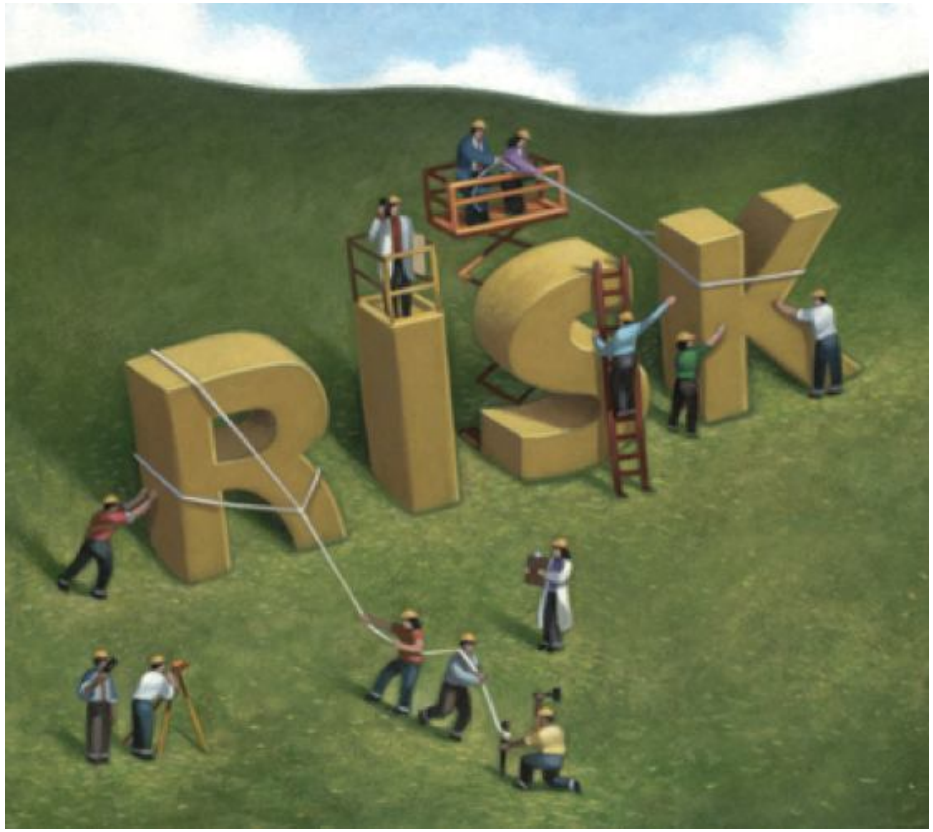
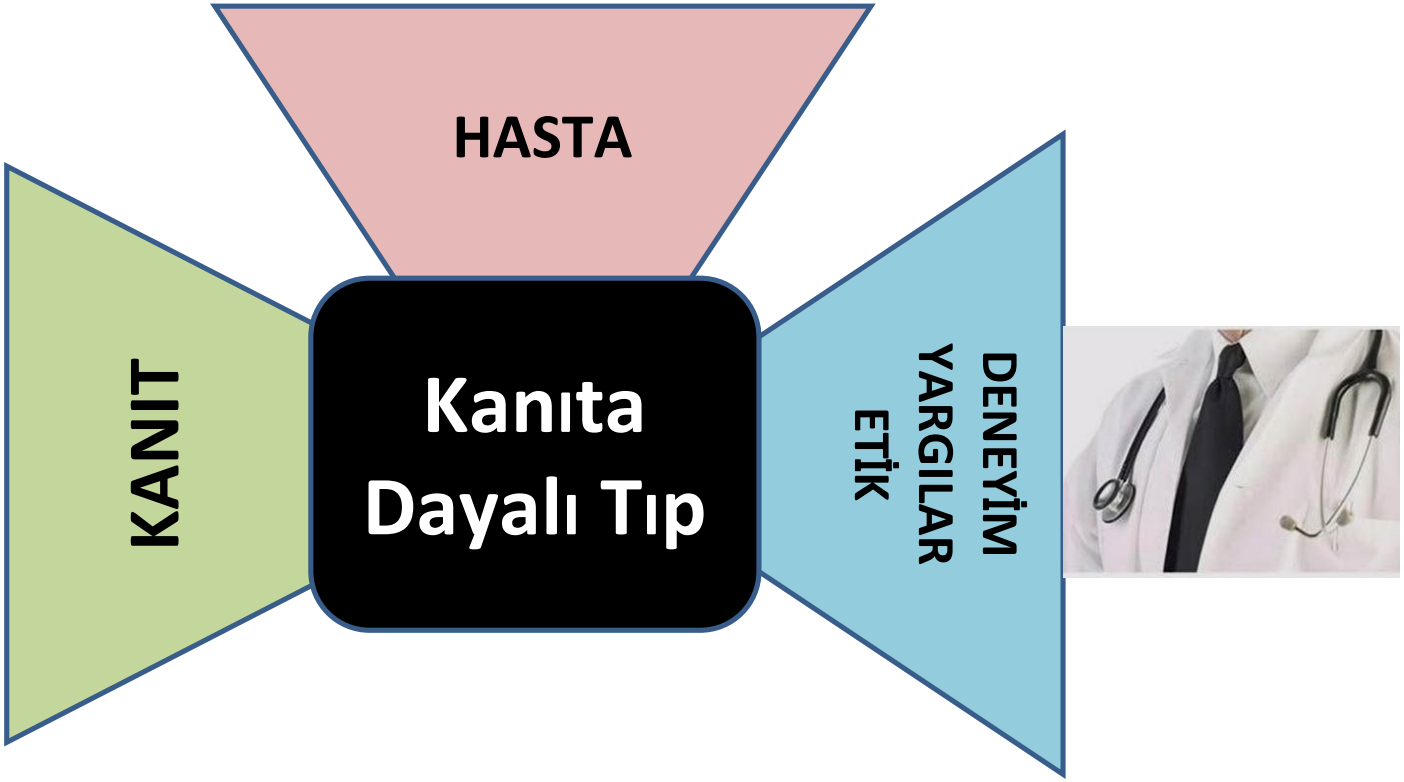
KANITA DAYALI KLİNİK LABORATUVARLARDA RİSK ANALİZİ ve TARAMA TEST UYGULAMALARI



Dr.Muhittin A.SERDAR

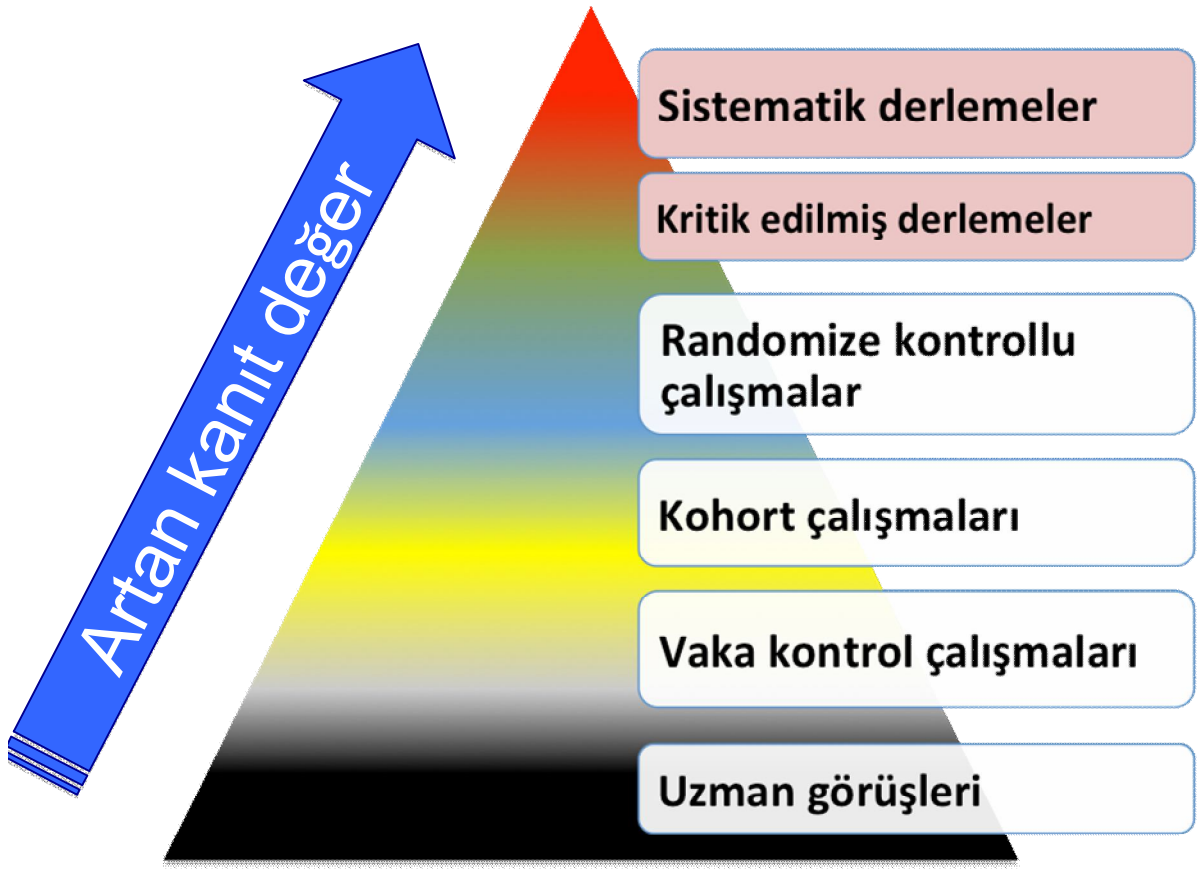
Kanıta Dayalı Tıp



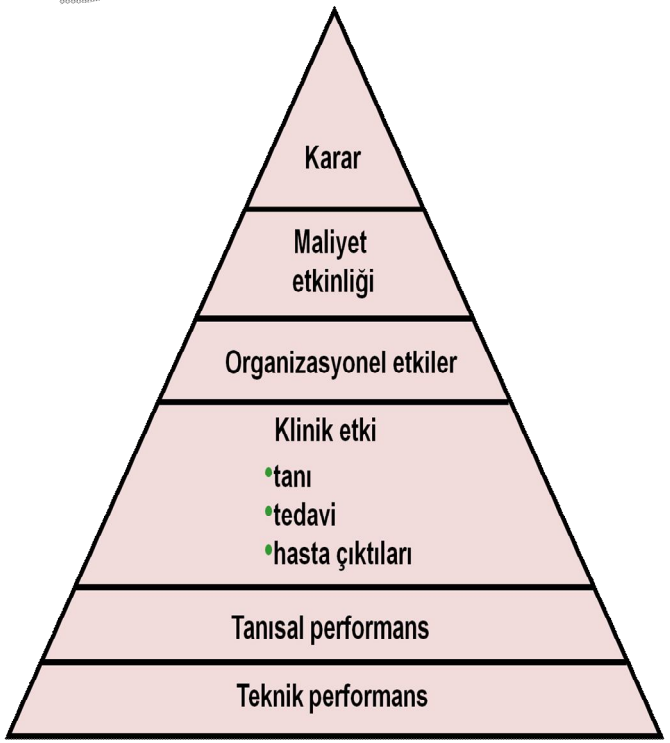
- **Hekimin deneyimi, hastanın tercihleri ve en iyi kanıtların entegre edildiği sistematik bir yaklaşım**

Sackett ve Guyatt

En iyi kanıt ! (Klinik- Laboratuvar)



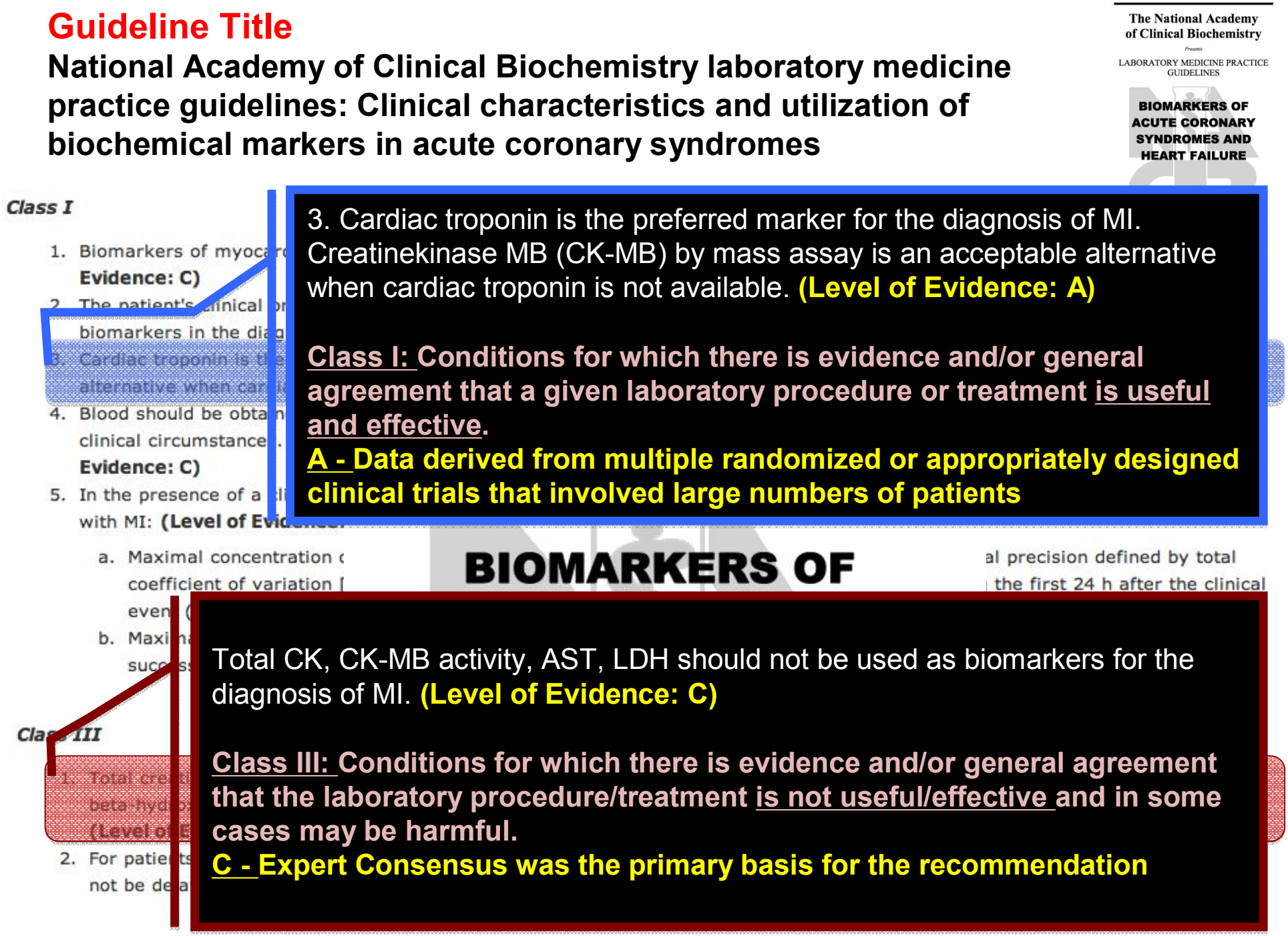
Filtre edilmiş bilgi



ClinChem 2000; 46: 1041-50.

Guideline Title

National Academy of Clinical Biochemistry laboratory medicine practice guidelines: Clinical characteristics and utilization of biochemical markers in acute coronary syndromes



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- NACB DiabetesEntireLMPG.pdf
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- uptodate.Overview of the risk factors for cardiovascular disease.mht
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- uptodate.Risk factors for prostate cancer.mht
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- uptotade.Diagnosis and acute mana...spected nephrolithiasis in adults.mht
- uptpdate.Screening for osteoporosis.mht
- USPSTF prostateart.pdf

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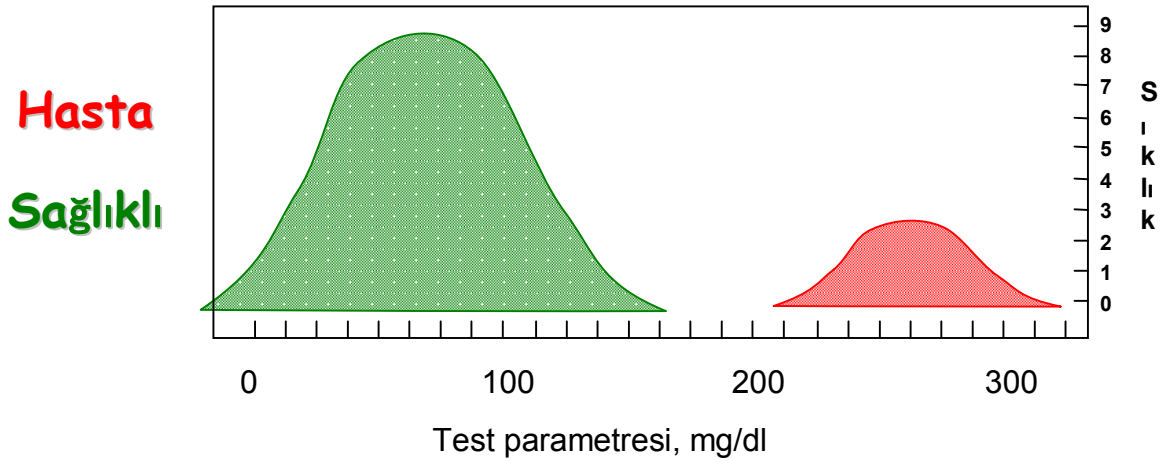
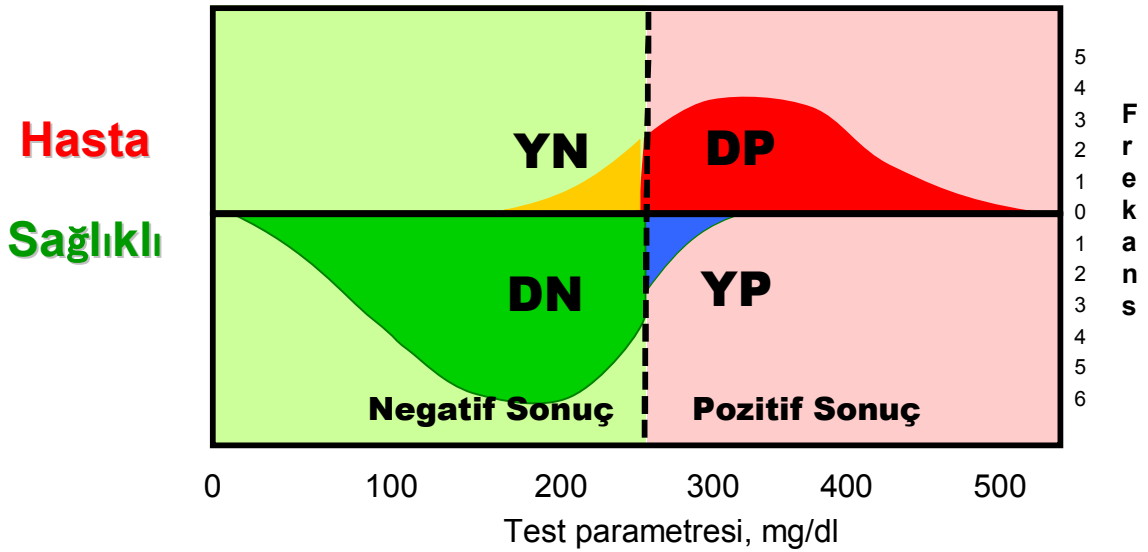
UYGULANAN TEST





YN (FN) Yalancı negatif DP (TP) Doğru pozitif

DN (TN) Doğru negatif YP (FP) Yalancı pozitif

Duyarlılık ve Özgüllük

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Duyarlılık (Sensitivite)

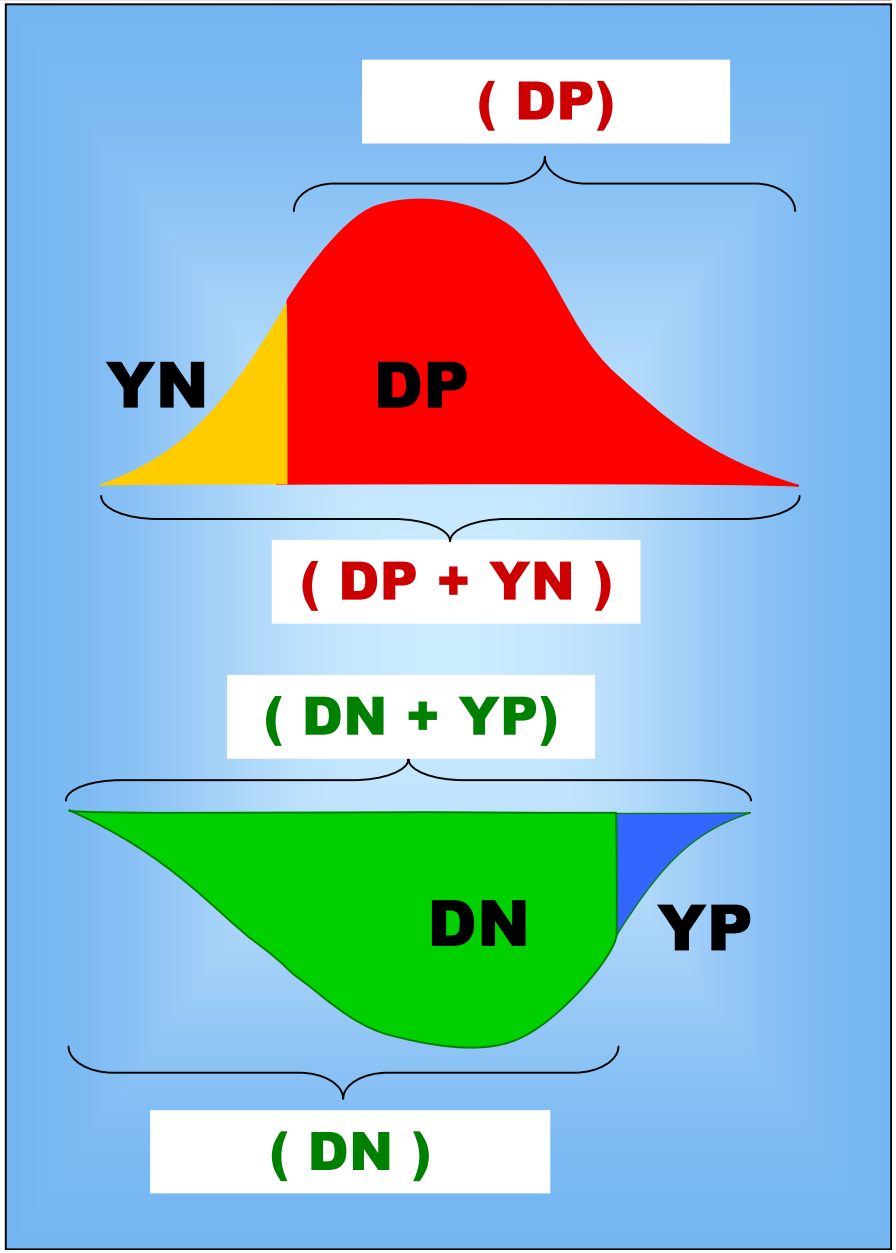
Bir testin gerçek hastaları bulma yeteneğidir.

Duyarlılık = DP / (DP + YN)

Özgüllük (Spesifisite)

Bir testin gerçek sağlamları bulma yeteneğidir.

Özgüllük = DN / (DN + YP)



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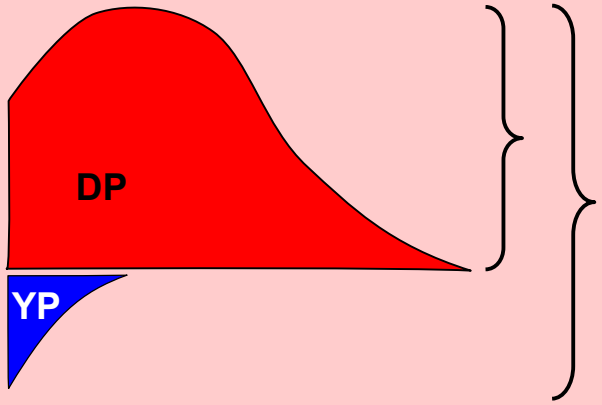
Pozitif Öngörü Değeri (Positive Predictive Value, PV+)

Bir testin verdiği sonucun gerçeği yansıtma gücüdür.

Pozitif öngörü değeri, pozitif sonuçla karşılaşan bir hekimin,

"bu sonucu alan hastanın gerçek bir hasta olma olasılığı nedir ?"

sorusunun yanıtını verir.

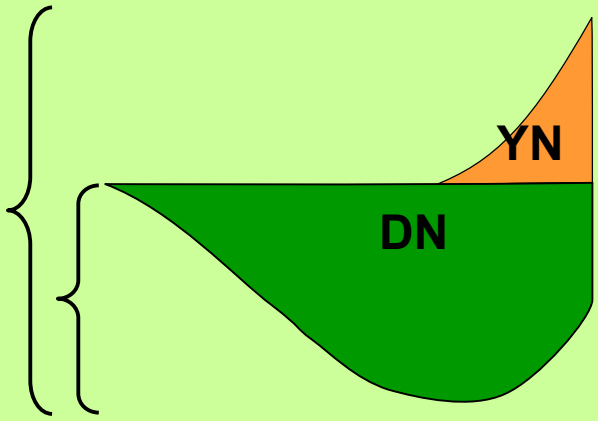


Pozitif öngörü değeri

(positive predictive value)

PV+ = Doğru Pozitif /Toplam Pozitif

Negatif Kestirim Değeri (Negative Predictive Value, PV-)



Negatif kestirim değeri

PV- = Doğru negatif/ Toplam negatif

Negatif kestirim değeri ise, aynı şekilde negatif test sonucu ile karşılaşıldığında,

"**bu kişinin gerçekten bir sağlam olma olasılığı nedir**?"

sorusunun cevabını oluşturur.

