

A MARKED DIFFERENCE BETWEEN TWO POPULATION UNDER MASS SCREENING OF NEONATAL hTSH AND BIOTINIDASE ACTIVITY

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Tarama testleri (Mass screening)



Erken girişim ve tedaviye olanak sağlar



Hastalıklar nadirdir ancak

Hasta bebekler

mental retardasyon ,
gelişme problemleri
ölümle karşıkarşıyadır.



Bebeklerin tanı konulduğu takdirde
önlenebilen komplikasyonlardan
kurtulmasına olanak sağlar



Aileleri belirsizlikten kurtarır.

De opsporing van aangeboren metabole aandoeningen :

- *Fenylketonurie*
- *Hypothyreoïdie*



Ministerie van de
Vlaamse Gemeenschap

PCMA Lab.
BELÇİKA

Haziran –Ağustos 2001

TÜBİTAK - NATO B2

Kit temini
FEBS / Province of ANTWERP



Fenilketonüri (Fenilalanin)



Kongenital hipotiroidi (nTSH)



Galaktozemi (Galaktoz 1-P, Galaktoz ,GALT)



Kongenital Adrenal hiperplazi (17-OH progesteron)



Biotinidaz eksikliğı (Biotinidaz)

*The Journal NIH research (1991),
Lab Methods for Neonatal Screening (1993)*

AMAÇ

Akredite (ISO IEC 17025) bir metabolizma laboratuvarında
Kan Biotinidaz ve nTSH ölçümü ile,

