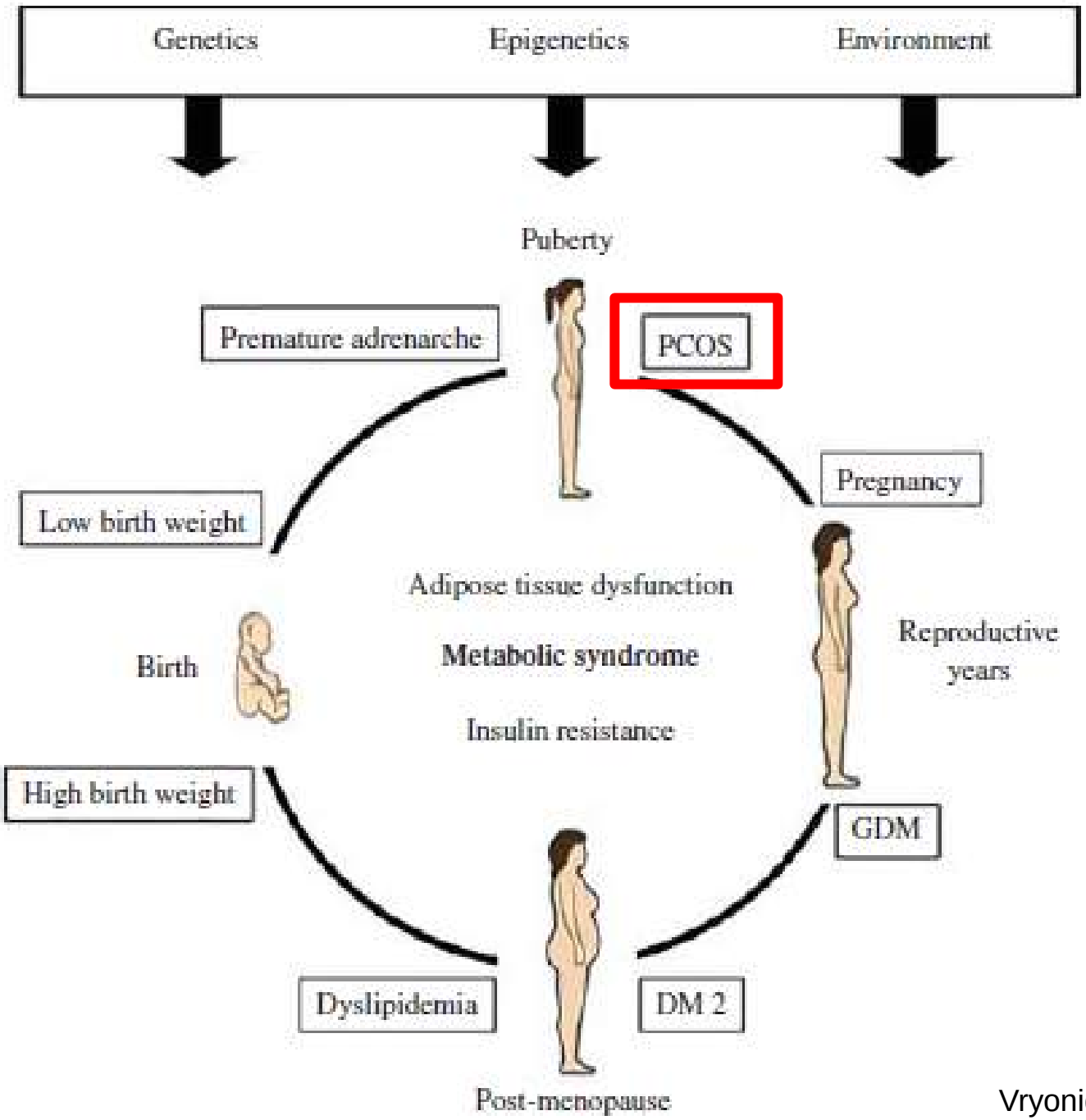


Metabolik reprodüktif durum
«İnsülin direnci ve reprodüktif bozukluk»

- Metabolizma ve reprodüktif durum birbiriyle sıkı ilişkide
- Çevresel, nütrisyonel ve hormonal faktörler enerji metabolizmasını reprodüktif ihtiyaçlara göre düzenler
- Metabolizma – reprodüktif durum ilişkisinin bozulması over disfonksiyonu gibi bozukluklara neden olur



Vryonidu et al. EJE 2015



Vryonidu et al. EJE 2015

PKOS Tanı Kriterleri
(2003 Rotterdam)

1. **Oligo-anovulasyon**
2. **Klinik hiperandrojenizm ve/veya hiperandrojenemi**
3. **Polikistik overler (PKO)**

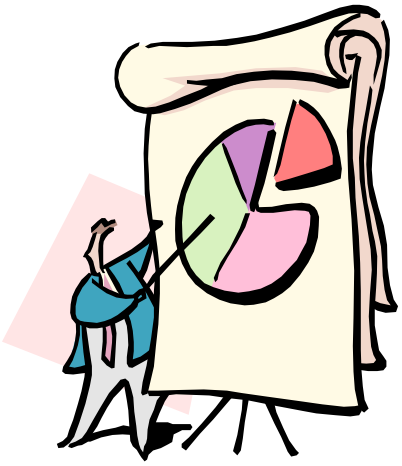
(3 kriterden 2'si tanı için gerekli)

- **Diğer ilişkili hastalıkların ekarte edilmesi**

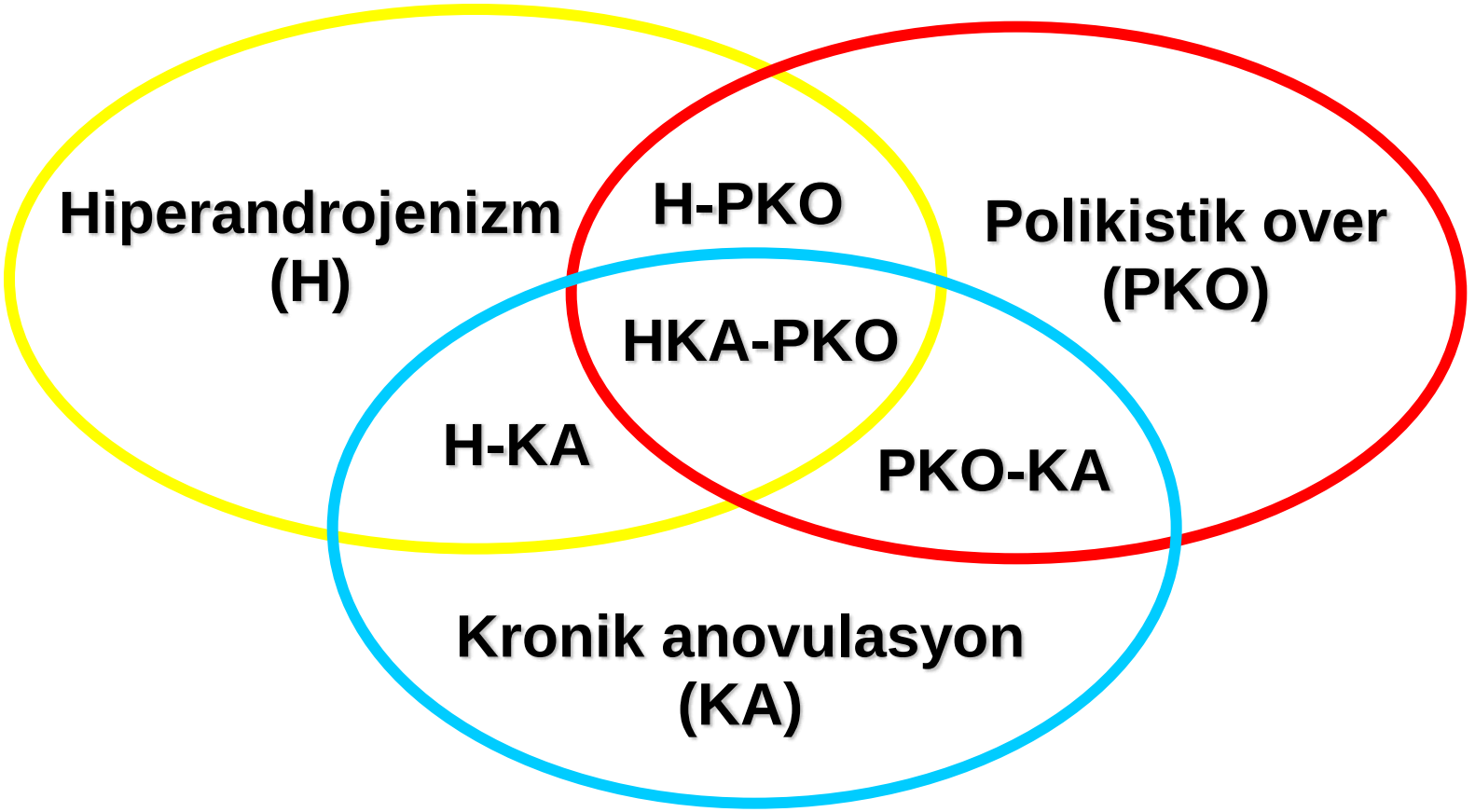
***Rotterdam ESHRE/ASRM-sponsored PCOS Consensus Workshop Group, Hum Reprod & Fertil Steril 2004**

PKOS- Belirti ve bulgular

- Hirşutizm %60-90
- Oligomenore %50-90
- İnfertilite %55-75
- PKO %50-75
- Obezite %40-60
- Amenore %25-50
- Akne %25
- Disfonksiyonel uterus kanaması %30
- Normal adet düzeni %22



PKOS - Fenotip



Yaşam boyu değişen fenotip!

Yildiz, in Polycystic Ovary Syndrome Karger 2008, Editors:Dunaif&Chang&Franks&Legro

NIH 1990, ROTTERDAM 2003, ve AE-PCOS 2006 kriterlerine göre PKOS fenotipleri

	Fenotip			
Özellik	***A***	***B***	***C***	***D***
Hiperandrojenizm	√	√	√	
Oligo-anovulasyon	√	√		√
Polikistik overler	√		√	√
NIH 1990	√	√		
Rotterdam 2003	√	√	√	√
AE-PCOS 2006	√	√	√	

Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) | National Institutes of Health | U.S. Department of Health and Human Services

Office of Disease Prevention

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NIH Office of Disease Prevention
Evidence-based Methodology Workshop on

POLYCYSTIC OVARY SYNDROME (PCOS)

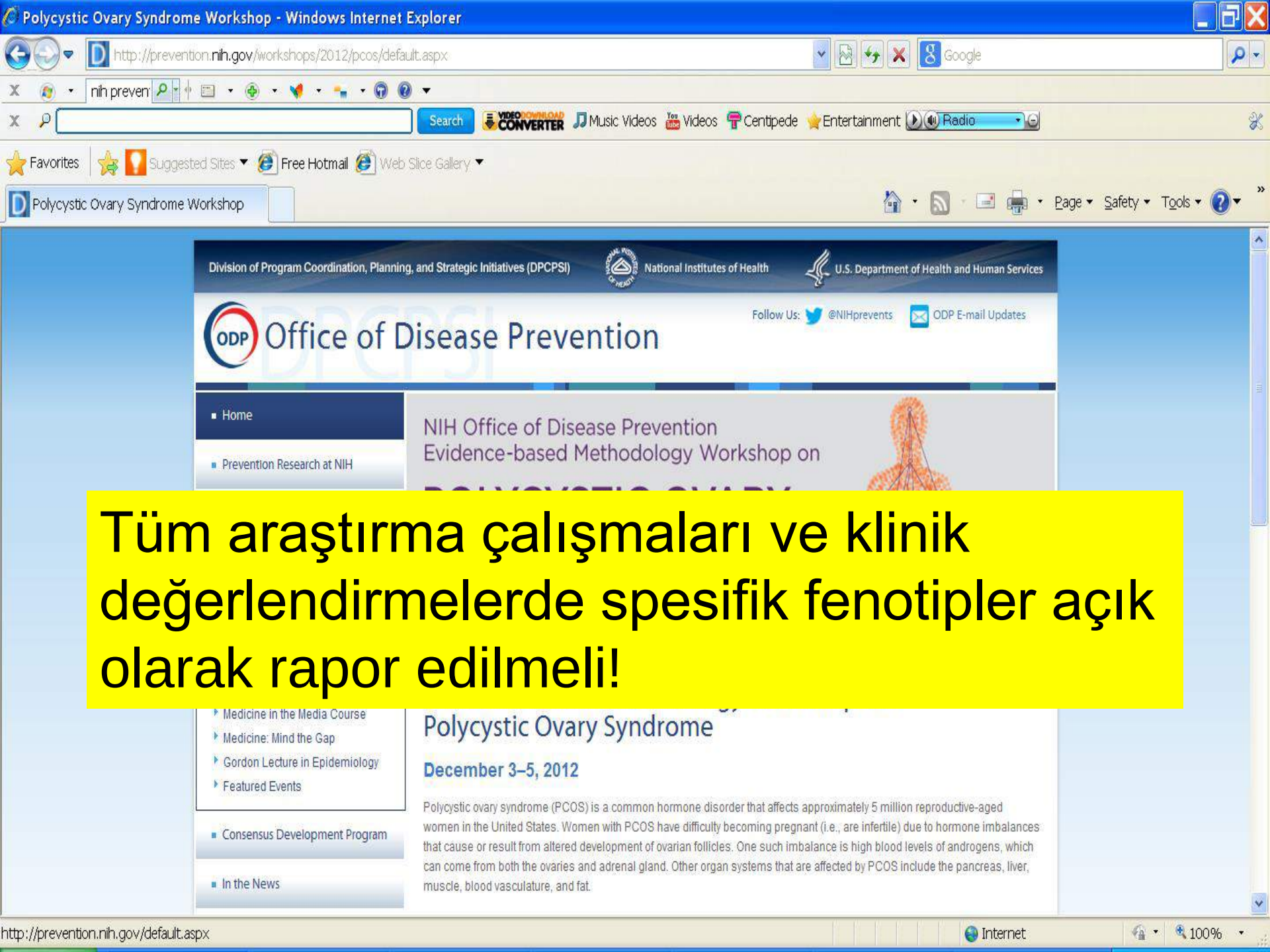
DECEMBER 3-5, 2012

ODP Home > Events and Programs > Polycystic Ovary Syndrome Methodology Workshop

Evidence-based Methodology Workshop on Polycystic Ovary Syndrome

December 3–5, 2012

Polycystic ovary syndrome (PCOS) is a common hormone disorder that affects approximately 5 million reproductive-aged women in the United States. Women with PCOS have difficulty becoming pregnant (i.e., are infertile) due to hormone imbalances that cause or result from altered development of ovarian follicles. One such imbalance is high blood levels of androgens, which can come from both the ovaries and adrenal gland. Other organ systems that are affected by PCOS include the pancreas, liver, muscle, blood vasculature, and fat.


Polycystic Ovary Syndrome Workshop - Windows Internet Explorer
http://prevention.nih.gov/workshops/2012/pcos/default.aspx
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Tüm araştırma çalışmaları ve klinik değerlendirmelerde spesifik fenotipler açık olarak rapor edilmeli!
Medicine in the Media Course
Medicine: Mind the Gap
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http://prevention.nih.gov/default.aspx
Internet
100%

PKOS – A.B.D.'de prevalans

0021-972X/04/$15.00/0
Printed in U.S.A.

The Journal of Clinical Endocrinology & Metabolism 89(6):2745–2749

doi: 10.1210/jc.2003-032046

The Prevalence and Features of the Polycystic Ovary Syndrome in an Unselected Population

RICARDO AZZIZ, KESLIE S. WOODS, ROSARIO REYNA, TIMOTHY J. KEY, ERIC S. KNOCHENHAUER, AND BULENT O. YILDIZ

Departments of Obstetrics and Gynecology (R.A., K.S.W., R.R., E.S.K.), Medicine (R.A.), and Occupational Health and Safety (T.J.K.), The University of Alabama at Birmingham, Birmingham, Alabama 35233; and Department of Internal Medicine (B.O.Y.), Endocrinology and Metabolism Unit, Hacettepe University Faculty of Medicine, Ankara, Turkey, 06100

%6.6 - NIH kriterleri

PKOS – Türkiye'de prevalans

Human Reproduction, Vol.27, No.10 pp. 3067–3073, 2012
Advanced Access publication on July 9, 2012 doi:10.1093/humrep/des232

human reproduction

ORIGINAL ARTICLE *Reproductive endocrinology*

Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria

Bulent Okan Yildiz[1], Gurkan Bozdag[2], Zuhal Yapici[2], Ibrahim Esinler[2], and Hakan Yarali[2,*]

[1]Endocrinology and Metabolism Unit, Department of Internal Medicine, Hacettepe University School of Medicine, Hacettepe, 06100 Ankara, Turkey [2]Department of Obstetrics and Gynecology, Hacettepe University School of Medicine, Hacettepe, 06100 Ankara, Turkey

MAIN RESULTS AND THE ROLE OF CHANCE: The prevalence of PCOS under NIH, Rotterdam and AE-PCOS Society criteria were 6.1, 19.9 and 15.3%, respectively. While the prevalence of metabolic syndrome was 6.1% in the whole study group, within the patients diagnosed as PCOS according to NIH, Rotterdam and AE-PCOS Society criteria, it was 12.5, 10.3 and 10.0%, respectively.