Pozitif Olabilirlik Oranı (Likelihood Ratio (+), LR+)

Pozitif olabilirlik oranı; pozitif sonuçların içindeki gerçek ve yanlış sonuçların oranını verir.

LR+ = Duyarlılık /(1-Özgüllük)

Doğru (+) / Yanlış (+)

Örnek:

Bir test için **duyarlılık 0.90**, **özgüllük 0.85** olarak bulunmuş olsun.

0.90 / (1 - 0.85) = 6

Test yaklaşık her **6 doğru** pozitife karşı **1 yanlış** pozitif sonuç verir.

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ODD Ratio (Şans Oranı)

ODDS, iki seçenekli bir olayda, bir seçeneğin gerçekleşme şans oranını anlatır.

Vaka: Fenilketonuri taraması yapıyorsunuz. Hastalığın insidansı 1/2000. Fenilalanin tarama testinin LR (+) =40. Pozitif çıkan bir sonucun gerçek hasta olma olasığı nedir.

Test öncesi olasılık = 1/ 2000

(TÖ Odd oranı)

Test sonrası Odd ratio= TÖ Odd oranı x LR

Test sonrası Odd ratio= (1/ 2000) x 40= 1/50

ihtimal 40 katı arttı ve 1/50 oldu. Atrık bu 50 kişiden ileri test yapabilirsiniz

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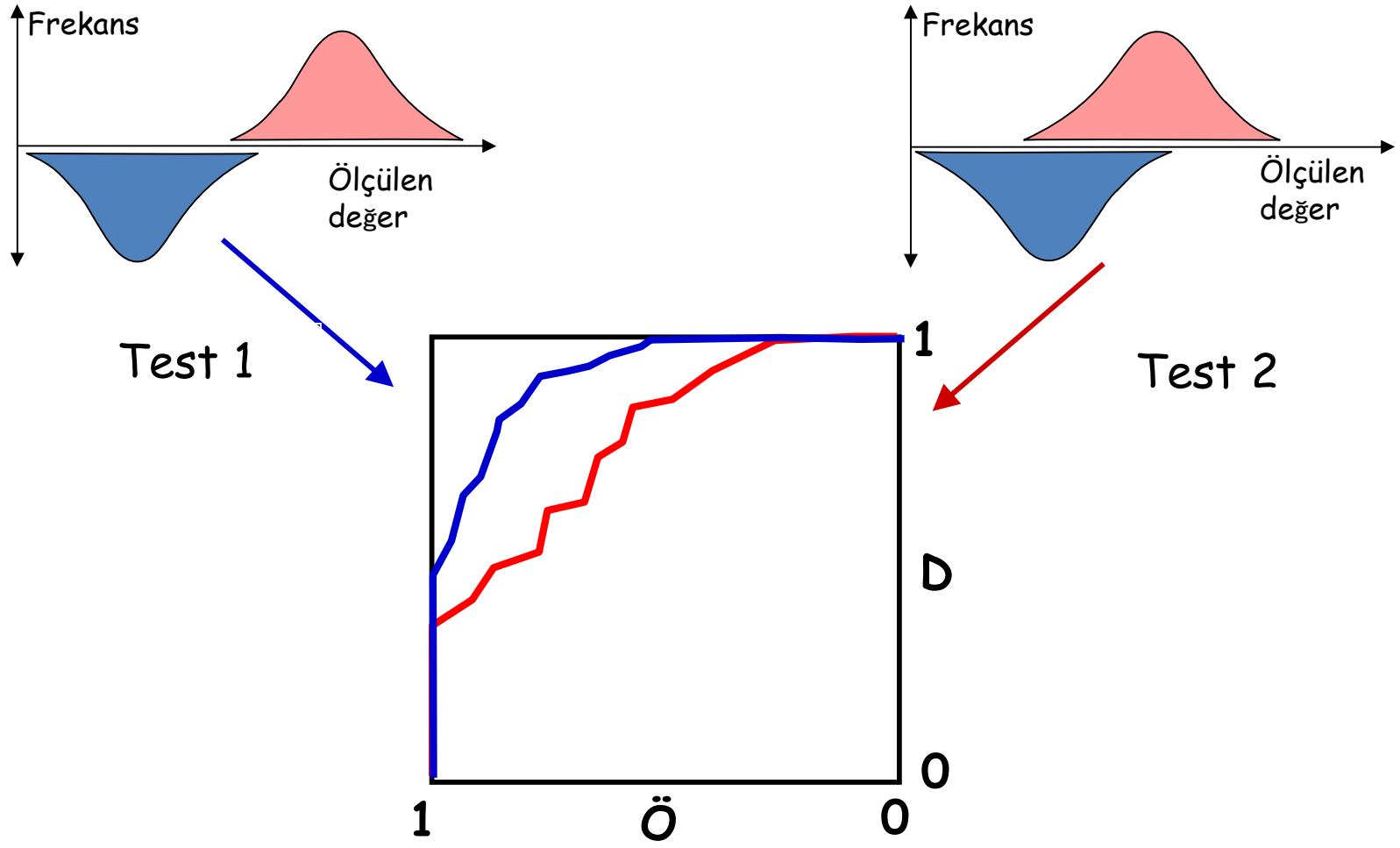
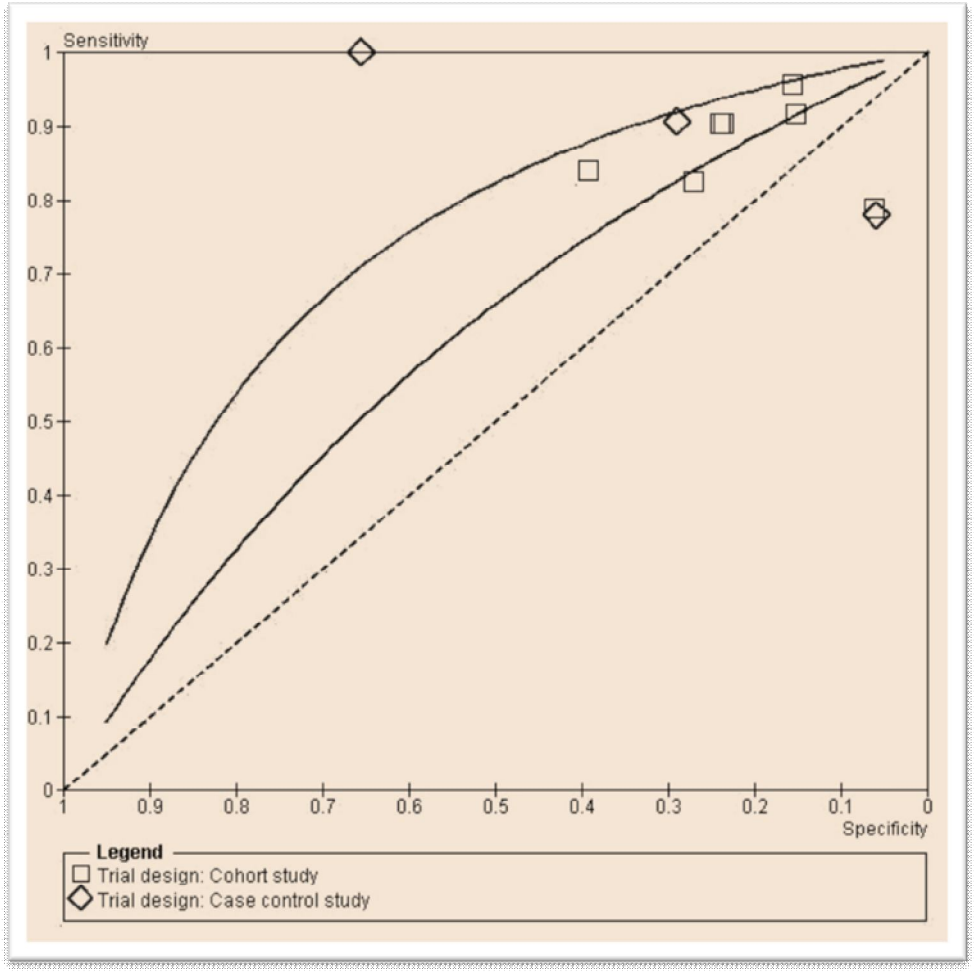
"Receiver Operating Characteristic" (ROC) Grafiği

ROC grafiği, iki ya da daha fazla testin, tanısal ayırım gücünü karşılaştırmak üzere kullanılabilir.

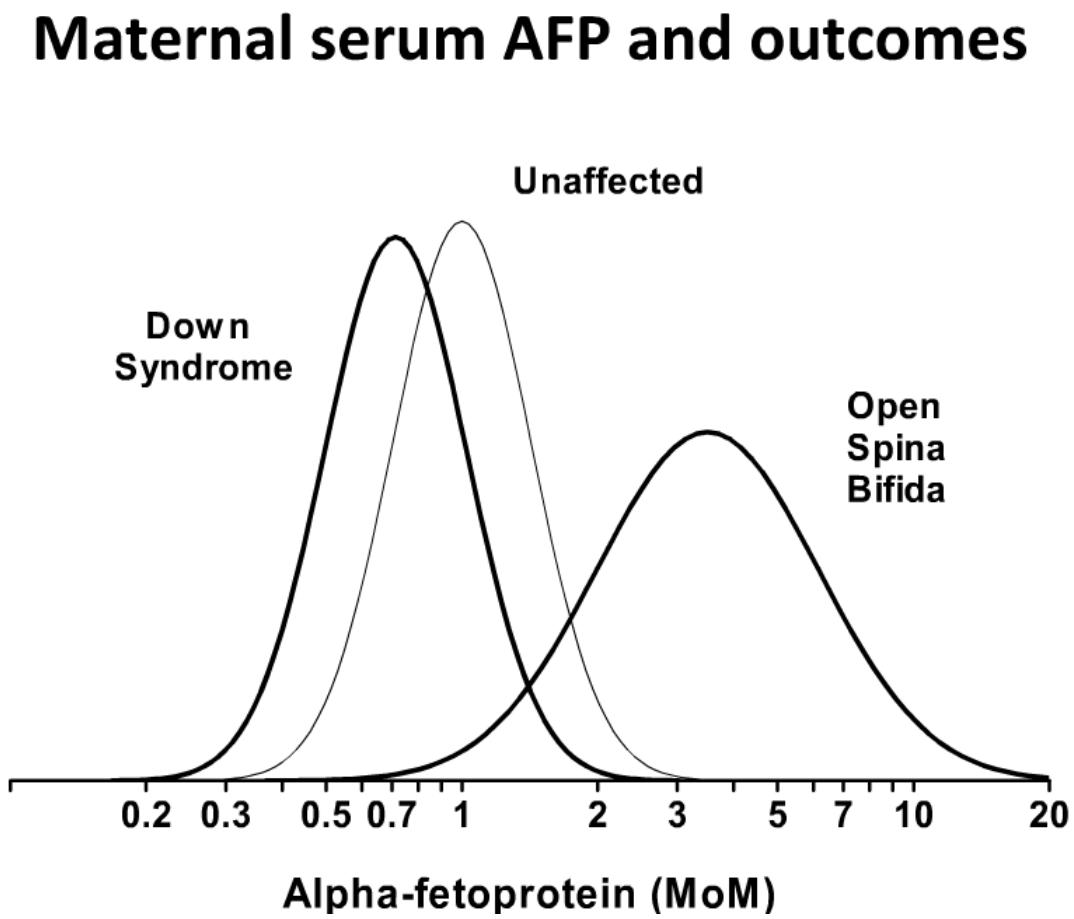


PSA ve performans değerlendirmesi randomizasyonun önemi



Forest plot of sensitivity and specificity of tPSA testing.
Harvey *et al. BMC Urology* 2009 **9**:14

Risk analizi örneği



Spina Bifida için örnek risk belirleme

Sonuçlar (UL)				
30	28	47	20	25
32	33	39	37	15
31	50	28	18	45
25	25	42	27	57
36	23	21	38	30
23	34	37	53	
43	20	30	29	
11	62	19	28	

Soru 1: 41 gebe için belirlenen AFP median değeri nedir?

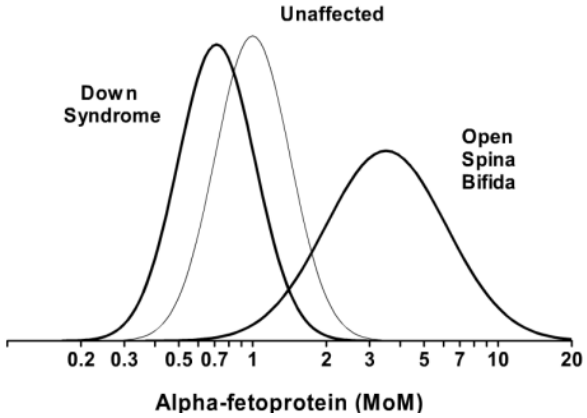
20-20-23-…-30- …47-53-57= 30 U/L

Soru 2: AFP sonucu 60 U/L olan gebenin MoM değeri nedir?

60/30= 2

Soru 3: Test öncesi ihtimal (Odd oranı) 1:2000 olan bu gebe için spin abifida riski nedir?

2 x 1:2000= 1:1000



Örnek vaka

Son altı ay içerisinde sizin laboratuvarınızda toplam 10000 bayan için tarama SB taraması yapılmıştır. > 2 MoM üzerinde gebe sayısı 350 dir. Yapılan ileri testler ile 7 gebenin pozitif olduğu 3 gebenin ise yanlış negatif olduğu gözlenmiştir.

	Hasta (+)	Sağlıklı (-)	
>2 MoM (+)	7 DP	343 YP	350
<2 MoM (-)	3 YN	9647 DN	9650
	10	9990	10000

Soru 4: Yanlış pozitif oranı nedir?

343/9990= %3.4

YP / YP+DN

Soru 5: Saptama oranı nedir?

7/10 = %70

DP / YN+DP

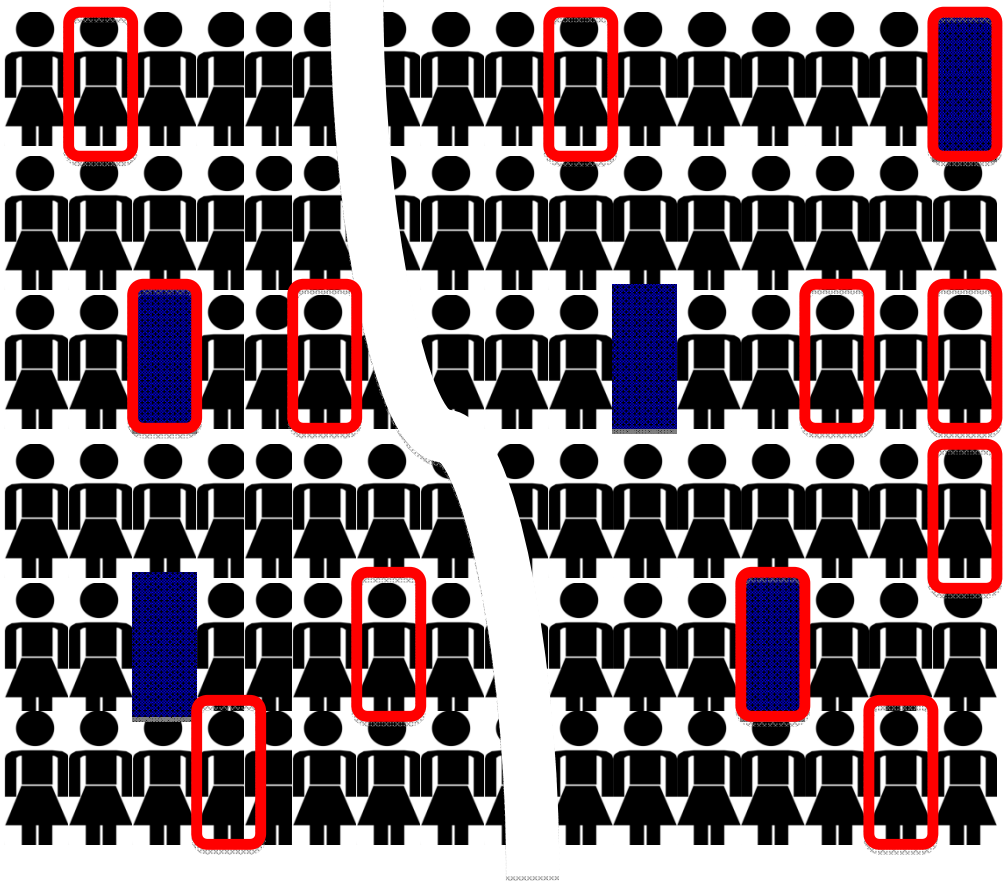
Soru 6: Pozitif sonuçlardaki hasta olasılığı nedir (PPV)?

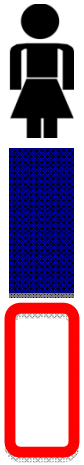
7/350 = 1:50 (%2)

DP / YP+DP

Örnek -2

1000 gebe tarıyoruz





Sağlıklı

Down sendromu

Test sonucupozitifgebe

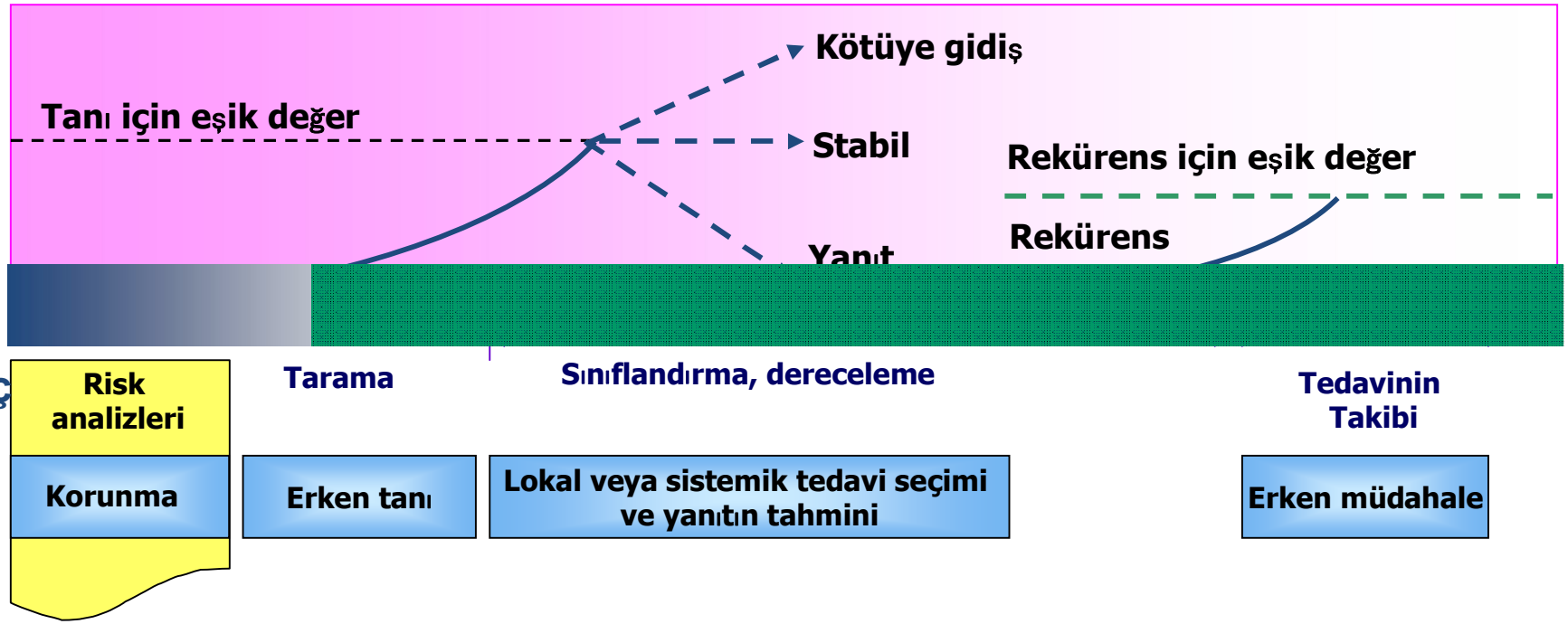
Saptama oranı (SO-DR) nedir?

3/5 = % 60

Yanlış pozitif oranı (YP-FP) nedir?

90/995 = % 9

YP / YP+DN



Örnek: Meme Kanseri

Klinik metod	Aile Hikayesi	Mamografi ve muayene	Fizik muayene, görüntüleme, biopsi, lenf nodu durumu ve patolojik inceleme	Fizik mauyene Görüntüleme
Belirteç	BRCA1 BRCA2	-	ER,PR,HER2/NEU, moleküler inceleme, PET	Ca 15-3

Risk

İstenmeyen etkilerin ortaya çıkma durumu ve sonuçlarıdır

Risk Yönetimi

İstenmeyen etkilerin görülme olasılığının hesaplanması ve değerlendirilmesini ve azaltılması ile ilgili önlerleri kapsar.

ISO Guide 73:2009
Risk management - Vocabulary

Risk ne kadar önemlidir (Olasılık x şiddet)
Ne yapılmalıdır?

Risk matriksi

Likelihood	Consequences				
	Insignificant	Minor	Moderate	Major	Severe
Almost certain	M	H	H	E	E
Likely	M	M	H	H	E
Possible	L	M	M	H	E
Unlikely	L	M	M	M	H
Rare	L	L	M	M	H

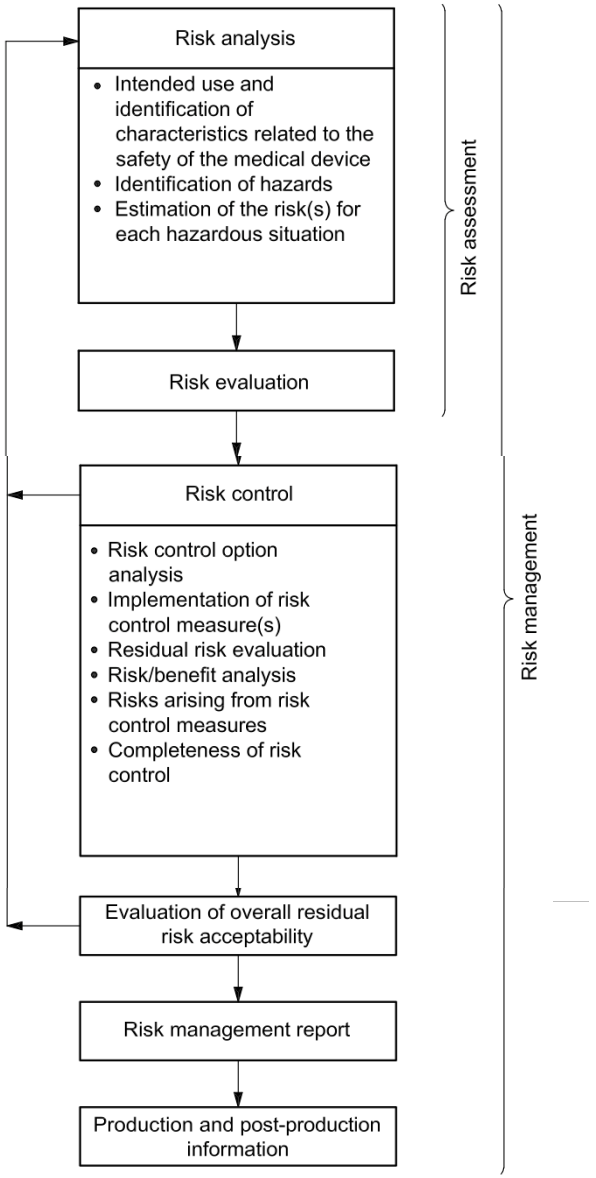
INTERNATIONAL STANDARD

ISO 14971

Second edition
2007-03-01

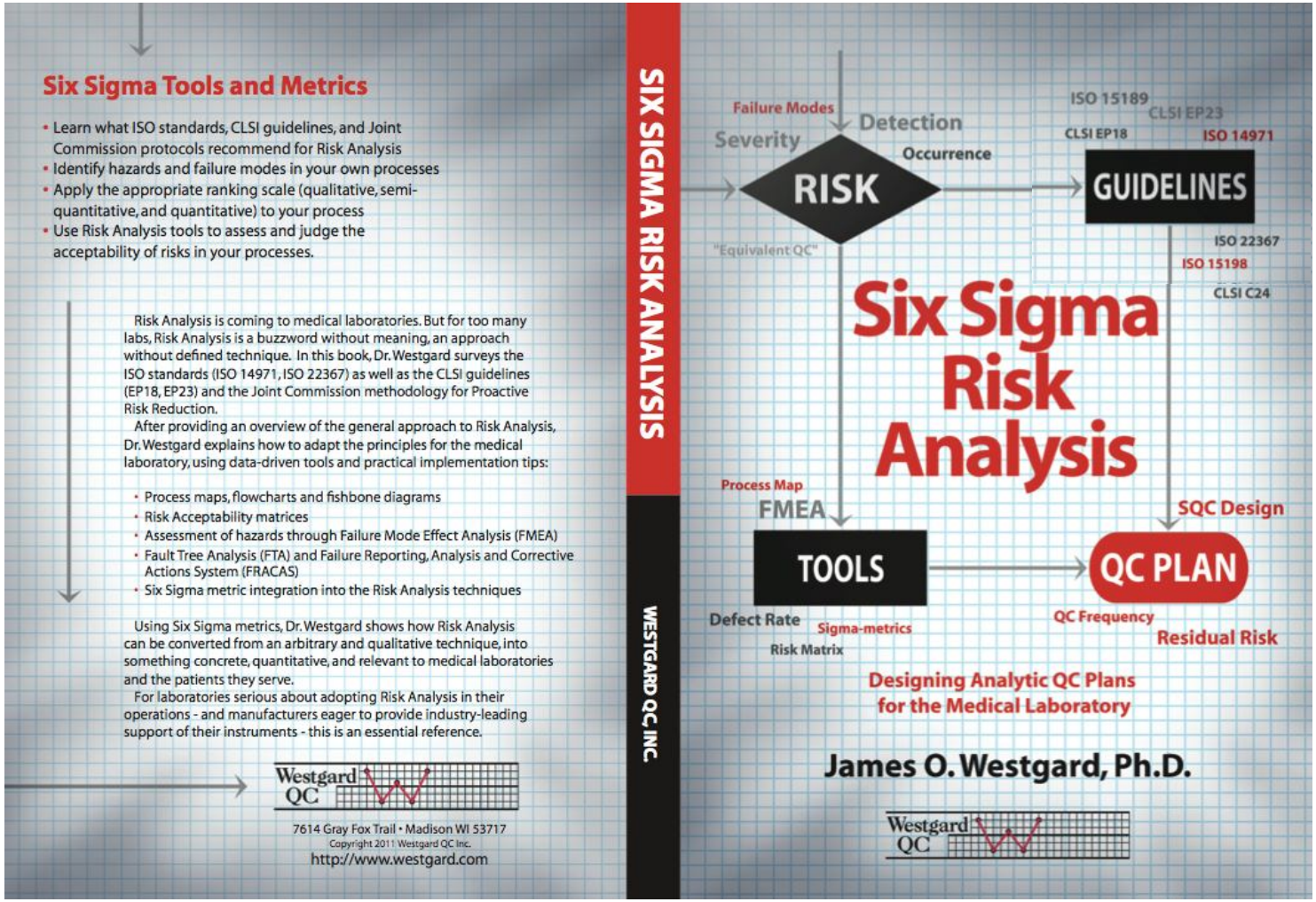
Medical devices — Application of risk management to medical devices

Dispositifs médicaux — Application de la gestion des risques aux dispositifs médicaux



14971:2007 specifies a process for a manufacturer to identify the hazards associated with medical devices, including *in vitro diagnostic (IVD) medical devices, to estimate and evaluate the associated risks, to control these risks, and to monitor the effectiveness of the controls. The requirements of ISO 14971:2007 are applicable to all stages of the life-cycle of a medical device*

Laboratuvarların farklı bir bakış açısı!