1. Türk toplumunda Ege Bölgesi referans aralığını belirlemek
2. İki popülasyona ait referans aralıklarını karşılaştırmak



Lizin veya lizil peptidler

BIOTİN

BIOTİNİDAZ

Holokarboksilaz sentetaz

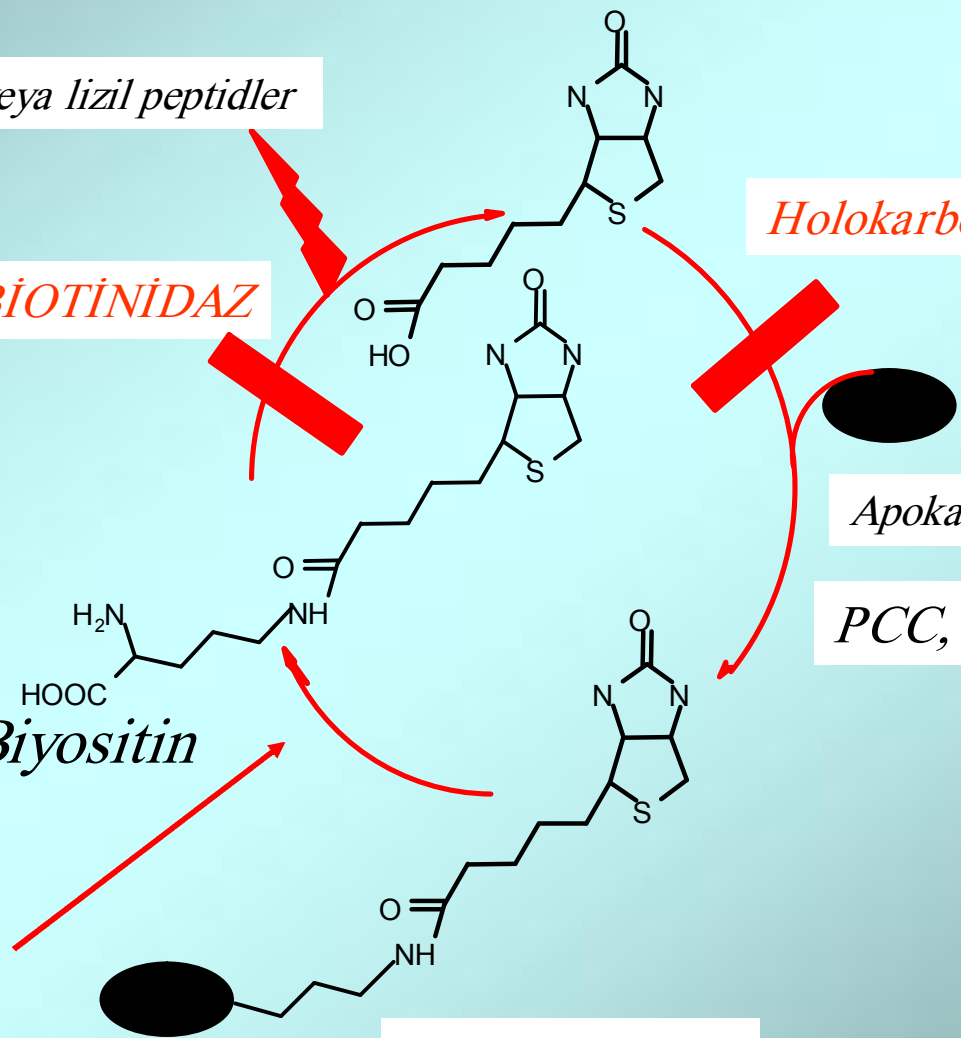
Apokarboksilazlar

PCC, MCC, PC, ACC)

Biyositin

Proteolitik yıkım

Holokarboksilazlar



Glukoz

Lösin

Valin
İzolösin
Metiyonin
Treonin
Yağ asidleri
Kolesterol yan zincir

MCC

3-metil krotonil KoA

3-metil glutakonilKoA

ACC

Yağ asidleri

Pirüvat

AsetilKoA

Malonil KoA

PC

Laktat

Sitrat

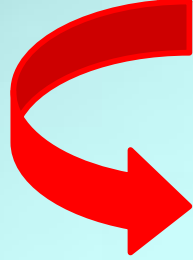
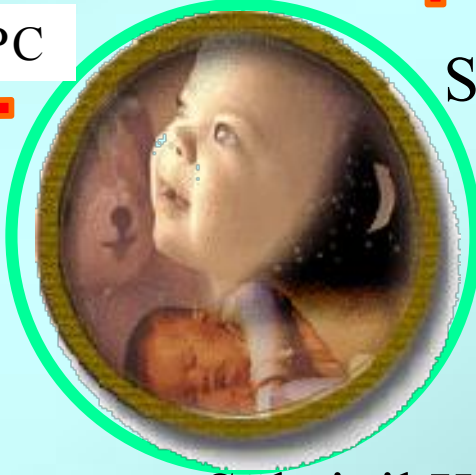
Propiyonil KoA

OAA

PCC

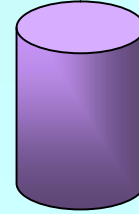
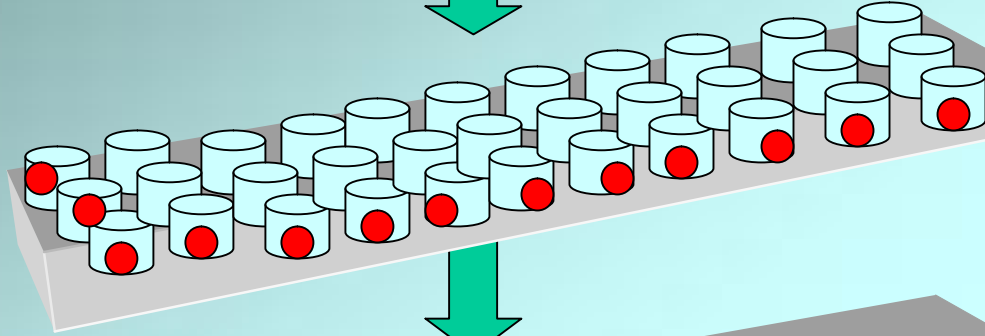
Süksinil KoA