Human Reproduction, Vol.31, No.12 pp. 2841–2855, 2016
Advanced Access publication on September 22, 2016 doi:10.1093/humrep/dew218

human reproduction

META-ANALYSIS ***Reproductive epidemiology***

The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis

Gurkan Bozdag[1], Sezcan Mumusoglu[1], Dila Zengin[1], Erdem Karabulut[2], and Bulent Okan Yildiz[3,*]

STUDY QUESTION: What is the reported overall prevalence of polycystic ovary syndrome (PCOS) according to the criteria of the National Institutes of Health (NIH), Rotterdam or the Androgen Excess and PCOS Society (AE-PCOS Society)?

SUMMARY ANSWER: The reported overall prevalence of PCOS (95% CI) according to diagnostic criteria of the NIH, Rotterdam and the AE-PCOS Society is 6% (5–8%, $n = 18$ trials), 10% (8–13%, $n = 15$ trials) and 10% (7–13%, $n = 10$ trials), respectively.

Dünyada PKOS prevalans çalışmaları-2015

THE PREVALENCE AND PHENOTYPIC FEATURES OF POLYCYSTIC OVARY SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

- Kalitatif ve kantitatif değerlendirme

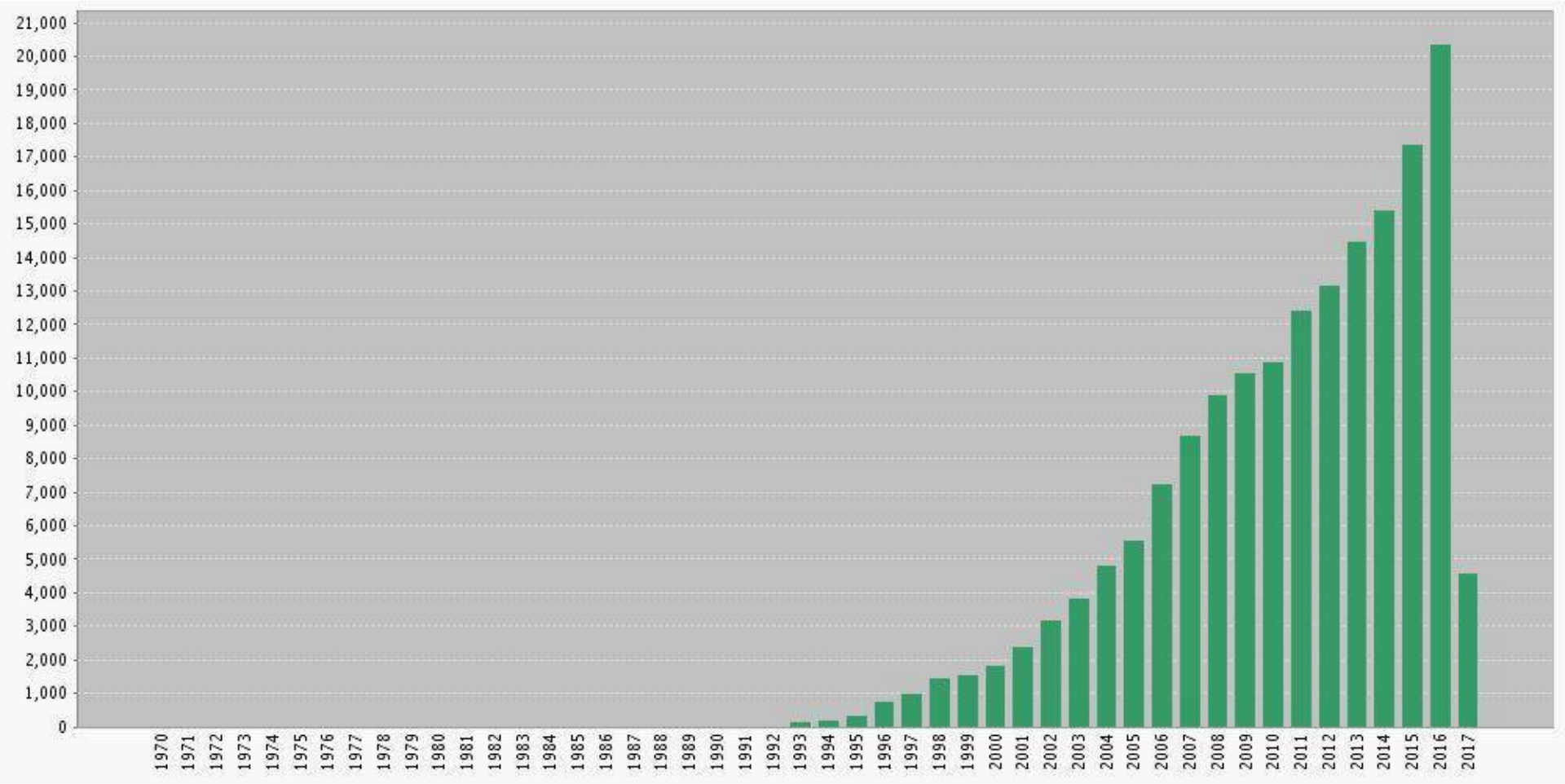
	Çalışma sayısı	Prevalans (%95 CI)
NIH	18	%6 (5-8)
Rotterdam	15	%10 (8-13)
AE-PCOS Society	10	%10 (7-13)
Hirşutizm	14	%13 (8-20)
Hiperandrojenemi	9	%11 (8-15)
PKO	12	%28 (22-35)
Oligo-anovulasyon	19	%15 (12-18)

Bozdag et al. Hum Reprod 2016

PKOS – Neden önemli?

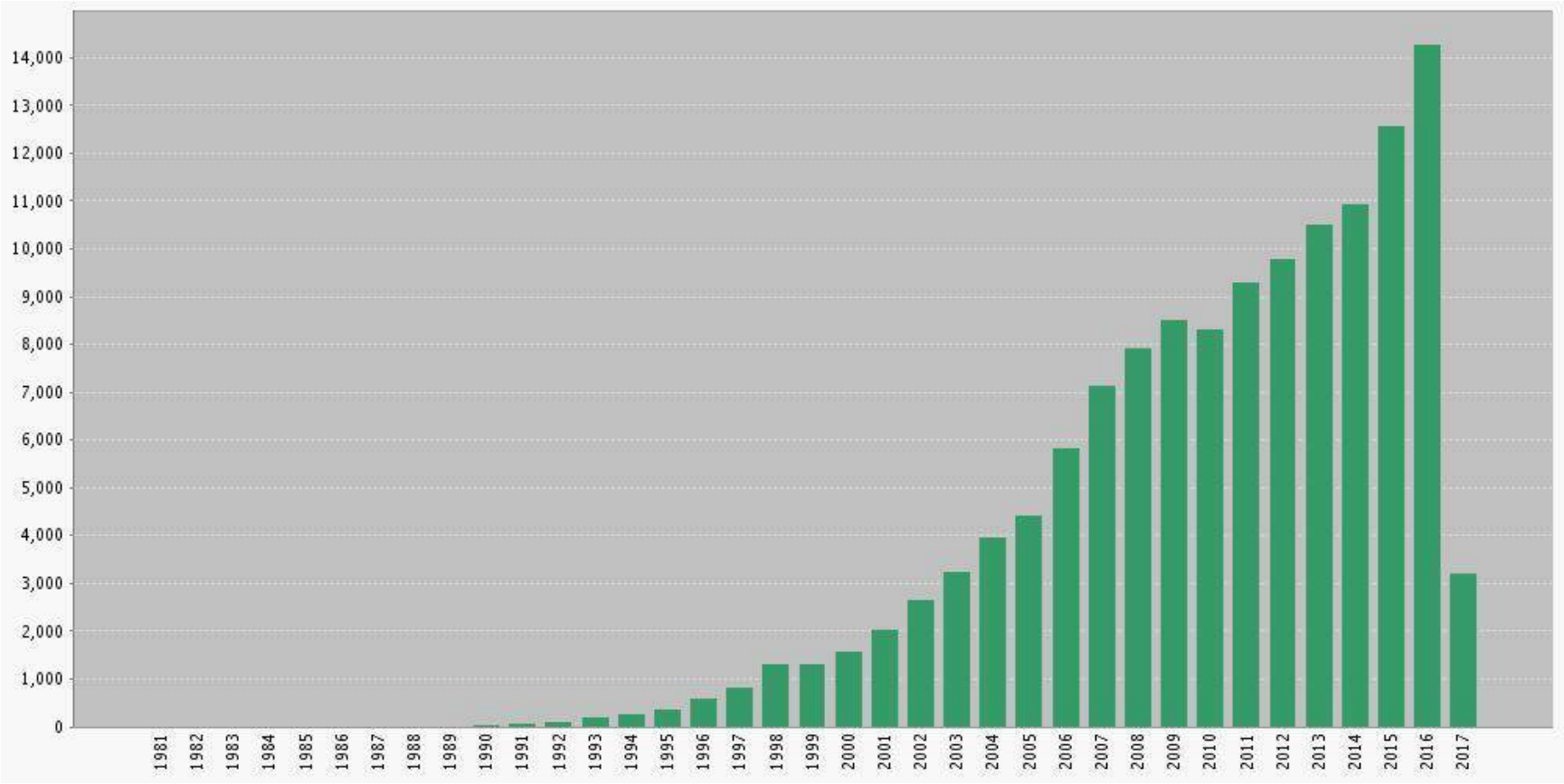
- **Doğurganlık çağındaki kadınlarda en sık görülen endokrin problem**
- **Anovulatuvar infertilitenin en sık nedeni**
- **Toplum sağlığı etkileri**
  - **artmış tip 2 diyabet riski ve prevalansı**
  - **artmış kardiyovasküler hastalık riski**

PKOS



>8500 makale, >170.000 atıf – WoS 19.04.2017

PKOS ve insülin direnci



>5000 makale, >131.000 atıf – WoS 19.04.2017

Metabolik reprodüktif durum

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0021-972X/80/5001-0113$02.00/0
Journal of Clinical Endocrinology and Metabolism

Vol. 50, No. 1
Printed in U.S.A.

Correlation of Hyperandrogenism with Hyperinsulinism in Polycystic Ovarian Disease*

GEORGE A. BURGHEN,† JAMES R. GIVENS, AND ABBAS E. KITABCHI

Departments of Pediatrics, Medicine, and Obstetrics and Gynecology and the Clinical Research Center, University of Tennessee Center for the Health Sciences, Memphis, Tennessee 38163

ABSTRACT. We evaluated basal plasma total immunoreactive insulin (insulin), androstenedione, and testosterone in 14 obese women: 8 with polycystic ovarian disease (PCOD) and 6 obese controls. All 3 hormones were significantly elevated ($P < 0.02$ to $P < 0.001$) in PCOD patients. A significant correlation among basal levels of plasma insulin, androstenedione, and testosterone was demonstrated. The PCOD group had significantly higher levels of glucose at 1, 2, and 3 h, with similar significant increases in plasma insulin levels at 0, 2, and 3 h. A significant correlation was found between plasma insulin response areas and plasma testosterone ($P < 0.001$) in the control and PCOD patients. These studies demonstrate that hyperandrogenism correlates with hyperinsulinism. (*J Clin Endocrinol Metab* **50:** 113, 1980)

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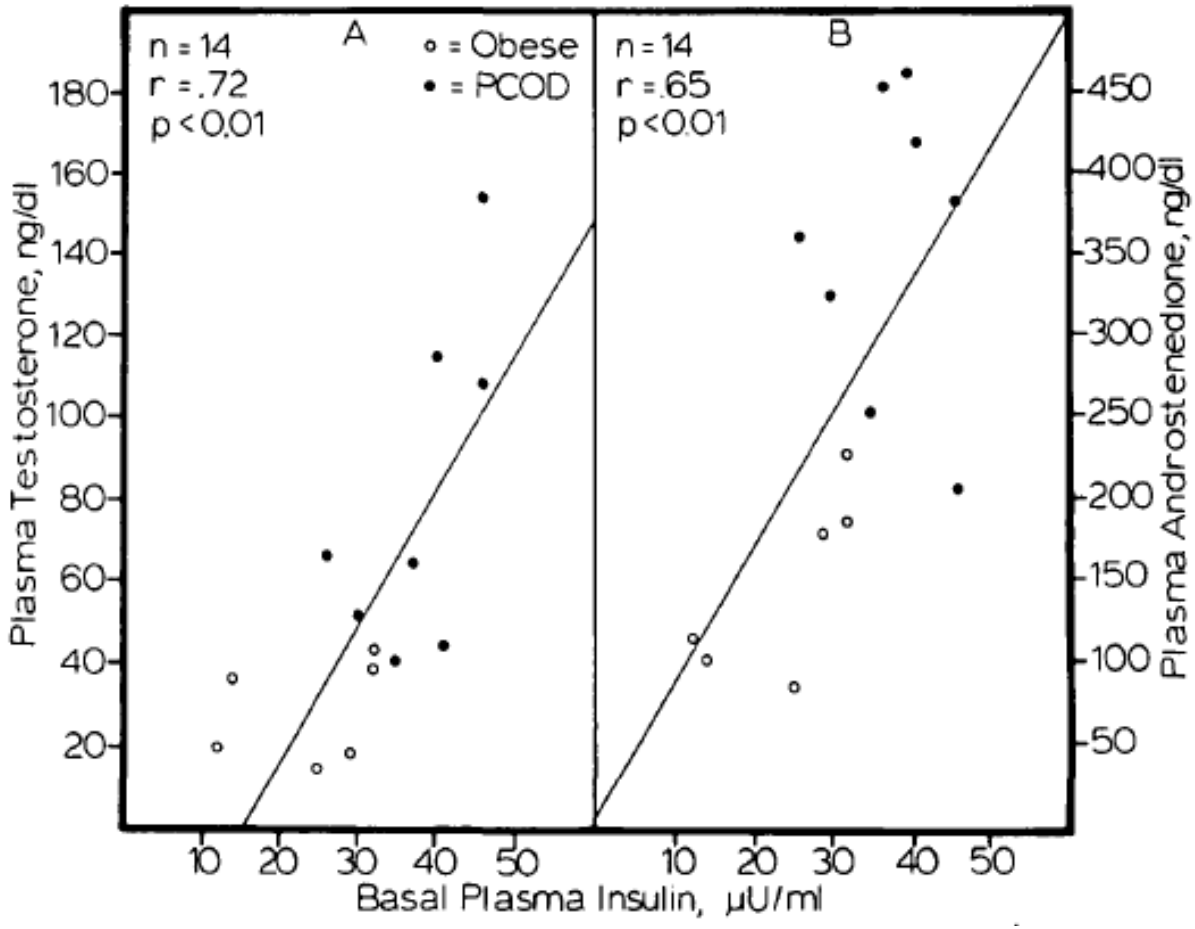

JCEM 1980

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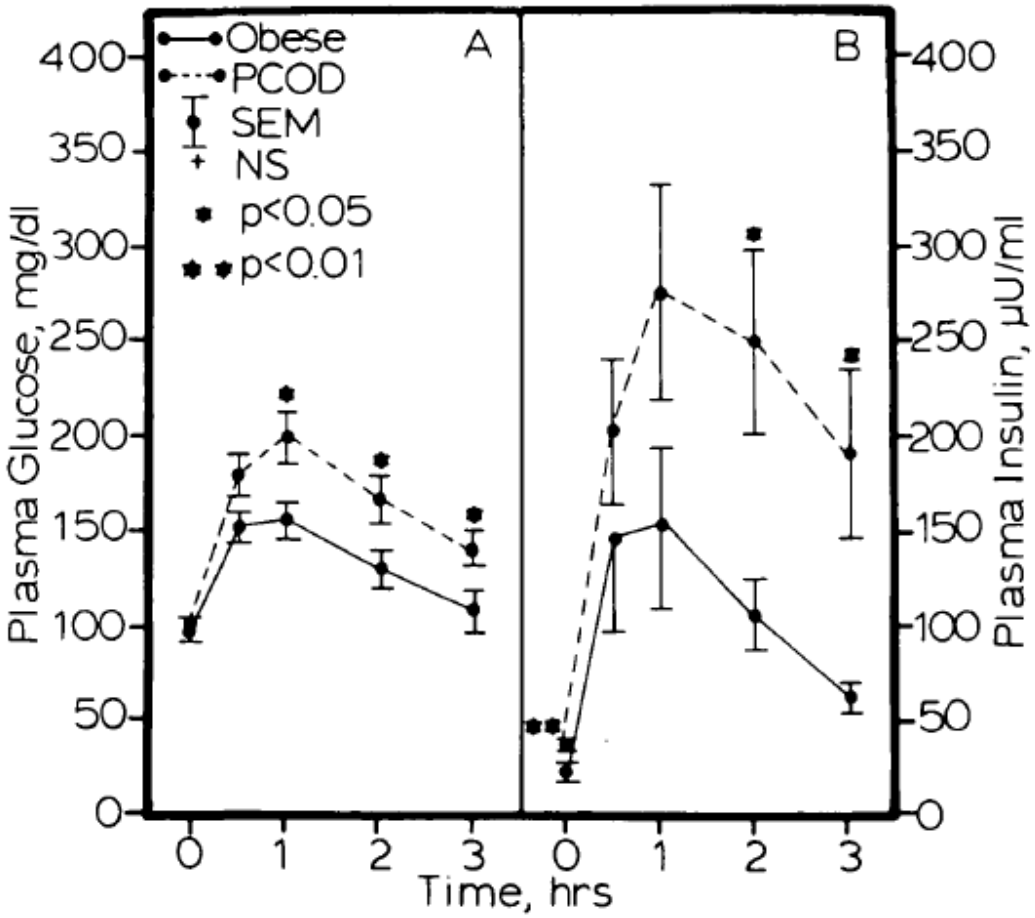