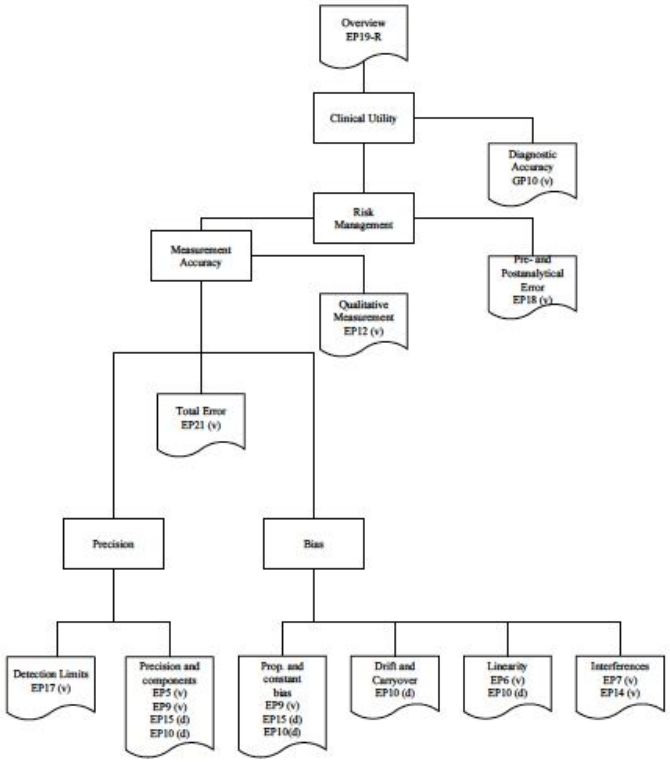


CLINICAL AND LABORATORY STANDARDS INSTITUTE®

EP18-A2
Vol. 29 No. 26
Replaces EP18-A
Vol. 22 No. 28

Risk Management Techniques to Identify and Control Laboratory Error Sources; Approved Guideline—Second Edition

Laboratory Failure Sources and CLSI Evaluation Protocols Documents



Hastalıkların etyolojisi

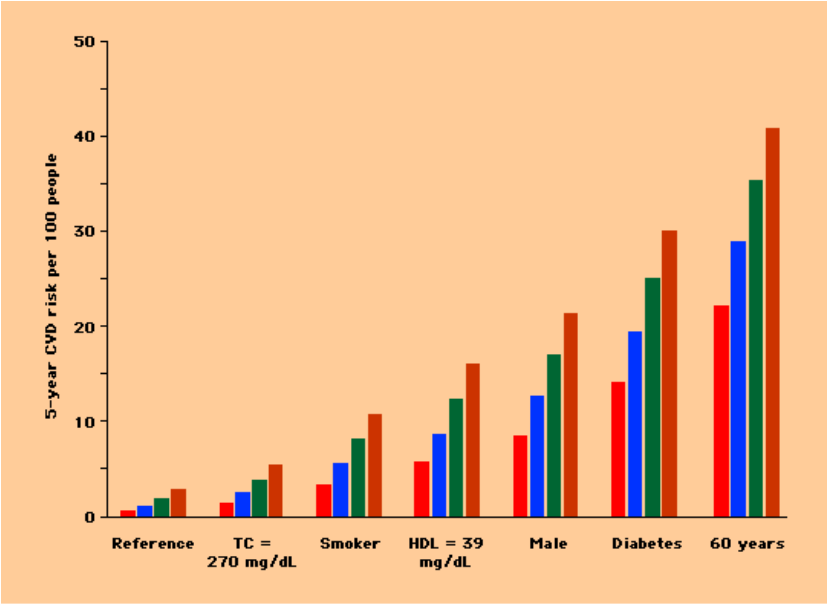
- **Çevresel faktörler** (diyet, alkol, enfeksiyonlar, sigara içmek.....)
- **Genetik faktörler** (mutasyonlar, lipoprotein seviyeleri, homosistein ve lipit metabolizmasındaki genler, pıhtılaşma, lökosit adezyonu, inflamasyon.....)

Toplam riske katkıları nedir ?

RİSK ANALİZLERİNİ HANGİ HASTALIKLAR İÇİN KULLANILIYOR?

- **KARDİYOVASKÜLER HASTALIK**
- **KANSERLER**
- **OSTEOPOROZ**
- **FMF (Ailevi Akdeniz Ateşi)**
- **Alzheimer**
- **Haemokromatoz**
- **Gaucher hastalığı**
- **Kistik fibroz**
- **Alfa 1 antitripsin eksikliği**
- **Sitokrom P450* CYP2C9, CYP2C19**
- **Çölyak Hastalığı, HLA DQ2 ve DR4(DQ8)**
- **.....**
- **.....**

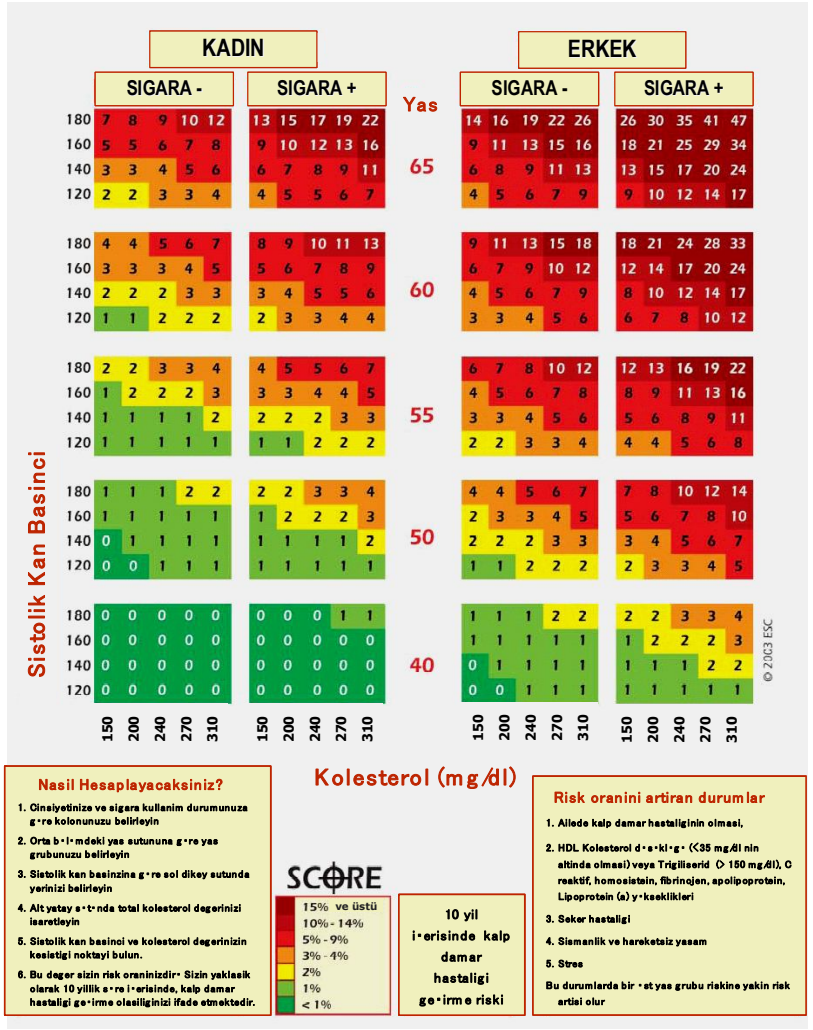
KORONER KALP HASTALIĞI RİSK FAKTÖRLERİ



Cumulative absolute risk of CVD at five years Cumulative absolute risk of cardiovascular disease (CVD) at five years according to systolic blood pressure and specified levels of other risk factors. The reference category is a nondiabetic, nonsmoking 50 year-old woman with a serum total cholesterol (TC) of 154 mg/dL (4.0 mmol/L) and HDL-cholesterol of 62 mg/dL (1.6 mmol/L). The CVD risks are given for systolic blood pressure levels of 110, 130, 150, and 170 mmHg. In the other categories, the additional risk factors are added consecutively. As an example, the diabetes category is a 50-year-old diabetic man who is a smoker and has a total cholesterol (TC) of 270 mg/dL (7 mmol/L) and HDL-cholesterol of 39 mg/dL (1 mmol/L). (Adapted from Jackson, R, Lawes, CM, Bennett, DA, et al, Lancet 2005; 365:434).

KALP DAMAR HASTALIGI RISKINIZI BILIYOR MUSUNUZ ?

CINSIYET, YAS, KAN BASINCI, TOTAL KOLESTEROL DEGERLERINE GÖRE 10 YILLIK KALP DAMAR HASTALIGI RISKININ BELIRLENMESI



Nasil Hesaplayacaksiniz?

1. Cinsiyetinize ve sigara kullanim durumunuza göre kolonunuzu belirleyin
2. Orta büyüklükteki yas sutununa göre yas grubunuzu belirleyin
3. Sistolik kan basinizina göre sol dikey sutunda yerinizi belirleyin
4. Ait yatay satırda total kolesterol degerinizi isaretleyin
5. Sistolik kan basinci ve kolesterol degerinizin kesistigi noktayi bulun.
6. Bu deger sizin risk oraninizdir. Sizin yaklasik olarak 10 yillik süre içerisinde, kalp damar hastaligi geçirme olasiliginizi ifade etmektedir.

SCORE

15% ve üstü
10% - 14%
5% - 9%
3% - 4%
2%
1%
< 1%

10 yil içerisinde kalp damar hastaligi geçirme riski

Risk oranini artiran durumlar

1. Ailede kalp damar hastaliginin olmasi,
2. HDL Kolesterol düsük (<35 mg/dl nin altinda olmasi) veya Trigliserid (> 150 mg/dl), C reaktif, homosistein, fibrinojen, apolipoprotein, Lipoprotein (a) yüksekilikleri
3. Seker hastaligi
4. Sigara ve hareketsiz yasam
5. Stres

Bu durumlarda bir üst yas grubu riskine yakin risk artisi olur

www.escardio.org/Prevention

'European Guidelines on CVD Prevention: third Joint European Societies' Task Force on Cardiovascular Disease Prevention in Clinical Practice' De Backer G., Ambrosioni E., Borch-Johnsen K., et al. Eur J Cardiovasc Prev Rehabil 2003; 10(suppl 1): S1-S78

EUROPEAN SOCIETY OF CARDIOLOGY

Framingham / ATP III point scores in men

Age, years	Points
20 to 34	-7
35 to 39	-3
40 to 44	0
45 to 49	3
50 to 54	6
55 to 59	8
60 to 64	10
65 to 69	12
70 to 74	14
75 to 79	16

Total cholesterol mg/dL (mmol/L)	Age 20 to 39	Age 40 to 49	Age 50 to 59	Age 60 to 69	Age 70 to 79
<160 (3.4)	0	0	0	0	0
160 to 199 (3.4 to 5.15)	4	3	2	1	1
200 to 239 (5.17 to 6.18)	8	6	4	2	1
240 to 279 (6.2 to 7.21)	11	8	5	3	2
≥280 (7.24)	13	10	7	4	2

	Age 20 to 39	Age 40 to 49	Age 50 to 59	Age 60 to 69	Age 70 to 79
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

HDL cholesterol mg/dL (mmol/L)	Points
≥60 (1.55)	-1
50 to 59 (1.29 to 1.53)	0
40 to 49 (1.03 to 1.27)	1
<40 (1.03)	2

Systolic blood pressure, mmHg	Untreated	Treated
<120	0	0
120 to 129	1	3
130 to 139	2	4
140 to 159	3	5
≥160	4	6

Point total	10-year risk, percent	Point total	10-year risk, percent
<9	<1	17	5
9	1	18	6
10	1	19	8
11	1	20	11
12	1	21	14
13	2	22	17
14	2	23	22
15	3	24	27
16	4	≥25	≥30

Estimation of cardiovascular risk in an individual patient without known cardiovascular disease

Diğer Risk faktörleri

Laboratory Medicine Practice Guidelines

Emerging Biomarkers for Primary Prevention of Cardiovascular Disease and Stroke

Table 1. Emerging Risk Factors for Cardiovascular Disease

C-Reactive Protein	Interleukins (eg, IL-6)
Serum amyloid A	Vascular and cellular adhesion molecules
Soluble CD-40 ligand	Leukocyte count
Fibrinogen	Plasminogen activator inhibitor 1
D-dimer	Tissue-plasminogen activator
Factors V, VII, VIII	Small dense LDL
Lipoprotein(a)	Apolipoproteins A1 and B
LDL and HDL subtypes	Oxidized LDL
Homocysteine	Lipoprotein-associated phospholipase A_2
Microalbuminuria	creatinine (glomerular filtration rate)
Cystatin C	Infectious agents
Apo E genotype	Fibrinopeptide A
Remnant lipoproteins	von Willebrand factor antigen

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İnflamasyon belirteçleri

hsCRP

Öneri	Kanıt Değeri / Öneri
Klasik risk analizleri < %5 ise ölçümüne gerek yoktur	**I - A**
Klasik risk analizleri %5- 10 ise yaşam yaşam sitilini belirlemek için önerilir	**II - B**
Klasik risk analizleri %10-20 tedavi planlamasında hsCRP ölçümü yapılabilir	**I - A**
Tedavi takibinde kullanımı	**Yetersiz veri**

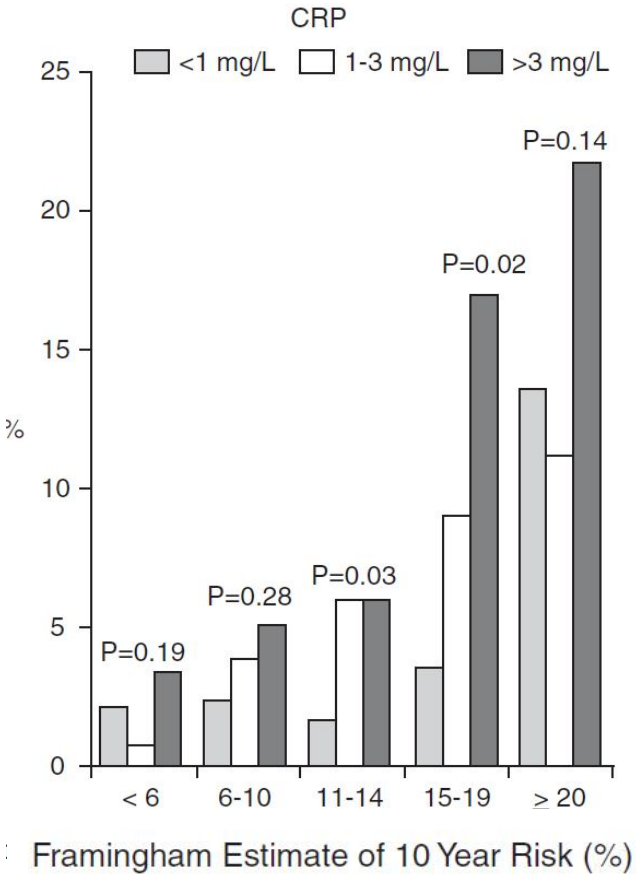

Table 2. American Heart Association/American College of Cardiology Classifications Summary of Indications

I Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective

II Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment

IIa Weight of evidence/opinion is in favor of usefulness/efficacy

IIb Usefulness/efficacy is less well established by evidence/opinion

III Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and insome cases may be harmful

Weight of Evidence

A Data derived from multiple randomized clinical trials that involved large numbers of patients

B Data derived from a limited number of randomized trials that involved small numbers of patients or from careful analyses of nonrandomized studies or observational registries

C Expert consensus was the primary basis for the recommendation

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Using Nontraditional Risk Factors In Coronary Heart Disease Risk Assessment

Release Date: October 2009

This topic page summarizes the U.S. Preventive Services Task Force (USPSTF) recommendations on using nontraditional risk factors in screening for coronary heart disease.

Summary of Recommendation / Supporting Documents

Summary of Recommendation

- The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to assess the balance of benefits and harms of using the nontraditional risk factors discussed in this statement to screen asymptomatic men and women with no history of CHD to prevent CHD events (select "Clinical Considerations" for suggestions for practice when evidence is insufficient).

  The nontraditional risk factors included in this recommendation are [redacted] ankle-brachial index (ABI), leukocyte count, fasting blood glucose level, periodontal disease, carotid intima-media thickness (carotid IMT), coronary artery calcification (CAC) score on electron-beam computed tomography (EBCT), homocysteine level, and lipoprotein(a) level.

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Supporting Documents

Using Nontraditional Risk Factors In Coronary Heart Disease Risk Assessment, October 2009

▶ Recommendation Statement (PDF File, 230 KB; PDF Help)

İnflamasyon belirteçleri

hsCRP

Table 4. Population Distributions of hsCRP (mg/L; N = 35,930)*

	Percentile						
	5th	10th	25th	50th	75th	90th	95th
American women†	0.2	0.3	0.6	1.5	3.5	6.6	9.1
American men	0.3	0.4	0.8	1.5	3.2	6.1	8.6
European women†	0.3	0.4	0.9	1.7	3.4	6.2	8.8
European men	0.3	0.6	0.8	1.6	3.3	6.5	8.6

*Data from Rifai (103) and Imhof (104).
†Only women not taking hormone replacement therapy.

CDC/AHA

sınır değer > 3.0 mg/L artmış risk

> 10.0 mg/L yüksek risk

Tekrarlanabilirlik < %10 (daha dar olması isteniyor)

Stabil (4 C'de 60 gün)

Biyolojik varyasyon yaklaşık %30

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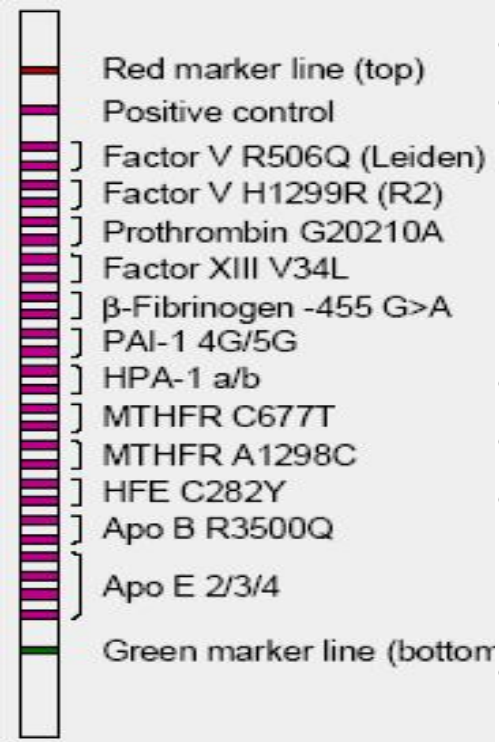
Diğer belirteçleri

	Öneri	Öneri/ Kanıt Değeri	Açıklama
Lipoprotein alt grupları (small dance LDL)	**Önerilmiyor**	**III- A**	**Metodlar yetersiz Standardizasyon yok Veriler yetersiz**
Lipoprotein a	Önerilmiyor	III-A	Metod yetersiz (CV %20) Veriler yeterli ve gerekliliği saptanamamıştır
ApoB **Apo A-I**	**Tedavi takibi Risk belirleme**	**I-A II-B**	**Uygun. Ancak LDL-C ve non-HDL-C'ye katkısı olmadığı için önerilmiyor**
Kreatinin, Cyctatin C, eGFR	Önerilmiyor	III-C	
Homosistein	< 10 umol/L 10-15 int. risk 15-30 yüksek risk >30 çok yük. risk	**II-C**	**hsCRP ile paralellik gösteriyor. Analitik problemleri mevcut. Örnek toplama ve ölçüm sorunları mevcut.**

Koroner kalp hastalığında polimorfizm ve genetik risk faktörleri



- Çalışmalar arsında önemli çelişkiler mevcut
- Meta analizler
  - faktor II (G20210A variant),
  - faktor V Leiden (G1691A)
  - faktor VII (R353Q),
  - glikoprotein (GP) IIIa reseptor (PIA1/A2)
  - methylenetetrahydrofolate reduktase (MTHFR, C677T).
- factor II ve factor V polimorfizmlerini ilişkisi yok
- GP IIIa PIA1/A2 (OR 1.12, 95% CI 1.01 to 1.24)
- factor VII R353Q –
  RQ ve RR genotipi iç (OR 0.78, 95% CI 0.65 to 0.93)
  QQ genotipi (OR 0.53, 95% CI 0.27 to 1.03)
- MTHFR TT homozigot (OR 1.30, 95% CI 1.11 to 1.52)

Kanserler

Major Breast Cancer Susceptibility Genes

Gene	Associated syndrome	Chromosome site	Gene frequency	Gene penetrance for breast cancer
BRCA1	HBOC*	17q21	Rare	Very high
BRCA2	HBOC	13q12-13	Rare	High
p53	Li-Fraumeni	17p13.1	Very rare	High
PTEN	Cowden	10q22-23	Very rare	High
ATM	Ataxia-telangiectasia (heterozygotes)	11q22-23	Common	Low to moderate
STK11	Peutz-Jeghers	19p13.3	Very rare	High

* HBOC : Hereditary breast ovarian cancer syndrome

Risk of Breast Cancer

	Percent of population	Percent of all breast cancer cases	Average lifetime risk of breast cancer, percent
General population	~90	80 to 85	11 to 12
Positive family history breast cancer†	~12	15 to 20	20 to 25
Positive BRCA1 or 2 mutation	~0.1	5 to 6	65 to 85

† Breast cancer in a first-degree relative

Breast Cancer Risk Assessment Models[†]

	Gail model	Claus model
Data derived from	BCDDP	CASH
Characteristics of study population	2852 cases, age ≥35 years In situ and invasive cancer 3146 controls Caucasian Annual screening	4730 patients, aged 20-54 years Invasive cancer 4688 controls Caucasian Not routinely screened
Variables in model	FH of breast cancer Age of menarche Age at first live birth Number of breast biopsies Presence of atypical hyperplasia in breast biopsy Race	FH of breast cancer
Definition of family history	Mother or sister	First- or second-degree relatives (maternal or paternal)
Validated?	Yes	No
Strengths	Incorporates risk factors other than FH	Maternal and paternal FH Age of onset of breast cancer Separate tables to calculate risk of breast cancer based on FH of ovarian cancer +/- breast cancer Calculation of risk dependent on age of proband
Limitations	Does not incorporate paternal FH of breast or ovarian cancer Does not consider age of onset of breast cancer in relatives Effect of number of breast biopsies (without atypical hyperplasia) may cause inflated risk estimates	Limited to specific combinations of affected relatives (eg, no table for mother-maternal grandmother) Does not incorporate risk factors other than FH
Best use	Calculation of breast cancer risk in absence of family history in women Determination of eligibility for tamoxifen for breast cancer risk reduction	Calculation of breast cancer risk in presence of family history

BCDDP: Breast Cancer Detection Demonstration Project; CASH: Cancer and Steroid Hormone Study; FH: family history.

[†] Reproduced with permission from: Domchek, SM, Eisen, A, Calzone, K, et al. Application of breast cancer risk prediction models in clinical practice. J Clin Oncol 2003; 21 :593. Copyright © 2003 American Society for Clinical Oncology.