Metilmalonil KoA

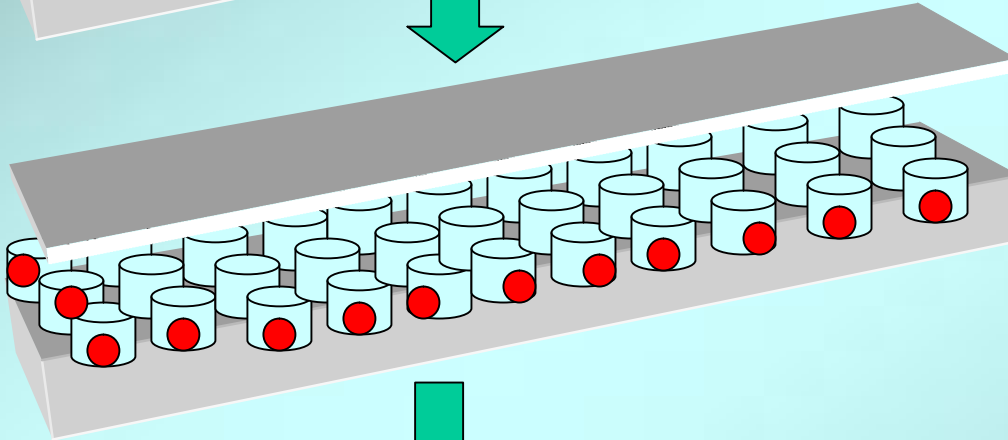




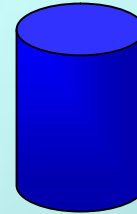
Schleicher & Schuell
2992 3mm puncher



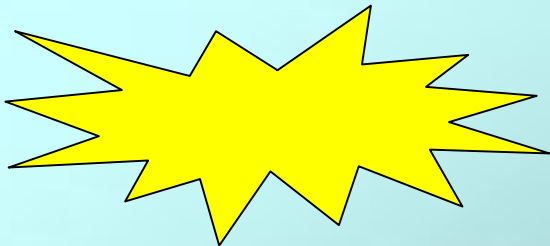
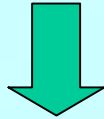
Biotin 6 amidoquinoline