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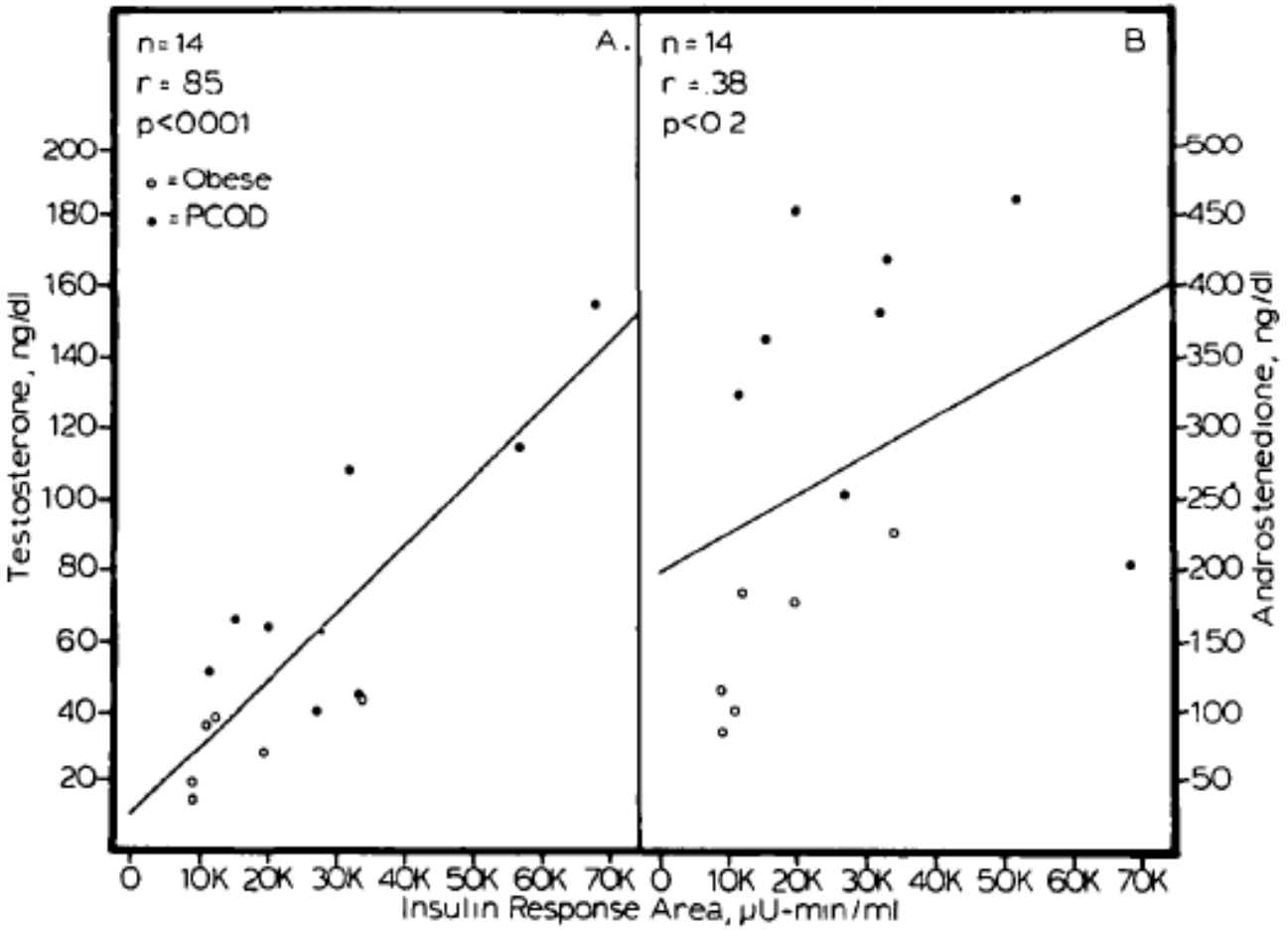

JCEM 1980

0021-972X/87/6503-0499$02.00/0
Journal of Clinical Endocrinology and Metabolism

Vol. 65, No. 3
Printed in U.S.A.

Characterization of Groups of Hyperandrogenic Women with Acanthosis Nigricans, Impaired Glucose Tolerance, and/or Hyperinsulinemia*

ANDREA DUNAIF†, MAGARET GRAF, JOHN MANDELI, VIMLA LAUMAS, AND ARETA DOBRJANSKY

Departments of Medicine, Obstetrics, Gynecology, and Reproductive Science, and Biomathematical Sciences, Mt. Sinai School of Medicine, City University of New York, New York, New York 10029

ABSTRACT. This study examined the prevalence of both basal and glucose-stimulated hyperinsulinemia and acanthosis nigricans (AN) as well as the relationship between insulin and androgen levels in hyperandrogenic women. Sixty-two women who had an elevation of 1 or more plasma androgen levels were studied. The results in these women, grouped for analysis on the basis of obesity and ovulatory status, were compared to those in 36 control women of similar ages and weights. The anovulatory hyperandrogenic women had the clinical and biochemical features of the polycystic ovary syndrome (PCO). Oral glucose tolerance tests were performed with measurement of glucose, insulin, sex hormone-binding globulin (SHBG), and total and non-SHBG-bound sex steroid levels.

AN was present in 29% of the hyperandrogenic women, the majority of them obese. Fifty percent of obese PCO women had AN, but they did not otherwise differ from PCO women lacking this dermatological change. Only women with PCO had significant hyperinsulinemia independent of obesity, and obese PCO women with AN had the highest serum insulin levels. Plasma glucose values during the oral glucose tolerance test were significantly increased in obese PCO women independent of the presence of AN, and 20% of these women had frank impairment of glucose tolerance. Ovulatory hyperandrogenic women had normal insulin levels and glucose tolerance. Obese and nonobese women had different relationships between sex steroid and insulin levels; obese women had significant correlations between insulin and non-SHBG testosterone levels ($r = 0.30$; $P < 0.05$), whereas nonobese women had significant correlations between insulin and FSH ($r = 0.40$; $P < 0.01$), dehydroepiandrosterone sulfate ($r = 0.33$; $P < 0.05$), and SHBG ($r = -0.37$; $P < 0.05$) levels, suggesting that the mechanisms underlying the association between sex steroid and insulin levels are complex.

These findings suggest that 1) only women with PCO have hyperinsulinemia independent of obesity; hyperinsulinemia is not a feature of hyperandrogenic states in general; 2) AN is a common finding in obese hyperandrogenic women, particularly those with PCO; 3) only obese PCO women are at risk for impairment of glucose tolerance, independent of the presence of AN, suggesting that the negative impact of PCO and obesity on insulin action is additive; and 4) PCO women with AN can be considered as a subgroup of PCO and do not appear to have a distinct endocrine disorder. (*J Clin Endocrinol Metab* **65**: 499, 1987)

Characterization of Groups of Hyperandrogenic Women with Acanthosis Nigricans, Impaired Glucose Tolerance, and/or Hyperinsulinemia*

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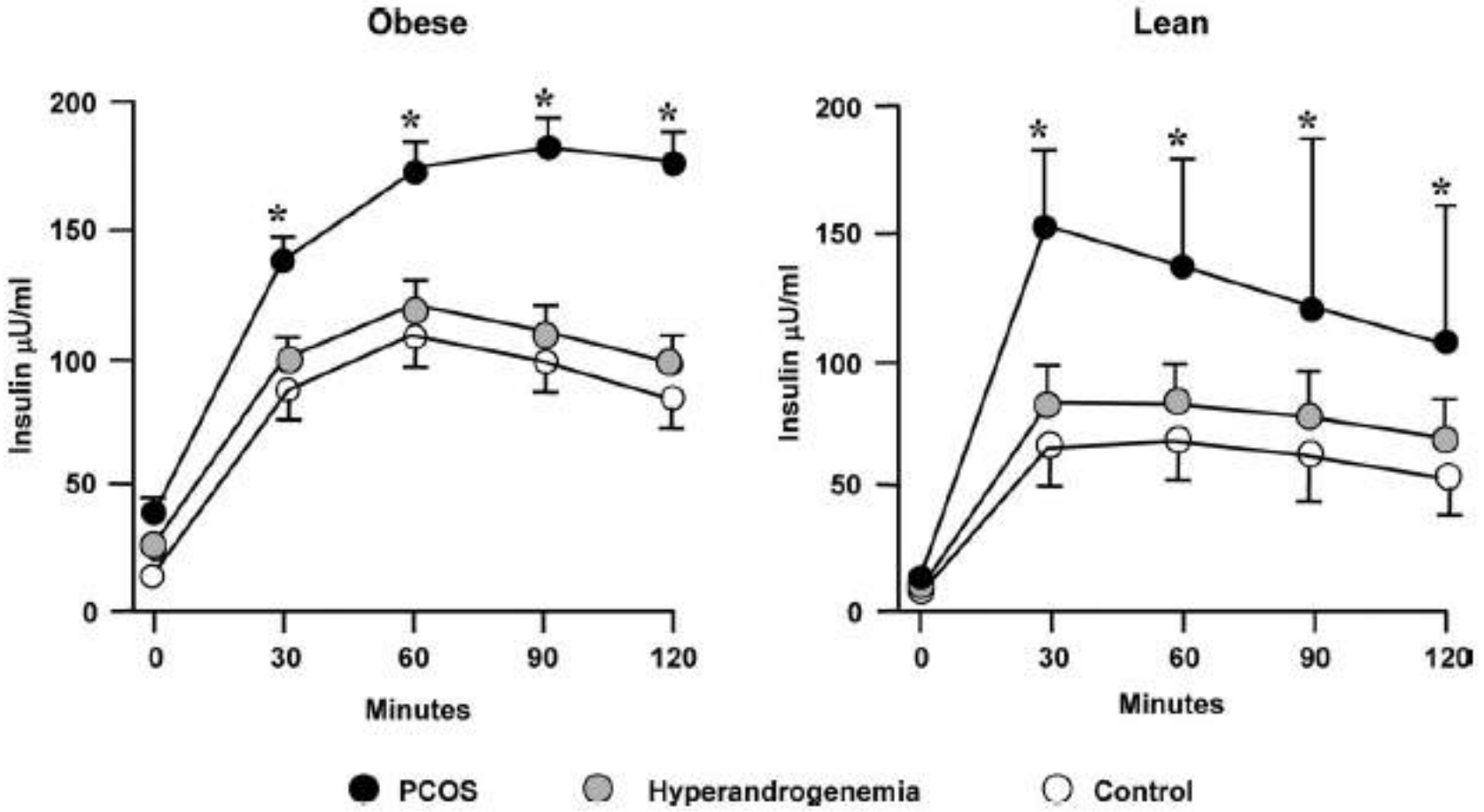
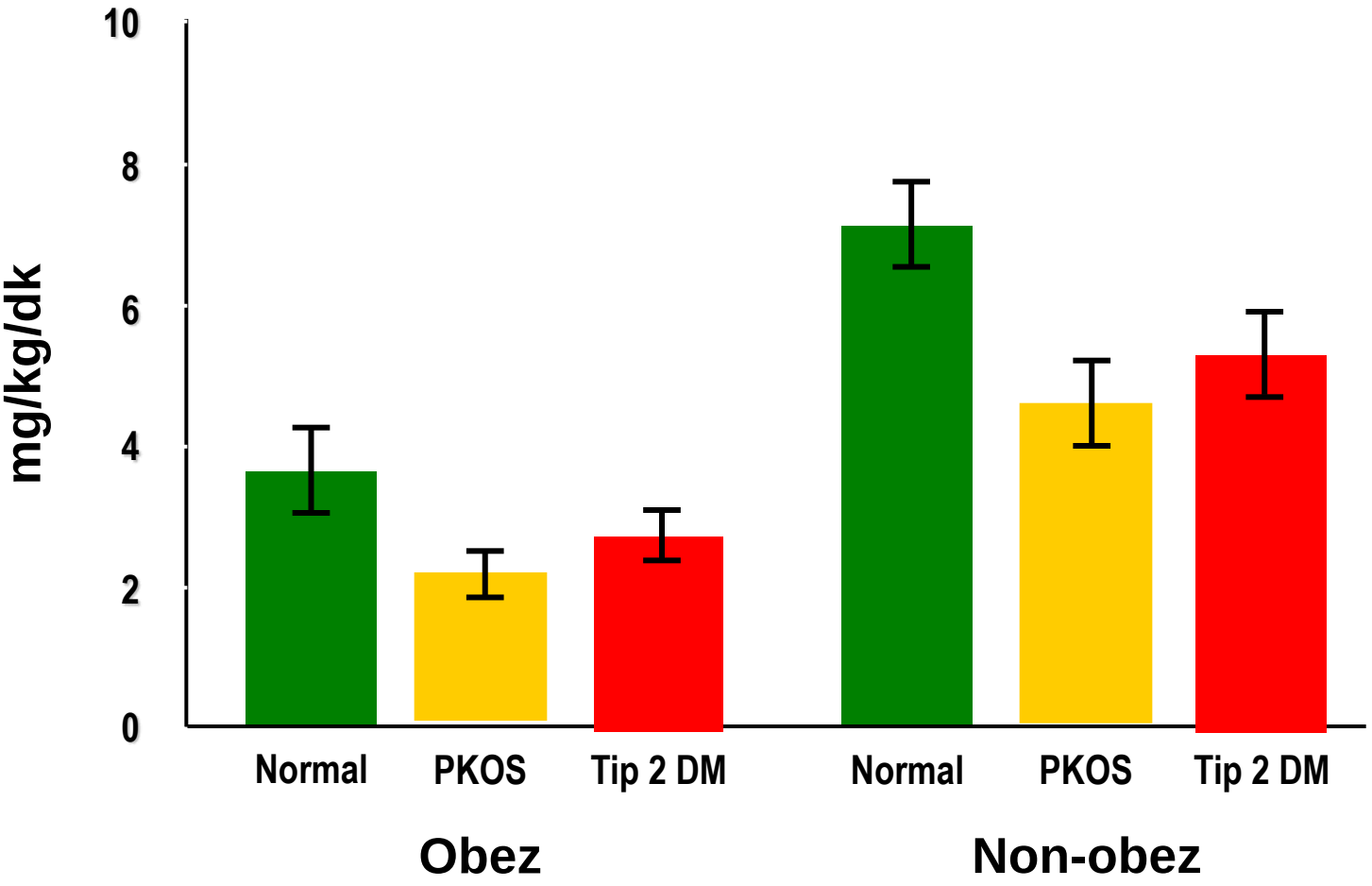