UpToDate 16.1 (2011)

OSTEOPOROZ

Kemik mineral dansitesi

Nam L
Patient ID: 57121
DOB: 01 January 1948

Sex: Female
Ethnicity: White
Menopause Age: 45

Height: 157.0 cm
Weight: 75.0 kg
Age: 58

Referring Physician: DAHILIYE

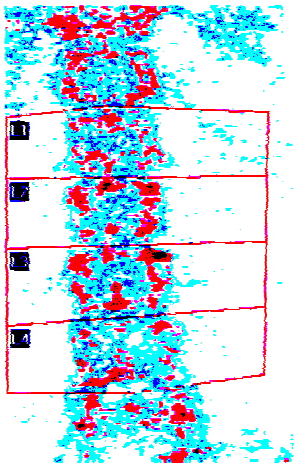


Image not for diagnostic use
116 x 128

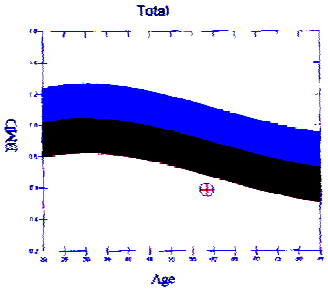
Scan Information:

Scan Date: 18 May 2006 ID: A05180619
Scan Type: f Lumbar Spine
Analysis: 18 May 2006 14:14 Version 12.3
Lumbar Spine (auto low density)
Operator: ERSAN
Model: QDR 4500C (S/N 49458)
Comment:

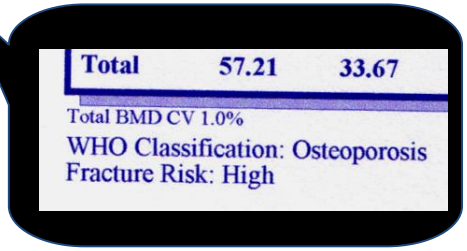
DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T - Score	Z - Score
L1	12.80	6.94	0.543	-3.5	-2.3
L2	12.66	7.92	0.626	-3.7	-2.4
L3	14.65	8.97	0.612	-4.3	-3.0
L4	17.11	9.84	0.575	-4.9	-3.3
Total	**57.21**	**33.67**	**0.588**	**-4.2**	**-2.9**

Total BMD CV 1.0%
WHO Classification: Osteoporosis
Fracture Risk: High

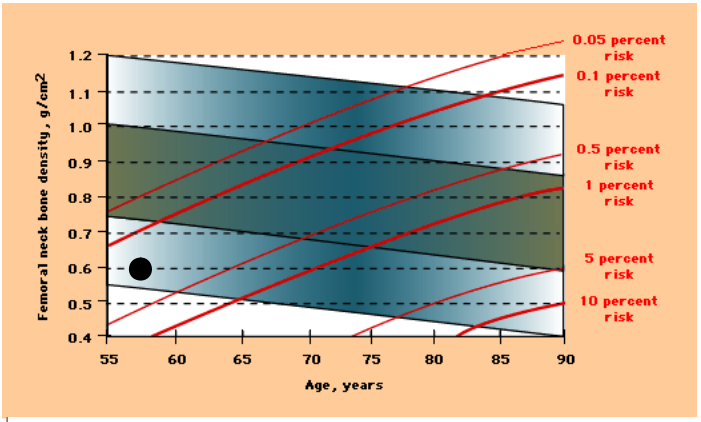


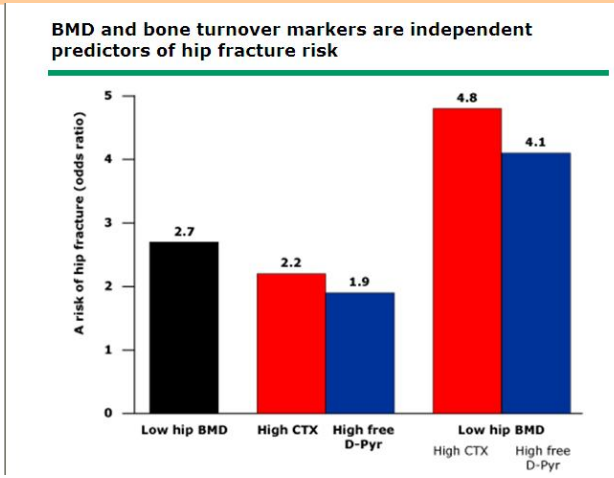
Physician's Comment:



Osteoporoz nedenleri.

1. Daha önce kırık hikayesi
2. Aile hikayesi
3. Sigara
4. Düşük vücut ağırlığı (< 58 kg)
5. Östrojen düşüklüğü
6. Düşük kalsiyum alımı
7. Alkol kullanımı
8. Sık düşmeler
9. Görme bozukluğu olanlar
10. Hastalık ve zayıflık





Kırık riski belirleme

Roche Wyeth NOVARTIS Abdi İbrahim SCHERING making medicine work

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care • www.ahrq.gov
USPSTF

SCREENING FOR OSTEOPOROSIS
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Women age ≥65 years without previous known fractures or secondary causes of osteoporosis	Women age <65 years whose 10-year fracture risk is equal to or greater than that of a 65-year-old white woman without additional risk factors	Men without previous known fractures or secondary causes of osteoporosis
Recommendation	Screen		No recommendation
	Grade: B		Grade: I (insufficient evidence)

Anoploidi ve Risk Analizleri

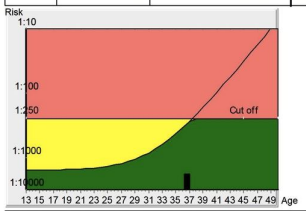
Laboratory Name
Laboratory Adress

Result Down syndrome screening

Name	Imaginary Patient	Sample ID		diabetes	no
		D.O.B.	01/01/69	Fetuses	1
Day of serum taking	18/02/05	Age at delivery	36.6	Smoker	no
Date of report:	02/04/05	Weight [kg]	61	IVF	no
		LMP	20/10/04	Ethnic origin	Caucasian

Corrected MoM's and calculated risks

AFP	71.3	IU/ml	1.93	Corr. MoM	Gestational age at sample date	17	+	2
uE3	4.4	ng/ml	1.49	Corr. MoM	determination method			LMP
HCG	15600	mUI/mL	0.70	Corr. MoM	Physician			



Tr.21 risk
at term
1:3408

Age risk
at term
1: 302

Down Syndrome Risk

The calculated risk for Trisomy 21 is below the cut off which represents a low risk.
After the result of the Trisomy 21 test it is expected that among 3408 women with the same data, there is one woman with a trisomy 21 pregnancy and 3407 women with not affected pregnancies.
The calculated risk by PRISCA depends on the accuracy of the information provided by the referring physician.
Please note that risk calculations are statistical approaches and have no diagnostic value!

Neural tube defects risk	Risk for trisomy 18
The corrected MoM AFP (1.93) is located in the low risk area for neural tube defects.	**The calculated risk for trisomy 18 is < 1:10000, which indicates a low risk.**

below cut off | Below Cut Off, but above Age Risk | above cut off

Estimated Risk of Down Syndrome by Maternal Age and Gestational Age†

Maternal age (years)	Risk at 12 weeks	Risk at 16 weeks	Risk at 40 weeks
20	1/1068	1/1200	1/1527
25	1/946	1/1062	1/1352
30	1/626	1/703	1/895
31	1/543	1/610	1/776
32	1/461	1/518	1/659
33	1/383	1/430	1/547
34	1/312	1/350	1/446
35	1/249	1/280	1/356
36	1/196	1/220	1/280
37	1/152	1/171	1/218
38	1/117	1/131	1/167
39	1/89	1/100	1/128
40	1/68	1/76	1/97
41	1/51	1/57	1/73
42	1/38	1/43	1/55

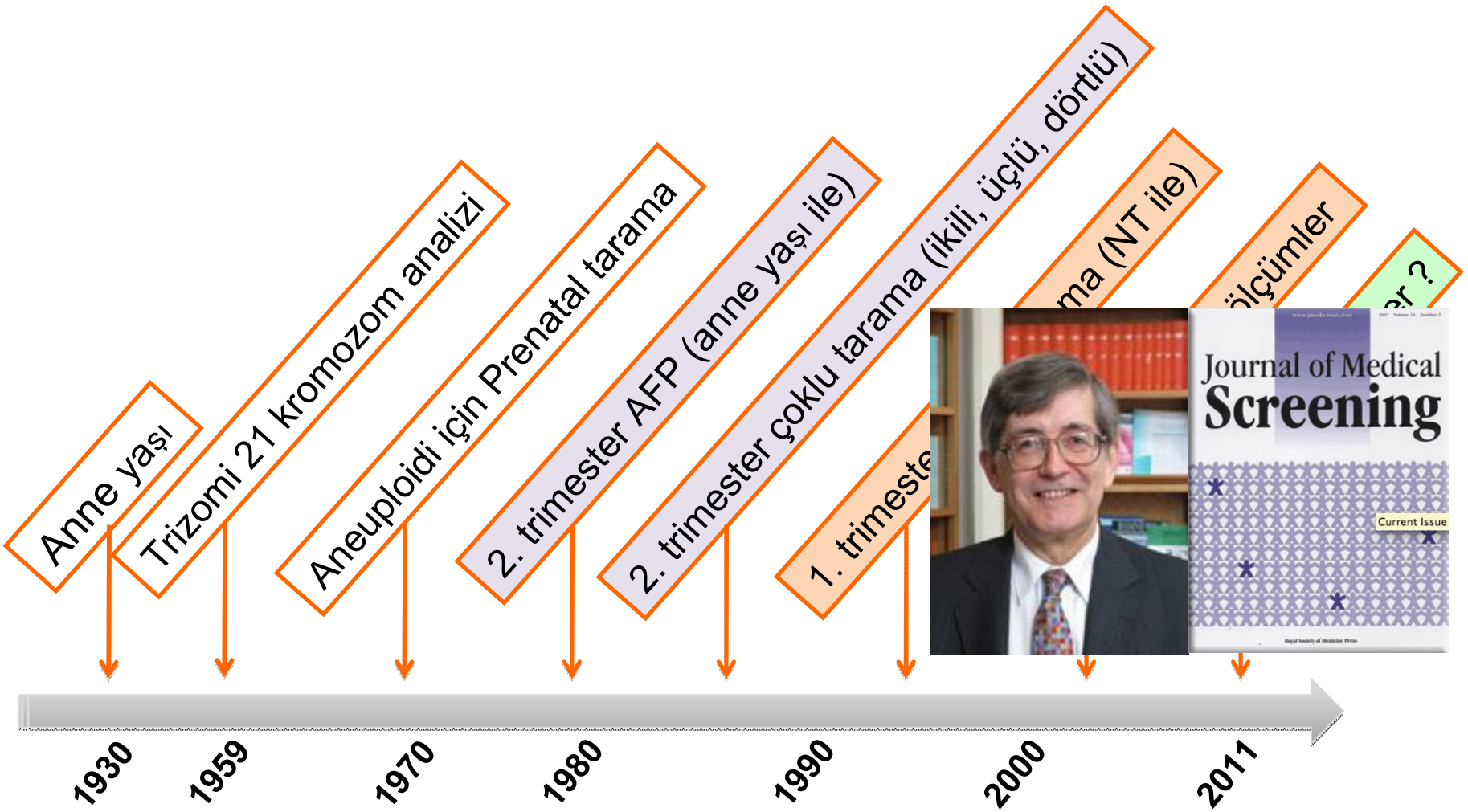
†Adapted from Nicolaides, KH. Am J Obstet Gynecol 2004; 191 :45.

The Effect of Selecting Different Risk Cut-offs on Triple Test Performance†

Term risk cut-off	Equivalent to maternal age cut-off of	Detection rate, percent	False positive rate, percent
≥ 1 in 250	≥ 37	69	4.9
1 in 300	≥ 36	72	5.9
1 in 350	≥ 35	74	6.8

†Reproduced with permission from Wald et al.Triple marker performance with gestational age estimated by ultrasound.

Anoploidi hikayesi



Down Sendromu tanısı

Prenatal Screening for Down Syndrome
in 14 EUROCAT Countries *(Special Report 2010)*

	Nat'l Policy	1st Trimester	2nd Trimester
Austria	NO		
Belgium	YES	NT/serum	
Croatia	NO	NT	serum
Denmark	YES	combined	
Finland	YES	combined	
France	YES	combined	
Ireland	NO		
Italy	YES	NT/combined	triple
Malta	NO		
Netherlands	YES	NT/serum/combined	triple
Spain (Catalonia)	YES	combined	quad
Sweden	NO	combined *(routine in parts of Sweden)*	
Switzerland	YES	combined	triple
UK	YES	combined *(>90% DR at <2% FPR by April 2010)*	triple/quad

EUROCAT: European Surveillance of Congenital Anomalies

Risk Formülleri *

Calculating Risks for DS

- Determine the “marker dependent” likelihood ratio by calculating H_{DS} and $H_{Unaffected}$

$$H = \frac{1}{\prod\sigma(2\pi)^{p/2}\cdot\det(\mathbf{R})^{1/2}}\exp\left[-\frac{\mathbf{Z}^T\mathbf{R}^{-1}\mathbf{Z}}{2}\right]$$

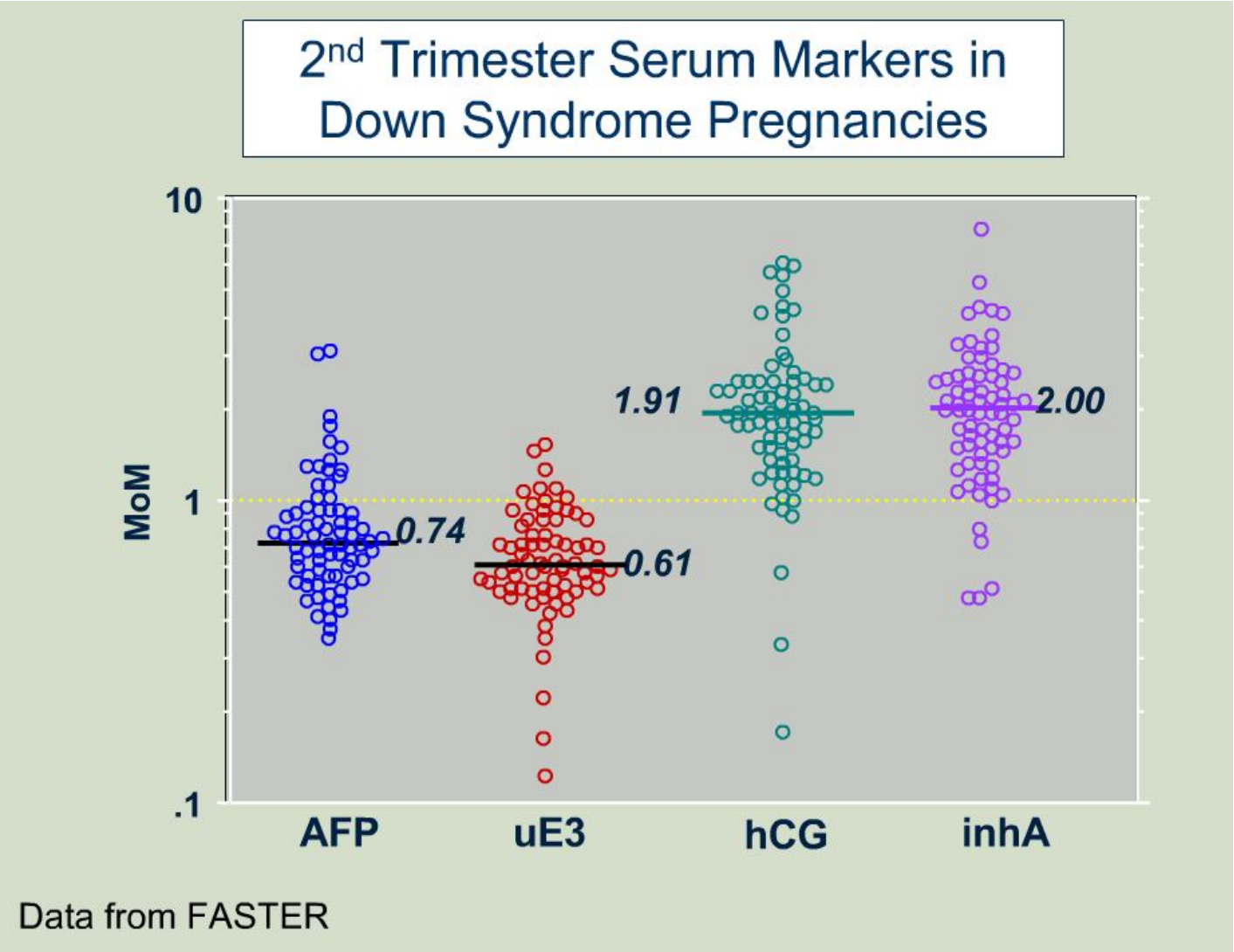
- LR = H_{DS} divided by $H_{Unaffected}$

- Post-test Odds = Pre-test Odds × LR

*** First-trimester risk calculation for trisomy 13, 18, and 21: comparison of the screening efficiency between 2 locally developed programs and commercial software.** Clin Chem. 2011 Jul;57(7):1023-31.

2. trimester tarama

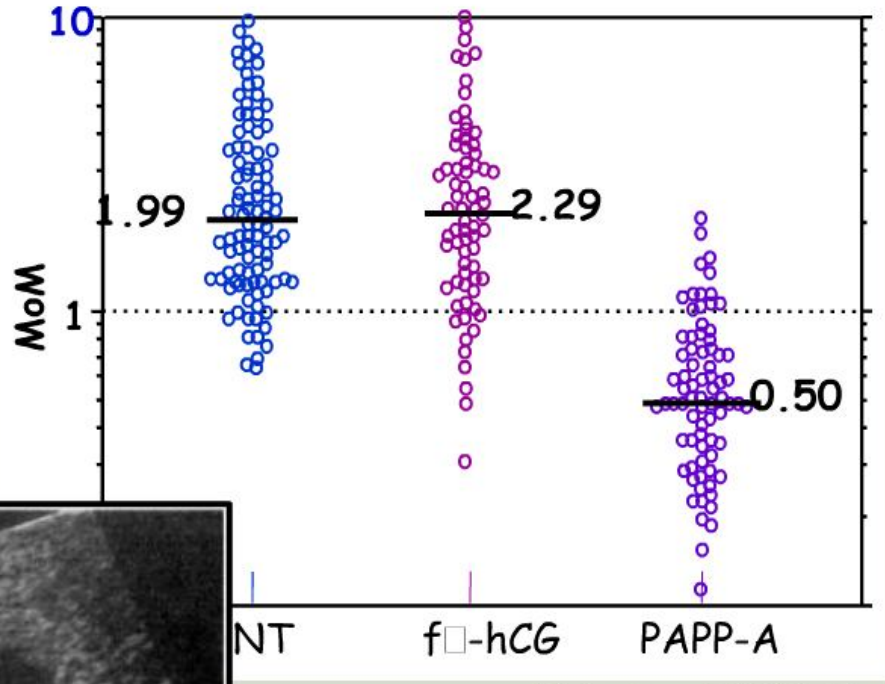
$$\text{Risk} \approx \frac{hCG^2}{AFP^2 \times uE3}$$



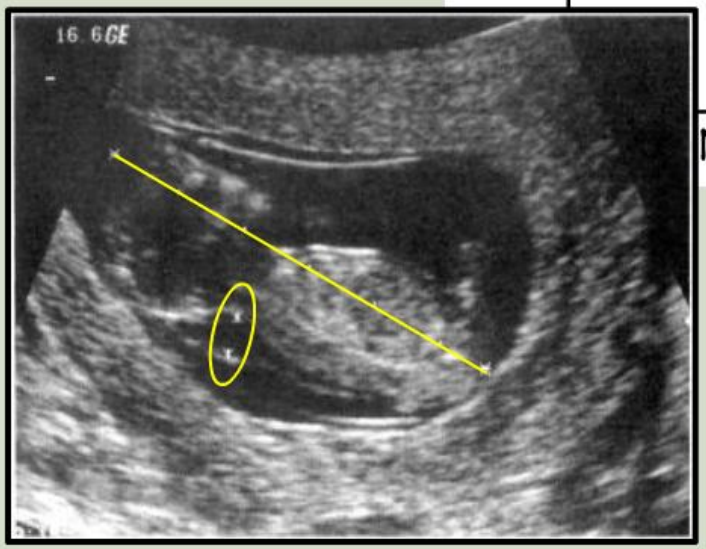
Birinci trimester test

First Trimester Combined Test:

- *NT ultrasound*
- *serum PAPP-A*
- *serum □-hCG*



Data from FASTER

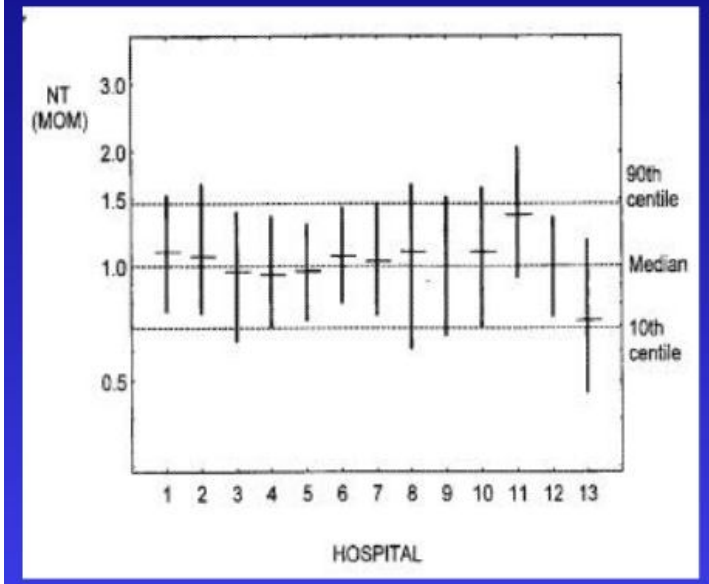


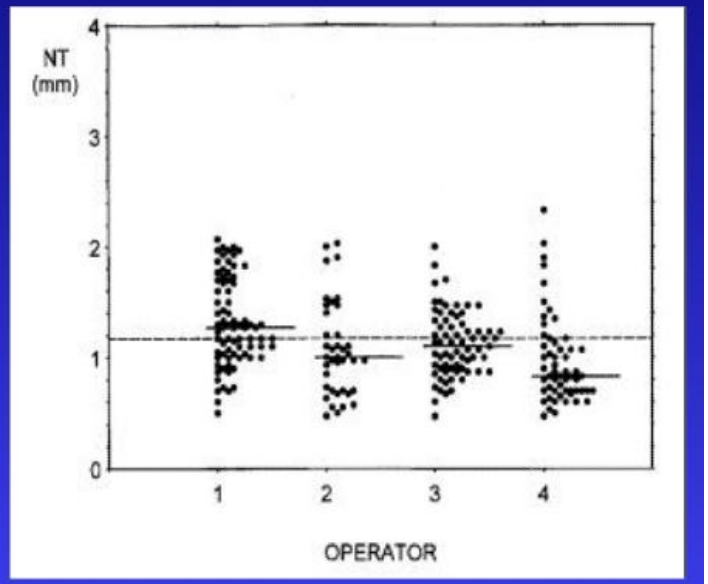
F Malone, with permission

NT değerlendirilmesi

NT reference data (medians)

Can a single set of medians be used for all sonographers?



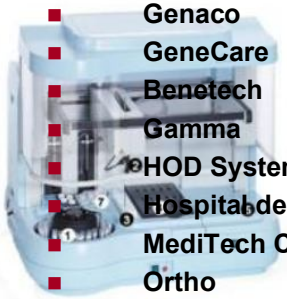


Crossley J et al., 2002 (Glasgow) – all FMF trained sonographers

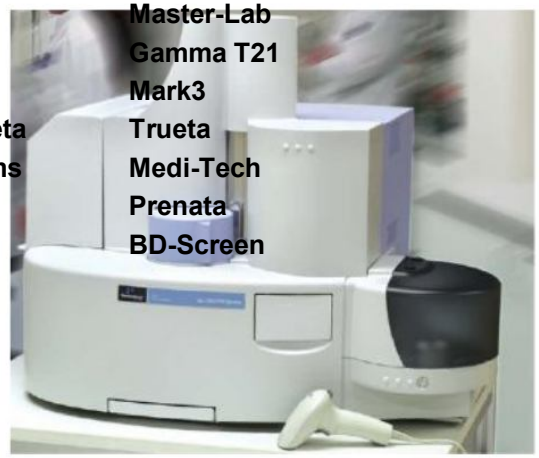
Dünya ve Türkiye ne kullanıyor

YAZILIMCI	PROGRAM
Typolog	Prisca
Logical Medical Systes	Alpha
PerkinElmer Life Sciences	Wallac Multi-Calc
NTD Laboratories	Ultra-Screen
Genaco	Genaco
GeneCare	GeneCare
Benetech	Master-Lab
Gamma	Gamma T21
HOD Systems	Mark3
Hospital de Girona, Dr. Trueta	Trueta
MediTech Computer Systems	Medi-Tech
Ortho	Prenata
Technische EDV-Systeme	BD-Screen

Point of Care 1st Trimester Platforms



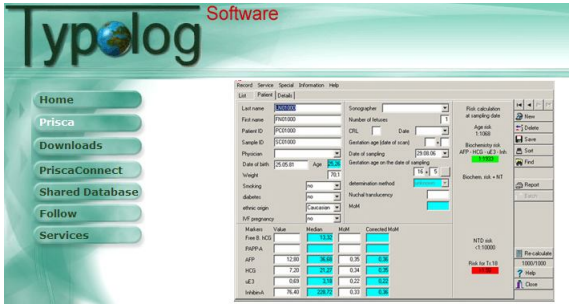
Kryptor



DelfiaXpress

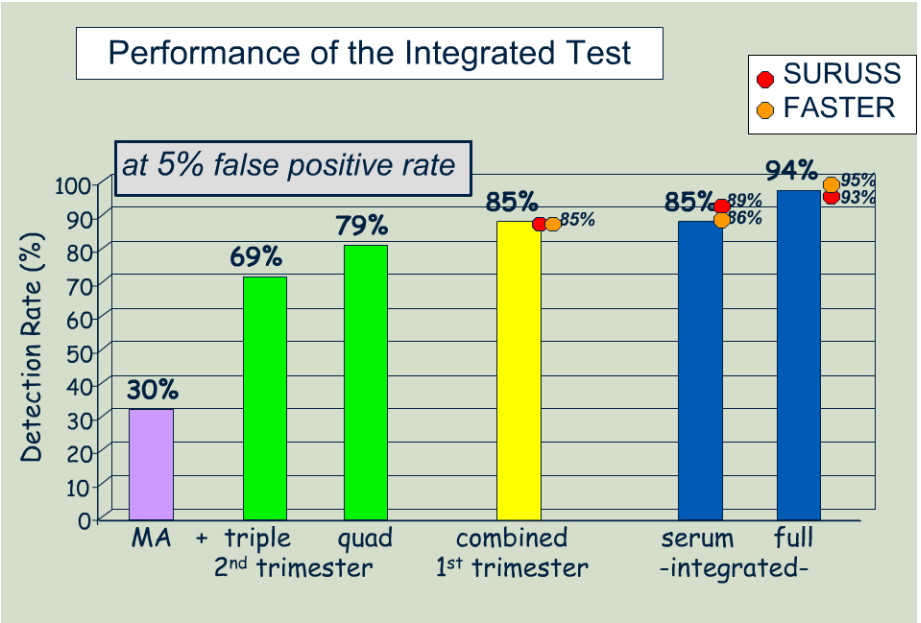
Instruments not available for this application in the US

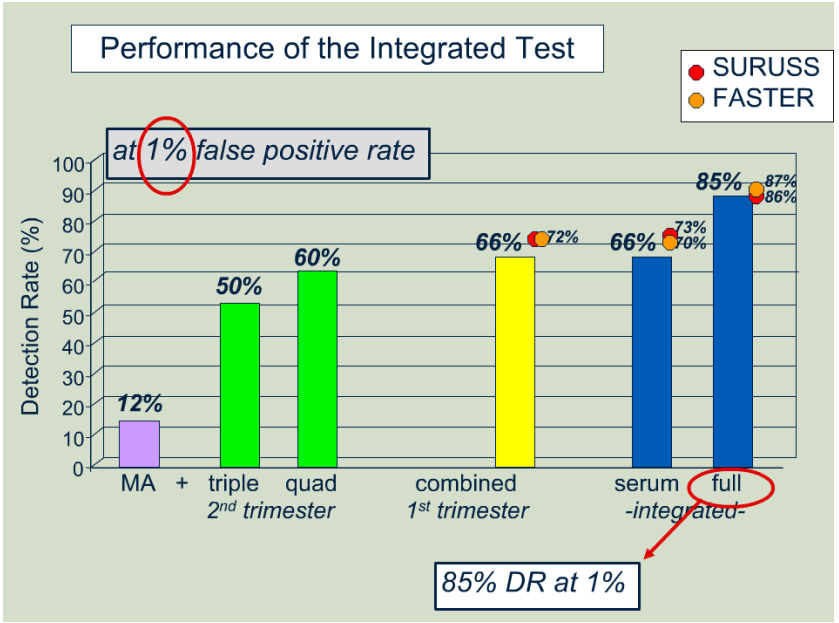
IMMULITE® 1000



BECKMAN COULTER.