Enkübasyon 17±1 saat

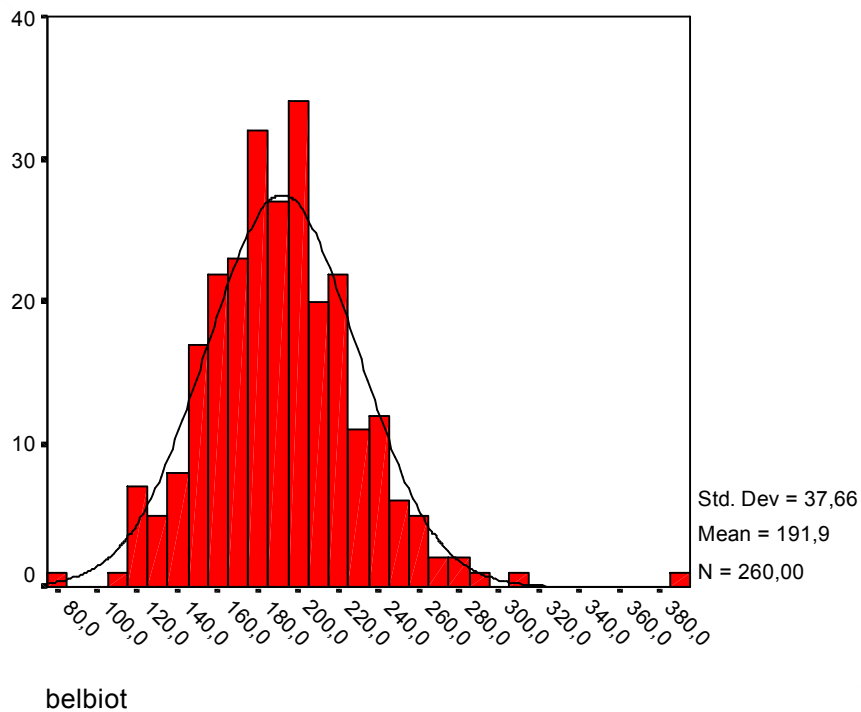


Absolut etanol

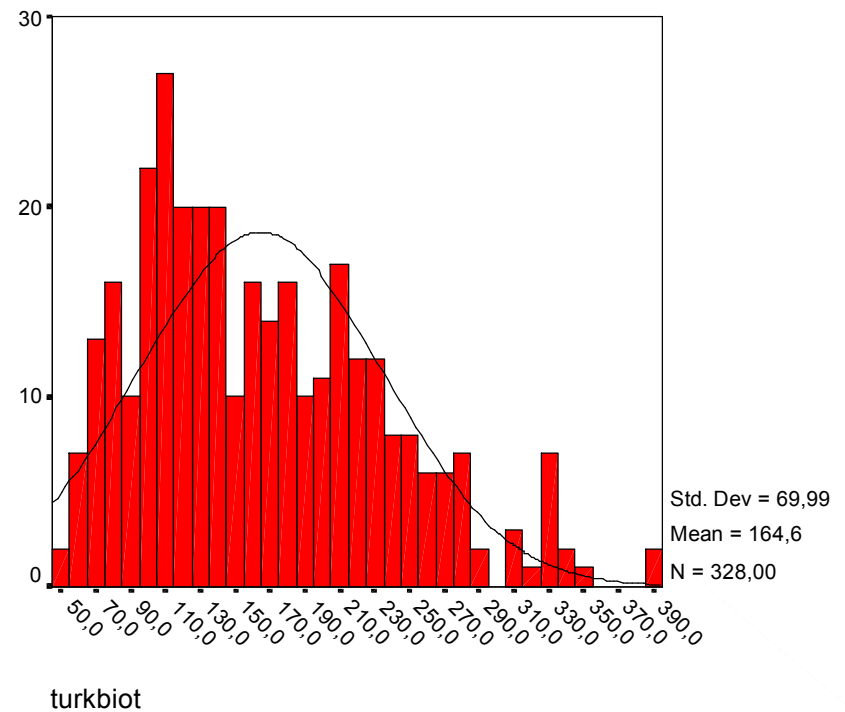


Floresan ölçüm (355 -544 nm)

BELÇİKA Biotinidaz

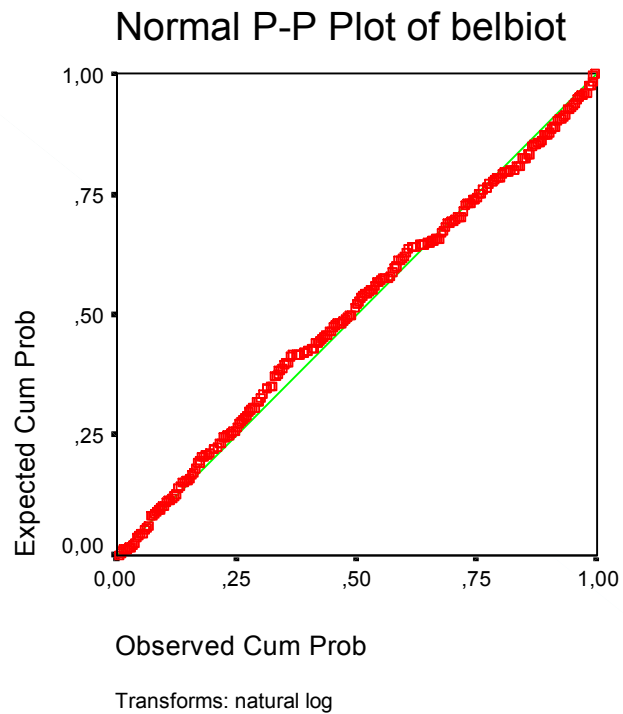


TÜRK Biotinidaz

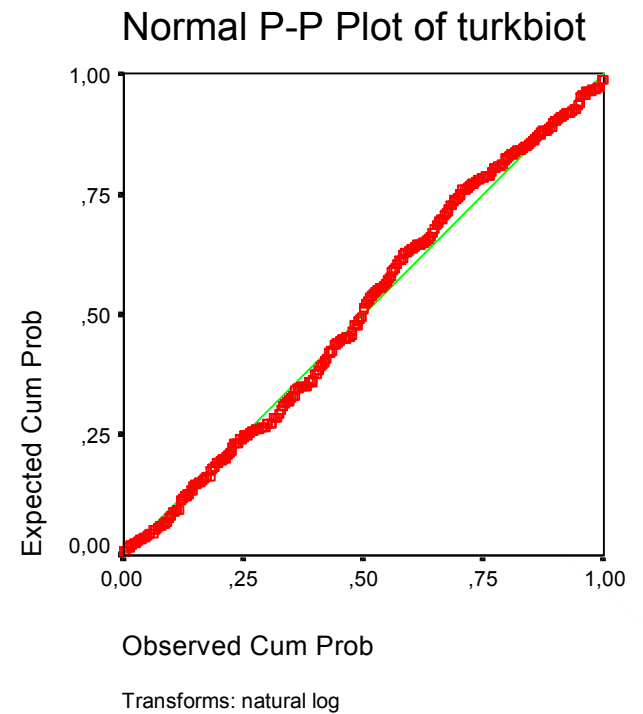


Mann-Whitney U Asymp. Sig. (2-tailed) 0,000

BELÇİKA Biotinidaz



TÜRK Biotinidaz





REFERANS DEĞERLER BİOTİNİDAZ (IU)
(1 nmol / ml / dak / blood spot = 50 iu)