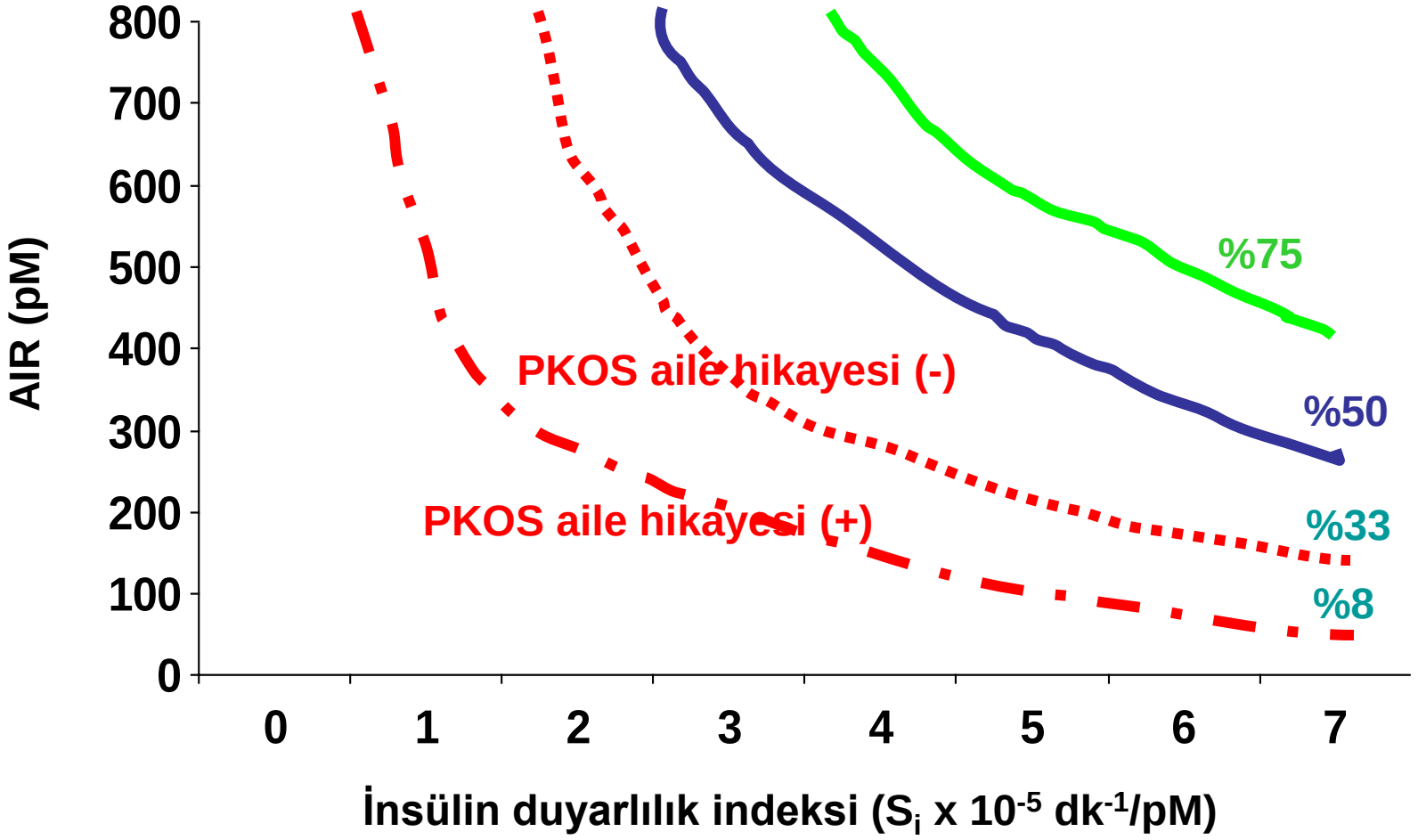
JCEM 1987

PKOS'da insülin aracılı glukoz alınımı



Dunaif A., Endocr Rev 1997

PKOS'da β-hücre disfonksiyonu



Ehrmann et al., J Clin Invest 1995

PKOS ve insülin direnci

- **İnsülin direnci prevalansı**

  - tanım

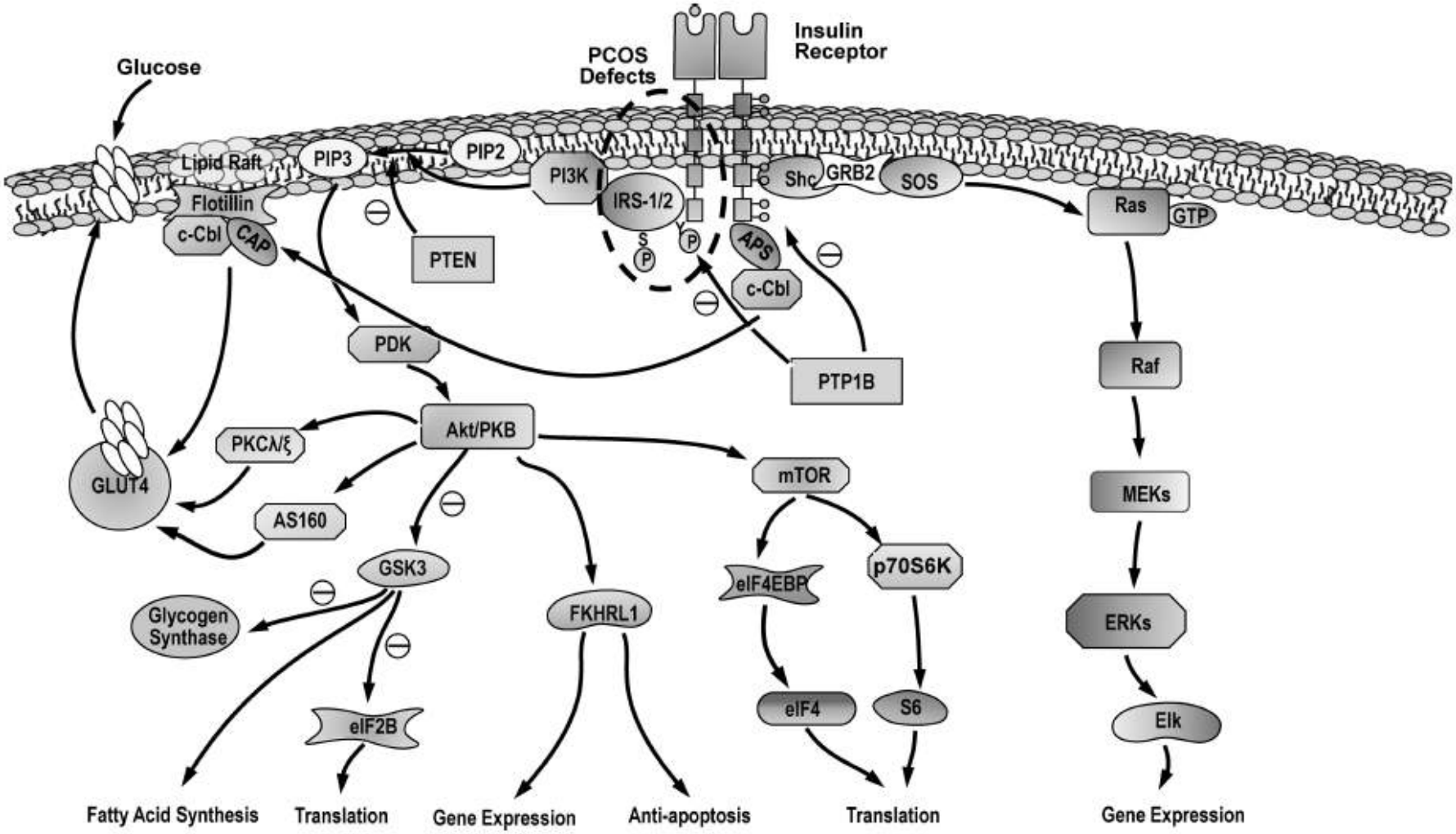
  - ölçüm metodu

  - çalışılan populasyon

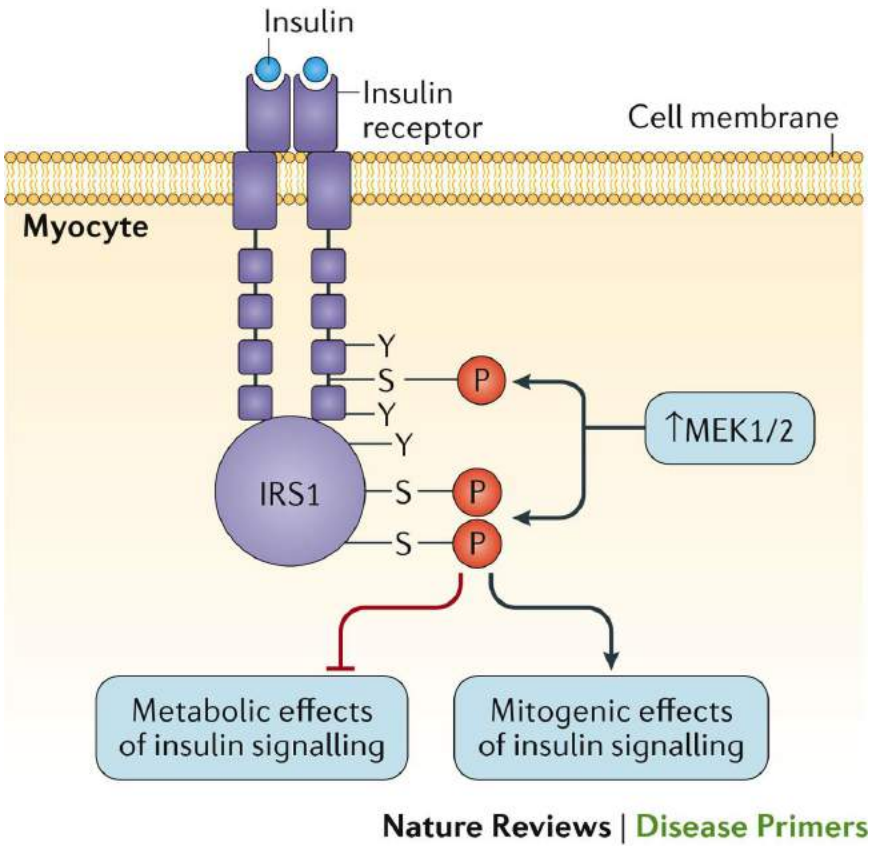
- **PKOS'da yaş, VKİ ve etnik yönden eşleştirilmiş kontrol grubu kullanıldığında insülin direnci prevalansı %65'e varan oranlarda***

*Dunaif et al., Diabetes 1989
Legro et al., JCEM 1998
DeUgarte et al., Fertil Steril 2005

İnsülin reseptör sinyal yolağı



PKOS'da kasta insülin direncinin moleküler mekanizmaları



Azziz, R. *et al.* (2016) Polycystic ovary syndrome
Nat. Rev. Dis. Primers doi:10.1038/nrdp.2016.57

Evolutionary determinants of polycystic ovary syndrome: part 1

Uğur Ünlütürk, M.D.,[a] Efe Sezgin, Ph.D.,[b] and Bulent Okan Yildiz, M.D.[a]

[a] Division of Endocrinology and Metabolism, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara; and [b] Department of Food Engineering, Laboratory of Nutrigenomics and Epidemiology, Izmir Institute of Technology, Izmir, Turkey

Polycystic ovary syndrome (PCOS) is a common and complex genetic disorder that develops under varying degrees of hyperandrogenemic and hyperinsulinemic conditions that cause phenotypic variability ranging from mild hirsutism to anovulation and infertility. In addition to increased risk of reproductive disability, PCOS is associated with metabolic diseases including type 2 diabetes, dyslipidemia, and cardiovascular disease. Similar prevalence rates and shared genetic susceptibility of PCOS among different populations suggest that genetic risk factors were already present in the ancestors of humans. Contemporary human genetic studies inform us that the origin of human ancestors is from Africa. Sharing common susceptibility loci between Chinese and European ancestry suggests that PCOS may have persisted for more than 50,000 years, before the migration of humans out of Africa. Although PCOS is the most common cause of anovulatory infertility, its high prevalence is still a paradox. From an evolutionary perspective, the pathogenic mechanisms underlying PCOS might be candidate factors for survival advantage of the human being. Former compensatory advantageous factors may become pathogenic mechanisms underlying complex metabolic disease with prolonged life expectancy and transition to sedentary lifestyle.
(Fertil Steril® 2016;106:33–41. ©2016 by American Society for Reproductive Medicine.)

- Populasyonlar arasında allel frekanslarında önemli farklılıklar
- Değişik çevresel koşullarda PCOS ilişkili genler üzerinde pozitif ve negatif faktörlere bağlı kompleks seçicilik
- PKOS'ta kalıtsal duyarlılık lokuslarından biri INSR ile ilişkili

Fertil Steril 2016

TABLE 1

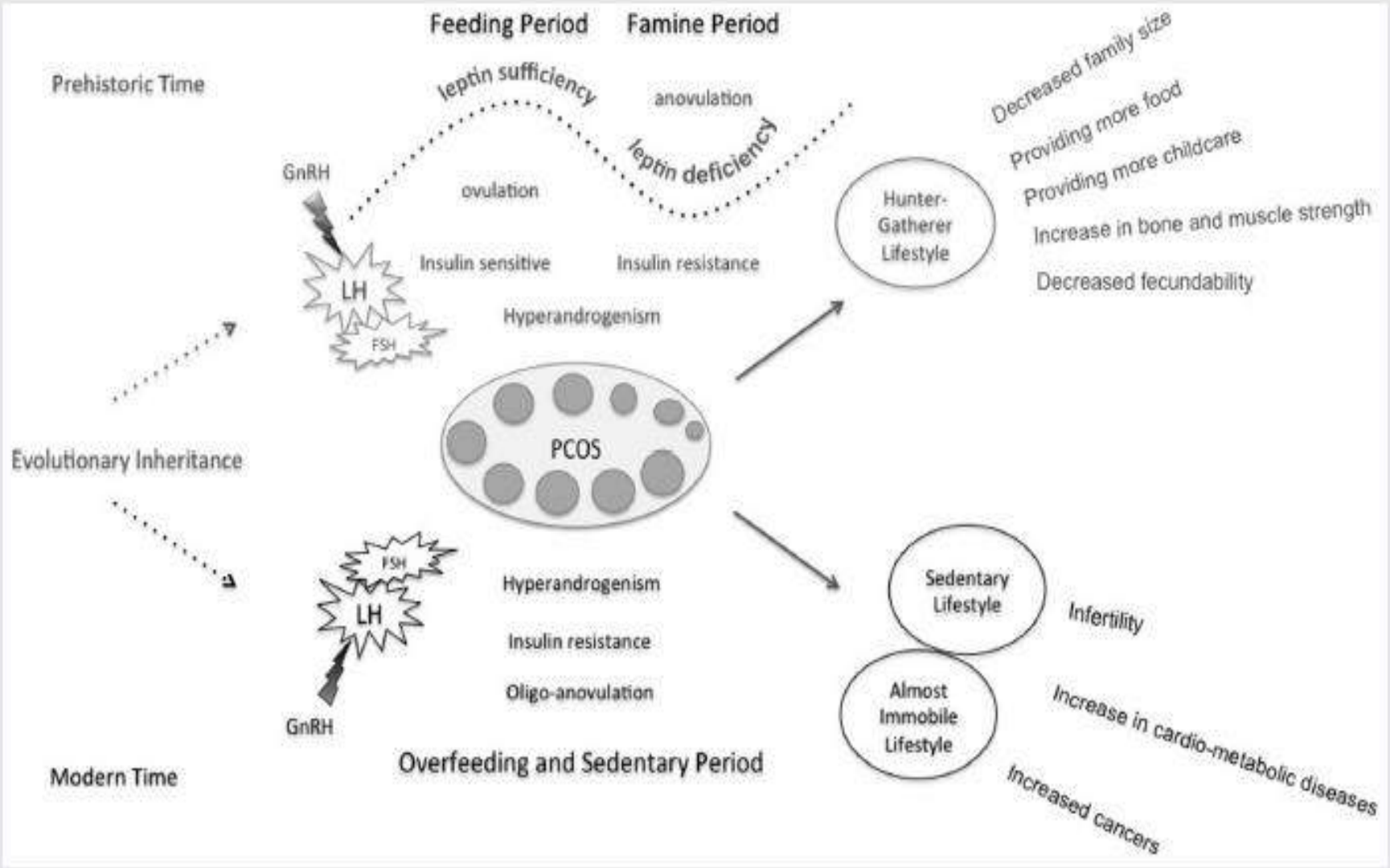
Allelic nature and population frequency distribution of genetic variants associated with polycystic ovary syndrome (PCOS) in multiple GWAS.

		Allelic nature[a]				Effect allele population frequency[b]				
Gene	SNP	Ancestral	Derived	PCOS[c]	Effect on PCOS	African	European	East Asian	South Asian	American
FSHR	rs2268361	C	T	C	Protective	0.75	0.36	0.50	0.46	0.37
C9orf3	rs4385527	G	A	G	Protective	0.90	0.60	0.18	0.77	0.65
	rs3802457	G	A	G	Protective	0.72	0.98	0.89	0.97	0.97
	rs10993397	C	T	C	Protective	0.87	0.60	0.73	0.71	0.65
DENND1A	rs10986105	T	G	T	Susceptible	0.15	0.04	0.05	0.06	0.08
SUMO1P1	rs6022786	A	G	A	Susceptible	0.57	0.41	0.41	0.44	0.34
GATA4/NEIL2	rs804279	A	T	A	Protective	0.64	0.73	0.81	0.74	0.78
KRR1	rs1275468	C	T	C	Susceptible	0.62	0.70	0.57	0.68	0.66
ERBB3	rs7312770	C	T	C	Susceptible	0.51	0.46	0.22	0.31	0.31
THADA	rs12468394	A	C	C	Protective	0.54	0.48	0.73	0.34	0.70
	rs12478601	T	C	C	Protective	0.18	0.41	0.71	0.34	0.60
	rs7563201	G	A	A	Protective	0.37	0.53	0.28	0.55	0.31
LHCGR	rs13405728	A	G	G	Protective	0.32	0.07	0.27	0.17	0.19
DENND1A	rs10818854	G	A	A	Susceptible	0.08	0.05	0.05	0.08	0.07
	rs10760321	G	A	A	Susceptible	0.65	0.71	0.65	0.66	0.73
YAP1	rs1894116	A	G	G	Susceptible	0.07	0.08	0.18	0.22	0.05
	rs11225154	A	G	A	Susceptible	0.02	0.08	0.19	0.24	0.05
RAB5B/SUOX	rs705702	A	G	G	Susceptible	0.05	0.32	0.22	0.20	0.23
HMGA2	rs2272046	A	C	C	Protective	0.001	0.03	0.08	0.03	0.01
TOX3	rs4784165	T	G	G	Susceptible	0.44	0.26	0.36	0.27	0.33
INSR	rs2059807	G	A	G	Susceptible	0.82	0.62	0.37	0.68	0.47
KHDRBS3	rs10505648	A	G	G	Protective	0.28	0.52	0.09	0.27	0.36
KCNA4/FSHB	rs11031006	G	A	A	Susceptible	0.05	0.15	0.03	0.10	0.10
ERB4	rs1351592	C	G	G	Susceptible	0.64	0.19	0.09	0.28	0.21
RAD50	rs13164856	C	T	T	Susceptible	0.63	0.70	0.62	0.69	0.58
ERBB2	rs7218361	G	A	A	Susceptible	0.002	0.05	0.0	0.02	0.03

[a] Information based on dbSNP and 1000 Genomes data.
[b] Allele state associated with PCOS.
[c] Frequency of PCOS-associated alleles among human population samples in 1000 Genomes project.