Performanslar

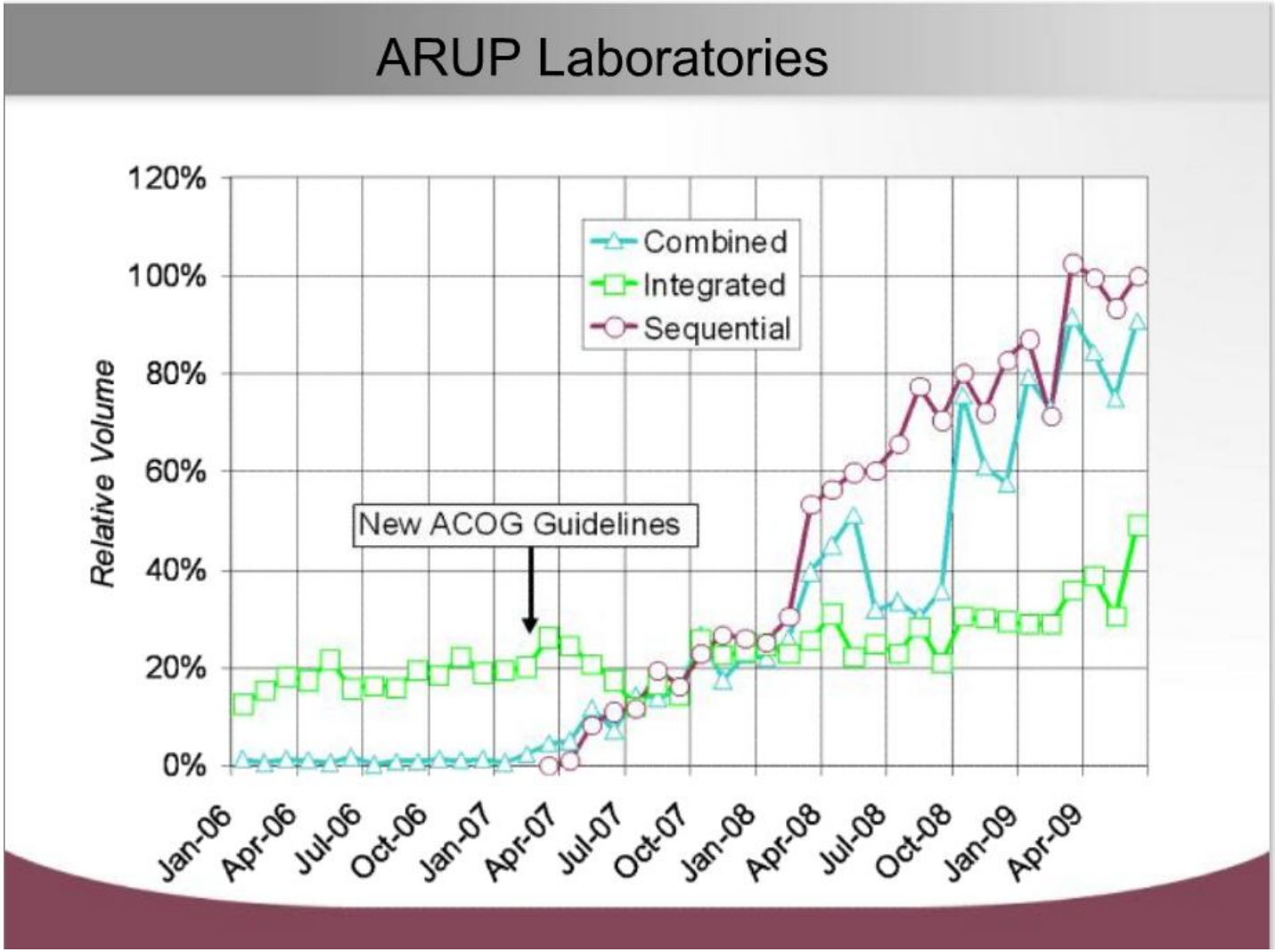




SURUSS study: (n=47053) Serum, Urine and Ultrasound Screening Study (Semin Perinatol. 2005 Aug;29(4):225-35)
The FASTER study-NIH, (n=38167) ((NEJM 2005;353:2001)

AFP, free β -hCG , total hCG, uE 3 ve PAPP-A – flouroimmunoassay (AutoDELFIA, Perkin Elmer™ (Life Sciences, USA)
Inhibin A- ALISA (Oxford Bioinnovation and Diagnostic Systems Laboratories Incorporated, UK)

Kombine kullanımlar artmaktadır



Ardışık test

Contingent Screening

Step 1: - 1st trim. NT + PAPP-A (+ β-hCG)

- very high risk (≥1 in 25 or 1 in 50) called *Screen Positive* and offered CVS *(<1% of all women screened)*

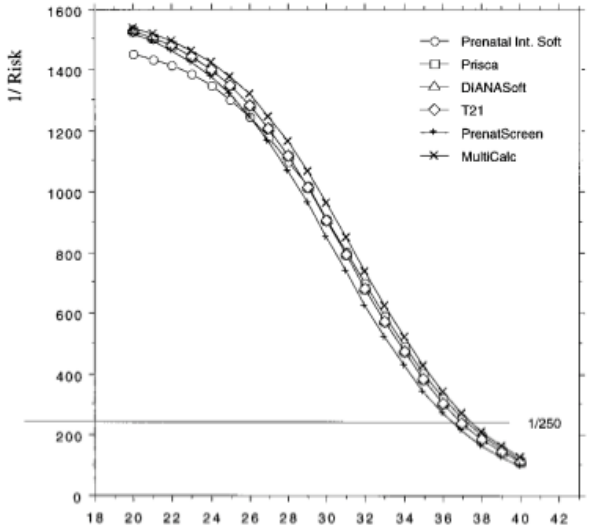
- very low risk (<1 in 2000) called *Screen Negative* and have no further testing *(60-70% of all women screened)*

Step 2: - all between 1 in 25 or 1 in 50 and 1 in 2000 go on to full integrated test *(30-40% of all women screened)*

- high risk by integrated test (≥1 in 100) called *Screen Positive* and offered amniocentesis *(1-2% of all women screened)*

Software for Prenatal Down Syndrome Risk Calculation: A Comparative Study of Six Software Packages Clinical Chemistry 45, No. 8, 1999

- Detection rate of 54.4 – 66.4.% and a false-positive rate of 2.4 – 6.8%.
- For example, at 20 years, the risk varied from 1 in 710 (Prenat Screen) to 1 in 378 (DIANASoft and Prisca)



	Abbott Prenatal Soft		BioChem DIANASoft	Chiron T21	CIS bio PrenatScreen	Wallac MultiCalc
Control cases						
Patients <30 years (n = 321)	10 (3.1%)		7 (2.2%)	6 (1.8%)	6 (1.87%)	4 (1.2%)
Patients 30–34 years (n = 163)	13 (7.9%)		7 (4.3%)	5 (3.0%)	4 (2.45%)	2 (1.2%)
Patients 35–37 years (n = 45)	13 (28.8%)		9 (20%)	9 (20%)	9 (20%)	7 (15.5%)
Total (%) (n = 529)	36 (6.8%)		23 (4.3%)	20 (3.8%)	19 (3.6%)	13 (2.4%)
Down syndrome cases						
Patients <30 years (n = 25)	10 (40%)		9 (36%)	8 (32%)	7 (28%)	5 (20%)
Patients 30–34 years (n = 45)	29 (64.4%)		29 (64.4%)	29 (64.4%)	27 (60%)	26 (57.7%)
Patients 35–37 years (n = 55)	44 (80%)		39 (70.9%)	40 (72.7%)	37 (67.2%)	37 (67.3%)
Total (%) (n = 125)	83 (66.4%)		77 (61.6%)	77 (61.6%)	71 (56.8%)	68 (54.4%)

DO %61.6, FPR %4.3

Comparison of combined, stepwise sequential, contingent, and integrated screening in 7292 high-risk pregnant women.

Guanciali-Franchi P, Iezzi I, Palka C, Matarrelli B, Morizio E, Calabrese G, Benn

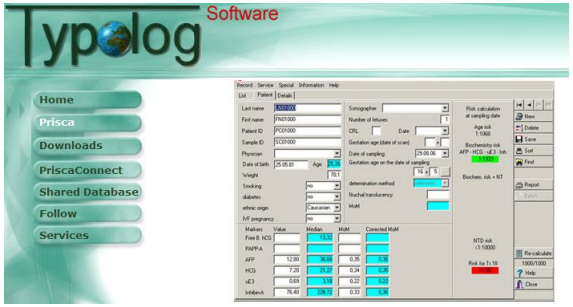
Prenat Diagn. 2011 Nov;31(11)

Table 1. Summary of Down syndrome DR and FPRs for each protocol

	First trimester		Second trimester		Net	
Protocol	**DR (%)**	**FPR (%)**	**DR (%)**	**FPR (%)**	**DR (%)**	**FPR (%)**
Combined test	17/21 (81)	294/7271 (4.0)	—	—	17/21 (81)	294/7271 (4.0)
Integrated test	—	—	19/21 (90)	247/7271 (3.4)	19/21 (90)	247/7271 (3.4)
Sequential test	17/21 (81)	294/7271 (4.0)	2/21 (10)	87/7271 (1.2)	19/21 (90)	381/7271 (5.2)
Contingent test	11/21 (52)	10/7271 (0.1)	8/21 (38)	180/7271 (2.5)	19/21 (90)	190/7271 (2.6)

DR, detection rate; FPR, false-positive rate.

Immulite 1000 chemiluminescent immunometric assays (Immulite, Medical System; Genoa, Italy)



Laboratuvar performansları

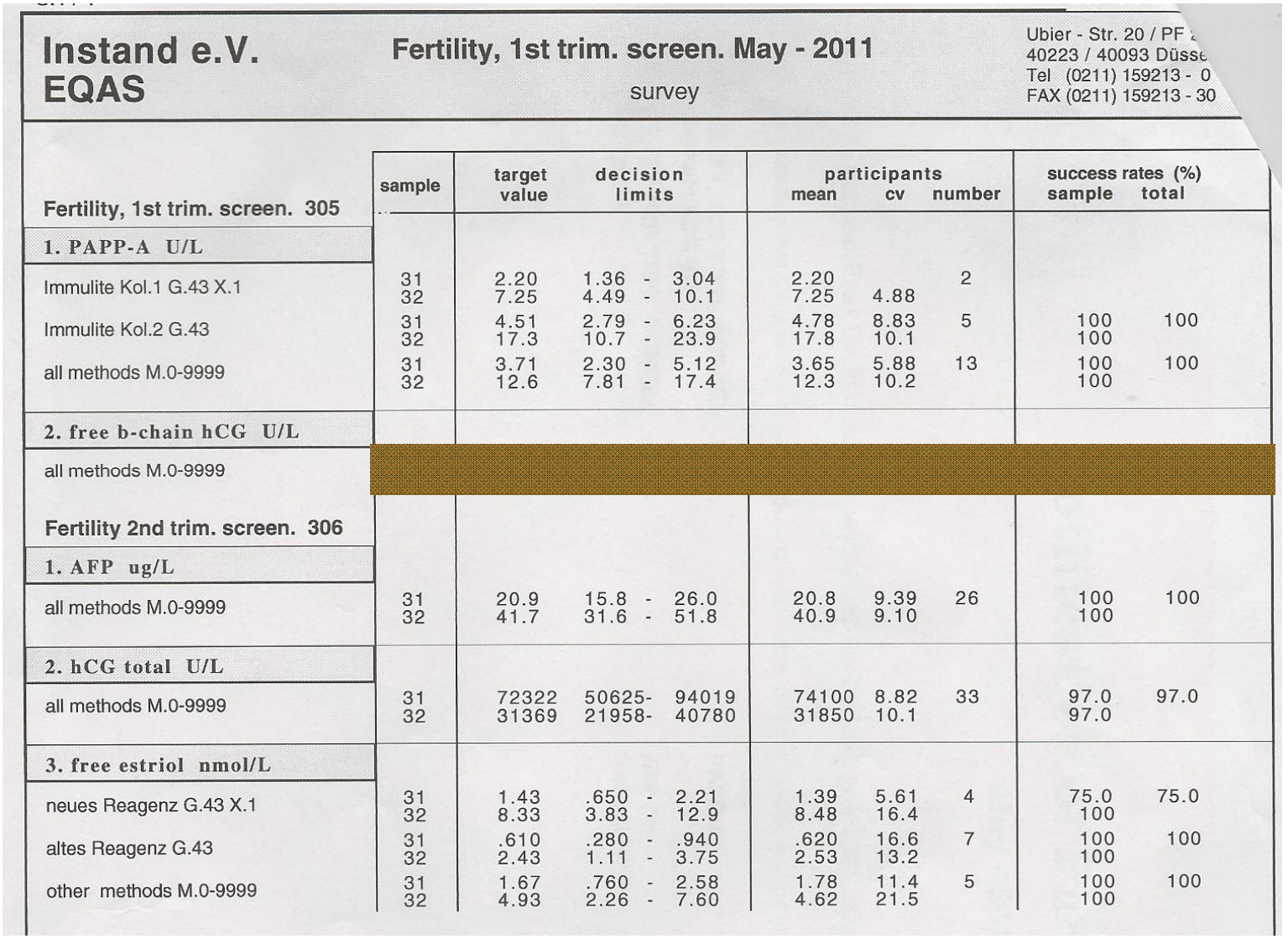
The National Academy of Clinical Biochemistry

Presents

LABORATORY MEDICINE PRACTICE GUIDELINES

MATERNAL-FETAL RISK ASSESSMENT AND REFERENCE VALUES IN PREGNANCY

Dış Kalite Değerlendirme



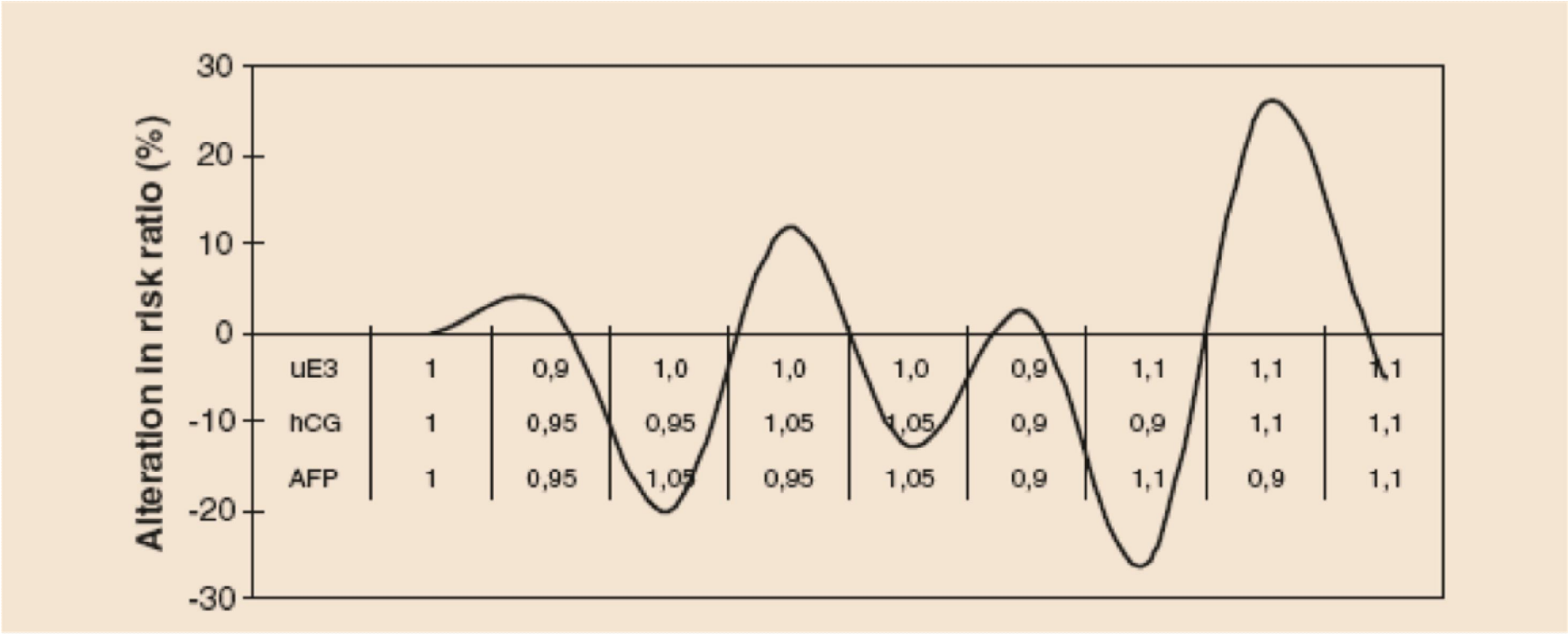
Instand e.V.
EQAS

Fertility, 1st trim. screen. May - 2011
survey

Ubier - Str. 20 / PF
40223 / 40093 Düsse
Tel (0211) 159213 - 0
FAX (0211) 159213 - 30

Fertility, 1st trim. screen. 305	sample	target value	decision limits	participants mean	cv	number	success rates (%) sample	total
1. PAPP-A U/L								
Immulite Kol.1 G.43 X.1	31	2.20	1.36 - 3.04	2.20		2		
	32	7.25	4.49 - 10.1	7.25	4.88			
Immulite Kol.2 G.43	31	4.51	2.79 - 6.23	4.78	8.83	5	100	100
	32	17.3	10.7 - 23.9	17.8	10.1		100	
all methods M.0-9999	31	3.71	2.30 - 5.12	3.65	5.88	13	100	100
	32	12.6	7.81 - 17.4	12.3	10.2		100	
2. free b-chain hCG U/L								
all methods M.0-9999								
Fertility 2nd trim. screen. 306								
1. AFP ug/L								
all methods M.0-9999	31	20.9	15.8 - 26.0	20.8	9.39	26	100	100
	32	41.7	31.6 - 51.8	40.9	9.10		100	
2. hCG total U/L								
all methods M.0-9999	31	72322	50625- 94019	74100	8.82	33	97.0	97.0
	32	31369	21958- 40780	31850	10.1		97.0	
3. free estriol nmol/L								
neues Reagenz G.43 X.1	31	1.43	.650 - 2.21	1.39	5.61	4	75.0	75.0
	32	8.33	3.83 - 12.9	8.48	16.4		100	
altes Reagenz G.43	31	.610	.280 - .940	.620	16.6	7	100	100
	32	2.43	1.11 - 3.75	2.53	13.2		100	
other methods M.0-9999	31	1.67	.760 - 2.58	1.78	11.4	5	100	100
	32	4.93	2.26 - 7.60	4.62	21.5		100	

Üçlü testin tekrarlanabilirliği



Serdar MA, (International Journal of Gynecology and Obstetrics (2006) 93, 28—32)

Gülhane Askeri Tıp Akademisi

- **2008 yılı içerisinde**

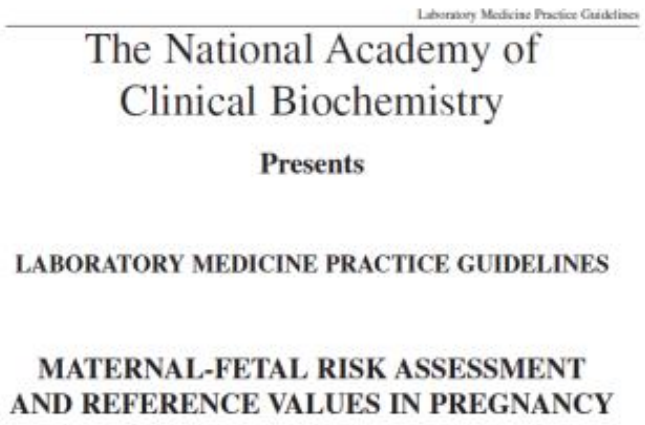
	Test sayısı	Pozitif test	
– 2.Trimester test	3192	228	% 7.14
– 1.Trimester test	540	30	% 5,55

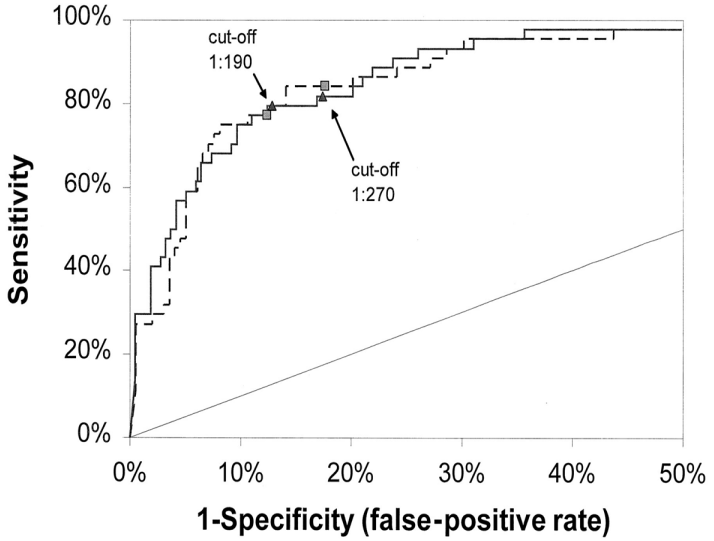
- 352 amniosentez 9 Down Sendromu
  - **252 Test pozitifliği**
  - **88 Maternal yaş nedeni**
  - **12 Diğer**
- 7 (%78) vaka 35 yaş üzerinde
- 352 amniyosentez komplikasyon görülmedi (ACOG 1/1600)
- 3 Down sendrom doğumu gerçekleşmiş
  - İki hastada da 2. trimester tarama negatif saptanmıştır

Cut off ?

Screening for Down syndrome is based on a risk estimate (*40*). The woman's age provides the *a priori* risk, which is adjusted based on the likelihood ratio of the analyte values in Down syndrome pregnancies compared to

one-third of the initial screen positives have overestimated gestational ages, giving falsely positive results. The detection rate of the screening program exceeds 60%. Since the population parameters in affected twin pregnancies are unknown, screening in twin pregnancies is performed by adjusting the analyte MOMs to the corresponding levels in a singleton pregnancy, and applying the risk algorithm.