Alt sınır

Üst sınır

Belçika N=257 (90 %CI)	124,39 120,14 134,16	264,59 253,94 275,80
Türk N=328 (90% CI)	61,38 51,37 66,92	275,58 268,45 281,55

Kongenital hipotiroidizm

İnsidans 1/4000

Tiroid hormon sentezinde yetersizlik

Tarama testi: Pimer TSH ölçümü

Cut off: 15 mU/L

Protokol

>15 mU/L

Tekrar örnek isteme (recall)

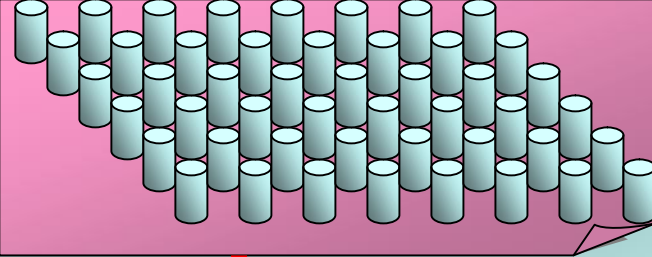
50-100 mU/L

Acil örnek isteme sonucu posta ile bildirme
ve serum da TSH ve T4 çalışılması

>100

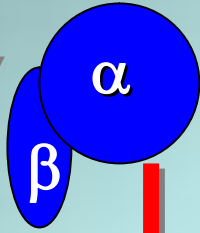
pediatrik endokrinolog ile görüşme ve tedavi





Anti β hTSH IgG (solid faz)