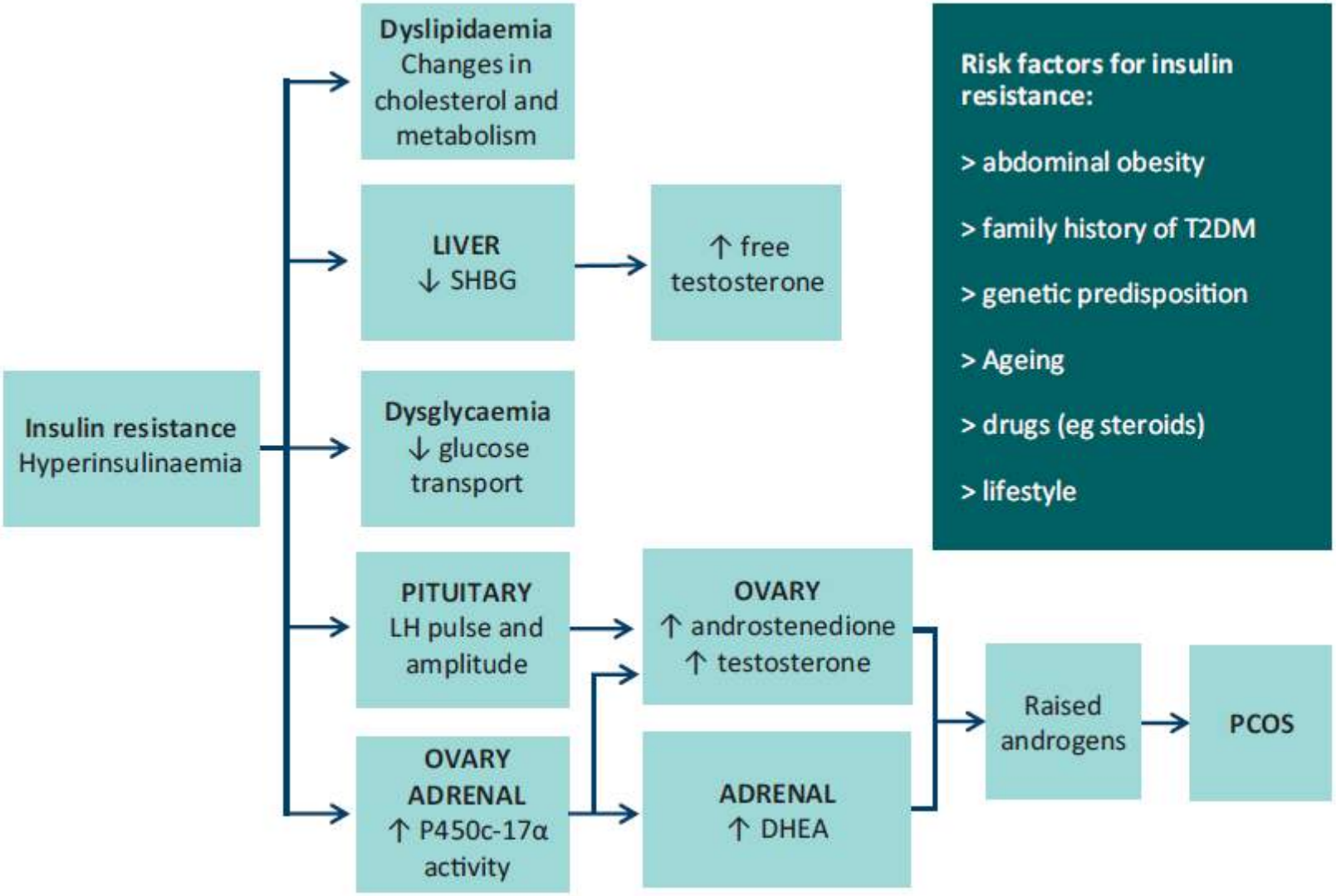
Fertil Steril 2016

FIGURE 1



Fertil Steril 2016

PKOS ve insülin direnci



Clin Med 2015

PKOS'da metabolik disfonksiyon

Human Reproduction Update, Vol.16, No.4 pp. 347–363, 2010
Advanced Access publication on February 16, 2010 doi:10.1093/humupd/dmq001

human reproduction update

Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: a systematic review and meta-analysis

Lisa J. Moran[1,*], Marie L. Misso[2], Robert A. Wild[3,†], and Robert J. Norman[4,†]

RESULTS: A total of 2192 studies were reviewed and 35 were selected for final analysis. Women with PCOS had increased prevalence of IGT (OR 2.48, 95% CI 1.63, 3.77; BMI-matched studies OR 2.54, 95% CI 1.44, 4.47), DM2 (OR 4.43, 95% CI 4.06, 4.82; BMI-matched studies OR 4.00, 95% CI 1.97, 8.10) and metabolic syndrome (OR 2.88, 95% CI 2.40, 3.45; BMI-matched studies OR 2.20, 95% CI 1.36, 3.56). One study assessed IGT/DM2 incidence and reported no significant differences in DM2 incidence (OR 2.07, 95% CI 0.68, 6.30). One study assessed conversion from normal glucose tolerance to IGT/DM2 (OR 2.4, 95% CI 0.7, 8.0). No studies reported metabolic syndrome incidence.

PKOS'da metabolik disfonksiyon*

	PCOS	Control	OR	95% CI
IGT	44/347	20/319	2.54	1.44-4.47
T2DM	19/441	63/1175	4.0	1.97-8.10
MetSend	61/273	37/276	2.2	1.36-3.56

2192 çalışmanın 35'i (24 NIH, 11 Rotterdam kriterleri)

*BMI-matched

PKOS'da metabolik disfonksiyon

Human Reproduction, Vol.27, No.10 pp. 3067–3073, 2012
Advanced Access publication on July 9, 2012 doi:10.1093/humrep/des232

human reproduction

ORIGINAL ARTICLE *Reproductive endocrinology*

Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria

Bulent Okan Yildiz[1], Gurkan Bozdag[2], Zuhal Yapici[2], Ibrahim Esinler[2], and Hakan Yarali[2,*]

[1]Endocrinology and Metabolism Unit, Department of Internal Medicine, Hacettepe University School of Medicine, Hacettepe, 06100 Ankara, Turkey [2]Department of Obstetrics and Gynecology, Hacettepe University School of Medicine, Hacettepe, 06100 Ankara, Turkey

MAIN RESULTS AND THE ROLE OF CHANCE: The prevalence of PCOS under NIH, Rotterdam and AE-PCOS Society criteria were 6.1, 19.9 and 15.3%, respectively. While the prevalence of metabolic syndrome was 6.1% in the whole study group, within the patients diagnosed as PCOS according to NIH, Rotterdam and AE-PCOS Society criteria, it was 12.5, 10.3 and 10.0%, respectively.

ORIGINAL ARTICLE

Polycystic Ovary Syndrome Is a Risk Factor for Type 2 Diabetes

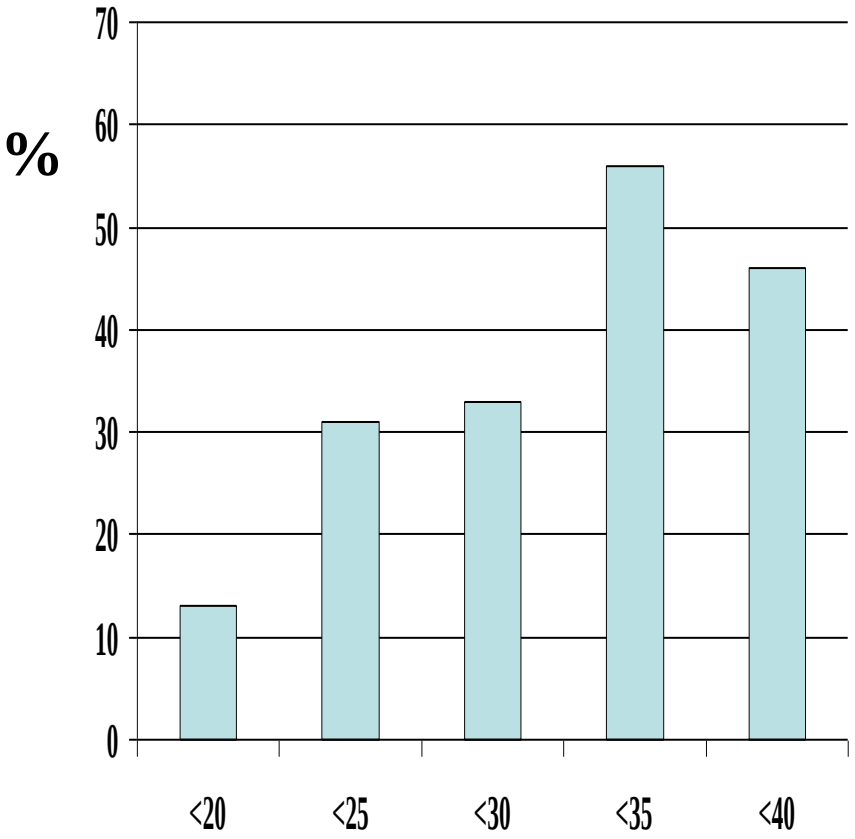
Results From a Long-Term Prospective Study

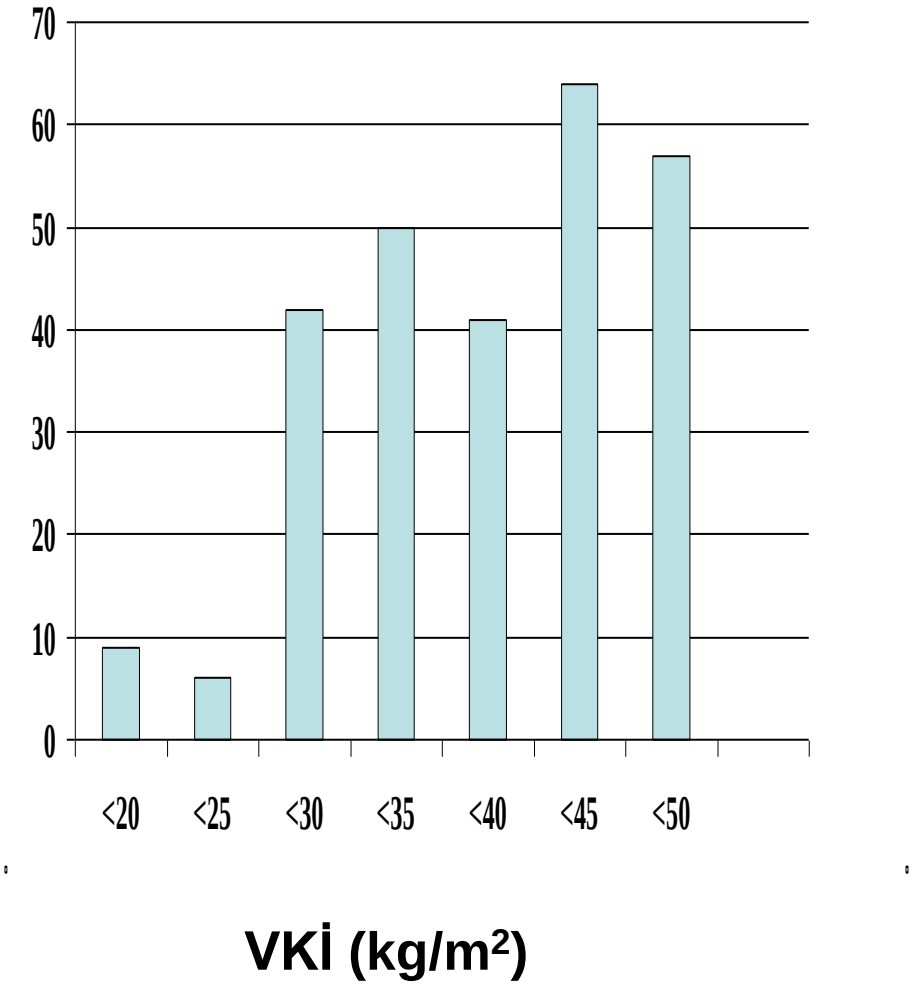
Alessandra Gambineri,[1] Laura Patton,[1] Paola Altieri,[1] Uberto Pagotto,[1] Carmine Pizzi,[2] Lamberto Manzoli,[3] and Renato Pasquali[1]

- 255 PKOS'lu hasta
- Ortalama 16.9 yıl takip
- Takip sonunda yaşa göre standardize edilmiş diyabet prevalansı %39.3 (Populasyon verisi %5.8)

Diabetes, 61:2369-74, 2012

PKOS'da yaş ve VKİ'ye göre glukoz intoleransı prevalansı



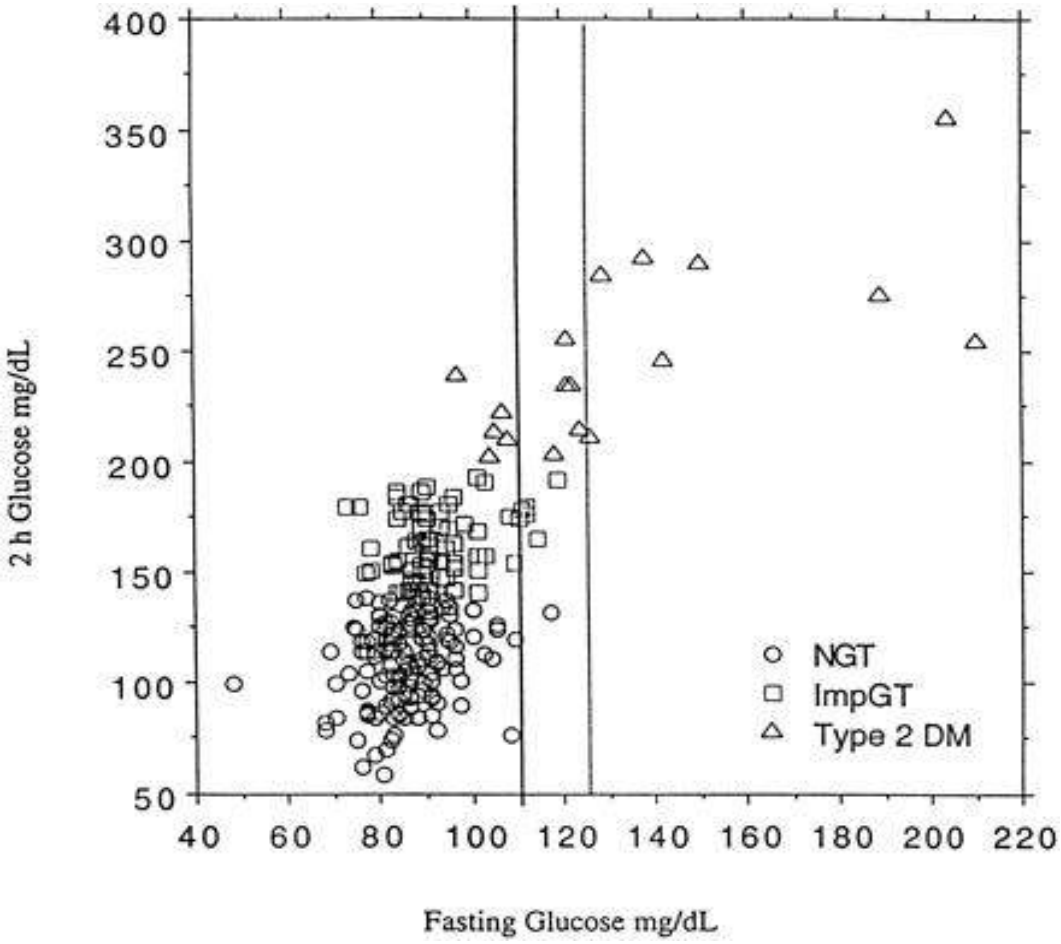


Legro et al, JCEM, 1999

PKOS'da APG'na karşılık 2. saat PG *

Glukoz intoleransı tanısı

OGTT – Tek başına APG (OR, 8.28; %95 CI 4.66-15.34)



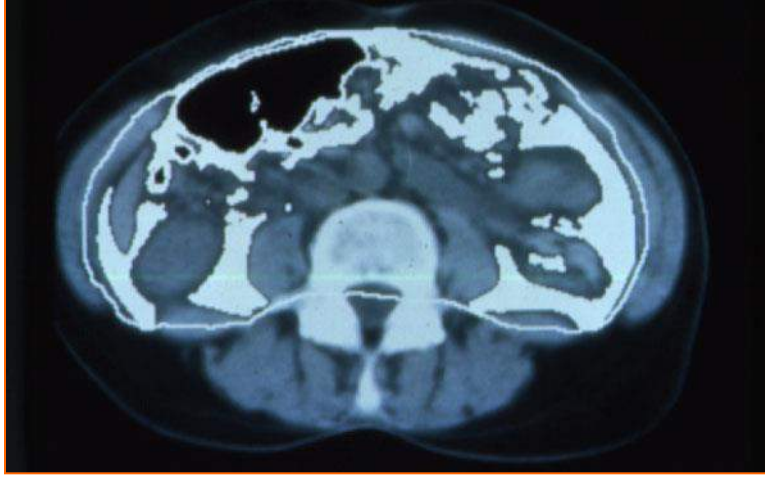
*Legro RS et al.,J Clin Endocrinol Metab 1999
Legro RS, Obstet Gynecol Clin North Am. 2001

Metabolik reprodüktif durum

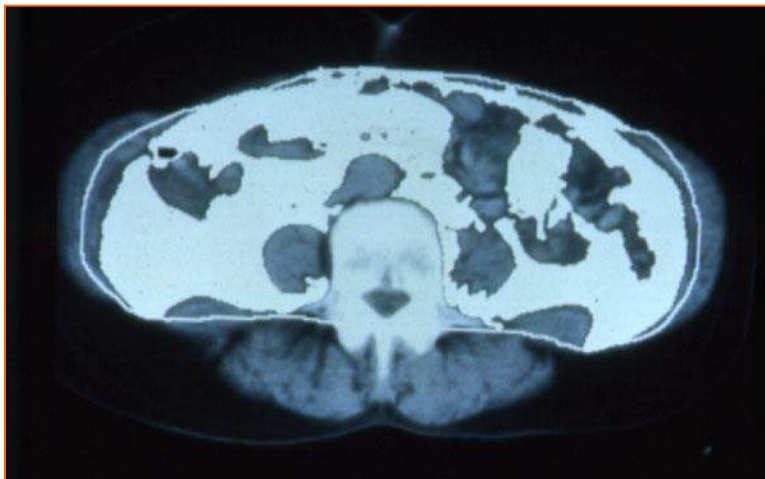
Sunum planı

- Metabolik reprodüktif durum ve PKOS
- PKOS, insülin direnci ve diyabet
- **PKOS ve obezite**
- PKOS mu yeni bir isim mi?