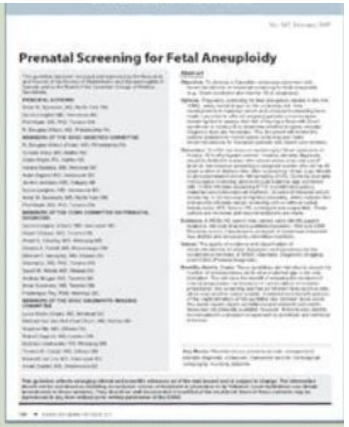
Clinical Chemistry. 2003;49:69-76

Minimum standartlar

SOGC 2007

Available Screening Options that Meet Minimum Standard
(75% DR with a 5% FPR)

- First Trimester Screen
- Second Trimester Quad Screen
- Two Step Screens:
- Contingent
- Integrated
- Serum Integrated
- Sequential


Prenatal Screening for Fetal Aneuploidy

3. “The screening strategy chosen will depend on availability of CVS and of personnel trained in NT measurement …

ACOG Practice Bulletin, No. 77, January 2007

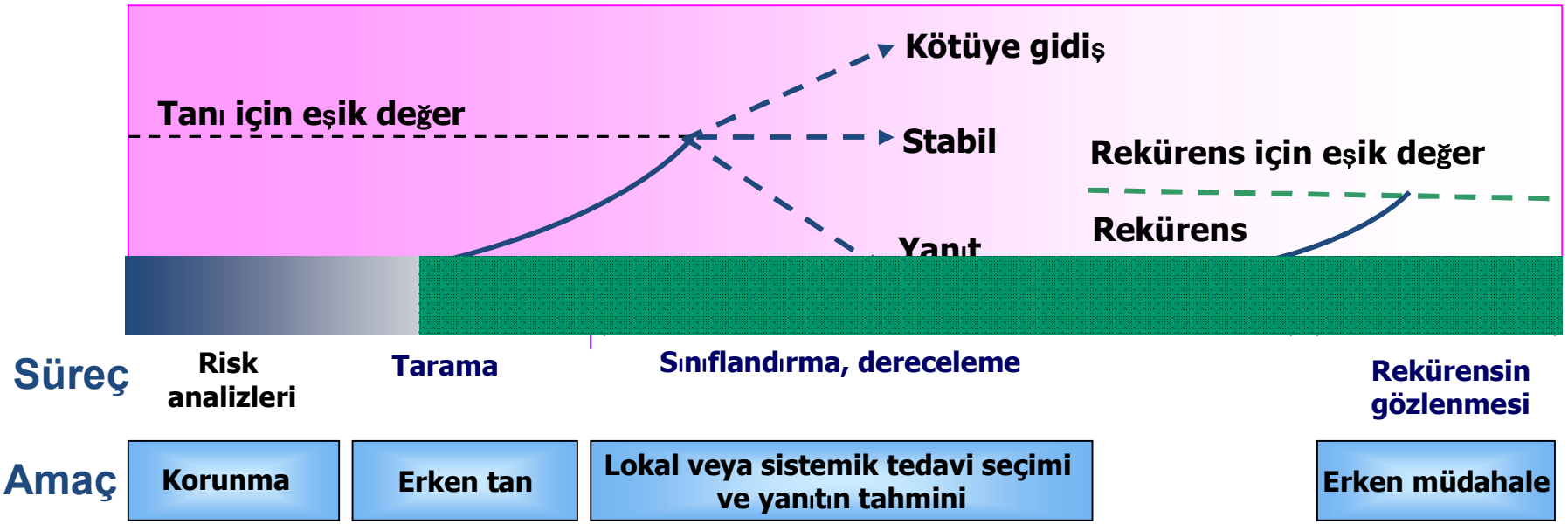
Risk kabul edilebilir mi?

Risk yönetiminde karar alma aşaması

- Kaçınılabilir mi?
  - Riski oluşturan faktörlerden uzak durma
- Azaltılabilir mi?
  - Riskin etkilerini azaltma
- Aktarılabilir mi?
  - Yönlendirme *(sigorta)*
- Kabul edilebilir mi?
  - Risk ile yaşamaya devam

Sonuçlar ve Yorumlar

- **Bugün için tıbbi risk belirleme tedavi takibinde önem kazanmıştır (kalp hastalığı, kırık riskleri vs gibi)**
- **Topluma uygulanmasında farklı görüşler vardır.**
- **Bireysel bilgi ve algı düzeyleri önemlidir**
- **Risk analizinde kullanılan laboratuvar testleri ile ilgili standardizasyon çalışmaları eksiktir. Ve laboratuvar grupları bu çalışmaların içerisinde yer alamamış veya geç kalmışlardır.**



Kalp hastalıkları
Kanserler
- **meme**
- **pankreas**
- **kolon**
- **.....**

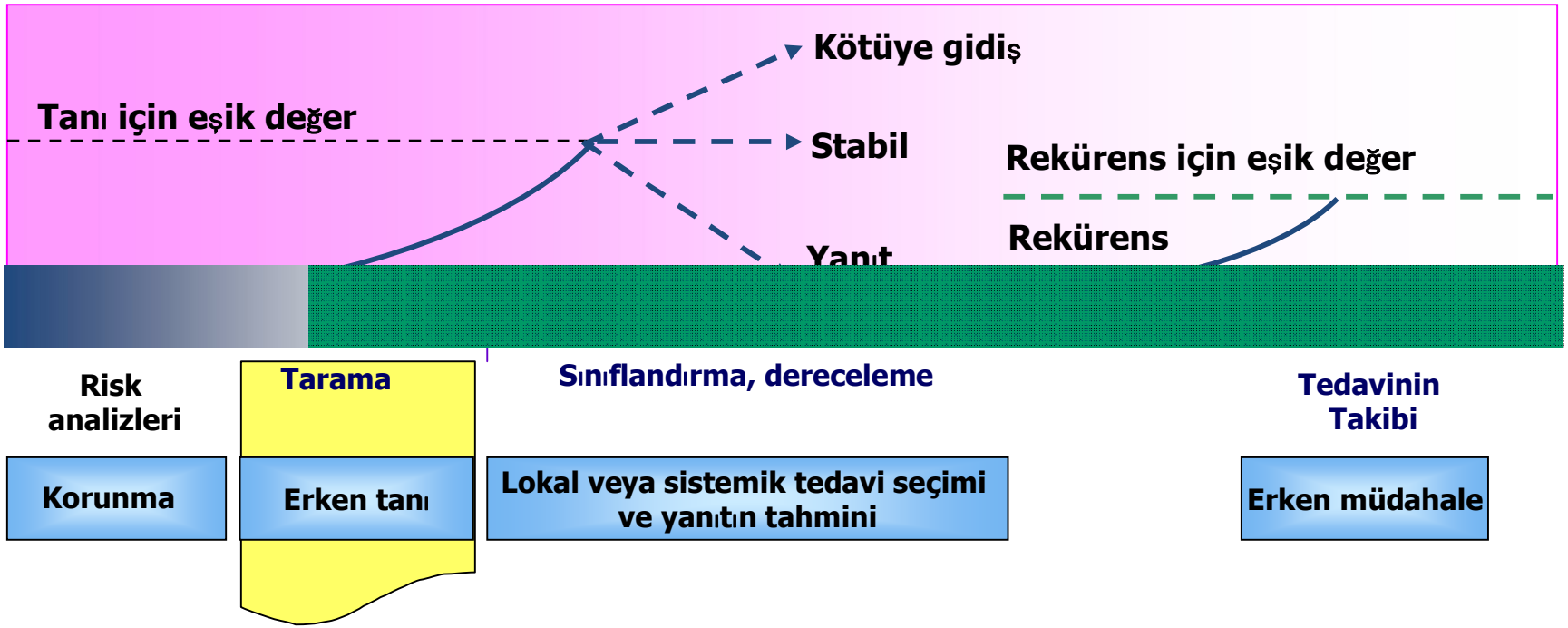
Osteoporoz
.....
.....
.....
.....
Uzun ve sağlıklı yaşamak için

}

Sigara tüketiminin azaltılması
Alkol kısıtlanması
Düşük kalorili ve yeterli mineral, vitamin desteği olan beslenme
Düzenli egzersiz
Gerekli aşıların yapılması
Tek eşlilik ve korunma
Stres yönetimi

Kime fayda sağlayacak ?

- SİGORTA ŞİRKETLERİNE
- İLAÇ ve TEST FİRMALARINA
- SAĞLIK ÇALIŞANLARINA (DOKTORLARA, HASTANELERE)
- HASTALARA

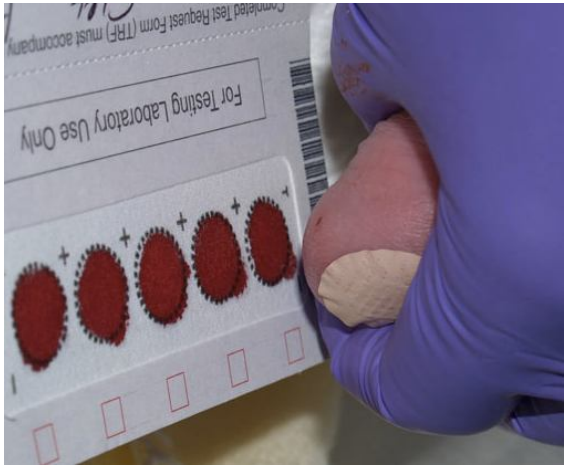


Örnek: Meme Kanseri

Klinik metod	Aile Hikayesi	Mamografi ve muayene	Fizik muayene, görüntüleme, biopsi, lenf nodu durumu ve patolojik inceleme	Fizik mauyene Görüntüleme
Belirteç	BRCA1 BRCA2	-	ER,PR,HER2/NEU, moleküler inceleme, PET	Ca 15-3

Amaç

- **<u>Hastalıkların erken</u> dönemde tanısının konması**
- **Hastalıkların önlenmesi veya ertelenmesi.**



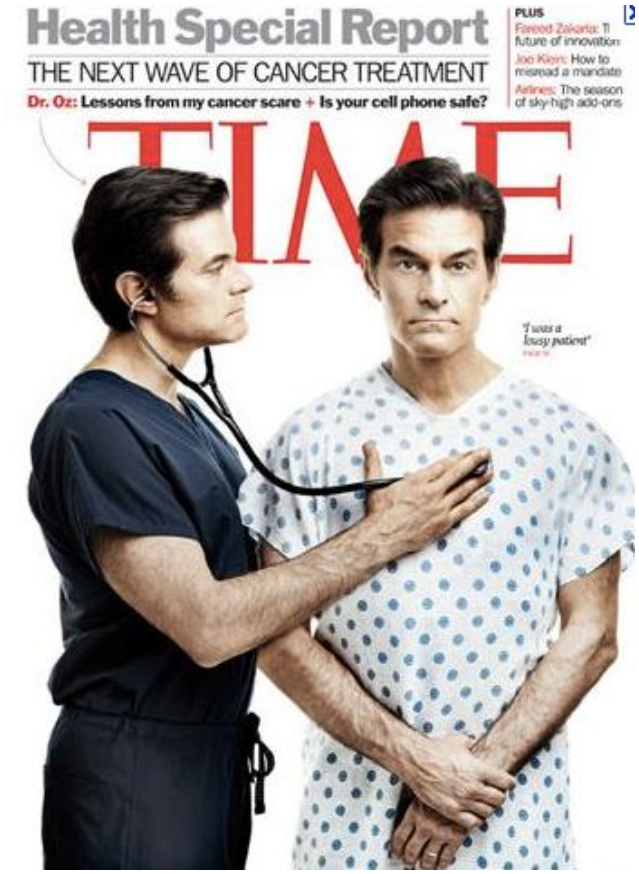
Tarama için

- **Uygun bir testiniz olacak ve kabul edilebilir PÖD (PPV) ve NÖD (NPV) değeri olmalı**
- **Önemli veya toplumsal sorun olan ve sık görülen durumlar olmalı**
- **Hastalık saptandığında etkin ve uygulanabilir tedavisi olmalı**
- **Ve bu tedavi, tanı erken konduğu için daha iyi sonuç vermeli**
- **Maliyet etkin olmalı**
- **Hedef popülasyon için kabul edilebilir olmalı**
- **Devamlı ve aralıksız uygulanabilmeli**
- **Hastalara güven vermeli ve onanmalı**

Shahram Shahangian,
Laboratory-Based Health Screening: Perception of Effectiveness, Biases, Utility, and Informed/Shared Decision Making
LABMEDICINE, Volume 37 Number 4, April 2006

Taramayı etkin kılan faktörler

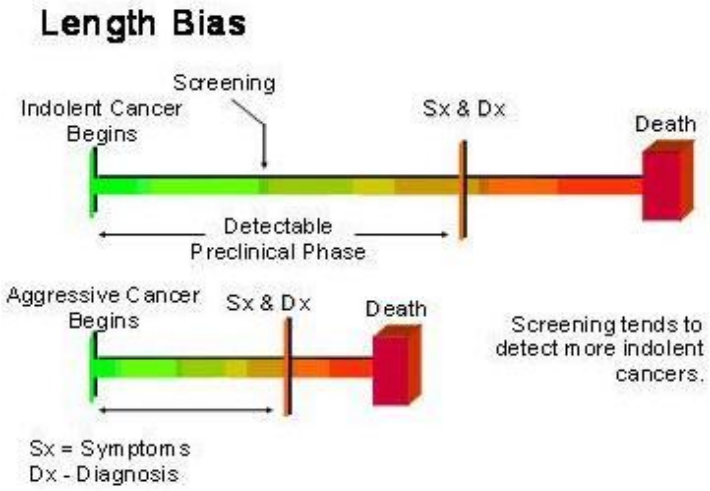
- **Klinisyenlerin önerisi önemli**
- **Tarama aralıkları - zamanı**
- **Taramanın uygun sunulması ve anlaşılır olması**
- **Karar ve uygulama süreci hakkındaki bilgilendirmeler**

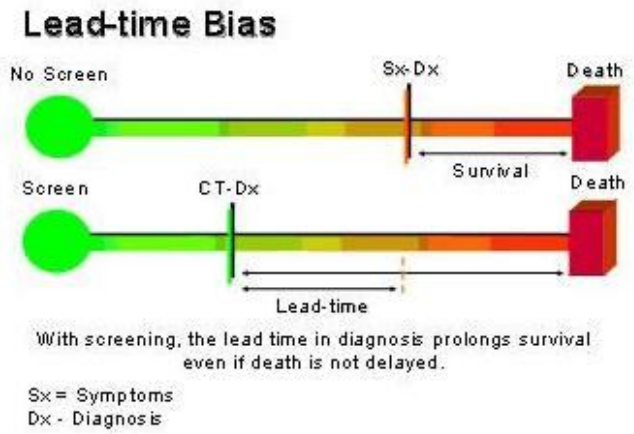


Shahram Shahangian,
Laboratory-Based Health Screening: Perception of Effectiveness, Biases, Utility, and Informed/Shared Decision Making
LABMEDICINE, Volume 37 Number 4, April 2006

Taramayı etkinliğini azaltan durumlar

- *Yavaş ilerleyen hastalıklar veya çok hızlı ilerleyen durumlar (Length bias)*
- *Erken tanı konması mümkün olmalı (Lead-time bias).*
- *Yanlış pozitif test sonuçları*
- *Psikolojik stres, korku, anksiyete*





Shahram Shahangian,
Laboratory-Based Health Screening: Perception of Effectiveness, Biases, Utility, and Informed/Shared Decision Making
LABMEDICINE, Volume 37 Number 4, April 2006

http://www.uspreventiveservicestaskforce.org

U.S. Preventive Services Task Force

USPSTF Home ■ Resource Links ✉ E-mail Updates

You Are Here: U.S. Preventive Services Task Force > Topic Index > Screening for Prostate Cancer

Screening for Prostate Cancer

Release Date: August 2008

This topic page summarizes the U.S. Preventive Services Task Force (USPSTF) recommendations on screening for prostate cancer.

Summary of Recommendations / Supporting Documents / Published Comments and Response

Summary of Recommendations

- The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits a
  Grade: I Statement.
- The USPSTF recommends against screening for prostate cancer in men age 75 years or
  Grade: D Recommendation.

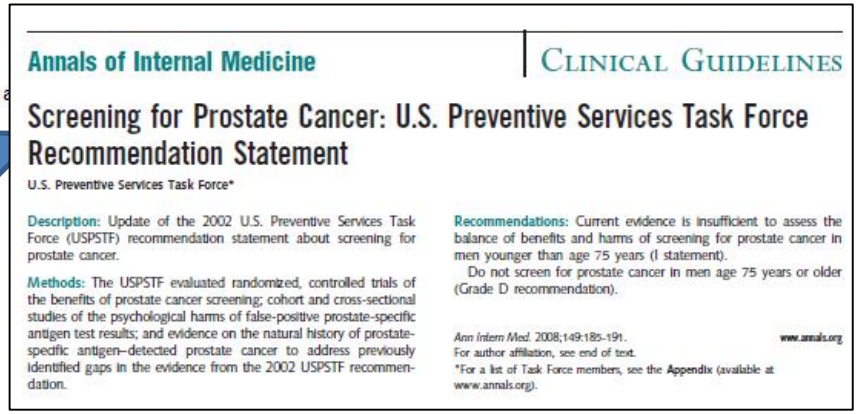
Top of Page

Supporting Documents

Screening for Prostate Cancer, August 2008

- Recommendation Statement (PDF File, 210 KB
- Supporting Article (PDF File, 195 KB; PDF Help)
- Evidence Synthesis (PDF File, 420 KB; PDF Help)
- Clinical Summary (PDF File, 115 KB; PDF Help)
- Video: How to Talk with Your Patients When Evidence Is Insufficient (3:40 minutes, Windows Media®)

Colorectal Cancer: Screening (2008)
Gynecologic Cancers: Counseling (Inactive)
Lung Cancer: Screening (2004)



Annals of Internal Medicine | CLINICAL GUIDELINES

Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

U.S. Preventive Services Task Force*

Description: Update of the 2002 U.S. Preventive Services Task Force (USPSTF) recommendation statement about screening for prostate cancer.

Methods: The USPSTF evaluated randomized, controlled trials of the benefits of prostate cancer screening; cohort and cross-sectional studies of the psychological harms of false-positive prostate-specific antigen test results; and evidence on the natural history of prostate-specific antigen–detected prostate cancer to address previously identified gaps in the evidence from the 2002 USPSTF recommendation.

Recommendations: Current evidence is insufficient to assess the balance of benefits and harms of screening for prostate cancer in men younger than age 75 years (I statement).

Do not screen for prostate cancer in men age 75 years or older (Grade D recommendation).

Ann Intern Med. 2008;149:185-191. www.annals.org
For author affiliation, see end of text.
*For a list of Task Force members, see the **Appendix** (available at www.annals.org).

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Listeriosis Outbreak: Labs Pinpoint Source of Illness

An outbreak of cantaloupe-borne listeriosis that began in late August and expanded to 28 states is the deadliest foodborne outbreak in the United States in over 25 years. The Centers for Disease Control and public health laboratories have coordinated throughout the outbreak to identify the source and limit the number of cases. Read the full article to learn more.

Topics in the News

New Study Finds No XMRV Link to Chronic Fatigue Syndrome, but Debate Continues

November 4, 2011

A recent study has concluded that current tests do not reproducibly detect Murine leukemia viruses (MLV), including xenotropic-MLV-related virus (XMRV/MLV), in blood samples from people with chronic fatigue syndrome (CFS), so blood donor screening is unwarranted. Debate, however, continues and more studies are in the works to further examine the association, if any, between XMRV and CFS.

Task Force and Other Health Organizations Revise Cervical Cancer Screening Guidelines

November 2, 2011

The U.S. Preventive Services Task Force (USPSTF) has released a draft recommendation statement that contains changes to its previous guidelines for cervical cancer screening. Three other health organizations have released their proposed joint recommendations as well. Both sets of guidelines recommend

Use the search box and menus below to quickly navigate Lab Tests Online

SEARCH

Tests

- List of all tests and synonyms
- Test not listed?
- 5-HIAA
- 17-Hydroxyprogesterone
- A/G Ratio
- A1c
- ACE

Conditions/Diseases

- List of all conditions/diseases
- Acidosis/Alkalosis
- ACS
- Addison's Disease
- Adrenal Insufficiency
- Alcoholism
- Allergies

Screening

- List of screening recommendations
- Newborns
- Infants
- Children
- Teens
- Young Adults
- Adults

KANITIN NİTELİĞİ (U.S. Preventive Services Task Force)		
Kod	**Randomize yöntemli çalışma**	**Kanıtların tanımı**
I	Evet	**Randomize kontrollü çalışma**
II-1	Evet	Randomize olmayan iyi tasarlanmış kontrollü çalışma
II-2	Hayır	İyi tasarlanmış kohort, vaka kontrol çalışmaları
II-3	Hayır	Bir çok seride kontrolsüz çalışmalarda dramatik sonuçlar
III	Hayır	Uzman görüşü, tanımlayıcı çalışma ve vaka raporları

ÖNERİNİN GÜCÜ		
A	**Mutlaka uygulanmalı**	**Yüksek oranda etkili**
B	**Uygulanmalı**	**Orata düzeyde etkin.**
C	**Zayıf**	**Net etkisi çok zayıf**
D	**Uygulanmamalı**	**Net faydası yok ve ya zararlı**
I	**Veri yetersiz**	**Etkin değil ve/veya etkinliği ile ilgili bilgiler yetersiz**

UPSTF'nin mutlaka uygulanmalı (A) grup tarama testleri

Hastalık / Test	Hedef popülasyon -YIL
Serviks kanseri **(Pap smear test)**	Cinsel aktif bayan (2003) >65 yaş üstü (D)(2003) HPV (I) (2003)
Rektum kolon kanseri **(Gaitada gizli kan)**	50 yaş üstü kadın ve erkek (2008) (her yıl) **(RR 0.85, CI: 0.78,0.92)** (Magstream/HemeSelect; FlexSure OBT/Hemoccult ICT; OC-Hemodia; Monohaem) Sen=%61-91, Spe= %91 **Hemoccult II için Sen= %25-38, Spe= %98**
Lipit metabolizması bozuklukları **(Total / HDL kolesterol)**	>35 yaş Erkek ve yüksek riskli, > 45 yaş kadınlar (2008) (2-5 yıl) (A) 20-35 (B) risk olanlara için 20-35 (C) risk olamayanlar için
Asemptomatik Bakteriüri	12-16 haftalık gebeler (2008)
Klamidya enfeksiyonu	> 24 yaş cinsel aktif ve gebe olmaya bayan (2007)

Figure 3A–C. Results of Meta-anlaysis of Statin Trials

Figure 3A: Effect of Treatment on Total CHD Events

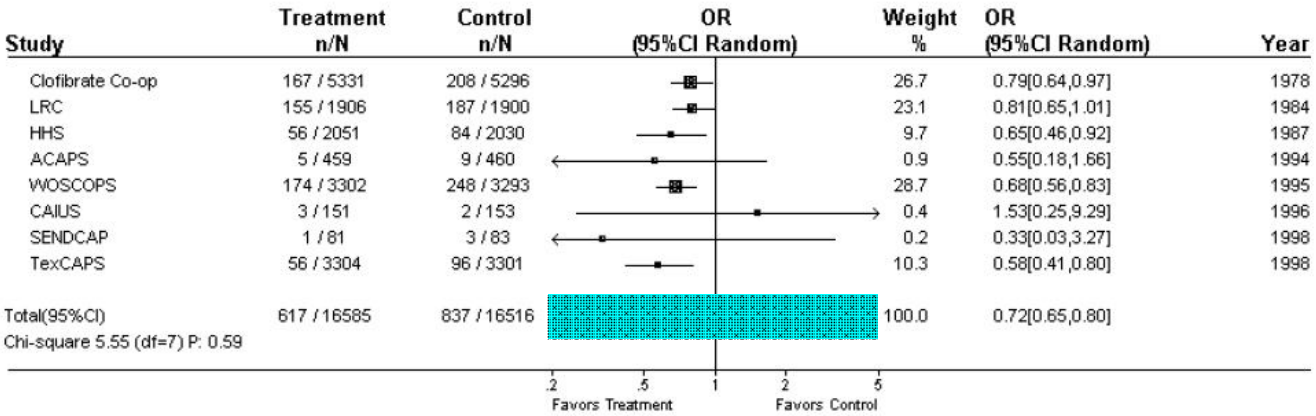


Figure 3B: Effect of Treatment on Total CHD Mortality

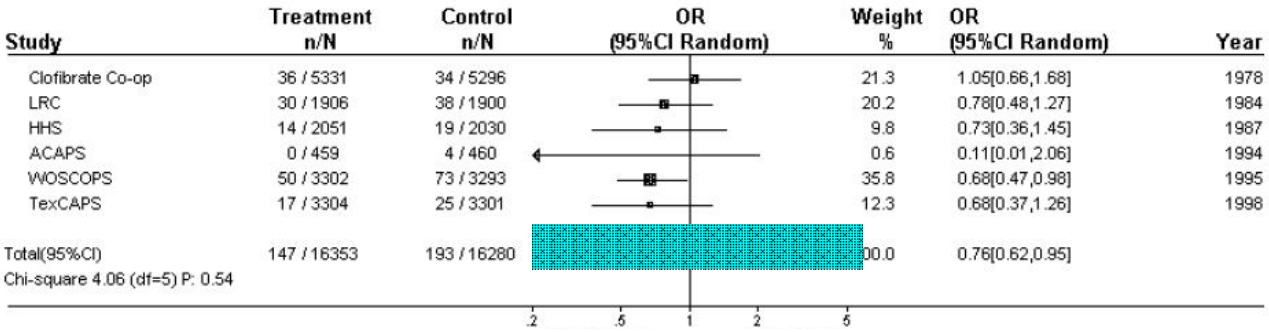
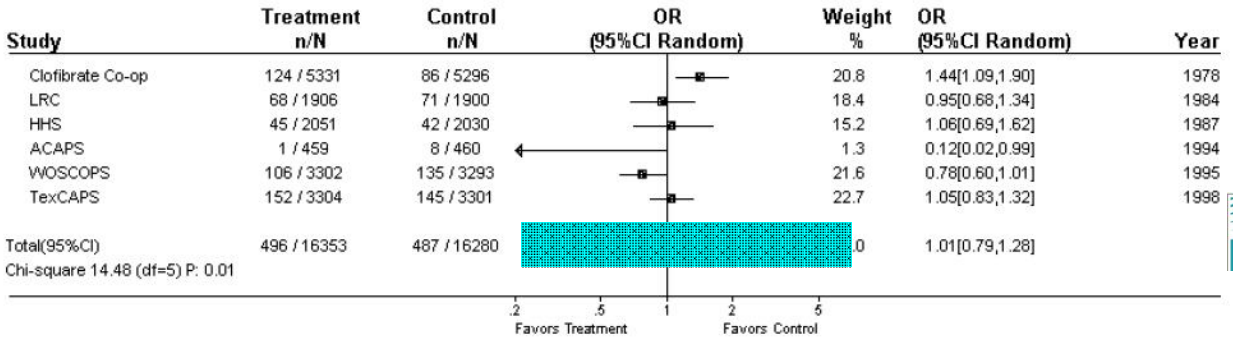


Figure 3C: Effect of Treatment on Total Mortality



UPSTF'nin mutlaka uygulanmalı (A) grup tarama testleri (devam)

Hastalık / Test	Hedef popülasyon -YIL
Hepatit B enfeksiyonu	Hamile kadınlar ilk müracatda (2006)
HIV enfeksiyonu	Erişkin bireyler ve gebeler (2006)
Sifilis enfeksiyonu	Yüksek riskli kadınlar ve gebeler (2004)
D (Rh) uyumsuzluk testi	Hamile kadınlar ilk müracaatda (2004)
Konjenital hipotroidi	Yeni doğanlar (2008)
Fenilketonüri	Yeni doğanlar (2008)
Hemoglobinopatiler /Orak hücreli anemi	Yeni doğanlar (2007)*