2992
S&S



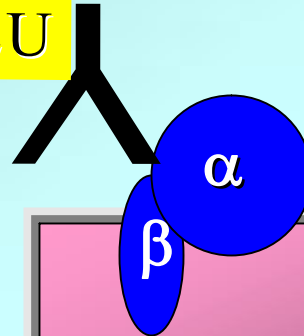
hTSH molekülü



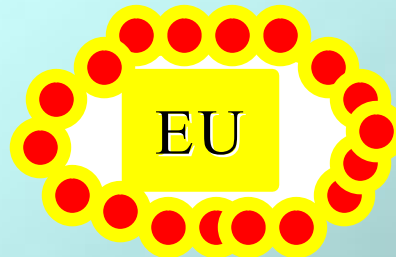
Monoklonal antikor



EU

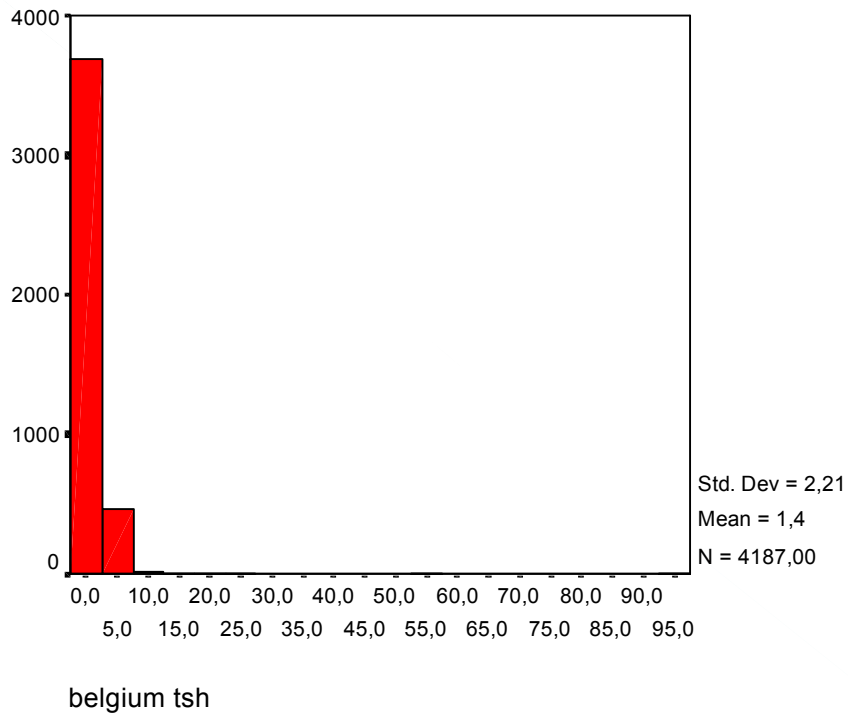


ES

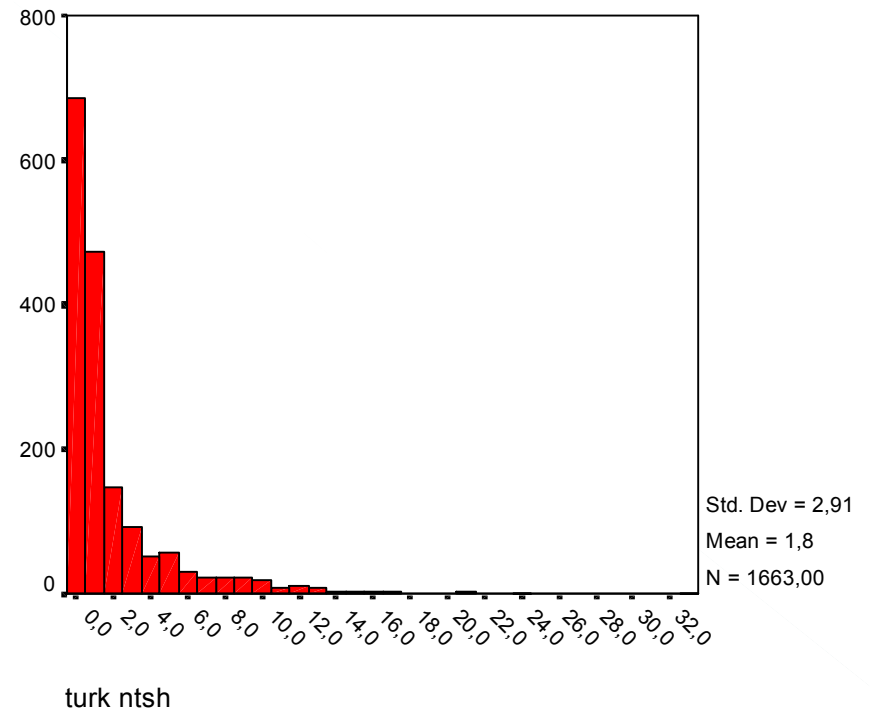


Floroimmunometrik
ölçüm

BELÇİKA nTSH



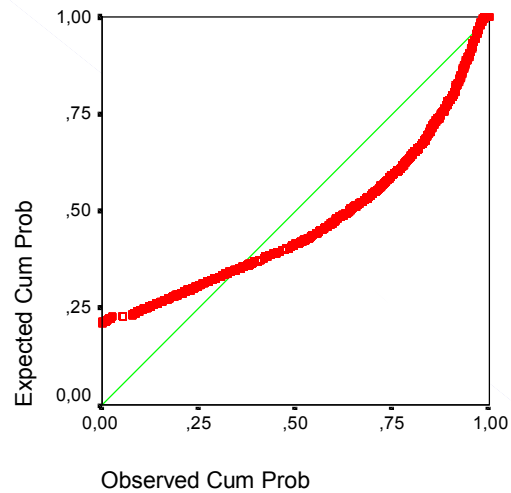
TÜRK nTSH



Mann-Whitney U Asymp. Sig. (2-tailed) 0,000

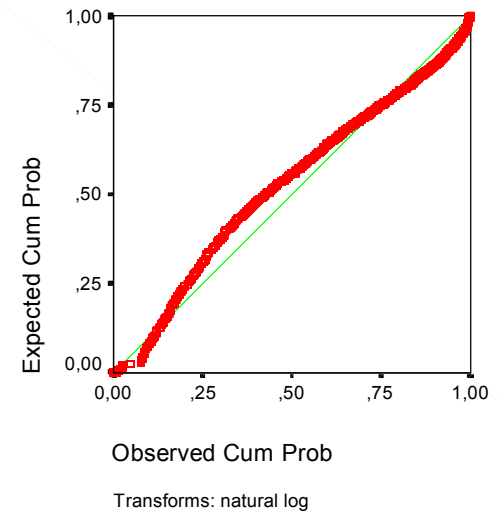
Belgium nTSH

normal values n=4186



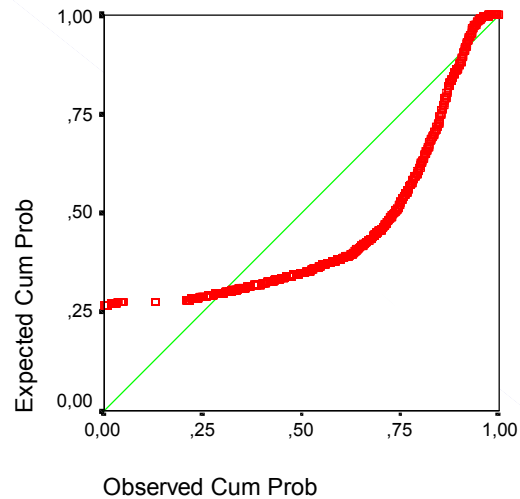
Belgium nTSH

Tranformed values n=4186



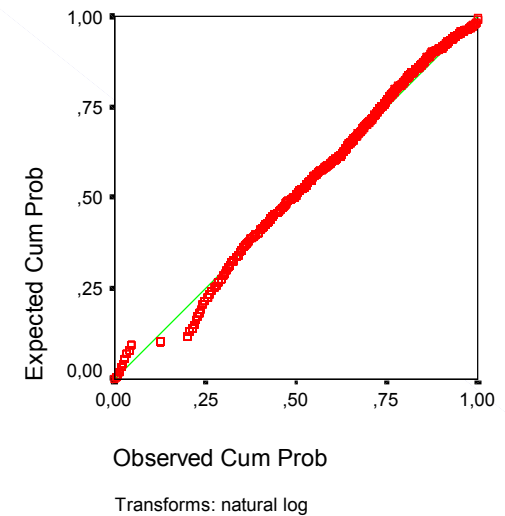
Turkish nTSH

Normal values n=1663



Turkish nTSH

Transformed values n=1663



A : Binomial normal approximation

$$pl, pr = \frac{x \pm 1/2 + \frac{c_2}{2} \pm |c| \sqrt{(x \pm 1/2)(1 - \frac{x \pm 1/2}{N})} + \frac{c_2}{4}}{N + c_2}$$



<http://members.aol.com/johnp71/confint.html#Binomial>

BELÇİKA

*N= 4186 95 % CI for 2,497 is between 2,05-3,00 %
95 % CI for 97,50 is between 96,97-97,92%*

TÜRKİYE

*N= 1663 95 % CI for 2,494 is between 1,83-3,33 %
95 % CI for 97,50 is between 96,60-98,12 %*

B: exact nonparametric