PKOS ve obezite



- PKOS hastalarının %50'si
- Android dağılım
- İnsülin direnci
- SHBG
- Dislipidemi
- Tip 2 diyabet riski



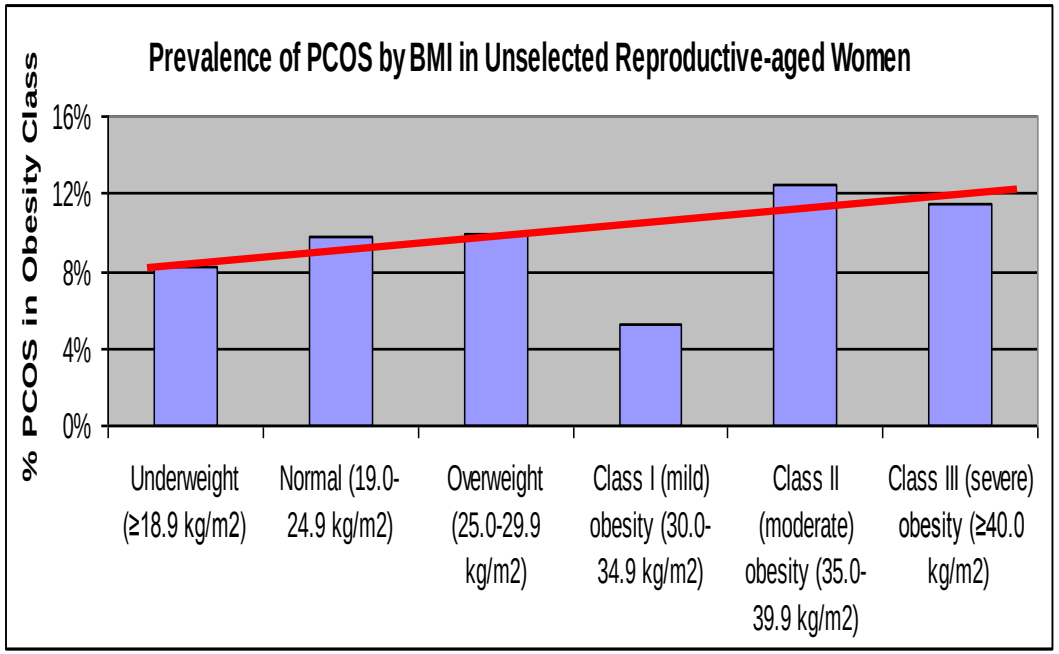
human reproduction update

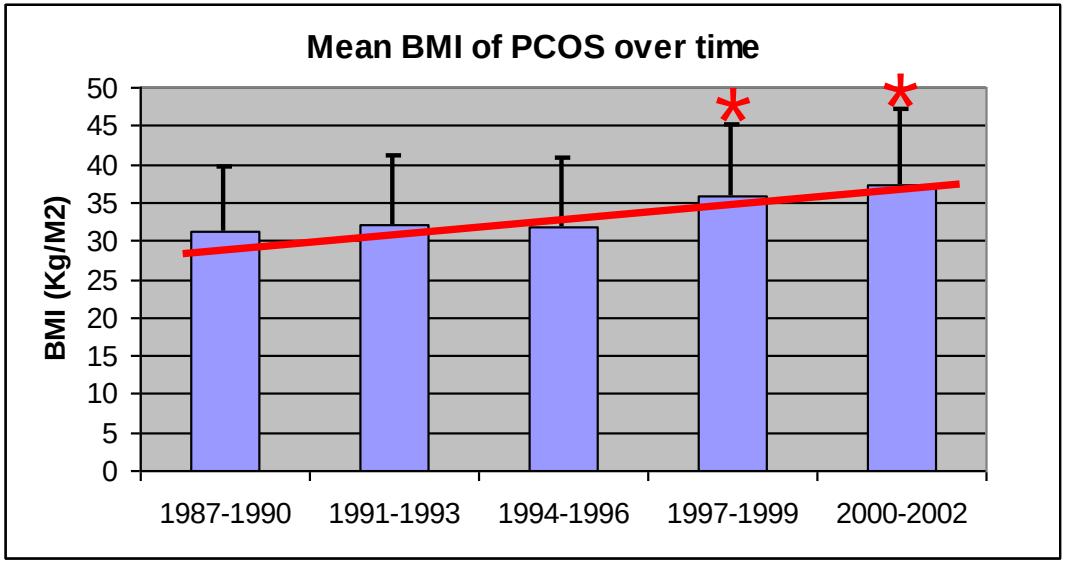
Overweight, obesity and central obesity in women with polycystic ovary syndrome: a systematic review and meta-analysis

- 35 PKOS çalışması
- Obezite ve santral obezite için 2.8 ve 1.7 kat artmış risk (önemli heterojenite)
- PKOS'ta obezite prevalansı: %49 (%12-100)
- Beyaz ırktan PKOS'lu kadınlar Asyalılara göre daha obez
- Güney Asyalı kadınlarda VKİ artışından ziyade santral obezite
- PKOS'lu adolesanlarda 6 kata varan obezite riski
- Tüm katılımcılar refere edilen hastalar

Lim et al. HRU 2012

Obezite ve PKOS – A.B.D. verisi





- 675 seçilmemiş kadın, 746 PKOS hastası
- Obezlerde PKOS riskinde minimal artış
- PKOS hastalarının VKİ değerlerinde genel popülasyona benzer şekilde artış
- PKOS'da obezite intrinsik faktörlerden çok çevresel faktörleri yansıtıyor

Yildiz et al, JCEM 2008

Obezite ve PKOS – Türkiye verisi

Table II Prevalence of PCOS according to BMI.

	Whole group	NIH	Rotterdam	AE-PCOS
Total prevalence	392 (100)	24 (6.1)	78 (19.9)	60 (15.3)
Non-obese (<30 kg/m^2)	352 (89.8)	18 (5.1)	66 (18.8)	51 (14.5)
Obese (≥ 30 kg/m^2)	40 (10.2)	6 (15.0)	12 (30.0)	9 (22.5)

Yildiz et al. Hum Reprod 2012

PKOS ve Obezite – Türkiye verisi

Table III Prevalence of obesity in PCOS.

	Whole group (n = 392)	NIH (n = 24)	Rotterdam (n = 78)	AE-PCOS (n = 60)
Non-obese (<30 kg/m^2)	352 (89.8)	18 (75.0)	66 (84.6)	51 (85.0)
Obese (≥30 kg/m^2)	40 (10.2)	6 (25.0)	12 (15.4)	9 (15.0)

Percentages are given in parentheses.

Yildiz et al. Hum Reprod 2012

JCEM ONLINE

Advances in Genetics—Endocrine Care

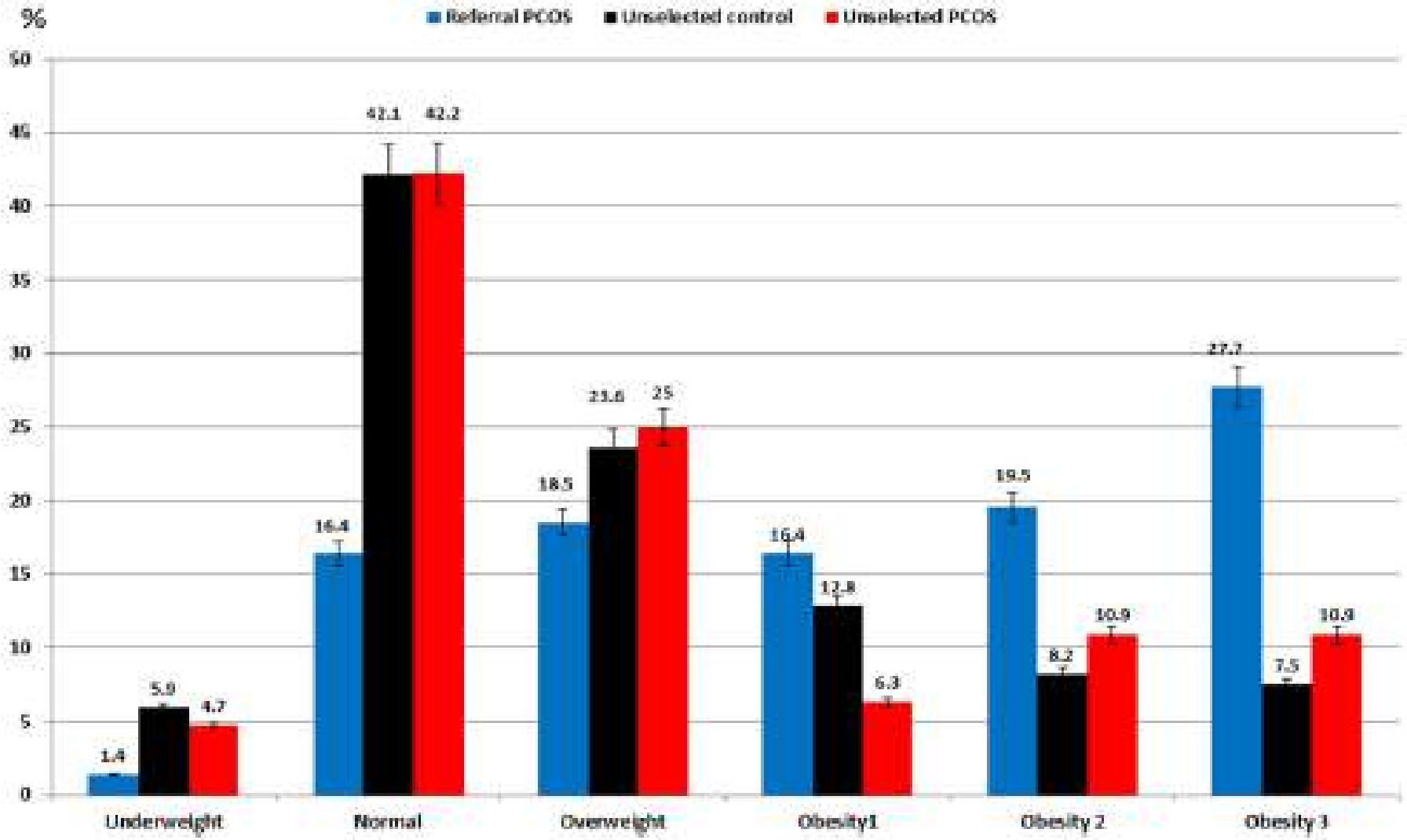
Referral Bias in Defining the Phenotype and Prevalence of Obesity in Polycystic Ovary Syndrome

Uche Ezeh, Bulent O. Yildiz, and Ricardo Azziz

- 292 refere PKOS, 64 seçilmemiş PKOS, 563 seçilmemiş kontrol
- Refere PKOS: daha yüksek VKİ, hirşutizm skoru, androjen değerleri, daha şiddetli PKOS subfenotipi
- Refere PKOS'da obezite sıklığı 2.2 kat daha fazla
- Obezite sıklığı seçilmemiş PKOS ve kontrol gruplarında benzer

JCEM 2013

Referral Bias in Defining the Phenotype and Prevalence of Obesity in Polycystic Ovary Syndrome



Ezeh et al. JCEM 2013

Ovarian and adipose tissue dysfunction in polycystic ovary syndrome: report of the 4th special scientific meeting of the Androgen Excess and PCOS Society

Bulent O. Yildiz, M.D.,[a] *and Ricardo Azziz, M.D., M.P.H., M.B.A.,*[b] *for the Androgen Excess and PCOS Society*

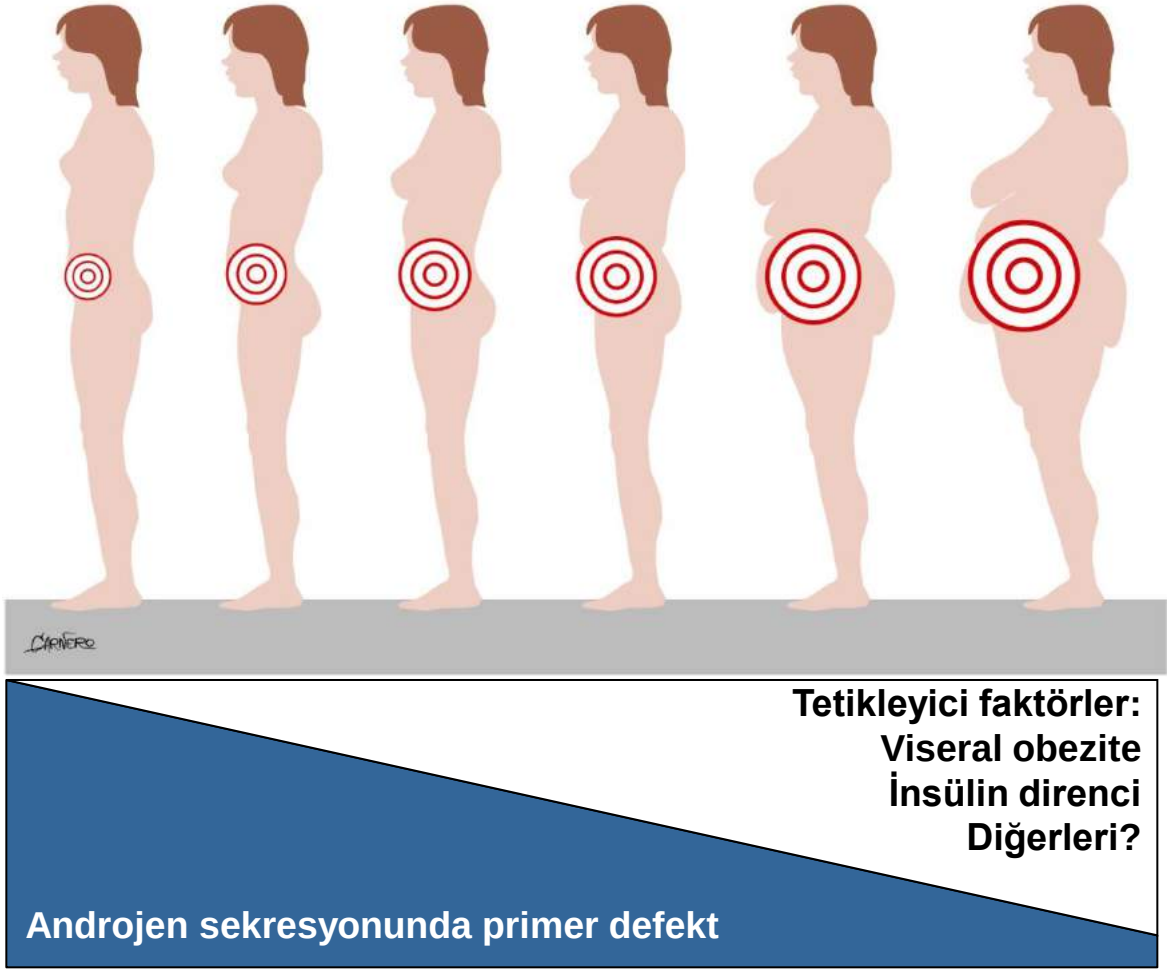
[a] Hacettepe University School of Medicine, Ankara, Turkey; and [b] Cedars-Sinai Medical Center and the David Geffen School of Medicine, University of California, Los Angeles, California

Significant advances have been made in our understanding of ovarian dysfunction in polycystic ovary syndrome (PCOS), and alterations in adipose tissue function are likely to play an important role in its pathophysiology. This review highlights the principal novel concepts presented at the 4th special scientific meeting of the Androgen Excess and PCOS Society, "Ovarian and Adipose Tissue Dysfunction: Potential Roles in Polycystic Ovary Syndrome," which occurred on June 6, 2008 in San Francisco, California. (Fertil Steril® 2010;94:690–3. ©2010 by American Society for Reproductive Medicine.)