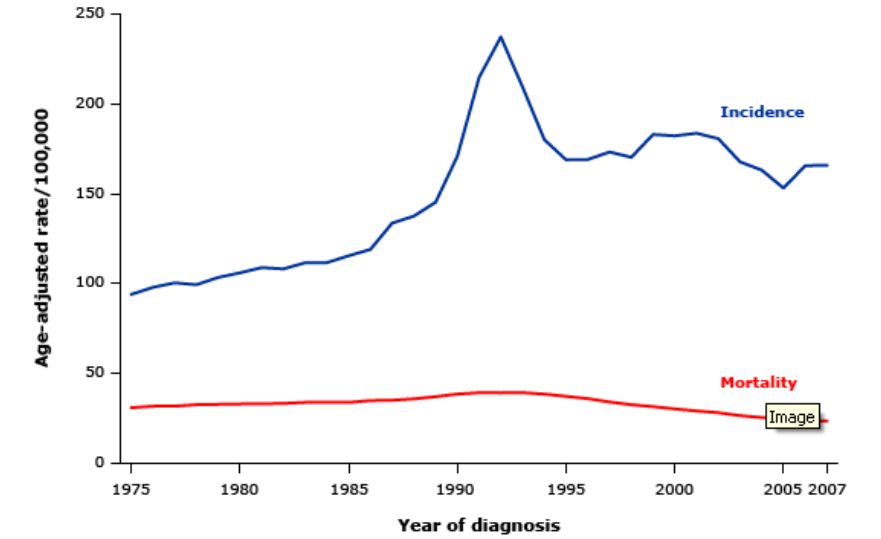
Penisilin prilaksisi orak hücre anemili çocuklarda pnömokok enfeksiyonunu azaltır odds ratio = 0.37, 95% CI 0.16 – 0.86)
Afrikan-Amerikalılarda 1/375. Türkiye genelinde sıklık % 0.37-0.6 arasında

UPSTF'nin diğer önerileri

Hastalık / Test	Hedef popülasyon -YIL
Mesane kanseri **İdrar analizi, NMP22**	I (2011)
Meme kanseri **(BRCA 1/BRCA 2)**	D (2004); B (2004)- Yüksek riskli kadınlar
Kolon ve Rektum kanseri **(Gaitada gizli kan)**	C (2008) 76-85 yaş (Rutin önerilmiyor) D (2008) > 85 yaş yaş üstü ((Önerilmiyor)
Kolon ve Rektum kanseri **(Fekal DNA)**	I (2003) (Fekal DNA= veri yetersiz)
Akciğer tümörü **(Balgam incelemesi)**	I (2004)
Pankreas	D (2004)
Prostat	I (2008); 50-74 yaş arası D (2008)- > 75 yaş üzeri

Prostat kanseri ve PSA

Prostate cancer: Changes over time average annual age-adjusted incidence and mortality rates in the United States, 1975-2007



)ecision aids for prostate cancer screening

Resource	Website	Available from
"Should I be tested for prostate cancer?"	www.cancer.org/prostatemd	American Cancer Society
"Prostate cancer screening: A decision guide"	www.cdc.gov/cancer/prostate/pdf/prosguide.pdf	Centers for Disease Control and Prevention
"Prostate cancer screening: A decision guide for African Americans"	www.ustoo.org/PDFs/CDC_PCa_Screen_Guide_AA.pdf	Centers for Disease Control and Prevention
"La Deteccion del Cancer de Prostata: Una guia para Hispanos en los Estados Unidos"	www.cdc.gov/cancer/prostate/pdf/prostate_cancer_spanish.pdf	Centers for Disease Control and Prevention
"Is a PSA test right for you?"	www.healthdialog.com	Foundation for Informed Medical Decision Making
"Prostate cancer screening: Should you get a PSA test?"	www.mayoclinic.com/health/prostate-cancer/HQ01273	the Mayo Clinic
"PROSDEX: A PSA decision aid"	www.prosdex.com	University of Cardiff, UK

ource: Wolf, AMD, Wender, RC, Etzioni, RB, et al. American Cancer Society Guidelines for the Early Detection of Prostate Cancer. Update 2010. CA Cancer J Clin 2010; 60:70.

Laboratory Medicine Practice Guidelines

Use of Tumor Markers in Testicular, Prostate, Colorectal, Breast, and Ovarian Cancers

Edited by Catharine M. Sturgeon and Eleftherios Diamandis

B – Moderate

III - Evidence from large prospective studies.

Table 6. NACB Recommendations for the Clinical Use of PSA Serum Markers in the Management of Prostate Cancer

Marker	Application	NACB Recommendations (2008)	LOE*	Strength of Recommendation**	Reference
	Early detection (with DRE)	Yes	III	B	(136, 183, 521, 522)
	Early Detection: Age-specific reference ranges	No	Expert opinion	B	(146)
	Staging/prognosis	Yes	III	B	(193, 201, 205, 206, 523-526)
	Surveillance/monitoring	Yes	III	B	(527, 528)
% fPSA	Differentiation of prostate cancer from benign	Yes	III	B	(160, 529)

Table 7. Recommendations by Different Expert Groups for Use of PSA, Complexed PSA, and Percent Free: Total PSA As Tumor Markers for Prostate Cancer

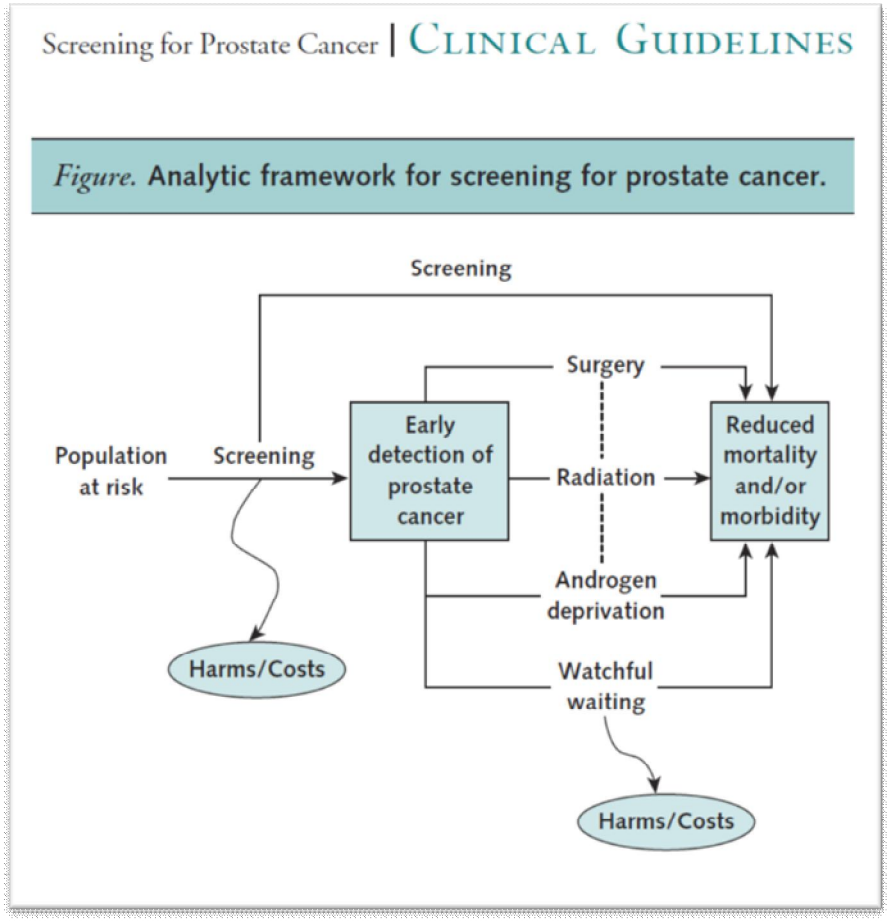
Marker	Application	ACS (138)	ACP (530)	ASTRO (527)	AUA (528)	EAU (531)	EGTM (148)	ESMO (532)	NACB/ EGTM 2002 (15)	NCCN (533)	USPSTF (534)	NICE 2008 (121, 139)	NACB 2008*
	(with DRE)			published							available for men <75 years of age. Screening for men 75 years or older not recommended (535)	available	present
	Early detection: Age-specific reference ranges	None published	None published	None published	None published	None published	**No**	None published	**Yes (NACB)**	None published	None published	None published	**No**
	Early detection: PSA velocity	None published	None published	None published	None published	None published	None published	None published	None published	**Yes**	None published	**Yes**	**Yes**

Genel olarak PSA ile ilgili öneriler

- **Eğer serum PSA taramaya karar verdiyseniz her 2 veya 4 yılda**
  - **(Grade 2 B)**
- **Taramada rektal muayene**
  - **(Grade 2 B)**
- **Anormal DRE veya PSA > 7 ng/ml üzerinde biyopsi önerilir**
  - **(Grade 2C)**
- **65 yaş üzerinde PSA 1 ng/ml altında ise tarama kesilir**
  - **(Hastalar 76 istiyor*)**

A Grade 2B: Recommendation is a weak recommendation.

A Grade 2C: Recommendation is a very weak recommendation; other alternatives may be equally reasonable.



•Optimization of PSA Screening Policies: A Comparison of the Patient and Societal Perspectives
Med Decis Making. 2011 Sep 20

AFP ve tarama

Table 2. Recommendations for Use of AFP in Liver Cancer by Different Expert Groups

Application	AASLD 2005 40	Asian Oncology Summit 136	BrSocGE 26 2003	EASL 131 2001	EGTM 137 1999	ESMO 2009 4	French SOR 132	Japanese EBCIGI 2007/2008 127, 128	NCCN 2010 135	NACB 2010		
											LOE	SOR
determination of AFP (with abdominal ultrasound) in high risk groups (i.e. patients with chronic hepatitis B or C virus or cirrhosis)	be used only if ultrasound not available)	6-month intervals)				with or without AFP)		AFP, AFP-L3, DCP)				

Laboratory Medicine Practice Guidelines

Follow-up Testing for Metabolic Diseases Identified by Expanded Newborn Screening Using Tandem Mass Spectrometry

Edited by Michael J. Bennett

NATIONAL ACADEMY of CLINICAL BIOCHEMISTRY
THE ACADEMY OF AACC

FOLLOW-UP TESTING FOR METABOLIC DISEASES IDENTIFIED BY EXPANDED NEWBORN SCREENING USING TANDEM MASS SPECTROMETRY

Table 3-1 Disease-Specific Follow-Up Testing Recommendations

Disorders of Amino Acid Catabolism and Transport	Screening Marker	Follow-Up Analyses	Follow-Up Markers	Additional Testing	Evidence	References
Phenylketonuria (includes benign hyperphenylalaninemia, and biopterin metabolic defects)	Phenylalanine Tyrosine	Plasma amino acids	Phenylalanine Tyrosine	Urine pterin metabolites Dihydropteridine reductase activity	A-I	23–26
Tyrosinemia						
Type 1	Tyrosine	Urine organic acids	Succinylacetone	No additional testing indicated	A-I	27–39
Type 2		Plasma amino acids	Tyrosine >1000 μM on presentation		A-I	
Maple Syrup Urine Disease	Isoleucine + leucine + alloisoleucine	Plasma amino acids	Isoleucine, Leucine, valine, alloisoleucine	No additional testing indicated	A-I	40–43
Citrullinemia						
Type 1 (ASA Synthase)	Citrulline	Plasma/Urine amino acids	Citrulline Argininosuccinate,	Ammonia, bilirubin, Alk Phos, GGT.	A-I	44–53
Type 2 (Citrin)	Citrulline			Genetic testing may distinguish I and II.	B-II	

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THE ACADEMY OF AACC

Yenidoğan taramaları

Dünya: 1/1500-3.000 (toplam KMH sıklığı)

Türkiye(2010)

Yenidoğan tarama sonuçları (~1.300.000 bebek/yıl)

	Hasta sayısı	Ülkemiz[1]	Dünya (genel)
Konjenital hipotroidizm	2543	1/1270	1/2000-4000[2]
Fenilketonuri	182 (479*)	1/6228	1/10.000-30.000[3]
Biotinidaz eksikliği	199	1/7116	1/60.000[4]

*Hiperfenilalaninemi (HPA) **Türkiye, PKU'nun en sık görüldüğü ülkelerden biridir.**

1.S.Özbaş. Türkiyede Yenidoğan Tarama Programı. XI.Metabolik Hastalıklar ve Beslenme Kongresi, İzmir, 14 Nisan 2011
2. Rastogi MV, LaFranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis. 2010 Jun 10;5:17.
3. http://emedicine.medscape.com/article/947781-overview
4. Wolf B. Worldwide survey of neonatal screening for biotinidase deficiency. J Inherit Metab Dis. 1991;14:923–7

Türkiye ne kullanıyor?

PISHTAZTEB DIAGNOSTICS Zaman

TSH PERFORMANSI

The TSH Standards used in this kit is calibrated against WHO 2nd I.R.P of hTSH 80/558.

7. Proficiency test:
Accuracy was studied using DGKL (GERMANY) Quality Control samples (TS1/08).

Sample No. **TS1/ 08**	DGKL Enriched Value (TSH µIU/ml, Whole blood)	NTSH Kit result (TSH µIU/ml, Whole blood)
9999751-1	**10.5** (6.30 -14.7)	10.3
9999751-2	**4.70** (2.30 -7.10)	3.4
9999751-3	**26.2** (15.7 -36.7)	29.2
9999751-4	**17.0** (10.2 -23.8)	15.8

3. Jenerasyon 81/565
2. Jenerasyon 80/558.

http://www.nibsc.ac.uk/documents/ifu/81-565.pdf

Türkiye ne kullanıyor?

ANI Labsystems

Phenylalanine test procedure

Punch 3 mm sample disks, add 80 µl eluent

Incubate 30 min at RT on a shaker

Transfer 50 µl eluate, add 50 µl incubation mixture.

Incubate
A) 1 h at 60 °C or **B)** 2 h at 37 °C

Add 200 µl copper reagent

Incubate 15 min at RT

Measure at ex. 390 nm, em. 485 nm

Reproducibility

Table 3 Procedure A

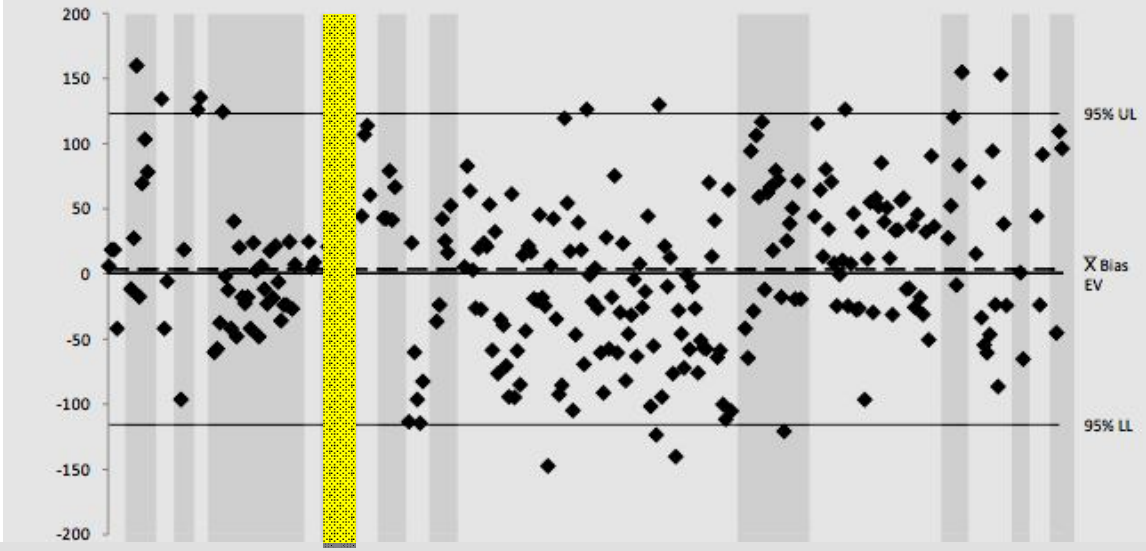
Sample no.	Mean concentration (mg/100 ml)	Standard deviation (mg/100 ml)	CV%
Within-run imprecision (10 replicates)			
1	1,5	0,2	12,1
2	5,2	0,3	5,9
3	9,3	0,6	6,3
Between-run imprecision (10 successive runs, averages of 4 replicates)			
4	1,8	0,2	11,4
5	5,2	0,5	9,4
6	10,6	0,8	7,9

1) the European Working Standard for Phenylalanine (EWS-Phe) since 1996 and the 1st ISNS Reference Preparation for Neonatal Screening for TSH, phenylalanine and 17 α-hydroxyprogesterone in blood spots since 2005

Phe

Figure 15. Bias Plot of Phenylalanine Values by Method
Quarter 1, Specimen 3
Expected Value (EV)[1] 406.02 µmol/L whole blood

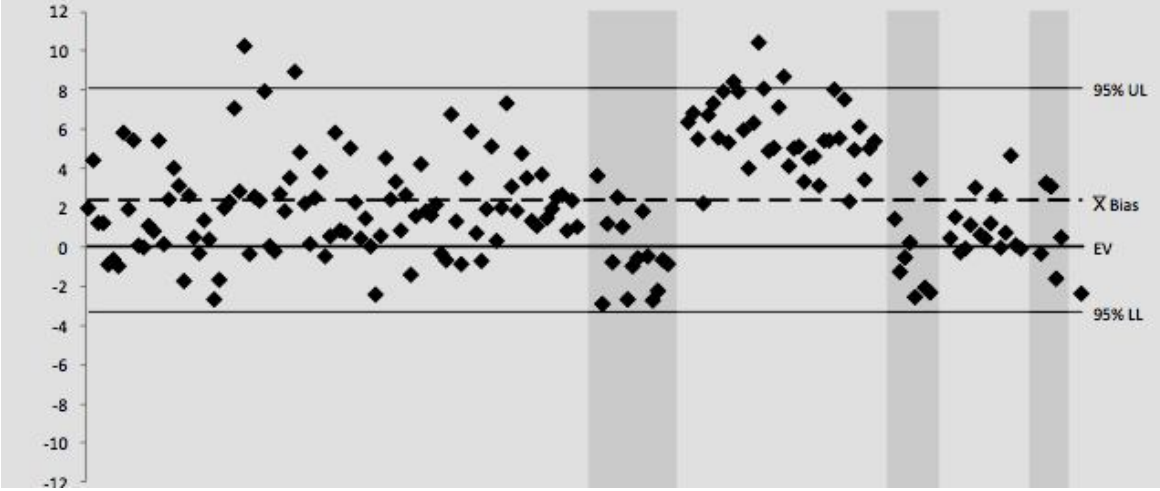
CV% 10-30



Cserbest

Figure 22. Bias Plot of Free Carnitine (C0(L)) Values by Method
Quarter 4, Specimen 3
Expected Value (EV)[1] 7.69 µmol/L whole blood

CV %20-50



EŞİK DEĞERLER

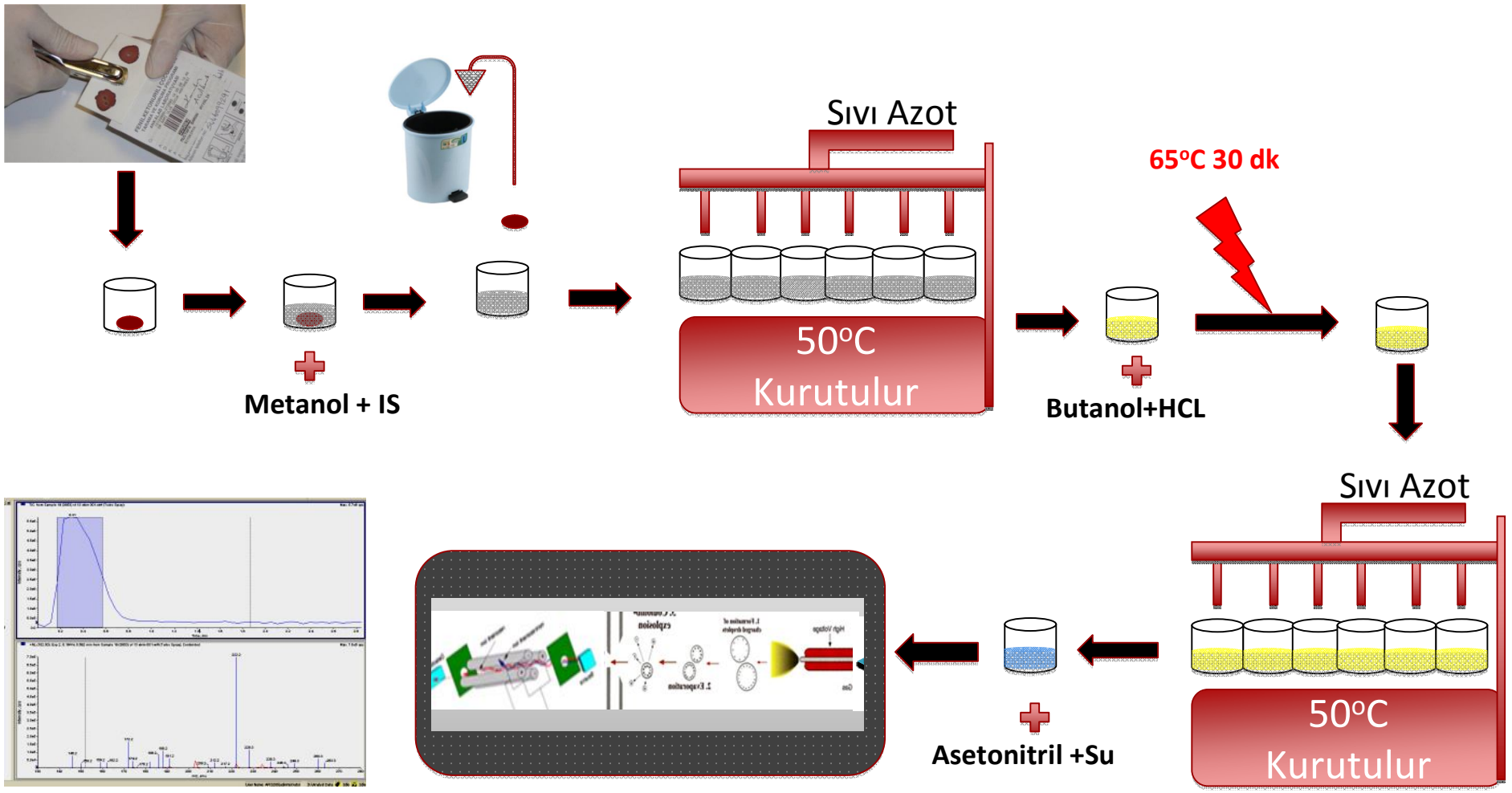
Domestic

Analyte	Min/Max
T4	3.5-8.0
TSH	19.4-61.0
17-OHP	25-105
Galactose	6.5-20.0
Phenylalanine	121-206
Tyrosine	138-414
IRT	39.6-170
GALT	0.7-4.0

Foreign

Analyte	Min/Max
T4	4.0-9.3
TSH	7.5-50.0
17-OHP	2.5-199.8
Galactose	3.0-30.0
Leucine	229-382
Tyrosine	200-500
IRT	40-150
GALT	1.2-5.0

Tandem MS ile tarama



Center for Disease Control and Prevention. Using tandem mass spectrometry for metabolic disease screening among newborns: a report of a work group. MMWR 2001; 50 (No. RR-3):1–40.