$$X_p = \frac{1}{\Phi(X_p)} \sqrt{\frac{p(1-p)}{N}}$$

B: exact nonparametric

BELÇİKA

N =4186	Lower limit	2,5 %	Upper limit	
Rank:	86 (0,070)	105 (0,090)	126 (0,100)	<i>Ranks of the CI around the Centile</i>
N =4186	Lower limit	97,5,5 %	Upper limit	
Rank:	4060 (4,260)	4081 (4,550)	4100 (4,94)	<i>Ranks of the CI around the Centile</i>

B: exact nonparametric

TÜRKİYE

N =1663	Lower limit	2,5 %	Upper limit	
Rank	31 (0,040)	42 (0,040)	56 (0,060)	<i>Ranks of the CI around the Centile 2,5 %</i>
N =1663	Lower limit	97,5 %	Upper limit	
Rank:	1607 (9,56)	1621 (10,50)	1632 (11,50)	<i>Ranks of the CI around the Centile 97,5 %</i>

nTSH

BELÇİKA / N=4186

TÜRKİYE / N=1663

% 2,497	% 97,50	% 2,497	% 97,50
2.1-3.0	97,44-97,94	1,8-3,4	96,05-97,76
mU/L 0,09	 mU/L 4,55	mU/L 0,04	 mU/L 10,50
0,07-0,1	4,26-4,94	0,04-0,06	9,56-11,50

SONUÇ

Türk Toplumunda (Ege Bölgesi)

REFERANS ARALIKLAR FARKLI !

Biotinidaz



nTSH



ÖNGÖRÜLEN ÇALIŞMALAR ?

1. Türkiye genelinde referans aralık /cut-off belirlenmesi
2. Çevresel faktör etkilerinin araştırılması
3. Folik asid , vit B₁₂ ve Biotin arasındaki ilişkinin araştırılması
4. Gen düzeyinde araştırmalar