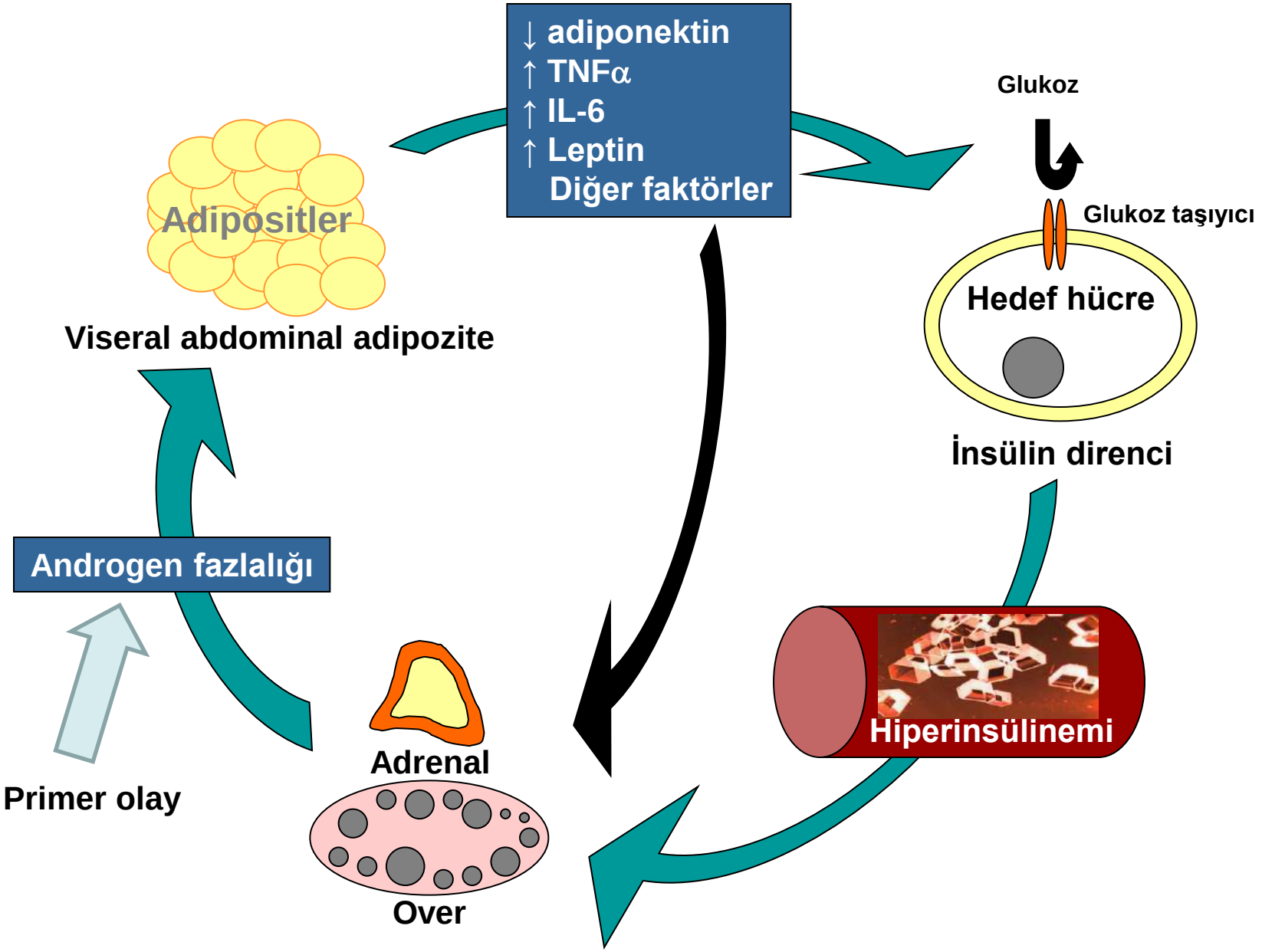
PKOS'da adipoz doku disfonksiyonu

- **Adipokin sekresyonunda disregülasyon**
- **İnsülin sinyal yolağında defektler**
- **Düşük dereceli kronik inflamasyon**
- **Disfonksiyonel steroidogenez**

Adipozite ve androjen sekresyonundaki defektin ciddiyeti



Escobar-Morreale & San Millán, Trends Endocrinol Metab 2007



Escobar-Morreale & San Millán, Trends Endocrinol Metab 2007

PKOS’da adipoz dokuda insülin direncinin moleküler mekanizmaları

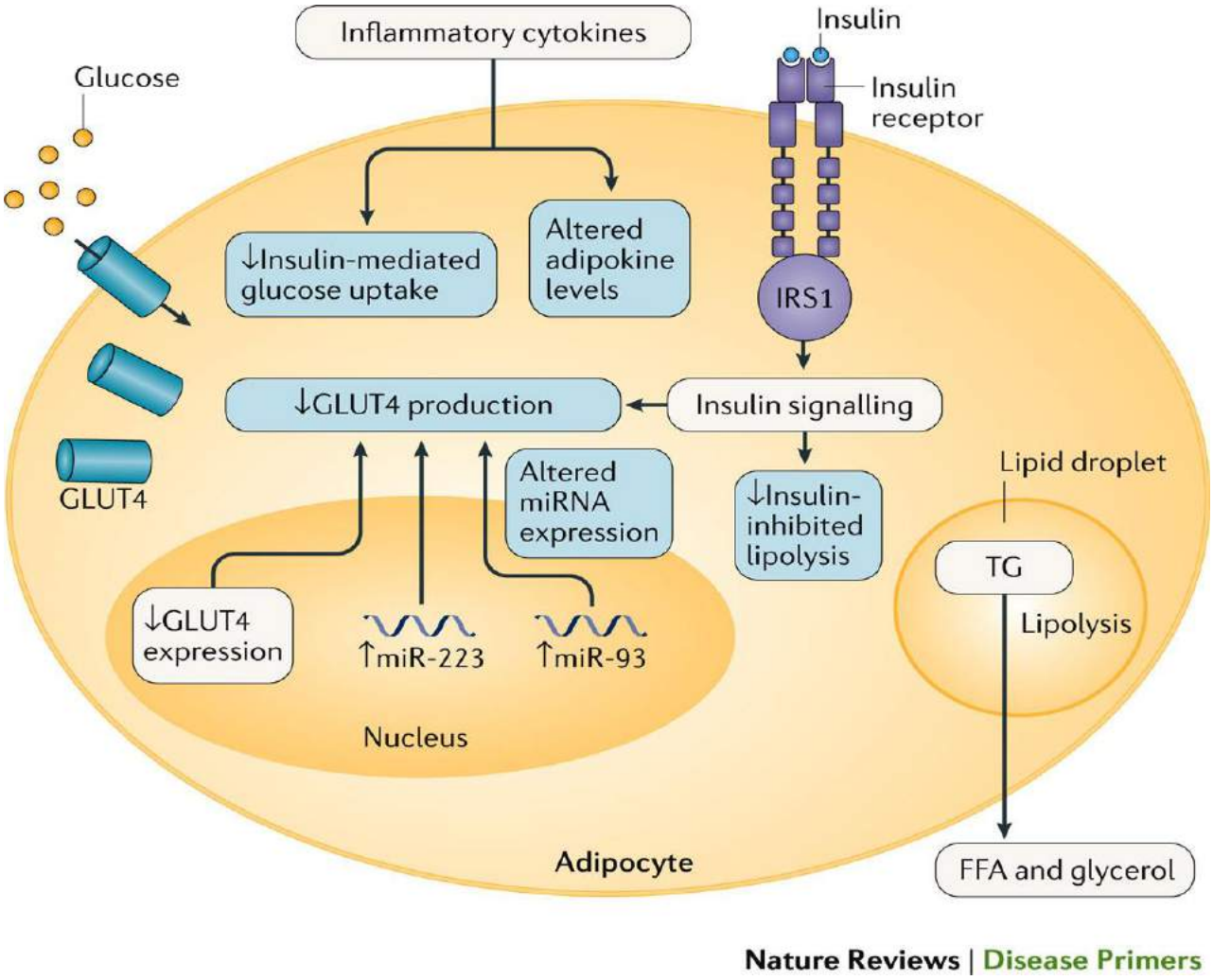
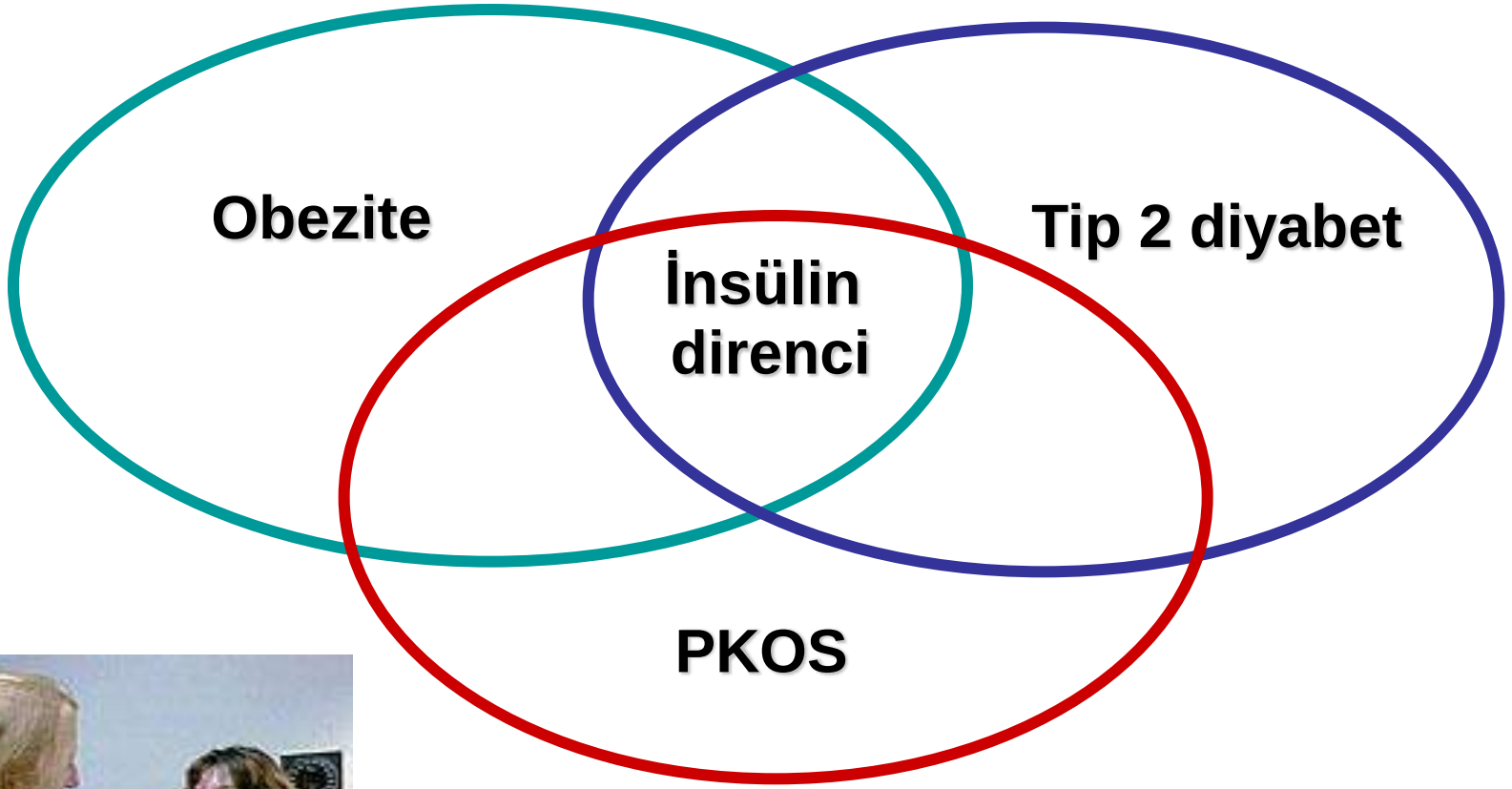
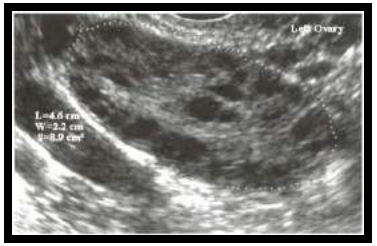


Image courtesy of Y.-H. Chen, Augusta University, Augusta, Georgia, USA

Azziz, R. *et al.* (2016) Polycystic ovary syndrome
Nat. Rev. Dis. Primers doi:10.1038/nrdp.2016.57

Tip 2 diyabet – Obezite - PKOS



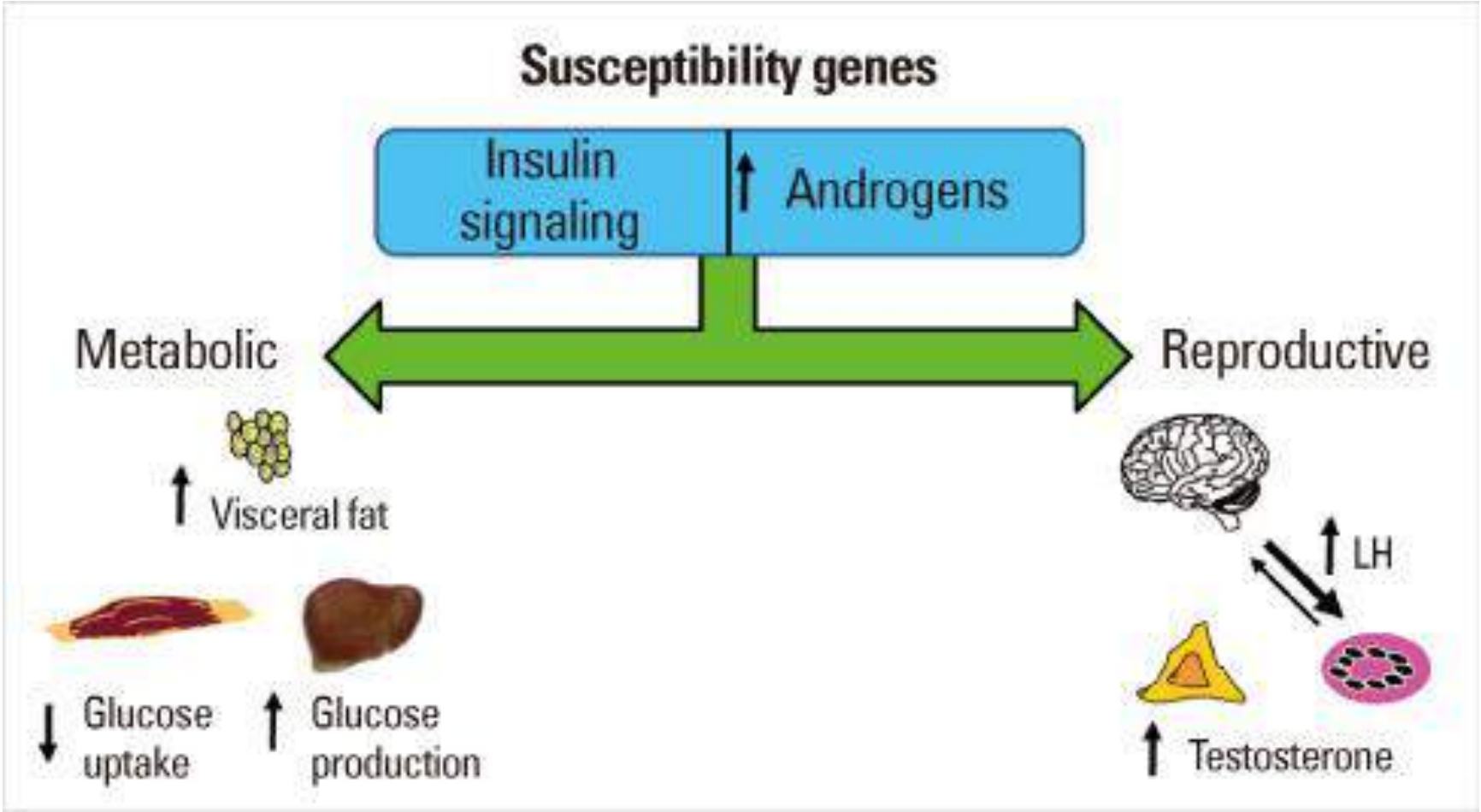


Metabolik reprodüktif durum

Sunum planı

- Metabolik reprodüktif durum ve PKOS
- PKOS, insülin direnci ve diyabet
- PKOS ve obezite
- **PKOS mu yeni bir isim mi?**

Bir metabolik reprodüktif durum olarak PKOS



1990 NICHD PCOS Konferansında tanı kriterleri üzerinde anlaşma oranları

Definite or probable	Possible
Hyperandrogenemia, 64%	Insulin resistance, 69%
Exclusion of other etiologies, 60%	Perimenarchal onset, 62%
Exclusion of CAH, 59%	Elevated LH/FSH, 55%
Menstrual dysfunction, 52%	PCO by ultrasound, 52%
Clinical hyperandrogenism, 48%	Clinical hyperandrogenism, 52%
	Menstrual dysfunction, 45%

CAH, Congenital adrenal hyperplasia.

Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) | National Institutes of Health | U.S. Department of Health and Human Services

Office of Disease Prevention

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- Events and Programs
  - Polycystic Ovary Syndrome Workshop
    - Agenda
    - Steering Committee
    - Register to Attend
    - Webcast Registration
    - Location & Logistics
    - Get Involved!
  - Medicine in the Media Course
  - Medicine: Mind the Gap
  - Gordon Lecture in Epidemiology
  - Featured Events
- Consensus Development Program
- In the News

NIH Office of Disease Prevention
Evidence-based Methodology Workshop on

POLYCYSTIC OVARY SYNDROME (PCOS)

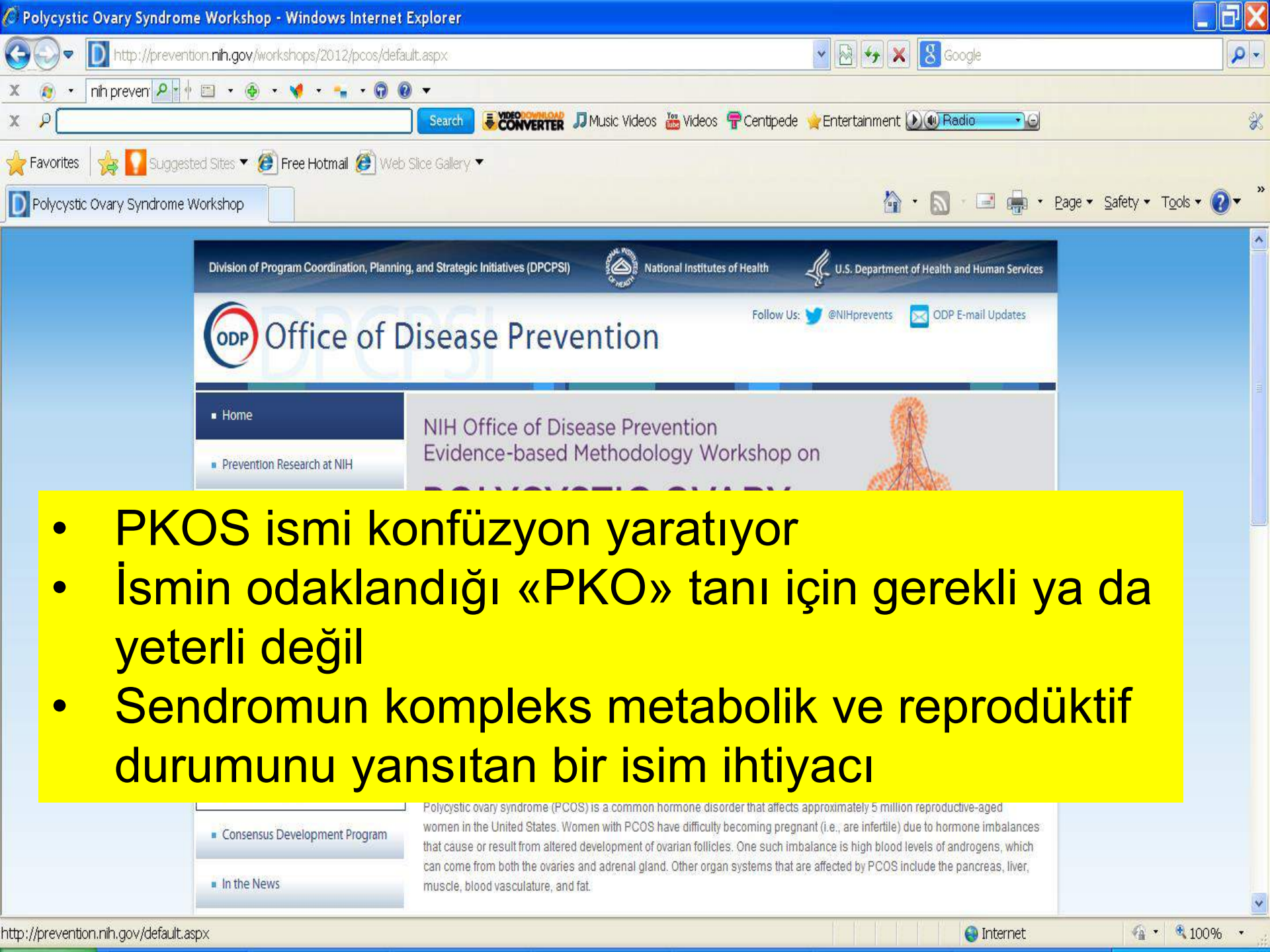
DECEMBER 3-5, 2012

ODP Home > Events and Programs > Polycystic Ovary Syndrome Methodology Workshop

Evidence-based Methodology Workshop on Polycystic Ovary Syndrome

December 3–5, 2012

Polycystic ovary syndrome (PCOS) is a common hormone disorder that affects approximately 5 million reproductive-aged women in the United States. Women with PCOS have difficulty becoming pregnant (i.e., are infertile) due to hormone imbalances that cause or result from altered development of ovarian follicles. One such imbalance is high blood levels of androgens, which can come from both the ovaries and adrenal gland. Other organ systems that are affected by PCOS include the pancreas, liver, muscle, blood vasculature, and fat.



- PKOS ismi konfüzyon yaratıyor
- İsmin odaklandığı «PKO» tanı için gerekli ya da yeterli değil
- Sendromun kompleks metabolik ve reprodüktif durumunu yansıtan bir isim ihtiyacı

Estrogenic ovulatory dysfunction or functional female hyperandrogenism: an argument to discard the term polycystic ovary syndrome

Millie Behera, M.D., Thomas Price, M.D., and David Walmer, M.D., Ph.D.

Reproductive Endocrinology and Fertility Division, Department Of Obstetrics and Gynecology, Duke University Medical Center, Durham, North Carolina

Polycystic ovarian syndrome: a misnomer for an enigmatic disease

P.-M. LAM† and N. RAINE-FENNING‡*

PCOS: what is in a name? an heterogeneous condition with multiple faces for multiple doctors

Philippe Bouchard and Bart C J M Fauser[1]

Correspondence should be addressed

Commentary: Polycystic Ovarian Disease (PCOD): A Misnomer, Looking for a New Name

Mahantesh Karoshi, M.D.
S. O. Okolo, Ph.D., FRCOG

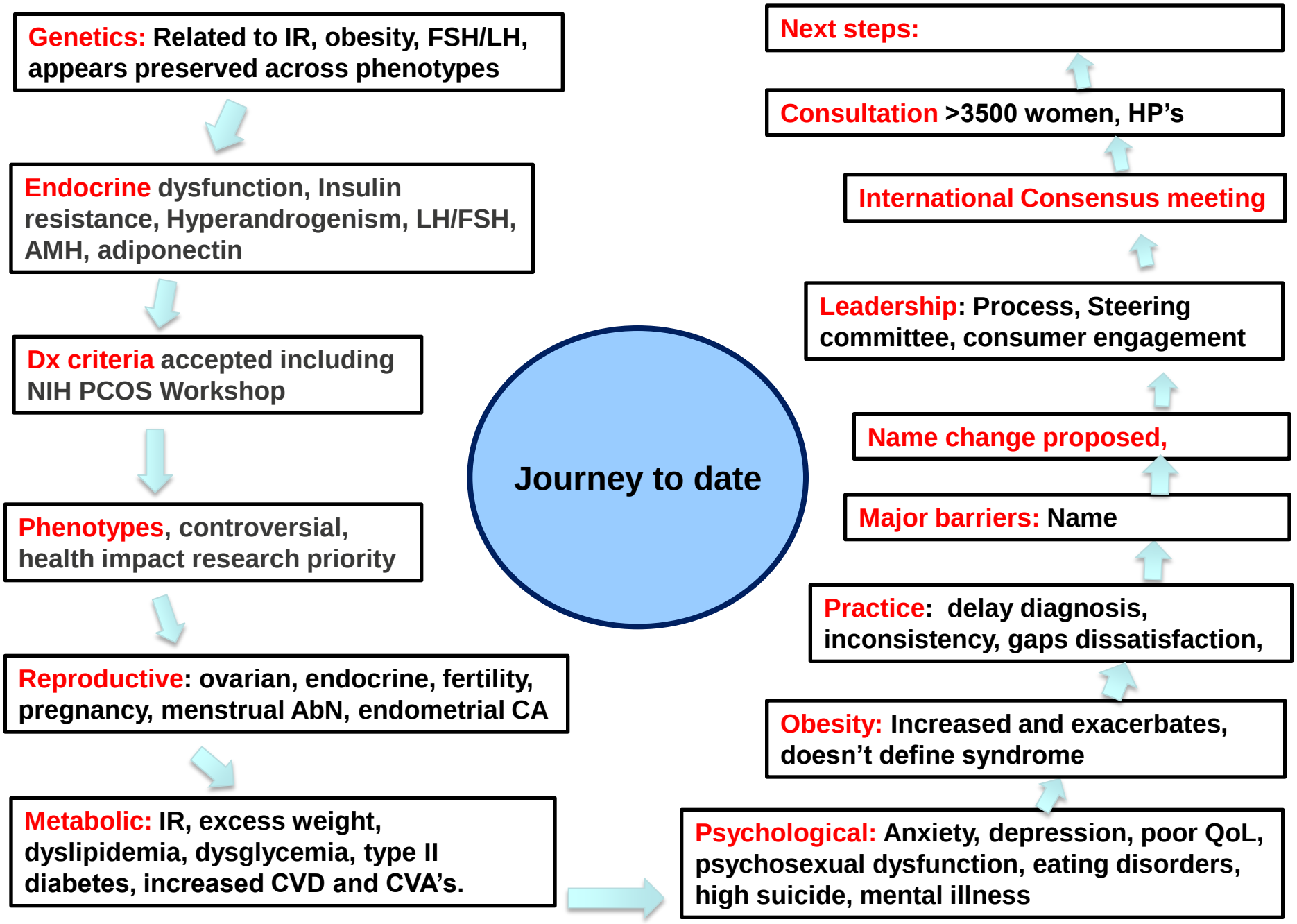
Delayed Diagnosis and a Lack of Information Associated With Dissatisfaction in Women With Polycystic Ovary Syndrome

Melanie Gibson-Helm,[1] Helena Teede,[1,2] Andrea Dunaif,[3] and Anuja Dokras[4]

[1]Monash Centre for Health Research and Implementation, School of Public Health and Preventive Medicine, Monash University, Clayton, Victoria 3168, Australia; [2]Monash Partners Academic Health Science Centre, Clayton, Victoria 3168, Australia; [3]Feinberg School of Medicine, Northwestern University, Chicago, Illinois 60611; and [4]Division of Reproductive Endocrinology, PENN PCOS Center, University of Pennsylvania, Philadelphia, Pennsylvania 19104

Participants: There were 1385 women with a reported diagnosis of PCOS who were living in North America (53.0%), Europe (42.2%), or other world regions (4.9%); of these, 64.8% were 18 to 35 years of age.

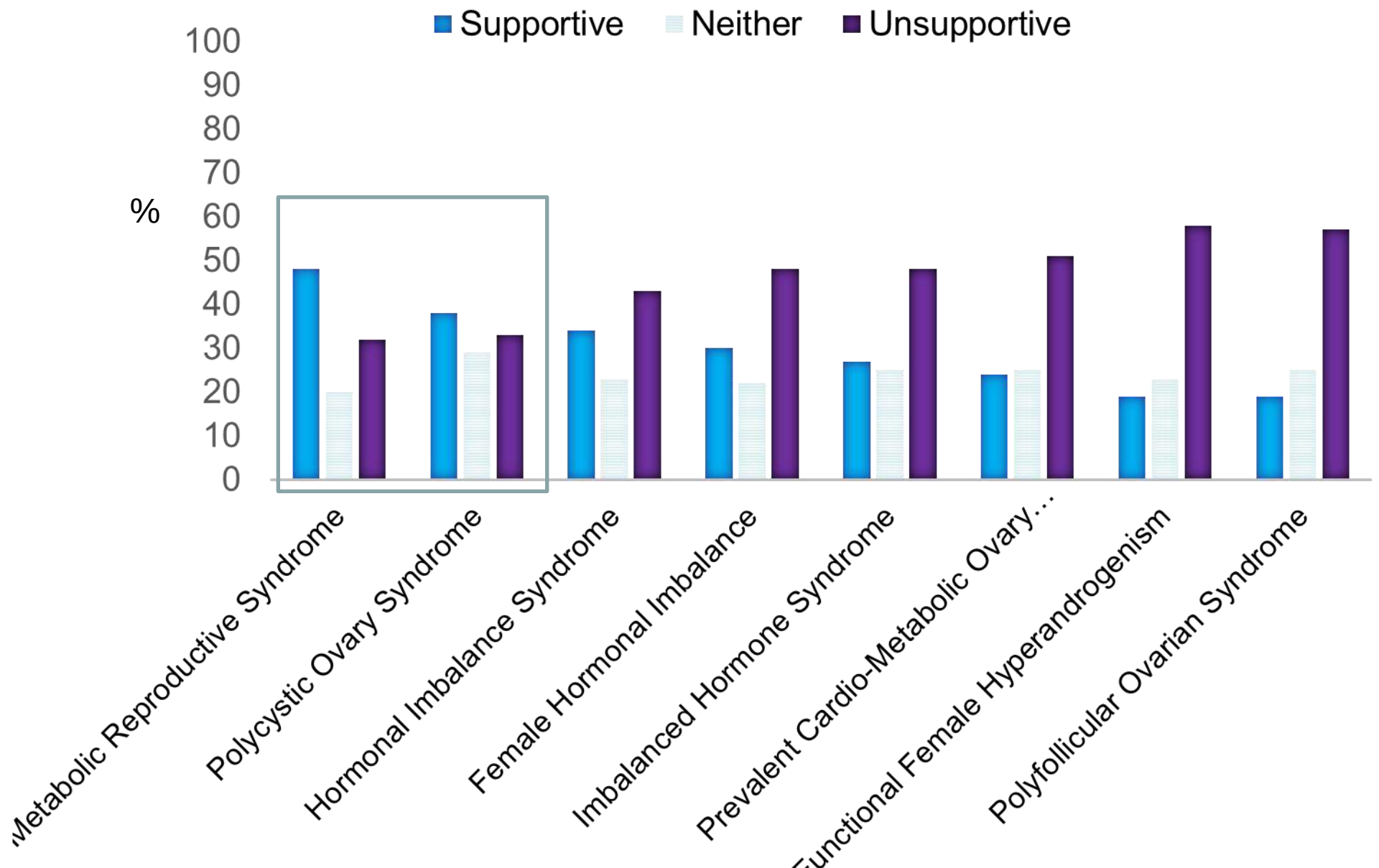
Conclusions: In the largest study of PCOS diagnosis experiences, many women reported delayed diagnosis and inadequate information. These gaps in early diagnosis, education, and support are clear opportunities for improving patient experience. (*J Clin Endocrinol Metab* 102: 604–612, 2017)


Genetics: Related to IR, obesity, FSH/LH, appears preserved across phenotypes
Endocrine dysfunction, Insulin resistance, Hyperandrogenism, LH/FSH, AMH, adiponectin
Dx criteria accepted including NIH PCOS Workshop
Phenotypes, controversial, health impact research priority
Reproductive: ovarian, endocrine, fertility, pregnancy, menstrual AbN, endometrial CA
Metabolic: IR, excess weight, dyslipidemia, dysglycemia, type II diabetes, increased CVD and CVA's.
Psychological: Anxiety, depression, poor QoL, psychosexual dysfunction, eating disorders, high suicide, mental illness
Obesity: Increased and exacerbates, doesn't define syndrome
Practice: delay diagnosis, inconsistency, gaps dissatisfaction,
Major barriers: Name
Name change proposed,
Leadership: Process, Steering committee, consumer engagement
International Consensus meeting
Consultation >3500 women, HP's
Next steps:
Journey to date

Uluslararası uzlaşı toplantısı

- Sunumlar, hasta grubu görüşleri
- Sunulan seçenekler
  - İsim değişmesin
  - Tüm ilgili gruplarla konsülte edilerek isim değişikliği değerlendirilsin
  - İsim hemen değişsin
- SWOT analizi
- Anonim oylama
- 2. seçenek kabul
- Devam eden konsültasyon süreçleri

Potansiyel isimler



Sonuçlar

- **Reprodüktif durum metabolizma ve insülin direnci ile kompleks ilişkili**
- **PKOS, insülin direnci, glukoz intoleransı ve obezitenin sık görüldüğü metabolik reprodüktif bir durum**
- **Sendromda isim değişikliği söz konusu olabilir (Metabolik reprodüktif sendrom?)**

ASRM PAGES

Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ ASRM-Sponsored 3rd PCOS Consensus Workshop Group

Bart C. J. M. Fauser, M.D.,[a] Basil C. Tarlatzis, M.D.,[b] Robert W. Rebar, M.D.,[c] Richard S. Legro, M.D.,[d] Adam H. Balen, M.D.,[e] Roger Lobo, M.D.,[f] Enrico Carmina, M.D.,[g] Jeffrey Chang, M.D.,[h] Bulent O. Yildiz, M.D.,[i] Joop S. E. Laven, M.D.,[j] Jacky Boivin, M.D.,[k] Felice Petraglia, M.D.,[l] C. N. Wijeyeratne, M.D.,[m] Robert J. Norman, M.D.,[n] Andrea Dunaif, M.D.,[o] Stephen Franks, M.D.,[p] Robert A. Wild, M.D.,[q] Daniel Dumesic, M.D.,[r] and Kurt Barnhart, M.D.[s]

Human Reproduction, Vol.27, No.1 pp. 14–24, 2012
Advanced Access publication on December 5, 2011 doi:10.1093/humrep/der396

human reproduction ESHRE PAGES

Consensus on women's health aspects of polycystic ovary syndrome (PCOS)†

The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group*,‡

Position Statement | G Conway and others | PCOS: an ESE perspective | 171:4 | P1–P29

The polycystic ovary syndrome: a position statement from the European Society of Endocrinology

Gerard Conway, Didier Dewailly[1], Evanthia Diamanti-Kandarakis[2], Héctor F Escobar-Morreale[3], Stephen Franks[4], Alessandra Gambineri[5], Fahrettin Kelestimur[6], Djuro Macut[7], Dragan Micic[7], Renato Pasquali[5], Marija Pfeifer[8], Duarte Pignatelli[9], Michel Pugeat[10], Bulent O Yildiz[11] on behalf of the ESE PCOS Special Interest Group

ECE2017

20 - 23 May 2017, Lisbon, Portugal

www.ece2017.org