Tandem MS ile tarama
İle tanısı konabilen hastalıklar

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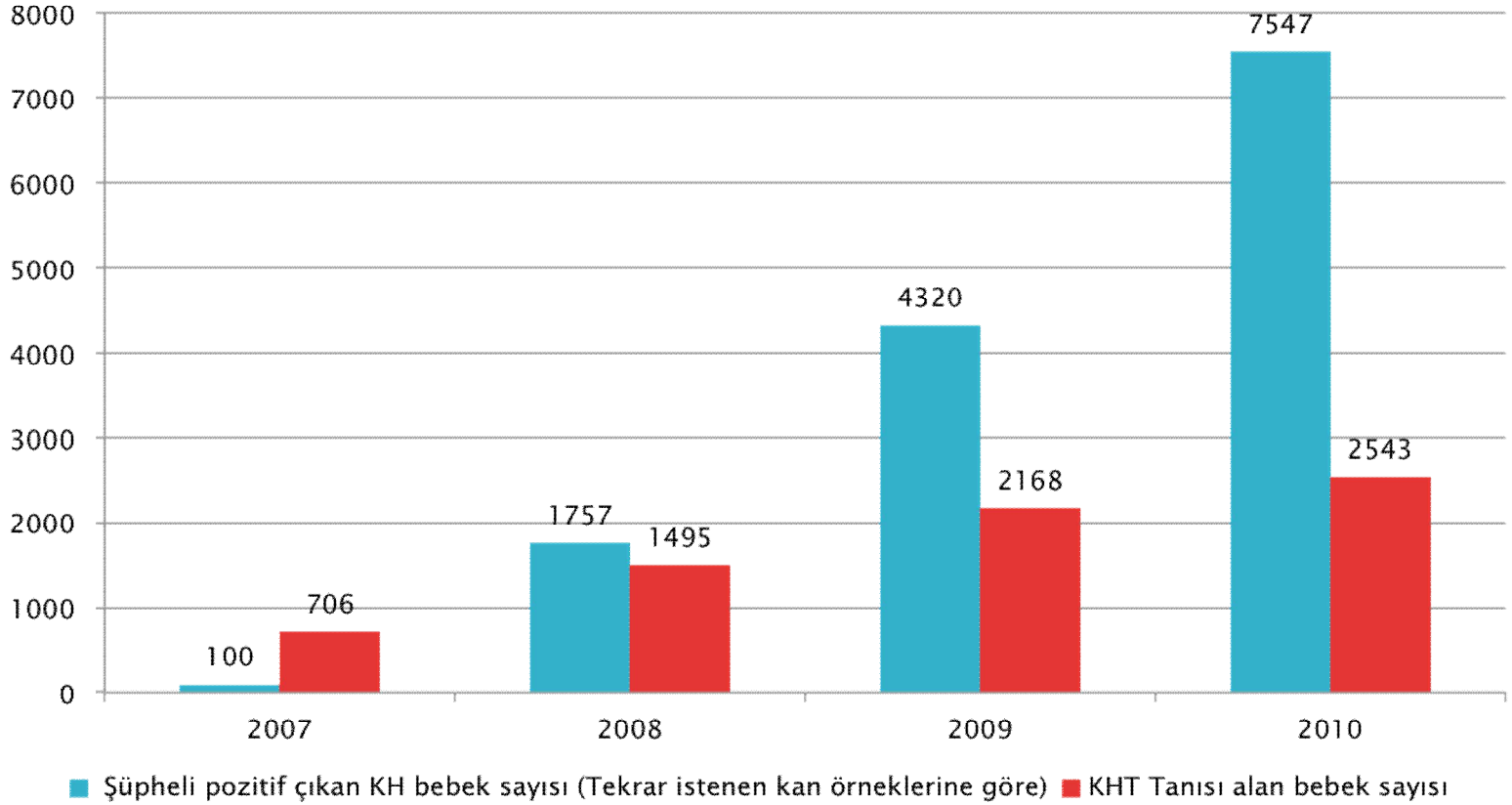
Table 1. List of Conditions, Abbreviations, and Levels of Evidence

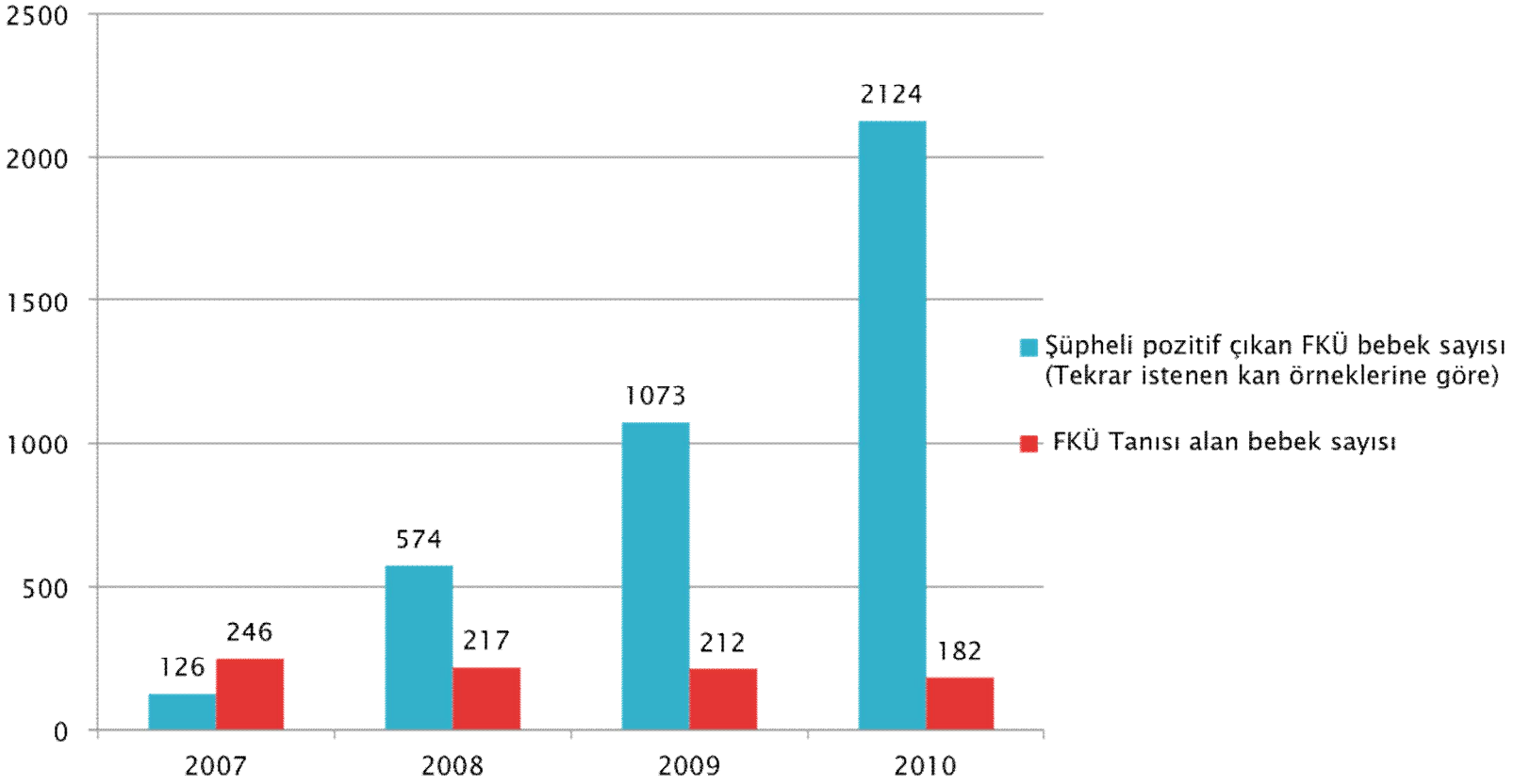
	Condition	Abbreviation	
1	Medium Chain Acyl CoA Dehydrogenase Deficiency	MCAD	A-I
2	Phenylketonuria (inc. benign hyper PHE, & BH4 defects)	PKU	A-I
3	Biotinidase Deficiency	BIOT	B-II
4	Congenital Adrenal Hyperplasia	CAH	A-I
5	Isovaleric acidemia	IVA	A-II
6	Very Long Chain AcylCoA Dehydrogenase Deficiency	VLCAD	A-II
7	Maple Syrup Urine Disease	MSUD	A-I
8	Long Chain Hydroxy AcylCoA Dehydrogenase Deficiency	LCHAD	B-II
9	Glutaric Acidemia (all forms)	GA	
	Type 1	*GA1*	A-I
	Type 2	*GA2*	B-II
10	HMGCoA Lyase Deficiency	HMG	A-II
11	Trifunctional Protein Deficiency	TFP	A-II
12	Multiple Carboxylase Deficiency	MCD	B-III
13	Methylmalonic Acidemia (all forms)	MMA	A-II
	Mutase	*MUT*	A-II
	Cbl	*CBL*	A-II
14	Homocystinuria	HCY	B-III
15	3-Methylcrotonyl CoA Carboxylase Deficiency	MCC	C-II
16	Propionic Acidemia	PA	A-II
17	Primary Carnitine Deficiency	PCD	B-II
18	Thiolase Deficiency	KT	B-II
19	Citrullinemia	CIT	B-III
20	Argininosuccinic Acidemia	ASA	B-III
21	Tyrosinemia (all forms)	TYR	
	Type 1	*TYR 1*	B-III
	Type 2	*TYR 2*	B-III
	Type 3	*TYR 3*	B-III
22	Short Chain AcylCoA Dehydrogenase Deficiency	SCAD	C-II/I*
23	Medium/Short Chain Hydroxyacyl Coa DH deficiency	SCHAD	B-III

Yıllar içinde şüpheli pozitif çıkan konjenital hipotroidi tanısı alan bebek sayısı



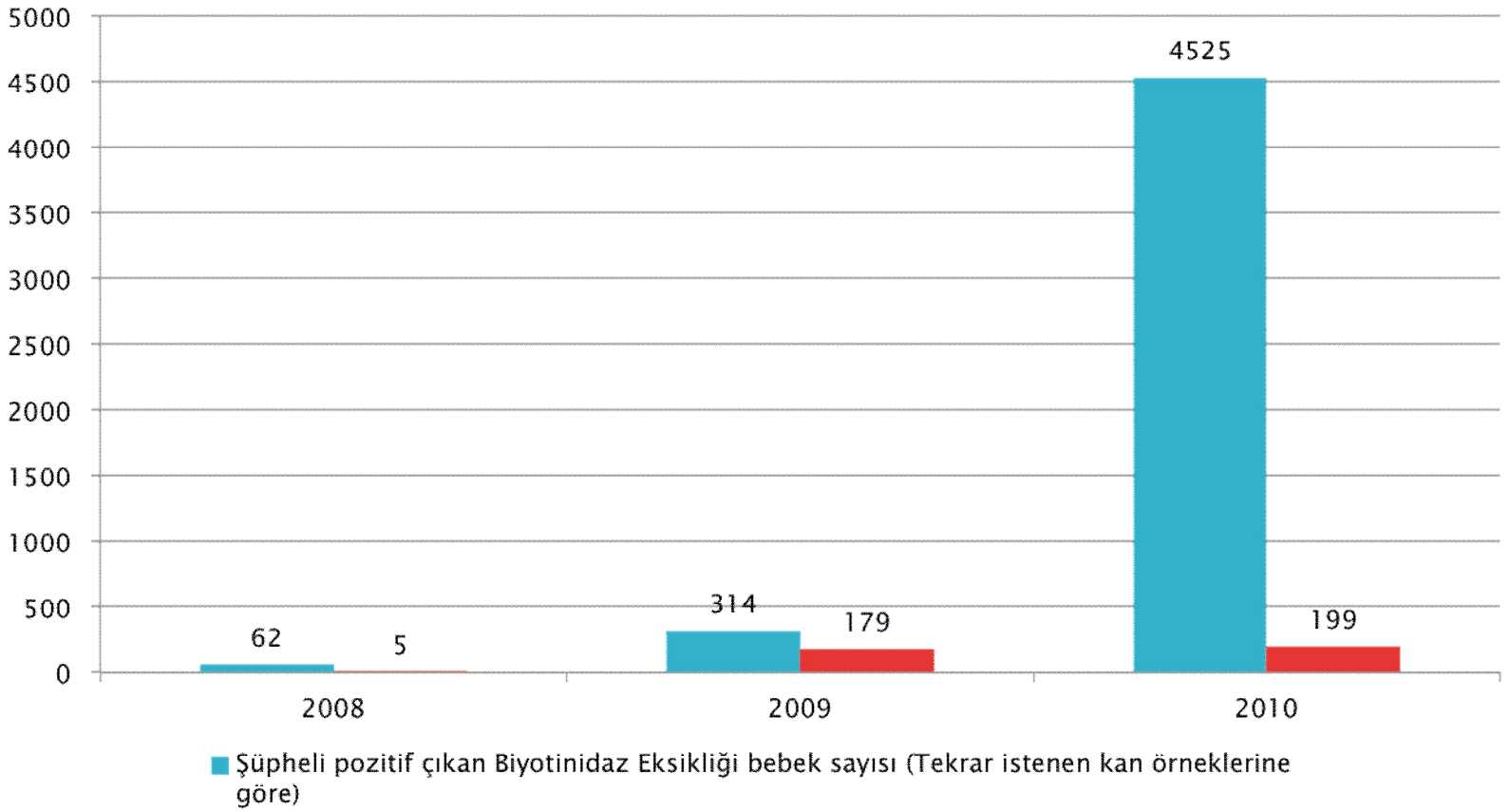
Uygunsuz kan alma oranı: % 2.15
Tekrar istenen kan örneği oranı: % 5.80

Yıllar içinde şüpheli/hasta çıkan fenilketonuri tanısı alan bebek sayısı



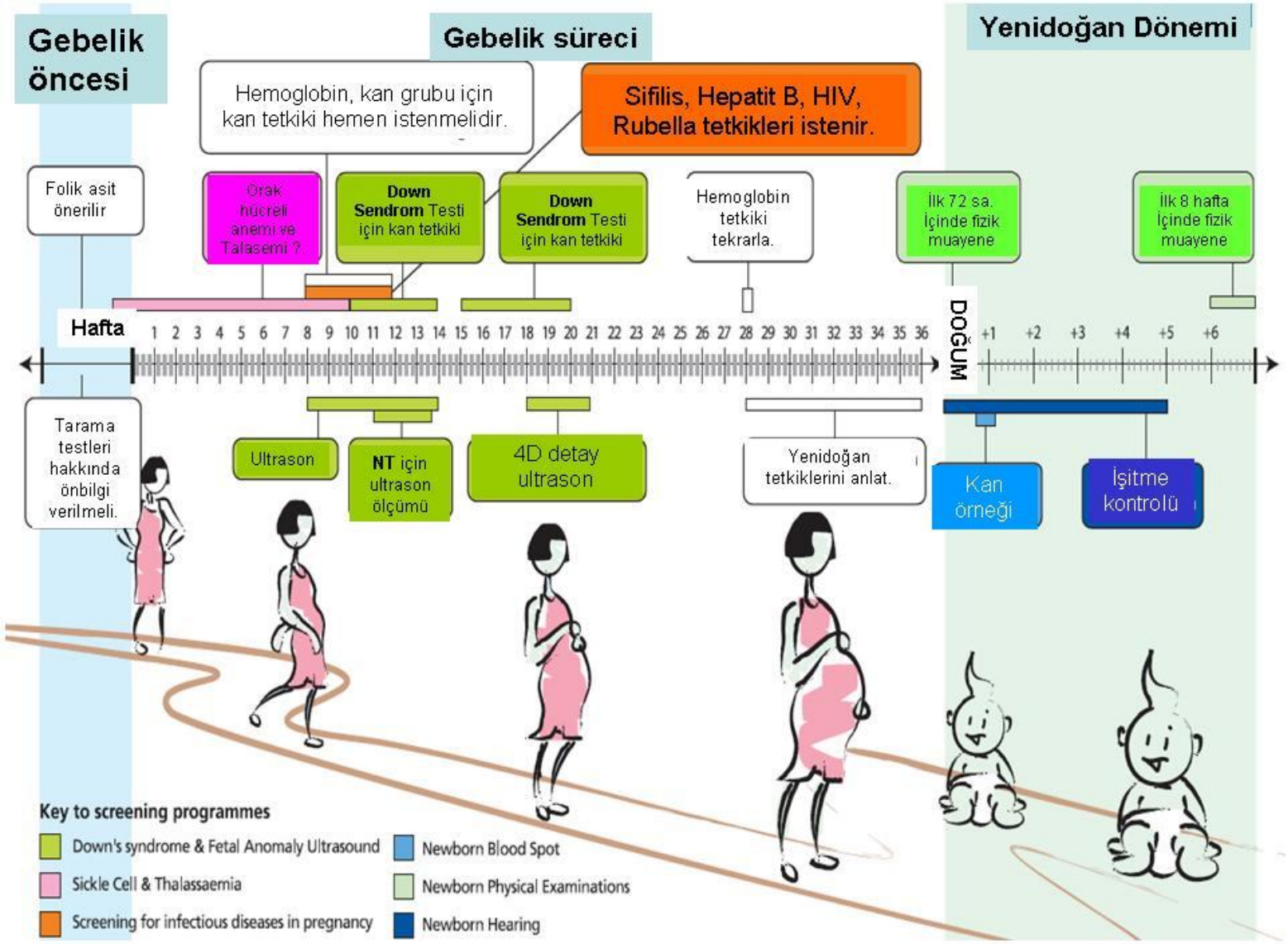
Uygunsuz kan alma oranı	: % 2.07
Tekrar istenen kan örneği oranı	: % 2.33

Şüpheli pozitif çıkan BE tanısı alan bebek sayısı



Uygunsuz kan alma oranı	: % 2.60
Tekrar istenen kan örneği oranı	: % 0.38

Gebelik süresi taramaları



Öneriler

Maternal-Fetal Risk Assessment and the Laboratory

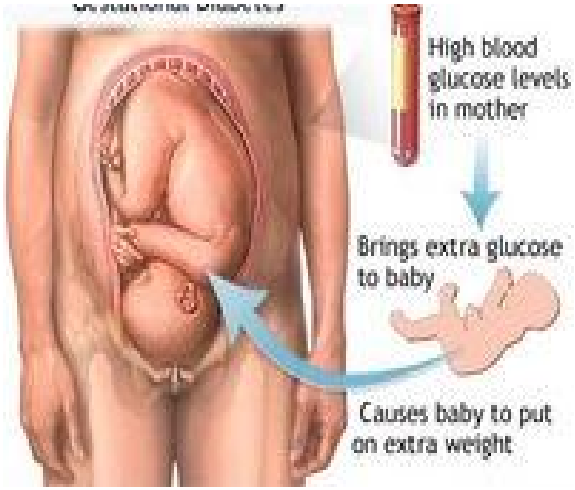
The laboratory role in risk management strategies varies with the strategy and the time of pregnancy in which it is important. Table I-2 indicates examples of such strategies.

Table I-2. Example of Laboratory-Based Gestation Specific Risk Reduction Strategies Decreasing Perinatal Risk in Diabetes

Time sensitivity	Intervention	Outcome objective
Pre-conception	Controlling blood glucose in known diabetics	Decrease risk of congenital abnormality
Second trimester 16 – 20 weeks	Maternal serum screen	Detect possible neural tube defect or other congenital anomalies
8 weeks	Glucose screen	Detect and manage abnormal glucose tolerance
Third trimester	Assess fetal lung maturity	Decrease neonatal respiratory distress syndrome
Post-natal	Monitor neonatal glucose, calcium	Prevent and manage neonatal metabolic problems

Gestasyonel Diabet

- Gestasyonel diabetes mellitus (GDM), gebelikte başlayan veya ilk tanısı gebelik sırasında konan çeşitli derecelerdeki glukoz intoleransı olarak tanımlanır.
- Gebelikte tanısı konan diyabet
  - Aşikar (overt)
  - Gestasyonel diyabet



Proceedings of the 4th. International Workshop-Conference on Gestational Diabetes Mellitus. Chicago, Illinois, USA. 14-16 March 1997. Diabetes Care 1998; 21 Suppl 2:B1.

American Diabetes Association. Standards of medical care in diabetes - 2010. Diabetes Care. 2010; 33: S11-S61.

Committee opinion no. 504: screening and diagnosis of gestational diabetes mellitus. Obstet Gynecol 2011; 118:751. ACOG

Gebelikte görülen hiperglisemi ile ilgili kabul görmüş tarama ve tanı testleri (1998–2011)

ADIPS (1998) The Australasian Diabetes in Pregnancy Society

Tarama: 50gr sınır 140

Tanı: 75 gr OGTT

ACOG (2001) American College of Obstetricians and Gynecologists

Tarama: 50 gr sınır 140

Tanı: 100 gr OGTT Carpenter/Coustan veya National Diabetes Data Group

SOGC (2002) Society of Obstetricians and Gynaecologists of Canada

ACE (2007) American Association of Clinical Endocrinologists

Tüm gebelere tarama yapılsın

Düşük riskli gebeler 24–28 haftada, yüksek riskli gebeler 20. haftada taransın

Tarama: 75gr

IADPSG (2008) International Association of Diabetes and Pregnancy Study Groups

ADA (2010) American Diabetes Association

ADA (2011) American Diabetes Association

ADA (2011) American Diabetes Association

8 Saatlik açlık sonrası uygulanan 75-g OGTT sonuçlarından birinin pozitif olması tanı koydurur.

- açlık ≥92 mg/dl (5.1 mmol/l)
- 1 h ≥180 mg/dl (10.0 mmol/l)
- 2 h ≥153 mg/dl (8.5 mmol/l)
- **Level of evidence (B)**

American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2011; 34 Suppl 1:S62.

İlave durumlar ve testler

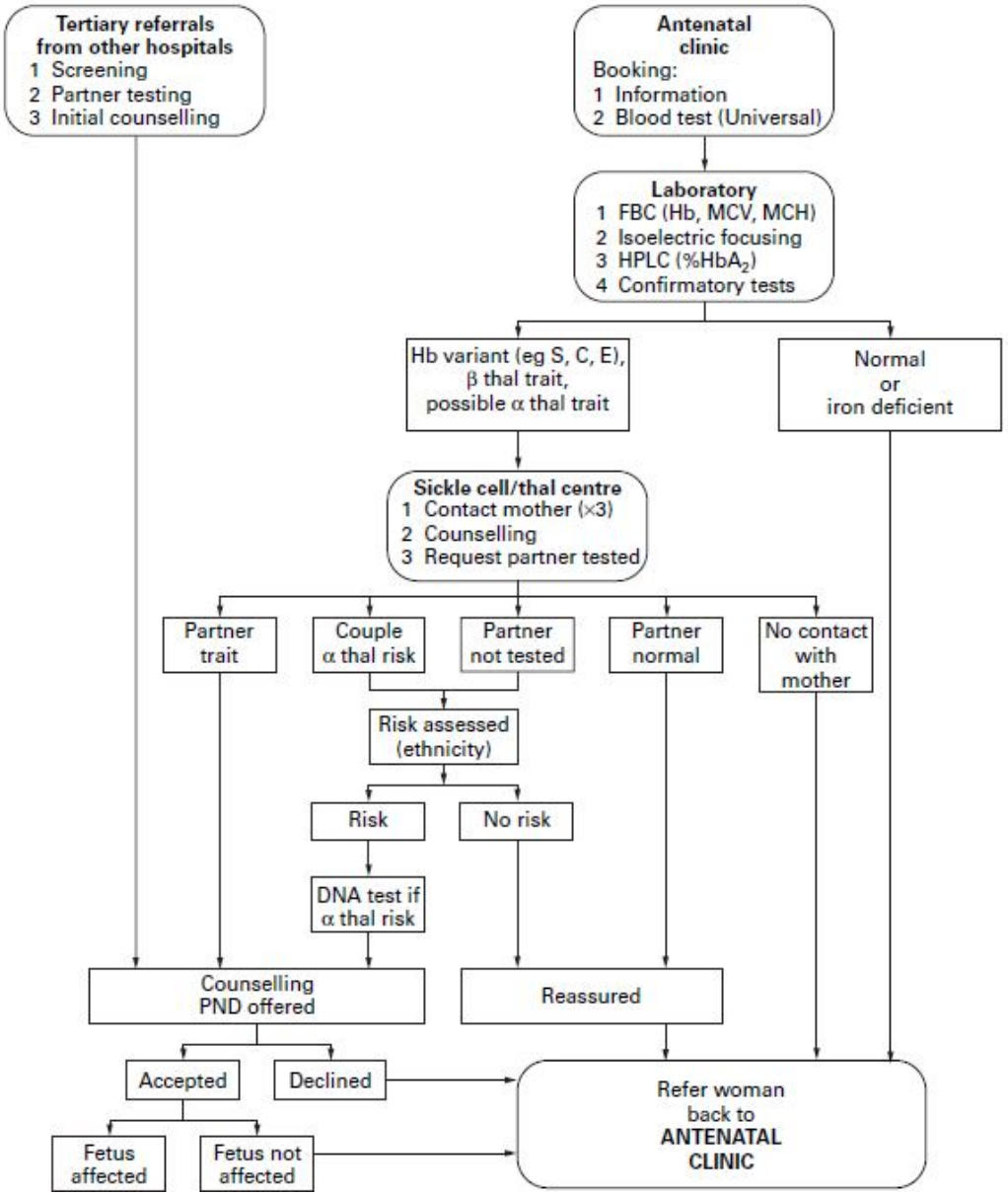
Table VI-3. Predictors of Preterm Birth < 35 wks*

Predictor	Odds Ratio
Fetal fibronectin (> 50 ng/mL)	6.6
Alkaline phosphatase (> 90th percentile)	4.0
History of preterm birth	4.0
Cervical length (≤ 25 mm)	3.9
Maternal serum alpha-fetoprotein (> 90th percentile)	3.9
Granulocyte CSF (> 75th percentile)	3.1

*From reference 75.

Laboratory Medicine Practice Guidelines
The National Academy of Clinical Biochemistry
Presents
LABORATORY MEDICINE PRACTICE GUIDELINES
MATERNAL-FETAL RISK ASSESSMENT AND REFERENCE VALUES IN PREGNANCY

Hemoglobinopati taramaları



National Guideline Clearinghouse

Carrier screening for thalassemia and hemoglobinopathies in Canada.

II A

2008 Oct.

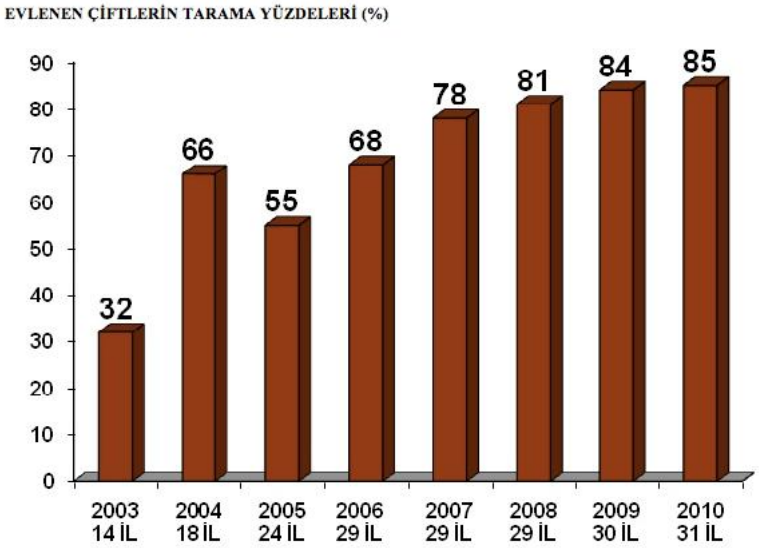
Hemoglobinopathies in pregnancy

American College of Obstetricians and Gynecologists (ACOG).

2007 Jan

Afrika, Akdeniz, ve Güney Asya orijinliler taranmalıdır

I A



Türkiye'de beta-talasemi taşıyıcı sıklığı %2,1 olup, yaklaşık 1.300.000 taşıyıcı ve 5500 civarında hasta vardır. Ayrıca her yıl taşıyıcı sıklığına göre 300–400 hasta çocuğun dünyaya gelmesi beklenmektedir.
Yıllık saptanan 150-250 arasındadır

GATA
Tıbbi Biyokimya AD
Ailesi